Coexisting severe mental illness and substance misuse: community health and social services

Review 3: The effectiveness and efficiency of service delivery models for health, social care and voluntary and community sector organisations at meeting the needs of people with a severe mental illness who also misuse substances

A systematic review

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Table of contents

GLOSSARY AND ABBREVIATIONS

AASE	Alcohol Abstinence Self-Efficacy Scale. The AASE assesses Bandura's construct of self-efficacy and evaluates an individual's efficacy (e.g., confidence) to abstain from drinking in 20 situations that represent typical drinking cues. These situations form 4 subscales comprised of 5 items each examining cues related to (1) negative affect, (2) social/positive, (3) physical and other concerns, and (4) withdrawal and urges. In addition, these same items can be assessed for an evaluation of an individual's temptation to drink providing a measure of cue strength to relate to the efficacy evaluation. Total scores range from 20 to 100. High scores indicate that an individual is confident in their ability to abstain from drinking alcohol.
ACT	assertive community treatment
ASI	Addiction Severity Index. The ASI is a semi-structured interview used for substance abuse treatment planning and evaluation. The ASI has 163 items, and each item is rated on a 4-point scale from 0 (not at all) to 4 (extremely). The index generates 7 composite scores; 1) Medical, 2) Employment, 3) Alcohol use, 4) Drug use, 5) Legal, 6) Family/social and 7) Psychiatric. Each of these is on a scale from 0 (lowest severity) to 9 (greatest severity).
AUS	Alcohol Use Scale. This is a clinician-rated measure of client alcohol-use over the past 6 months, scored on a scale from 1 (abstinence) to 5 (severe dependence).
BDI-II	Beck's Depression Inventory version II. This scale is used to assess the severity of depression. Scores range from 0 – 63, with higher scores indicating greater severity of symptoms.
BM	Beliefs Measure. Aims to identify the clients' substance-related beliefs (e.g., alcohol will help me relax) and their level of conviction in these beliefs. 0% (not at all true) to 100% (completely
BPRS	Brief Psychiatric Rating Scale (24 items). This is a brief measure of psychiatric symptoms. It is designed to be completed during a clinical interview and consists of 24 items, each scored on a Likert Scale from 1 (not present) to 7 (extremely severe). Scores range from 24 to 168 with higher scores indicating greater severity of psychopathology.
CAS	Covi Anxiety Scale. The CAS is a 3-item clinician-rated scale to assess severity of anxiety symptoms. Items are rated on a 5-point scale from 1 (not at all) to 5 (very much). Higher scores indicate greater symptom severity.
CAUS	Clinician's Rating for Drug Use Scale. This is a clinician-rated measure of client drug-use during the worst period over the past 6 months, scored on a scale from 1 (abstinence) to 5 (severe dependence).
CES-D	Centre for Epidemiological Studies – Depression Scale. The CES-D is a screening measure for symptoms of depression, as

	defined by the DSM-V. It is administered online and has 20 items each rated on a scale from 0 (not at all) to 4 (nearly every day for 2 weeks). The score range is 0-60, with scores above 16 indicating possible clinical significance.
CI	confidence interval
COMPASS	The COMPASS (combined psychosis and substance use) Programme is a specialist team working with people who have severe mental illness and who use drugs/alcohol problematically and is part of the Birmingham and Solihull Mental Health Foundation Trust.
CSI	Colorado Symptom Index. The Colorado Symptom Index is a 14-item self-report measure of psychiatric symptomatology. Items ask about psychiatric symptoms experienced within the past month and are each scored on a scale from 1 (not at all) to 5 (at least every day). Scores range from 14-70, with higher scores indicating greater symptom burden. The CSI has no official cut-off score, however a score of over 30 has been identified as clinically relevant. The CSI has excellent internal consistency (0.92), and good test-retest reliability (0.71).
CSQ	Client Satisfaction Questionnaire. This measure is designed to assess client satisfaction with services. Higher scores indicate a better outcome for participants.
DSS	Depressive Symptom Scale. The depression rating scale measures DSM-IV symptoms of depression. Scores range from 0 to 6, with higher scores indicating higher levels of depressive symptoms.
DUS	Drug Use Scale. This is a clinician-rated measure of client drug-use over the past 6 months, scored on a scale from 1 (abstinence) to 5 (severe dependence).
GAF	General functioning assessed with the Global Assessment of Function. This scale assigns a clinical judgment in numerical fashion to the individual's overall functioning level. Impairments in psychological, social and occupational/school functioning are considered, but those related to physical or environmental limitations are not. The scale ranges from 0 (inadequate information) to 100 (superior functioning).
GAS	Global Assessment Scale. This is a numeric scale (1 through 100) used by mental health clinicians and physicians to rate subjectively the social, occupational, and psychological functioning of adults, e.g., how well or adaptively one is meeting various problems-in-living. The score is often given as a range
GLSS	General Life Satisfaction Scale. General life satisfaction item from the Quality of Life Interview. Possible scores range from 1 to 7, with higher scores indicating more satisfaction with life in general.
HoNOS	Health of the Nation Outcome Scales. This is a clinician-rated measure of the health and social functioning of individuals with mental illness. The HoNOS has 12 items, each rated on a scale from 0 (no problem) to 4 (severe to very severe problem). Higher ratings indicate poorer functioning.
HSTI	Homicidal Suicidal Thought Index. The HSTI is the count of

	endorsed items related to killing or hurting someone else (for example, “During the past year, have you had significant problems with thoughts about killing or hurting someone else?”) or thoughts of, plans for action toward, or attempted suicide in the past year, with higher scores indicating increased risk of suicide or homicide (score range: 0 to 5).
IRR	incidence rate ratio
IV	intravariance
K10	Kessler 10 Scale. This is a 10-item screening measure to identify individuals with serious mental illness, and can be either self- or interviewer-administered. Items are scored on a scale of 0 (all of the time) to 4 (none of the time). Scores range from 0-40 with higher scores indicating better functioning.
LDQ	Leeds Dependence Questionnaire. This scale measures dependence on alcohol or other substances. The measure consists of 10 items each rated on a scale from 0 (never) to 3 (nearly always). Scores range from 0-30 with lower scores representing fewer difficulties. Scores below 10 indicate low dependence, whilst scores over 22 indicate high dependence.
LSP	Life Skills Profile. The LSP is a measure of aspects of functioning that affect how successfully people with a diagnosis of schizophrenia can care for themselves. The original version (the LSP-39) has 39 items rated 4 (always) to 1 (never) and 5 subscales; 1) self-care, 2) non-turbulence, 3) social contact, 4) communication and 5) responsibility. Higher scores indicate high levels of life skills.
MANSA	Manchester Short Assessment of Quality of Life. The MANSA is a measure of quality of life. It has 25 items that are rates either dichotomously (yes/no) or on a scale of 1 (couldn’t be worse) to 7 (couldn’t be better). Higher scores indicate better quality of life.
MCAS	The Multnomah Community Ability Scale. This is a clinician-report measure of client functioning. The MCAS consists of 17 items, each scored on a 5-point scale from almost never to almost always, with a 6th option of ‘don’t know’. Some items are reverse scored. Scores range from 17 to 85, with higher scores indicating better functioning.
MRAI	Major Role Adjustment Inventory measures social adjustment. Higher scores indicate a better outcome for participants.
MHTI	Mental Health Treatment Index. The MHTI assesses the nights or times of visiting the emergency room, staying in the hospital, or visiting an outpatient facility for mental health problems divided by the range of 90 days. Higher scores indicated increasing involvement in mental health treatment in the past 90 days.
n	number in subgroup
N	total number
NICE	National Institute for Health and Care Excellence
NR	not reported
OCDS	The Obsessive Compulsive Drinking Scale (OCDS). This scale is a 14-item, self-report questionnaire developed to measure

	alcohol-related craving. The OCDS may provide a measure of the state of illness among alcohol-dependent individuals and may have value in predicting subsequent drinking behaviour. It comprises 2 subscales: one which measures compulsion and one which measures obsession in relation to drinking in the last week. Each item is rated on a scale from 0 to 4, with higher scores indicating greater difficulty.
OECD	Organisation for Economic Co-operation and Development
PANSS	Positive and Negative Syndrome Scale. The PANSS is a scale that measures the severity of symptoms in people with psychosis. It includes 3 subscales: 1 for positive symptoms, 1 for negative symptoms and 1 for general psychopathology. Scores range from 30 to 210, with higher scores indicating greater severity of symptoms.
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QDIS-R	Quick Diagnostic Interview Schedule – Revised. The QDIS-R is a scale which measures past 12 month criteria for substance use disorders. Lower scores indicate a better outcome for participants.
QIDS-C16	Quick Inventory of Depressive Symptoms. The 16 item Quick Inventory of Depressive Symptomatology Clinician Rating scoring system converts responses to 16 separate items into the nine DSM-IV depression symptom criterion domains. The nine domains comprise: 1) sad mood; 2) concentration; 3) self-criticism; 4) suicidal ideation; 5) interest; 6) energy/fatigue; 7) sleep disturbance (initial, middle, and late insomnia or hypersomnia); 8) decrease/increase in appetite/weight; and 9) psychomotor agitation/retardation. The total score ranges from 0 to 27. Higher scores indicate greater severity of symptoms.
QOLI-20	Quality of Life Inventory. The QOLI assesses an individuals' quality of life for the importance they attach to each of 16 life domains (on a 3-point rating scale) as well as their current satisfaction with each domain (on a 6-point rating scale). Importance scores are multiplied by satisfaction scores for each domain, and then these scores are summed to determine an overall current quality of life for each individual. Higher scores indicate a higher overall quality of life.
RCT	randomised controlled trial
RDC	Raskin Depression Scale. This is a 3-item clinician-rated scale designed to assess baseline depression levels and change over time. Each item is rated on a 5-point scale from 1 (not at all) to 5 (very much). Higher scores reflect greater symptom severity with a score of 9 or above indicating moderate depression.
RQ	review question
RR	relative risk
RTC	Readiness to Change Questionnaire. This is a 12-item self-report instrument for measuring 'stage of change' reached by a client abusing alcohol. Clients respond to each statement on a 5-point

	scale from strongly disagree (−2) to strongly agree (+2). Three subscales are derived; 1) pre-contemplation (lower scores indicate greater readiness to change) 2) contemplation and 3) action (higher scores indicate greater readiness to change).
SAS-II	Social Adjustment Scale-II. This is an adaptation of the Social Adjustment Scale intended to assess the social adjustment of schizophrenic patients. The SAS-II contains 52 questions which are administered in a semi structured interview format and includes work role, sexual adjustment, romantic involvement, parental role, extended family relationships, social leisure activities, personal well-being and relationships with principal household member.
SATS	Substance Abuse Treatment Scale. This is a clinician-rated measure of the client's stage of substance abuse treatment over the past 6 months, scored on a scale from 1 (pre-engagement) to 8 (in remission or recovery).
SDS	Severity of Dependence Scale. This is a self-report scale comprised of a 5-item questionnaire that provides a score indicating the severity of dependence on opioids. Each of the five items is scored on a 4-point scale (0-3). The total score is obtained through the addition of the 5-item ratings. The higher the score the higher the level of dependence.
SFS	Social Functioning Scale. This was designed to measure social adjustment following family interventions in patients with diagnoses of schizophrenia. This measure has 79 items each scored on a 4-point scale assessing 7 domains; 1) social engagement, 2) interpersonal behaviour, 3) prosocial activities, 4) recreation, 5) independence-competence, 6) independence-performance, 7) employment. Higher scores indicate better functioning.
SMD	standardised mean difference
SOFAS	Social and Occupation Functioning Assessment Scale. This scale focuses exclusively on the individual's level of social and occupational functioning and is not directly influenced by the overall severity of the individual's psychological symptoms. Any impairment in social and occupational functioning that is due to general medical conditions is considered in making the SOFAS rating. The SOFAS is a global rating of current functioning ranging from 0 to 100, with lower scores representing lower functioning. Higher scores represent better outcomes.
TAF	Treatment Adherence Form. The form assesses mental health treatment appointments missed each month between assessment points.
TAU	treatment as usual
TPQ	Treatment Perceptions Questionnaire. The TPQ is 10-item questionnaire that also allows open-responses / feedback designed to assess client' satisfaction. A global score is obtained by summing the scores of all items. It was developed at the National Addiction Centre in London. It examines the perception of clients towards: 1) the nature and extent of their contact with a

	treatment programme's staff team (5 items); and 2) aspects of the operation of the treatment service and its rules and regulations (5 items). Items are scored on a five-point scale (strongly disagree – strongly agree; weighted 0-4). Higher scores reflect greater satisfaction with treatment.
VLQ	Valued Living Questionnaire. This is a two-part instrument designed to assess valued living. In the first part participants rate the importance of 10 domains of living on a 10-point Likert-style scale. These life domains are (1) family (other than parenting and intimate relations), (2) marriage/couples/intimate relations, (3) parenting, (4) friendship, (5) work, (6) education, (7) recreation, (8) spirituality, (9) citizenship, and (10) physical self-care. The instructions specify that not everyone values all of these domains, and that some domains may be more important, or important in different ways, at different times in an individual's life. The second part of the VLQ asks the client to rate, using the Likert-style scale, how consistently he or she has lived in accord with the valued behavioural pattern within each domain over the past week. Higher scores indicate a better outcome for participants.
WHODAS-2	World Health Organisation Disability Assessment Schedule 2. The WHODAS-2 is a 36-item disability assessment instrument investigating 6 domains of functioning; 1) cognition, 2) mobility, 3) self-care, 4) interaction, 5) life activities and 6) participation. Items are rated on a scale from 0 (none) to 4 (extreme). Higher scores indicate greater degree of disability.
WNSS	Wing Negative Symptom Scale. A simple classification of chronic schizophrenia, based on ratings of mental symptoms made at a standard interview, has been shown to have satisfactory reliability as between raters, and to be relatively stable over time. Scores representing different types of social behaviour provide some validity for the classification

1 EXECUTIVE SUMMARY

Severe mental illness (including schizophrenia, psychosis and bipolar disorder) coexists with drug and alcohol misuse in approximately 40% of users of secondary care mental health services. There is good evidence to suggest that outcomes for people with a dual diagnosis are worse than for other groups of service users who engage with health and social care services, and that they also have problems accessing services and are more likely to disengage with services (Mitchell et al., 2009; Crome et al., 2009).

Given the poor outcomes (and associated higher costs) (McCrone et al., 2000), there have been numerous attempts to provide better services for people with a dual diagnosis. Attempts to improve treatment outcomes can broadly be divided into 2 approaches. The first involved the development of specialist treatments, which have often taken the form of complex packages of care involving interventions known to be effective for either severe mental illness (for example, cognitive behavioural therapy) or substance misuse (for example, motivational interviewing). The second involved the development of particular models of care delivery often built around a specialised team (for example, assertive community teams or intensive case management). The former might be characterised as trying to achieve maximum therapeutic benefit, the latter to improve engagement with services.

The National Collaborating Centre for Mental Health (NCCMH) was commissioned by the NICE Centre for Public Health (now Public Health Internal Guidelines, Centre for Guidelines) to conduct four evidence reviews to help inform the development of a guideline aimed at optimising service organisation and delivery of community health and social care services for adults and young people with coexisting severe mental illness and substance misuse. This systematic review is the third of these 4 evidence reviews and focuses on which service delivery models are effective and efficient at meeting the needs of people with a dual diagnosis.

This review was conducted in accordance with *Developing NICE Guidelines: The Manual* (NICE, 2014a). A systematic search was conducted in 20 electronic databases (for studies published from 2000 onwards), 13 websites and 2 research registries. This review considered data from randomised controlled trials (RCTs) and observational studies (based in the UK and Ireland only) in order to address the following review question:

- RQ 3: Which service models for health, social care and voluntary and community sector organisations are effective and efficient at meeting the needs of people with a severe mental illness who also misuse substances?

For RCTs, meta-analysis using a random-effects model was used to combine results from similar studies. Where this was not possible (for instance, because of different outcomes) a narrative synthesis was used. Observational studies were analysed separately from the RCTs and synthesised narratively.

Overall, 22 studies met the inclusion criteria: 20 were RCTs, 1 was a non-randomised controlled trial and 1 was a before-and-after study. For the RCT evidence, the quality of individual studies was assessed using the Cochrane

Collaboration's tool for assessing risk of bias in randomised trials. For observational studies, the 'Effective Practice and Organisation of Care (EPOC) Risk of Bias Tool' and the NICE-adapted 'Checklist to Assess Evidence of Prevalence and Incidence, Descriptive or Longitudinal Studies' was used (checklist 1.6 in NICE's Interim methods guide for developing service guidance 2014). Out of the 22 included studies, 9 were rated moderate quality [+] and 13 were rated poor quality [–]. The key findings from these studies are summarised below in evidence statements, ordered by intervention type and comparison.

Review question 3: Which service models for health, social care and voluntary and community sector organisations are effective and efficient at meeting the needs of people with a severe mental illness who also misuse substances?

Assertive community treatment

Evidence statement 3.1: ACT compared with TAU

There is weak evidence from 5 RCTs (2[+][2,4] and 3[−][1,3,5]) comparing ACT with TAU on mental health and substance use outcomes, the acceptability of services, adaptive functioning and service utilisation. Two RCTs[2,3] reported that the intervention was delivered with 'good fidelity' to the treatment model.

Mental health

There is evidence from a meta-analysis and 4 US RCTs on the effectiveness of ACT compared with TAU to improve mental health outcomes. Consistent evidence from a meta-analysis of a 3-armed RCT [-][3] (n=147) comparing ACT or integrated ACT to TAU showed no difference between groups for mental health symptoms (assessed on the BPRS-24) (SMD=0.01; 95% CI, −0.33 to 0.36; p=0.94; I^2=0%) at 130 weeks' follow-up. There was also consistent evidence from 4 RCTs. One US RCT (1[+][4]; n=120) showed a small increased involvement in mental health treatment in the enhanced case management group compared to TAU at 52 weeks' follow-up, but the effect was not statistically significant (SMD=0.18; 95% CI, −0.18 to 0.54; p=0.33). Four US RCTs (2[+][2,4] and 2[−][1,5]) suggested no difference in psychiatric symptoms for ACT compared with TAU at follow-ups ranging from 52 to 156 weeks' post-randomisation.

Substance use

There is evidence from a meta-analysis and 3 RCTs on the effectiveness of ACT compared with TAU on substance use outcomes. Consistent evidence from a meta-analysis of a 3-armed RCT (1[−][3]) conducted in the US showed a small increase in the severity of substance use in the ACT group compared with TAU at 52 week's follow-up (SMD=0.18; 95% CI, −0.17 to 0.52; p=0.32; I^2=0%), but this was not statistically significant. There was also consistent evidence from 3 US RCTs (1[+][2], 2[−][1,5]) which indicated no significant differences in levels of alcohol, drug or overall substance use between ACT and TAU at 156 weeks' follow-up (p-values not reported).

Acceptability of services

There is consistent evidence from a meta-analysis of a 3-armed RCT (1[−][3]) conducted in the US which found that service users were significantly more satisfied with TAU compared with ACT at 130 weeks' follow-up (SMD=−0.44; 95% CI, −0.78 to −0.09; p=0.01; I^2=0%).

Adaptive functioning

There is consistent evidence from a meta-analysis and 2 RCTs on the effectiveness of ACT compared with TAU on adaptive functioning outcomes. A

meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US showed a small improvement in stable housing for ACT compared with TAU at 130 weeks' post-randomisation (SMD=0.22; 95% CI, −0.13 to 0.56; p=0.22; I^2=0%), however the difference was not significant. Two US RCTs (2[−][1,5]) reported no significant difference between groups for housing, employment, social contact or quality of life outcomes (p-values not reported). One US RCT (1[+][2]) reported no significant difference between groups for general functioning, life satisfaction or community housing (p-values not reported).

Service utilisation

There is consistent evidence from a meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US to suggest a moderate to large effects in favour of ACT for days in physical contact (SMD=0.65; 95% CI, 0.30 to 1.00; p=0.0003; I^2=0%) and telephone contact (SMD=0.94; 95% CI, 0.58 to 1.30; p<0.00001;I^2=0%) with the assigned programme compared with TAU at 130 weeks' follow-up; reasons for contacts were not reported. There was no difference between groups in the number of contacts with substance misuse services (SMD=−0.09; 95% CI, −0.46 to 0.28; p=0.62; I^2=13%).

Applicability to the UK:

This evidence is only partially applicable to the UK. This is because all included studies were conducted in the US and TAU is likely to differ from that provided in the UK, which has better co-ordinated services for severe mental illness than the US.

[1]Drake et al. (2004) [−]
[2]Essock et al. (2006) [+]
[3]Fletcher et al. (2008) [–]
[4]Striley et al. (2013) [+]
[5]Xie et al. (2005) [–]

Integrated treatment

Evidence statement 3.2: Integrated treatment[1] compared with TAU

There is moderate evidence from 6 RCTs (4[+][1,2,5,6] and 2[–][3,4]) comparing integrated treatment in combination with TAU with TAU alone for mental health, substance use and adaptive functioning outcomes. One before-and-after study (1[–][7]) assessed the effectiveness of integrated treatment in combination with TAU on substance use outcomes. One RCT[2] reported 81-100% fidelity to the intervention and another RCT[6] reported only 'minor variations' to the intervention.

Mental health

There is evidence from a meta-analysis and 4 RCTs on the effectiveness of integrated treatment on mental health symptoms. There was inconsistent evidence from a meta-analysis (n=466) of 2[+][1,2] UK RCTs and 1[+][5] Danish RCT which overall indicated no significant difference in psychotic symptoms between the integrated treatment and TAU (SMD=0.03; 95% CI, −0.27 to 0.33; p=0.83; I^2=44%) at follow-ups ranging from 43 to 104 weeks. There was also evidence from 2 RCTs: 1[−][3] RCT (n=62) conducted in Switzerland indicated a small reduction in severity of positive symptoms (SMD=−0.22; 95% CI, −0.72 to 0.27; p=0.38) and negative symptoms (SMD=−0.30, 95% CI, −0.80 to 0.21; p=0.25) in the integrated treatment group compared with TAU at 52 weeks' follow-up however the difference was not significant, and 1[−][4] US RCT (n=31) showed lower levels of mental health symptoms in the cognitive enhancement therapy group compared with TAU at 78 weeks' follow-up (SMD=0.20, 95% CI, −0.57 to 0.98; p=0.61), however this difference was not significant.

There is consistent evidence from 3 RCTs on relapse due to mental health problems. At 78 weeks' follow-up 1[+][1] UK RCT (n=36) suggested that an integrated treatment may reduce the risk of relapse (defined as a hospital admission or an exacerbation of symptoms lasting 2 or more weeks) (RR=0.58, 95% CI, 0.30 to 1.13; p=0.11; 7/18 [39%] versus 12/18 [67%]), but this was not significant. One UK RCT 1[+][2] (n=327) suggested no difference between groups in the risk of relapse (defined as an exacerbation of symptoms lasting 2 or more weeks) (RR=1.03, 95% CI, 0.78 to 1.36; p=0.82; 63/161 [39%] versus 61/161 [38%])) at 104 weeks' follow-up. Consistent evidence from a meta-analysis of 2 RCTs (1[+][2] and 1[–][3]; n=388) suggested no difference in the risk of hospital admission between groups at follow-ups ranging from 52 to 104 weeks (RR=1.08, 95% CI, 0.75 to 1.54; p=0.69; event rate ranging from 20% to 34% in the TAU group).

Substance use

There is consistent evidence from 3 RCTs on substance use outcomes. One UK RCT (1[+][2]) suggested no significant difference between intervention groups for abstinence from the participants' main substance at 104 weeks' follow-up (SMD=0.06, 95% CI, −0.19 to 0.31; p=0.62). One RCT conducted in Switzerland

[1] Integrated treatment here refers to any intervention which was delivered in the context of a multidisciplinary team in combination with usual care

(1[–][3]) suggested a reduction in cannabis use with motivational interviewing compared with TAU at 24 weeks' follow-up (Mann-Whitney U=308.0; p=0.015), but at 52 weeks' follow-up there was no evidence of a significant difference (Mann-Whitney U=378.5 (not significant, p-value not reported). One US RCT (1[–][4]) reported no significant difference between cognitive enhancement therapy and TAU in the number of participants who were abstinent from drugs or alcohol by study completion (p=0.347).One UK RCT (1[+][1]) reported a larger increase in the proportion of days abstinent from the most frequently used substance in the intervention group (change from baseline (median, range): 15.22, −35 to 98) than in TAU (change from baseline (median, range): 8.08, −25 to 50) but this was not significant (Mann-Whitney U=90.50, p-value not reported). There was also no significant difference between groups in the severity of substance misuse (p-values not reported). One RCT conducted in Denmark (1[+][5]) suggested no significant difference between intervention groups in the proportion of days using cannabis during a 1 month period at 43 weeks' follow-up (IRR=0.80, 95% CI 0.21–3.10; p=0.75).

Adaptive functioning

There is evidence from a meta-analysis and 4 RCTs on the effectiveness of integrated treatment on adaptive functioning outcomes. Consistent evidence from a meta-analysis (n=425) of 2[+][1,2] UK RCTs and 1[–][3] RCT conducted in Switzerland suggested no difference in general functioning between integrated treatment and TAU (SMD=−0.03; 95% CI, −0.24 to 0.18; p=0.81) at follow-ups ranging from 52 to 104 weeks. There was also evidence from 4 RCTS. One UK RCT (1[+][1]) and 1[−][4] US RCT suggested a small increase in social functioning with the integrated treatment compared with TAU, however these were not significant (SMD=0.19; 95% CI, −0.54 to 0.92; p=0.61[1]; SMD=0.22; 95% CI, −0.56 to 0.99; p=0.59[4]). One RCT conducted in Australia (1[+][6]; n=49) reported no significant difference between treatment groups in levels of health and social functioning (p=0.068).One RCT conducted in Switzerland 1[–][3] indicated a small increase in social and occupational functioning at 52 weeks' follow-up but this was not significant (SMD=−0.16; 95% CI, −0.66 to 0.33; p=0.52). In 1[+][5] RCT conducted in Denmark there was a small increase in quality of life at 43 weeks' follow-up in favour of TAU compared with integrated treatment, however this was not significant (SMD=−0.21,95% CI, −0.60 to 0.18; p=0.29).

Observational evidence

One UK before-and-after study (1[−][7]; n=173) reported a significant improvement in alcohol use (p<0.001), drug use (p<0.05) and overall substance use (p<0.001) for clinician-rated measures following a consultation-liaison service. For self-report measures there was a significant improvement in alcohol use (p<0.05) but not for the severity of substance use dependence.

Applicability to the UK:

This evidence is only partially applicable to the UK. This is because 4 out of the 7 studies were conducted in the Australia, Denmark, Switzerland and the US where TAU is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Also, for the study conducted in Australia this included people from indigenous communities so there is limited applicability to UK populations. Most of the interventions that comprise the

integrated treatment components assessed in this question are available in the UK but cognitive enhancement therapy[4] (or its equivalent) is not widely available in the UK, with its use restricted to a small number of specialist centres concerned with its development and evaluation.

[1]Barrowclough et al. (2001) [+]
[2]Barrowclough et al. (2010) [+]
[3]Bonsack et al. (2011) [–]
[4]Eack et al. (2015) [–]
[5]Hjorthøj et al. (2013) [+]
[6]Nagel et al. (2009) [+]
[7]Copello et al. (2013) [–]

Evidence statement 3.3: Integrated treatment compared with an active comparator

There is weak evidence from 1[+][1] RCT, comparing integrated treatment with an active comparator (enhanced assessment and monitoring), on mental health and substance use outcomes, adaptive functioning and service utilisation. Fidelity to intervention was reported to be average to high.

In 1[+][1] US RCT (n=30) of participants with bipolar disorder and a substance-use disorder, the authors reported significant improvements in the integrated treatment group (n=14) compared with the active control (n=16) in manic symptoms (b^2=−1.19, SE=0.45, p<0.05) and depressive symptoms (b=−0.92, SE=0.39, p<0.05), as well as psychosocial and physical disability (b=−1.84, SE=0.86, p<0.05) and daily activities (b=4.82, SE=2.09, p<0.05) at 24 weeks' follow-up. The authors reported no significant differences between groups in the number of standard drinks (b=7.19, SE=8.11, p-value not reported), number of days drinking (b=0.64, SE=0.94, p-value not reported), number of heavy drinking days (b=0.81, SE=1.04, p-value not reported), number of days using drugs (b=−1.67, SE=0.83, p<0.10), number of hospital admissions (b=0.02, SE=0.13, p-value not reported), emergency department visits (b=0.16, SE=0.08, p<0.10) or in the number of intervention sessions attended (b=−1.34, SE=1.20, p-value not reported).

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. There has been a decline in the number of integrated services in the UK.

[1]Wenze et al. (2015) [+]

[2] b here refers to multi-level regression coefficients which reflect change in the relationship between scores and time for the average participant in the Integrated Treatment Adherence Program (vs. Enhanced Assessment and Monitoring)

Other interventions

Evidence statement 3.4: Brokerage case management compared with an active comparator

There is weak evidence from 1[–][1] RCT, comparing brokerage case management with an active comparator (expanded brokerage case management), on mental health and substance use outcomes, adaptive functioning and service utilisation.

One 1[–][1] US RCT (n=268) included participants with severe mental illness and substance dependence who were discharged from inpatient care at the start of the trial. At 24 weeks' follow-up the authors reported no significant differences between brokerage case management and an active comparator for: depressive symptoms, use of inpatient care, substance use, quality of life, number of outpatient services used or emergency psychiatric visits (p-values not reported).

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Brokerage case management is compatible with the personalised budget approach to care in the UK.

[1]Havassy et al. (2015) [–]

Evidence statement 3.5: Contingency management combined with compensated work therapy compared with compensated work therapy alone

There is weak evidence from 2[–][1,2] RCTs comparing contingency management in combination with compensated work therapy with compensated work therapy alone on substance use and adaptive functioning outcomes.

Substance use

One US RCT (1[–][2]; n=101), which included veterans with a severe mental illness and substance-use disorder, suggested a reduced risk of substance use relapse with contingency management at 16 weeks' follow up (RR=0.69; 95% CI, 0.50 to 0.96; p=0.03; 25/50 [50%] versus 36/50 [72%]) and at 39 weeks' follow-up (RR=0.89; 95% CI, 0.70 to 1.14; p=0.38; 34/50 [68%] versus 38/50 [76%]), although for the later time-point this was not significant.

Adaptive functioning

There is evidence from 2 US RCTs on the effectiveness of contingency management on improved adaptive functioning.

One US pilot RCT (1[–][1]; n=19) which included veterans with a severe mental illness and substance-use disorder, suggested higher wage earnings with contingency management at 16 weeks' follow-up compared with compensated work therapy (Mann-Whitney U=20; p<0.05; $4,701 vs. $2,796). The contingency management group also showed a significantly shorter time to first job interview (Hazard ratio=6.23, 95% CI, 1.31 to 29.64, p<0.05), and had more weeks of competitive employment during the study period, however this was not significant (Mann-Whitney U=31; p<0.28; 4.2 weeks vs. 0.8 weeks).

In 1[-][2] RCT, at 39 weeks' follow-up, there was increased employment with contingency management compared with compensated work therapy alone (RR=1.79; 95% CI, 1.06 to 3.02; p=0.03; 25/50 [50%] versus 14/50 [28%]).

Applicability to the UK:

This evidence is only partially applicable to the UK because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. There is an increasing use of contingency management in UK health services however the service style changes and training required to support its implementation are limited. There are also ethical and social concerns about incentivising people to take up health care interventions.

[1]Drebing et al. (2005) [–]
[2]Drebing et al. (2007) [–]

Evidence statement 3.6: Time-limited care co-ordination compared with a matched attention control

There is weak evidence from 1[–][1] RCT comparing time-limited care co-ordination with a matched attention control on mental health and substance use outcomes.

One US study 1[–][1], which included 102 veterans with schizophrenia spectrum disorders or bipolar I disorder and a substance-use disorder, reported no significant difference between groups in the number of days experiencing depression, anxiety and hallucinations in the previous 30 days at 24 weeks' follow-up (p-values not reported). For substance use outcomes, there was a reduced risk of alcohol use with time-limited care co-ordination at 24 weeks' follow-up (RR=0.60, 95% CI, 0.34 to 1.07; p=0.08), however this was not significant. Other drug use was also measured but the difference between groups at follow-up was not reported. Significantly more participants in the time-limited care co-ordination group attended an outpatient appointment compared with those in the matched attention control group (RR=2.08, 95% CI, 1.14 to 3.80; p=0.02; 29/39 [69%] versus 8/24 [33%]).

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. A time-limited care co-ordination approach is compatible with current standard models of care in the UK.

[1]Smelson et al. (2012) [–]

Evidence statement 3.7: Shelter-based psychiatric clinic compared with TAU

There is weak evidence from 1[–][1] RCT comparing a shelter-based psychiatric clinic with usual shelter care on adaptive functioning outcomes and service utilisation.

One US study 1[–][1] which included 102 homeless people with a mental health problem (of whom 72% had a substance-use disorder) suggested a higher rate of participants who had stable housing (RR=1.17, 95% CI, 0.73 to 1.89; p=0.51) and a higher rate of employment (RR=1.67, 95% CI, 0.85 to 3.27; p=0.14) in the shelter-based psychiatric clinic group at shelter exit, however both findings were not significant. There was a significantly higher proportion of participants who attended 1 or more community mental health centre appointments (RR=1.74; 95% CI, 1.15 to 2.62; p=0.008; 33/51 [65%] versus 19/51 [37%]), however this was not significant when those who attended 2 or more (RR=1.89; 95% CI, 0.93 to 3.84; p=0.08; 17/51 [33%] versus 9/51 [18%]) and 3 or more appointments were considered (RR=1.43; 95% CI, 0.59 to 3.46; p=0.43; 10/51 [20%] versus 7/51 [14%]). Considering only the sub-sample of participants with a substance-use disorder (n=69), a higher proportion of participants in the psychiatric clinic group compared with the usual shelter care group attended a substance use programme (RR=4.11; 95% CI, 1.56 to 10.82; p=0.004; 19/37 [51%] versus 4/32 [12.5%]) during the study period.

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Such models of care have already been developed in the UK with a focus on homelessness, many of whom would meet criteria for dual diagnosis although these are not currently widely developed.

[1]Bradford et al. (2005) [–]

Evidence statement 3.8: Staff training compared with no training

There is weak evidence from 1[–][1] non-randomised controlled trial and 1[–][2] RCT comparing staff training with no training on mental health and substance use outcomes, the acceptability of services, adaptive functioning outcomes and service utilisation. One RCT[2] reported that fidelity to the training intervention was low, with 35% of the intervention group receiving the intervention as intended.

Mental health

There is inconsistent evidence from 1 RCT and 1 non-randomised controlled study on the effectiveness of training on mental health outcomes. One UK RCT (1[–][2]; n=232) suggested a small to moderate reduction in the severity of mental health symptoms at 78 weeks' follow-up in the intervention group (SMD=−0.44, 95% CI, −0.71 to −0.16; p=0.002) but no significant difference between groups in the risk of hospital admission (RR=0.89, 95% CI, 0.67 to 1.20; p=0.46; 49/113 [43%] versus 47/97 [48%]), or the use of hospital beds (SMD=0.02, 95% CI, −0.25 to 0.29; p=0.87). One UK non-randomised controlled study (1[−][1]; n=58) indicated no significant difference between groups in mental health symptoms at 78 weeks' follow-up (p-value not reported).

Substance use

There is inconsistent evidence from 1 RCT and 1 non-randomised controlled trial on the effectiveness of training on substance use outcomes. One UK RCT 1[–][2] suggested no significant difference between groups in alcohol use (SMD=−0.13; 95% CI, −0.45 to 0.19; p=0.43; RR=1.04, 95% CI, 0.85 to 1.26; p=0.72; 56/76 [74%] versus 54/76 [71%]), cannabis use (SMD=0.03; 95% CI, −0.29 to 0.35; p=0.86; RR=0.89, 95% CI, 0.57 to 1.39; p=0.61; 24/76 [32%] versus 27/76 [36%]) or other drug use (SMD=−0.26; 95% CI, −0.58 to 0.06; p=0.11; RR=0.92, 95% CI, 0.45 to 1.89; p=0.83; 12/76 [16%] versus 13/76 [17%]) at 78 weeks' follow-up. One UK non-randomised controlled study 1[−][1] indicated no significant difference between groups in service user engagement with substance use treatment or in substance-related beliefs (p-values not reported). The authors did report significantly less alcohol consumed by participants in the intervention group compared with control at 78 weeks' follow-up (p-value not reported).

Acceptability of services

One UK RCT 1[–][2] suggested no difference in service user satisfaction in the intervention group at 78 weeks' follow-up (SMD=0.02, 95% CI, −0.26 to 0.29; p=0.91), and greater satisfaction with treatment for the intervention group, which was not significant when controlling for baseline scores (adjusted difference=0.68, 95% CI, −2.1 to 3.5).

Adaptive functioning

One UK RCT 1[–][2] suggested no difference in social functioning at 78 weeks' follow-up between the intervention and control group (SMD=0.03, 95% CI, −0.24 to 0.30; p=0.82), and greater quality of life in the intervention group, which was not significant when adjusting for baseline scores (adjusted difference=0.62; 95% CI, −3.8 to 2.9).

Applicability to the UK:

The evidence is directly applicable to the UK as both included studies were

conducted in the UK. This model has been implemented in a number of UK services but resources for this have been reduced significantly in recent years.

[1]Graham et al. (2006) [–]
[2]Johnson et al. (2007) [–]

Evidence statement 3.9: Supportive housing compared with treatment as usual

There is moderate evidence from 1[+][1] RCT, comparing a supportive housing intervention with TAU, on mental health and substance use outcomes and adaptive functioning. The study reported that the intervention was delivered on average with a 'high level' of fidelity.

One study 1[+][1] conducted in Canada, which included 950 homeless people with a mental health problem (of whom 73% had a substance use problem), suggested improved mental health symptoms in the intervention group compared with TAU at 52 weeks' follow-up (SMD=−0.10; 95% CI, −0.23 to 0.02; p=0.11), however the difference was not significant. There was no difference between groups in levels of substance use (RR=1.00, 95% CI, 0.86 to 1.17; p=0.96; 188/469 [40%] versus 192/481 [40%]). At 52 weeks' follow-up the evidence suggested a higher rate of housing (RR=2.35, 95% CI, 2.01 to 2.75; p<0.00001; 316/433 [73%] versus 124/400 [31%]), a small to moderate improvement in quality of life (SMD=0.42, 95% CI, 0.29 to 0.55; p<0.00001) and a small improvement in general functioning (SMD=0.24, 95% CI, 0.11 to 0.37; p=0.0002) in favour of the supportive housing group.

Applicability to the UK:
The evidence is only partially applicable to the UK because the study is conducted in Canada where policies regarding access to supported housing are likely to differ from those provided in the UK. A number of community services provide housing support in the UK; these services are often located in the third sector and are linked to statutory mental health services. Such services could provide the basis for an extension for this work to support people with dual diagnosis.

[1]Aubry et al. (2015) [+]

Evidence statement 3.10: Supportive text messaging compared with control text messaging

There is moderate evidence from 1[+][1] RCT, comparing supportive text messaging with control text messaging, on mental health and substance use outcomes and adaptive functioning.

One RCT 1 [+][1] (n=54) conducted in Ireland compared 3 months of supportive text messaging with control text messaging in people with major depressive disorder and an alcohol-use disorder who had been discharged from an inpatient unit. At 24 weeks' follow-up, there were lower levels of depression in the intervention group compared with the control group (SMD=−0.17, 95% CI, −0.71 to 0.36, p=0.52), however the difference was not significant. The evidence suggested small to moderate effects in favour of the intervention group for preoccupation with alcohol (SMD=−0.45, 95% CI, −1.00 to 0.09; p=0.10), mean number of days abstinent from alcohol (SMD=0.42, 95% CI, −0.12 to 0.97; p=0.12) and confidence in abstaining from alcohol (SMD=0.35; 95% CI, −0.19 to 0.89; p=0.20), however these were not significant. A moderate effect in favour of the intervention group was found at 24 weeks' follow-up for participants' general functioning (SMD=0.53; 95% CI, −0.01 to 1.08; p=0.05).

Applicability to the UK:
Although the study was conducted in Ireland, the findings are directly applicable to a UK setting as the effect of receiving supportive text messages on peoples' behaviour is not likely to differ between countries.

[1]Agyapong et al. (2013) [+]

2 INTRODUCTION

The National Institute for Health and Care Excellence (NICE) has been asked by the Department of Health to develop a guideline on effective multi-agency working to improve access to community health and social care services for people with severe mental illness and substance misuse (referred to as a dual diagnosis). This review is the third of 4 reviews to inform the guideline.

- Review 1 considers the epidemiology and current configuration of UK health and social care community services for people with a dual diagnosis.
- Review 2 considers the views and experiences of service users, their families and carers, and providers and commissioners of health and social care community services for people with a dual diagnosis.
- Review 3 considers the effectiveness and efficiency of service delivery models.
- Review 4 considers the cost-effectiveness of service delivery models.

2.1 CONTEXT IN WHICH THE REVIEW IS SET

Severe mental illness (including schizophrenia, psychosis and bipolar disorder) coexists with drug and alcohol misuse in approximately 40% of users of secondary care mental health services. There is good evidence to suggest that outcomes for people with a dual diagnosis are worse than for other groups of service users who engage with health and social care services, and that they also have problems accessing services and are more likely to disengage with services (Mitchell et al., 2009; Crome et al., 2009). Furthermore, people with a dual diagnosis are more likely to have contact with the criminal justice system (Theriot & Segal., 2005).

Given the poor outcomes (and associated higher costs) (McCrone et al., 2000), there have been numerous attempts to provide better services for people with a dual diagnosis. Attempts to improve treatment outcomes can broadly be divided into 2 approaches. The first involved the development of specialist treatments, which have often taken the form of complex packages of care involving interventions known to be effective for either severe mental illness (for example, cognitive behavioural therapy) or substance misuse (for example, motivational interviewing). The second involved the development of particular models of care delivery often built around a specialised team (for example, assertive community teams or intensive case management). The former might be characterised as trying to achieve maximum therapeutic benefit, the latter to improve engagement with services.

Before describing the position of the 2 models of care in current UK services, a description of the various models and of their development in the wider context of mental health services is first provided in order to facilitate a better understanding of the models and also the assessment of the evidence considered in this review.

The specialist treatment model grew out of developments in the psychological treatment of severe mental illness and work in the field of drug and alcohol misuse. It has been established for some time (for example, Pilling et al., 2002) that psychological interventions (principally cognitive behavioural therapy and family intervention) can have a positive impact on both the severity of psychotic symptoms

and the likelihood of relapse. This research influenced the NICE guideline on psychosis and schizophrenia in adults (NICE, 2014b). In the field of drug and alcohol misuse, a range of psychological interventions (principally motivational interviewing, relapse prevention and contingency management) have been demonstrated to be effective in the reduction of drug and alcohol misuse and the prevention of relapse (Miller & Wilbourne, 2002, Burke et al., 2002) .This work has also influenced NICE guidelines (NICE 2011; NICE, 2007).

These 2 related streams of work came together to inform the development of what in this review is referred to as the integrated treatment approach. The integrated treatment approach seeks to combine interventions from both areas described above with standard care (often referred to as treatment as usual in clinical trials) with the aim of improving outcomes for those with a dual diagnosis. In the UK standard care is typically provided through community mental health teams which focus on the treatment of severe mental illness and provide a service to a defined catchment area. The primary means of delivering services is through case co-ordinator (other terms used to describe this role might include key worker or case manager); this will be provided by a staff member who will have specific training in health or social care, often nurses or social workers. Case co-ordination involves the delivery of assessment and a range of psychosocial interventions, liaison with family members and other care agencies and monitoring of treatment progress. Case co-ordinators are members of the community mental health team, which comprises specialist nursing, medical, psychology and social care and staff. Frequency of contact with service users will vary between every 2 to 4 weeks depending on need and may be more frequent (weekly) when establishing interventions or during a crisis. Community mental health teams will have close links with both inpatient services and other specialist treatment services such as Crisis resolution and home treatment teams.

In contrast, community-based care in the United States (which is where many trials are conducted) is typically more fragmented. Community mental health teams are much less common and care is often co-ordinated through outpatient care settings, with less integration between inpatient and community settings than in the UK. A typical example of integrated care might include the use of cognitive behavioural interventions together with motivational interviewing in a community mental health setting to address the needs of a person with dual diagnosis.

New models of care delivery, referred to above, developed out of the work on assertive community treatment (ACT) and intensive case management (ICM). Evidence, largely drawn from studies in the United States, suggested that both were effective (for example, Marshall & Lockwood, 1998). In particular, ACT and ICM were seen as a solution to better engage and help people with severe mental illness who often had poor contact with services and as a consequence had poorer outcomes. ACT and ICM share some common functions including a reduced case load (typically less than 20 per worker compared with that of a community mental health team, which typically may be over 40 per worker), long-term and consistent support and a central aim to promote better engagement with services. ICM locates the responsibility for the co-ordination of care with a single individual, even though case co-ordinators are members of a multi-disciplinary team. In contrast, in ACT

responsibility rests with the whole team as the task of managing a caseload of difficult to engage people for a single worker is seen as too challenging. In addition, in ACT the purpose of the team is to provide all key interventions from within the resources of the team, whereas in ICT interventions may well be provided outside of the team. Variations to the ICM model include brokerage case management where the sole function of the case manager is to organise care instead of providing care and time limited case co-ordination where the role is undertaken for a limited period of time (say for 3 to 6 months) in contrast to the 2 years or more of contact associated with ACT and ICM models.

Both models have influenced the delivery of care for dual diagnosis in England. Initial responses focused on the development of specialist dual diagnosis teams but few services were actually developed because it became evident that the large numbers of people with a dual diagnosis required the establishment of a parallel community mental health service. Few if any such teams still exist and where they do their role has moved away from the direct provision of care to provide a training and consultation role to community mental health services. The decline in the development of ACT or ICM models may also have been influenced by UK studies of ACT (for example Killapsy et al., 2006) and ICM (Burns et al., 1999) in people with severe mental illness, which suggested that neither were effective in the UK. One reason to account for this is that the better quality of standard care provided within the UK compared to poorer standard care in the United States meant that the benefits of ACT or ICM could not be achieved in the UK studies. The development of specialist therapeutic interventions has not gained much traction in England – again the model that has been followed has been in supporting the delivery of interventions in the context of community mental health services.

The response to the failure of the 2 models to establish a distinct role in mental health services has been to promote integration of both assertive engagement and specialist treatments into routine care. Common methods for doing this have been either the consultation and advice model (currently adopted by a number of services where nurse specialist or specialist teams provide the service) or the appointment of 1 or more specialist staff member to a community mental health team. This integrated model is currently the most common model but it is far from established in most mental health trusts. Staff turnover, in particular of staff with specific skills in dual diagnosis, has been a major problem in maintaining the specialist staff member model.

2.2 AIMS AND OBJECTIVES

To estimate the effectiveness and efficiency of service delivery models for health, social care and voluntary and community sector organisations at meeting the needs of people with a dual diagnosis.

2.3 REVIEW QUESTION AND PROTOCOL

The review protocol summary, including the review question and the eligibility criteria used for this review, can be found in Table 1. The full protocol is available here.

Table 1: Review protocol summary for RQ 3 (effectiveness and efficiency of service delivery models for health, social care and voluntary and community sector organisations at meeting the needs of people with a dual diagnosis)

Component	Description
Review question	Review question (RQ) 3: Which service models for health, social care and voluntary and community sector organisations are effective and efficient at meeting the needs of people with a dual diagnosis?
Condition or domain being studied	'Dual diagnosis' was defined as a severe mental illness combined with misuse of substances. Severe mental illness includes a clinical diagnosis of: • schizophrenia, schizotypal and delusional disorders • bipolar affective disorder • severe depressive episode(s) with or without psychotic episodes Substance misuse refers to the use of legal or illicit drugs including alcohol and medicine, in a way that causes mental or physical damage (this may include low levels of substance use that would not usually be considered harmful or problematic, but may have a significant effect on the mental health of people with a mental illness such as psychosis).
Context	Included: community settings (including a range of services provided by the NHS or other healthcare systems, social care and schools, as well as the community and voluntary sectors). Studies from any Organisation for Economic Co-operation and Development (OECD) member country will be included. However, applicability to the UK service setting will be considered during data analysis and synthesis. Excluded: • non-OECD studies • prisons and other custodial settings • young offenders units • forensic secure mental health settings
Population	Included: young people (aged 14 to 24 years) and adults (25 years and over) who have been diagnosed as having a severe mental illness and who misuse substances (dual diagnosis) who live in the community. Excluded: • children (aged under 14 years) • people with a severe mental illness but with no evidence of substance misuse • people who misuse substances who have not been diagnosed with a severe mental illness • people with a severe mental illness who smoke or use tobacco but do not misuse any other substances • people who have a severe mental illness and misuse substances, but who are not living in the community.

Component	Description
Intervention(s), exposure(s)	Included: Any service delivery model, including: • Integrated models of care: mental health and substance misuse treatments are delivered by the same service, clinician or team of clinicians at the same time (for example, assertive community treatment [ACT], case management, integrated motivational interviewing and cognitive behavioural therapy, mainstreaming) • Parallel models of care: separate treatment programmes are delivered in parallel by mental health and substance misuse services • Serial models of care: separate treatment programmes are delivered sequentially by mental health and substance misuse services • Measures aimed at improving accessibility and availability of services, for example, services available 24 hours a day, 7 days a week • Measures aimed at promoting uptake of and engagement with services, for example, practical help (such as reminders to attend) and non-clinical activities (such as 'coffee mornings') Excluded: Not applicable
Comparator(s)/control	Included: • Treatment as usual (TAU) • No treatment • Waitlist control • Placebo (including attention control) • Any alternative service delivery model Excluded: Not applicable
Primary/critical outcomes	• Mental and physical health outcomes (including mortality, recovery and relapse, physical morbidity) • Accessibility of services (for instance, transfer/referral times, waiting times, physical accessibility of services) • Acceptability of services (for instance, service user, carer and family satisfaction with care) • Adaptive functioning outcomes (for instance, employment, housing, quality of life) • Service utilisation (for instance, number of missed appointments, changes in treatment adherence)
Study design	Included: RCTs (including crossover randomised trials if data from the first phase is available) from all OECD countries If there are no RCTs found in the evidence search, or the results from the RCTs are inconclusive, the range of included studies will be expanded to include non-randomised studies. Preference will be given to quasi-randomised controlled trials (for example, allocation by alternation or date of birth), controlled non-randomised studies and large cohort studies. If little evidence meets the above criteria, then before-and-after studies will be considered cautiously. Systematic reviews will be used as a source for identifying any studies that may not have been picked up in the searches.

2.4 IDENTIFICATION OF POSSIBLE EQUALITY AND EQUITY ISSUES

The following equality issues were identified through scoping and the NICE equality impact assessment[3] and where possible, consideration was given to the specific needs of:

- older people
- people with a learning disability
- teenage parents
- people from black and minority ethnic groups
- travellers
- asylum seekers or refugees
- women
- lesbian, gay, bisexual, transsexual or transgender people
- people who are homeless or in insecure accommodation
- people from a low-income family or on a low income
- people who are socially isolated
- ex-offenders
- sex workers
- people who are, or have a history of being, 'looked after' or adopted
- adults who have a history of experiencing, witnessing or perpetrating violence or abuse
- young people who have experienced abuse or witnessed domestic violence or abuse
- young people who are excluded from school
- young people whose parents have mental health or substance misuse problems.

[3] Available at: http://www.nice.org.uk/guidance/gid-phg87/documents/severe-mental-illness-and-substance-misuse-dual-diagnosis-community-health-and-social-care-services-equality-impact-assessment-scoping2

3 METHODOLOGY

3.1 LITERATURE AND DATABASE SEARCH

Based on the scope, a systematic search strategy was developed to identify relevant evidence published between 2000 and July 2015. 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 systematic and exhaustive approach to the searches to maximise the retrieval of evidence. Searches were conducted in the following databases:

- Applied Social Sciences Index and Abstracts (ASSIA)
- Cost-Effectiveness Analysis (CEA) Registry
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Reviews of Effect (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- Econlit
- EconPapers
- Embase
- Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI) Centre databases - Bibliomap and Database of Promoting Health Effectiveness Reviews (DoPHER)
- Health Management Information Consortium (HMIC)
- International Bibliography of the Social Sciences (IBSS)
- MEDLINE and MEDLINE in Process
- NHS Economic Evaluations Database (NHS EED)
- PsycINFO
- Social Care Online
- Social Policy & Practice
- Social Science Citation Index
- Social Service Abstracts
- Sociological Abstracts.

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 test searches and discussions of the results of the searches with the project team to ensure that all relevant search terms were covered. In order to assure comprehensive coverage, search terms for dual diagnosis were kept purposefully 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. The search terms for the MEDLINE search are set out in full in appendix 1.

Search restrictions included the following:

- date (publication limit 2000-current)
- language (English-language studies) limits.
- animal studies, letters, editorials and other non-relevant publication types removed from results
- searching Embase using only major Emtree headings
- systematic reviews and RCTs using adaptations of filters developed by the Health Information Research Unit, McMaster University.

The following websites were searched:

- Campbell Collaboration
- European Observatory on Healthcare Systems and Policies
- Institute for Clinical Systems Improvement
- McMaster University Health Evidence
- NICE (guidelines and Evidence Search)
- National Institute for Health Research (NIHR) Health Services & Delivery Research Programme
- Public Health England (including National Treatment Agency for Substance Misuse)
- Public Health Wales
- Scottish Government
- Scottish Intercollegiate Guidelines Network (SIGN)
- Turning Research into Practice
- US National Guidelines Clearinghouse
- Welsh Government

In addition the following research registries were searched:

- ClinicalTrials.gov (US National Institutes of Health service)
- International Standard Randomised Controlled Trial Number (ISRCTN) Register

Citations from each search were downloaded into EndNote software and duplicates removed. Records were then screened against the eligibility criteria of the review before being appraised for methodological quality (see below). The unfiltered search results were saved and retained for future potential re-analysis to help keep the process both replicable and transparent. Additional hand searching of conference abstracts and references of recent high quality reviews was conducted to ensure all relevant trials were identified.

NICE issued a call for evidence to stakeholders between January and February 2015. From this call for evidence no reports were identified that met the criteria for this review.

3.2 SELECTION OF STUDIES

Citations from the database search were split into 2 separate files: (1) included RCTs and systematic reviews, and (2) observational studies only. This was

because different inclusion criteria were applied to the 2 types of research design. While the RCT and systematic review evidence included studies from any OECD country, evidence from observational studies was limited to the UK and Ireland.

Titles and abstracts of identified studies were screened for inclusion against agreed criteria. Two reviewers independently screened 10% of references. For the RCT and systematic review sift, overall inter-rater reliability was very good (percentage agreement of 99%). When considering the inter-rater reliability for only the proportion of studies that were included it was lower (percentage agreement of 75%). However as this was based on the inclusion of a small number of studies (n=8), the absolute number of studies on which there was disagreement was deemed low enough (n=2) not to warrant further double sifting. For the observational study sift, again, the overall inter-rater reliability was very good (percentage agreement of 99%), however when considering the inter-rater reliability for only the proportion of studies that were included, it was deemed too low (percentage agreement of 11%). A further 10% of references were screened independently by 2 reviewers. Again, despite good overall inter-rater reliability (percentage agreement of 99%), inter-rater reliability for included studies was poor (percentage agreement of 47%). In light of time pressures, a single reviewer completed the manual search on the remaining 80% of references, erring on the side of inclusion, to avoid exclusion of studies that might be relevant.

3.3 RETRIEVAL OF DATA AND FULL-TEXT APPRAISAL

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 entered into a study database (standardised template created in Microsoft Excel). The full text papers were screened by 2 reviewers using the inclusion criteria for reference. Any disagreements regarding inclusion/exclusion were resolved by discussion with a third reviewer. One researcher extracted data into the study database, of which 10% was checked by a second reviewer for reliability. Discrepancies or difficulties with coding were resolved through discussion between reviewers. Study characteristics, aspects of methodological quality, and outcome data were extracted from all eligible studies using an Excel-based form and Review Manager Version 5.3 (Cochrane Collaboration, 2014). At full-text appraisal stage it was agreed that in order to ensure inclusion of studies reporting integrated interventions was in a manner which would be consistent with the scope, single or multi-component interventions, delivered in the context of a specialist team or setting were included. Standalone interventions, for example those delivered in an outpatient clinic not linked to a specialist service, were excluded

3.4 QUALITY APPRAISAL

For the RCT evidence, the quality of individual studies was assessed using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (Higgins & Green, 2011). For observational studies, the Effective Practice and Organisation of Care (EPOC) Risk of Bias Tool and the NICE-adapted 'Checklist to Assess Evidence of Prevalence and Incidence, Descriptive or Longitudinal Studies' were used (checklist 1.6 in NICE's Interim methods guide for developing service guidance 2014). Each study was rated ++, + or – to denote its quality, where:

- ++ indicates that all or most of the checklist criteria have been fulfilled (and where they have not been fulfilled the conclusions are very unlikely to alter)
- + indicates that some of the checklist criteria have been fulfilled (and where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter)
- – indicates that few or no checklist criteria have been fulfilled (and the conclusions are likely or very likely to alter).

See appendix 2 and appendix 3 for example completed quality appraisal checklists. The review team also considered the applicability of individual studies to the review question.

3.5 DATA EXTRACTION

The data extracted (where available) were as follows:

- Study characteristics: research questions (RQ) addressed, study design, country, total number of participants (N), inclusion/exclusion criteria, severe mental illness, diagnostic criteria, substance misuse, method of substance misuse assessment, demographics (age, sex, ethnicity), treatment adherence (for instance, the proportion of participants who completed the intervention), treatment fidelity (whether the programme/intervention was delivered as planned), risk of bias (selection bias, performance bias, detection bias, attrition bias, other bias), overall study quality, funding, limitations identified by the review team and limitations identified by the authors.
- Comparisons: for both experimental and control conditions: service delivery model or control condition, group size, intensity/dose, frequency, duration and setting.
- Outcomes: outcome name, outcome measure, rater, direction of scale, time point (for instance, weeks post-randomisation), phase, outcome data (for instance, mean, standard deviation, N, events).

3.6 DATA ANALYSIS AND SYNTHESIS

For RCTs, meta-analysis using a random-effects model was used to combine results from similar studies. Where this was not possible (for instance, because of different outcomes) a narrative synthesis was used. Observational studies were analysed separately from the RCTs and synthesised narratively.

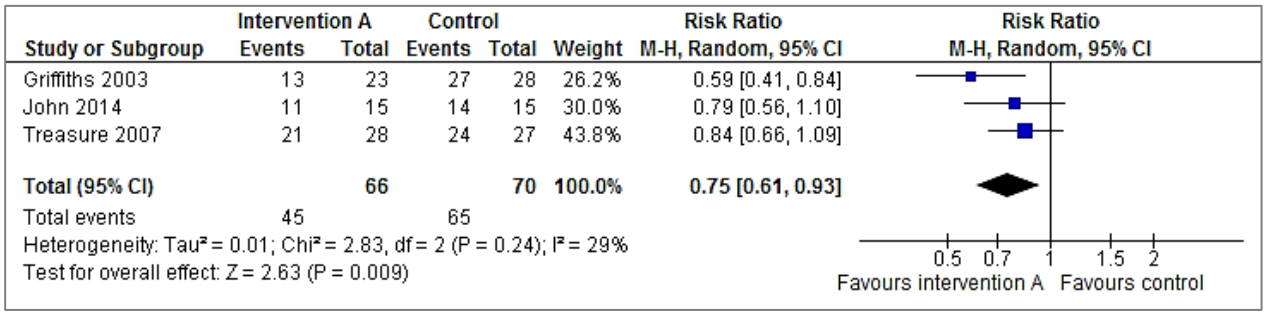
Meta-analysis

Where appropriate, meta-analysis using random effects models was used to synthesise evidence for the effectiveness of interventions using Review Manager Version 5.3. Dichotomous outcomes were analysed as relative risks (RR; also called a risk ratio) with the associated 95% confidence interval (see Figure 1for an example of a forest plot displaying dichotomous data). An RR is the ratio of the intervention event rate to the control event rate. An RR of 1 indicates no difference between intervention and control. In Figure 1, the overall RR of 0.75 indicates that the event rate (for instance, rate of unemployment) associated with intervention A is

about three-quarters of that of the control intervention, or, in other words, the reduction in the relative risk is 25%.

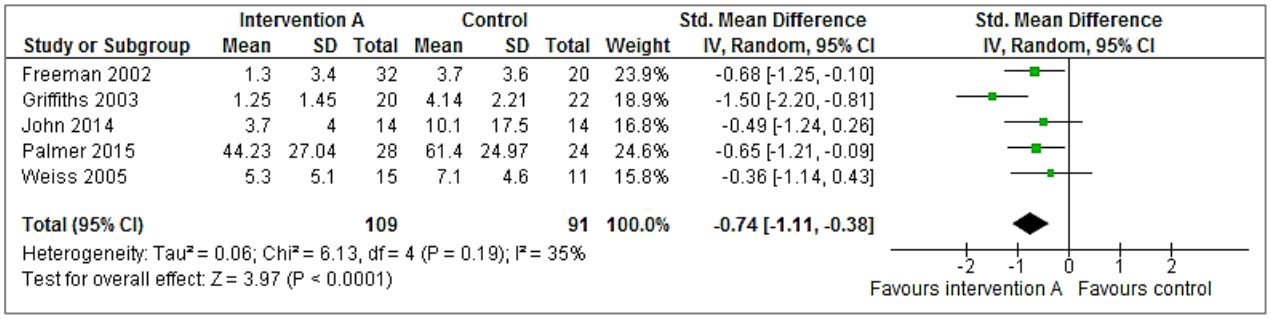
The confidence interval shows a range of values within which it is possible to be 95% confident that the true effect will lie. If the effect size has a confidence interval that does not cross the 'line of no effect', then the effect is commonly interpreted as being statistically significant.

Figure 1: Example of a forest plot displaying dichotomous data



Continuous outcomes were analysed using the standardised mean difference (SMD), or Cohen's d, which is the difference in the two groups' means divided by the average of their standard deviations (see Figure 2 for an example of a forest plot displaying continuous data). This means that a SMD of 1 indicates that the two groups' means differ by 1 standard deviation, whereas an SMD of 0.5 shows that the two groups' means differ by half a standard deviation. The size of the effect was reported according to Cohen's rule of thumb whereby an SMD of 0.2 can considered a small effect size, 0.5 a moderate effect size and 0.8 a large effect size (Cohen, 1988). 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. Where means and standard deviations were not reported by the authors, SMDs and their standard errors (either reported or calculated by the review team) were analysed using the generic inverse variance method.

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). For meta-analyses of

comparative effectiveness studies, the I^2 statistic was interpreted in the following way based on guidelines from the Cochrane Collaboration (Higgins & Green, 2011):

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity.

The Cochrane Collaboration advice suggests that overlapping categories are less misleading than simple thresholds since the importance of inconsistency depends on: (1) the magnitude and direction of effects, and (2) the strength of evidence for heterogeneity (for example, p value from the chi-squared test, or a confidence interval for I^2). Levels of heterogeneity will only be reported in the summary of findings when the I^2 statistic is above 40% and explored further when the I^2 statistic is above 50%.

Repeated observations on participants

Where studies reported results for several periods of follow-up (for example, 4 weeks, 12 weeks and 26 weeks' post-treatment) the longest follow-up from each study was utilised in analyses.

Method of dealing with missing data

Because imputation of missing data in order to perform a full intention-to-treat analysis is controversial, only the results for available participants will be analysed in meta-analysis. However, for dichotomous outcomes a sensitivity analyses was carried out whereby missing data was imputed according to worst case scenario. Outcomes from the sensitivity analysis are only presented if the intention-to-treat analysis differs significantly from the available case analysis.

It was proposed that a 'design-oriented' conceptual model which would build on a 'problem-oriented' conceptual model developed for RQ 1 (to map how changes to configuration of components impact on outcomes) would be produced. However, due to a lack of data it was not possible to develop either of the models.

3.7 PRESENTATION OF FINDINGS

Comparisons are reported within the following broad intervention categories:

- assertive community treatment
- integrated treatment
- other interventions.

Findings are reported within each comparison under headings for the following types of outcomes:

- Mental health outcomes (for instance symptoms, recovery and relapse)
- Substance use (for instance, severity of substance use and abstinence)
- Acceptability of services (for instance, service user satisfaction)
- Adaptive functioning (for instance, employment, housing and quality of life)
- Service utilisation (for instance, number of missed appointments and treatment adherence)

Throughout the summary of findings, the length of follow-up refers to the time from randomisation to assessment of the outcome.

For detailed presentation of study characteristics and findings, see appendix 10.

4 SUMMARY OF FINDINGS

4.1 STUDIES CONSIDERED

The electronic database search identified 11,654 records, 2,824 for RCT and systematic review evidence and 8,830 for observational studies. Of these, full-text appraisal was conducted for 155 records (and 11,499 were excluded on the basis of title and abstract). An additional 12 papers were located through hand-searching methods. Of these, 4 papers were included, which reported on studies which had already been identified in the RCT and systematic review search. After full-text review, and removal of duplicates, 22 studies were included (reported across 26 papers). See appendix 6 for the PRISMA diagram, appendix 7 for a bibliography of included studies and appendix 8 and appendix 9 for bibliographies of excluded studies with reasons for exclusion.

4.2 SUMMARY OF THE EVIDENCE

4.2.1 Overview of included studies

Twenty RCTs and 2 observational studies were included, with sample sizes ranging from 19 to 950 (mean: 156). Over half of the studies were conducted in the US (n=12) whereas 5 were conducted in the UK. Of those that reported the geographical location, 7 were conducted in urban settings, 3 in rural areas and 2 in mixed settings. The proportion of female participants ranged from 1%-56% across 21 studies which reported gender and the proportion of participants reported as white ranged from 14%-100% across 16 studies. Information on education level, employment or marital status were also reported in some of the studies. See Table 2 for a summary of included studies for RQ3 and appendix 10 for full evidence tables, which include detailed study information. Supporting information containing forest plots for each comparison can be found in appendix 11.

Table 2: Study information table of included studies for RQ3

Included studies	n=22
Sample size	19-950 (mean: 156)
Study design	RCTs (n=19), cluster RCT (n=1), non-RCT (n=1), before-and-after study (n=1)
Intervention	ACT (n=5), integrated treatment[4] (n=8), brokerage case management (n=1), contingency management and compensated work therapy (n=2), care co-ordination (n=1), shelter-based psychiatric clinic (n=1), staff training (n=2), supportive housing (n=1), supportive text messaging (n=1)
Severe mental illness	Any severe mental illness (n=9), bipolar disorder (n=2), major depression (n=2), schizophrenia spectrum disorder (n=5), schizophrenia spectrum disorder or bipolar disorder (n=1), unclear (n=2)
Substance misuse	Any substance-use disorder (n=15), alcohol-use disorder (n=1), cannabis-use disorder (n=2), cannabis- or alcohol-use disorder (n=2),

[4]Integrated treatment here refers to any intervention which was delivered in the context of a multidisciplinary team in combination with usual care

	alcohol-, cocaine- or opiate-use disorder (n=2)
Service setting	Community setting (n=3), location of choice (n=2), shelter (n=1), text messaging (n=1), NR (n=15)
Country	US (n=12), UK (n=5), Australia (n=1), Canada (n=1), Denmark (n=1), Ireland (n=1), Switzerland (n=1)
Geographical location	Urban setting (n=7); rural setting (n=3); mixed setting (n=2); NR (n=9)

4.2.2 Quality assessment

The general quality of the included studies was judges to be low to moderate. Out of 22 studies, 9 were rated moderate quality [+] and 13 were rated poor quality [–]. No studies were rated high quality [++]. This indicates that the evidence described in this section may be subject to bias, potentially influencing the outcomes reported. In all studies there was a high risk of performance bias because it was not possible to blind participants and providers to which intervention group they had been allocated. In 8 of the 22 studies there was a high risk of bias for missing outcome data, which was due to more than 20% of participants dropping out of the study and/or unequal dropout between different intervention groups. Other common limitations included: (1) a lack of information about the process of allocating participants to intervention group, (2) a lack of registered trials, which meant it was unclear whether selective outcome reporting had occurred, and (3) a lack of information regarding the blinding of outcome assessors. See appendix 4 and appendix 5 for completed methodology checklists.

4.3 ASSERTIVE COMMUNITY TREATMENT

4.3.1 Assertive community treatment compared with treatment as usual

Table 3: Summary of characteristics of studies contributing to the comparison: ACT compared with TAU

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Drake et al. (2004)* RCT Quality: [–]	US, New Hampshire, Rural	Bipolar disorder and substance-use disorder (n=54)	ACT	Standard case management	Community
Essock et al. (2006) RCT Quality: [+]	US, Connecticut, Urban	Severe mental illness and substance-use disorder (n=198)	ACT	Standard case management	Community
Fletcher et al. (2008) RCT Quality: [–]	US, NR	Severe mental illness and substance-use disorder (n=191)	Integrated ACT	Standard care	NR
			ACT	Standard care	
Striley et al. (2013) RCT Quality: [+]	US, Madison County, Illinois, NR	Major depression and substance-use disorder (n=120)	Enhanced case management	TAU	NR
Xie et al. (2005)* RCT Quality: [–]	US, New Hampshire, Rural	Schizophrenia spectrum disorders and substance-use disorder (n=169)	ACT	Standard case management	Community
** Drake et al. (2004) and Xie et al. (2005) were part of the same study, which was split by type of mental illness*					

Narrative summary

Five RCTs (n=732) compared ACT with TAU: Drake et al. (2004) [–], Essock et al. (2006) [+], Fletcher et al. (2008) [–], Striley et al. (2013) [+] and Xie et al. (2005) [–]. Fletcher et al. (2008) was a 3-armed trial that included 2 types of ACT and a TAU control group. For the purpose of this review, the control group was evenly split and compared with each intervention group separately, although overall differences between ACT and TAU are reported in this section. In 3 studies the authors did not provide sufficient data to calculate effect sizes: Drake et al. (2004), Essock et al. (2006) and Xie et al. (2005). Drake et al. (2004) and Xie et al. (2005) were part of

the same study, which was split by type of mental illness: Drake et al. (2004) only included people with bipolar disorder, whereas Xie et al. (2005) included people with a schizophrenia spectrum disorders. Essock et al. (2006) had a similar design to Drake et al. (2004) and Xie et al. (2005) as it was conducted by the same authors, but it was a separate study carried out in a different location. For these studies, findings are reported narratively. Because of differences in reported outcome measures it was not possible to meta-analyse data from Fletcher et al. (2008) and Striley et al. (2013). Essock et al (2006) and Fletcher et al. (2008) both reported that the intervention was delivered with good fidelity to the treatment model. Results are summarised for each type of outcome. Key characteristics of included studies are summarised in Table 3.

Mental health

A meta-analysis of a 3-armed RCT comparing ACT (n=53), or integrated ACT (n=46) to TAU (n=48), showed no difference between groups for mental health symptoms (assessed on the BPRS-24) (SMD=0.01; 95% CI, −0.33 to 0.36; p=0.94) at 130 weeks' follow-up (see appendix 11, forest plot 1.1.1).

One RCT by Striley et al. (2013), which included participants with major depression and a substance-use disorder, showed no difference between enhanced case management and TAU at 52 weeks' follow-up for depressive symptoms (assessed on the DSS) (SMD=−0.10; 95% CI, −0.46 to 0.26; p=0.58) or for homicidal and suicidal thoughts (assessed on the HSTI) (SMD=−0.03; 95% CI, −0.38 to 0.33; p=0.89) (see appendix 11, forest plots 1.1.2 and 1.1.4). There was evidence for a small increased involvement in mental health treatment (in the past 90 days) (assessed on the MHTI) for the enhanced case management group at 52 weeks' follow-up, but this was not significant (SMD=0.18; 95% CI, −0.18 to 0.54; p=0.33) (see appendix 11, forest plot 1.1.3).

Three RCTs did not report sufficient data to calculate effect sizes: Drake et al. (2004), Essock et al. (2006) and Xie et al. (2005). For all 3 trials, the authors reported no significant difference (p-values not reported) between ACT and standard care for psychiatric symptoms (assessed with the BPRS) at 156 weeks' follow-up.

Substance use

A meta-analysis of a 3-armed RCT (Fletcher et al. 2008) comparing ACT (n=53), or integrated ACT (n=46) to TAU (n=48), found that ACT was associated with a small increase in severity of substance use compared with TAU (SMD=0.18; 95% CI, −0.17 to 0.52; p=0.32) at 130 weeks' follow-up, however the difference was not significant (see appendix 11, forest plot 1.1.5).

Three RCTs did not report sufficient data to calculate effect sizes: Drake et al. (2004), Essock et al. (2006) and Xie et al. (2005). For all 3 trials, the authors reported no significant difference between ACT and standard care for alcohol use, drug use or overall substance use at 156 weeks' follow-up (p-values not reported).

Acceptability of services

Only 1 RCT reported outcomes associated with the acceptability of services. A meta-analysis of the different comparator arms in Fletcher et al. (2008) indicated

that service users were significantly more satisfied with TAU compared with ACT at 130 weeks' follow-up (SMD=−0.44; 95% CI, −0.78 to −0.09; p=0.01; control mean, SD: 4.36, 0.38) (see appendix 11, forest plot 1.1.6).

Adaptive functioning

A meta-analysis of the different comparator arms in Fletcher et al. (2008) found that ACT was associated with a small increase in days living in stable housing compared with TAU at 130 weeks' follow-up (SMD=0.22; 95% CI, −0.13 to 0.56; p=0.22), however this was not significant (see appendix 11, forest plot 1.1.7).

Three RCTs did not report sufficient data to calculate effect sizes: Drake et al. (2004), Essock et al. (2006) and Xie et al. (2005). Drake et al. (2004) and Xie et al. (2005) reported no significant difference between ACT and TAU for days of independent living, homelessness, employment, social contact and quality of life at 156 weeks' follow up (p-values not reported). Essock et al. (2006) reported no significant difference between ACT and TAU for general functioning, life satisfaction and community housing (p-values not reported).

Service utilisation

Only 1 RCT reported outcomes associated with service utilisation. A meta-analysis of the 2 comparator arms in Fletcher et al. (2008) found a moderate to large effect in favour of ACT for the number of days of physical contact with the assigned programme (SMD=0.65; 95% CI, 0.30 to 1.00; p=0.0003) and a large effect in favour of ACT for telephone contact (SMD=0.94; 95% CI, 0.58 to 1.30, p<0.00001) with the assigned programme at 130 weeks' follow-up (see appendix 11, forest plots 1.1.8 and 1.1.10). Reasons for contacts were not reported. There was no difference between groups in the number of days discussing substance use problems with the assigned programme (SMD=−0.09; 95% CI, -

−0.46 to 0.28; p=0.62) (see appendix 11, forest plot 1.1.9).

Evidence statement 3.1: ACT compared with TAU

There is weak evidence from 5 RCTs (2[+][2,4] and 3[−][1,3,5]) comparing ACT with TAU on mental health and substance use outcomes, the acceptability of services, adaptive functioning and service utilisation. Two RCTs[2,3] reported that the intervention was delivered with 'good fidelity' to the treatment model.

Mental health

There is evidence from a meta-analysis and 4 US RCTs on the effectiveness of ACT compared with TAU to improve mental health outcomes. Consistent evidence from a meta-analysis of a 3-armed RCT [-][3] (n=147) comparing ACT or integrated ACT to TAU showed no difference between groups for mental health symptoms (assessed on the BPRS-24) (SMD=0.01; 95% CI, - 0.33 to 0.36; p=0.94; I^2=0%) at 130 weeks' follow-up. There was also consistent evidence from 4 RCTs. One US RCT (1[+][4]; n=120) showed a small increased involvement in mental health treatment in the enhanced case management group compared to TAU at 52 weeks' follow-up, but the effect was not statistically significant (SMD=0.18; 95% CI, −0.18 to 0.54; p=0.33). Four US RCTs (2[+][2,4] and 2[−][1,5]) suggested no difference in psychiatric symptoms for ACT compared with TAU at follow-ups

ranging from 52 to 156 weeks' post-randomisation.

Substance use
There is evidence from a meta-analysis and 3 RCTs on the effectiveness of ACT compared with TAU on substance use outcomes. Consistent evidence from a meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US showed a small increase in the severity of substance use in the ACT group compared with TAU at 52 week's follow-up (SMD=0.18; 95% CI, −0.17 to 0.52; p=0.32; I^2=0%), but this was not statistically significant. There was also consistent evidence from 3 US RCTs (1[+][2], 2[−][1,5]) which indicated no significant differences in levels of alcohol, drug or overall substance use between ACT and TAU at 156 weeks' follow-up (p-values not reported).

Acceptability of services
There is consistent evidence from a meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US which found that service users were significantly more satisfied with TAU compared with ACT at 130 weeks' follow-up (SMD=−0.44; 95% CI, −0.78 to −0.09; p=0.01; I^2=0%).

Adaptive functioning
There is consistent evidence from a meta-analysis and 2 RCTs on the effectiveness of ACT compared with TAU on adaptive functioning outcomes. A meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US showed a small improvement in stable housing for ACT compared with TAU at 130 weeks' post-randomisation (SMD=0.22; 95% CI, −0.13 to 0.56; p=0.22; I^2=0%), however the difference was not significant. Two US RCTs (2[−][1,5]) reported no significant difference between groups for housing, employment, social contact or quality of life outcomes (p-values not reported). One US RCT (1[+][2]) reported no significant difference between groups for general functioning, life satisfaction or community housing (p-values not reported).

Service utilisation
There is consistent evidence from a meta-analysis of a 3-armed RCT (1[–][3]) conducted in the US to suggest a moderate to large effects in favour of ACT for days in physical contact (SMD=0.65; 95% CI, 0.30 to 1.00; p=0.0003; I^2=0%) and telephone contact (SMD=0.94; 95% CI, 0.58 to 1.30; p<0.00001;I^2=0%) with the assigned programme compared with TAU at 130 weeks' follow-up; reasons for contacts were not reported. There was no difference between groups in the number of contacts with substance misuse services (SMD=−0.09; 95% CI, −0.46 to 0.28; p=0.62; I^2=13%).

Applicability to the UK:
This evidence is only partially applicable to the UK. This is because all included studies were conducted in the US and TAU is likely to differ from that provided in the UK, which has better co-ordinated services for severe mental illness than the US.

[1]Drake et al. (2004) [–]
[2]Essock et al. (2006) [+]
[3]Fletcher et al. (2008) [–]

[4]Striley et al. (2013) [+]
[5]Xie et al. (2005) [–]

4.4 INTEGRATED TREATMENT[5]

4.4.1 Integrated treatment compared with treatment as usual

Table 4: Summary of characteristics of studies contributing to the comparison: integrated treatment compared with TAU

Author (year); study design; quality	Country, region, location	Population (N)	Intervention[†]	Comparator	Service setting
Barrowclough et al. (2001) RCT Quality: [+]	UK, Northwest of England, NR	Schizophrenia spectrum disorder and substance-use disorder (n=36)	Integrated intervention programme	Routine care	Home or clinic
Barrowclough et al. (2010) RCT Quality: [+]	UK, Greater Manchester, Lancashire and south London, Mixed	Schizophrenia spectrum disorders and substance dependence/ abuse (n=327)	Integrated intervention programme	Standard care	Location of choice, usually home
Bonsack et al. (2011) RCT Quality: [–]	Switzerland, Lausanne, NR	Schizophrenia spectrum disorders and cannabis dependence[β] (n=62)	Motivational intervention	TAU	NR
Copello et al. (2013) Before-and-after study Quality: [–]	UK, Birmingham and Solihull, Urban	Severe mental ilness and substance misuse (n=173)	COMPASS consultation-liaison service	No comparator	NR
Eack et al. (2015) RCT Quality: [–]	US, Pittsburgh, NR	Schizophrenia spectrum disorders and alcohol or cannabis abuse/ dependence (n=31)	Cognitive enhancement therapy	TAU	NR
Hjorthøj et al. (2013) RCT Quality: [+]	Denmark, Copenhagen, Urban	Schizophrenia spectrum disorders and cannabis abuse/ dependence (n=103)	Integrated intervention	TAU	NR
Nagel et al.	Three remote	Severe mental	Motivational	TAU	NR

[5] Integrated treatment here refers to any intervention which was delivered in the context of a multidisciplinary team in combination with usual care

(2009) RCT Quality: [+]	communities in northern Australia, Rural	illness and cannabis and/or alcohol use, from indigenous communities (n=49)	care planning		
†All interventions were delivered in combination with TAU *[β]Only 82.3% had a cannabis dependence*					

Narrative summary

Six RCTs (n=781) compared an integrated psychosocial intervention in combination with TAU with TAU alone: Barrowclough et al. (2001) [+], Barrowclough et al. (2010) [+], Bonsack et al. (2011) [–], Eack et al. (2015) [–], Hjorthøj et al. (2013) [+] and Nagel et al. (2009) [+]. Nagel et al. (2009) did not provide sufficient data to calculate effect sizes, therefore the findings are reported narratively. One before-and-after study (Copello et al. (2013) [–]) compared assessed outcomes following a brief intervention in combination with TAU and are reported separately from the RCT evidence. It should be noted that all the integrated treatment groups also received TAU (to improve readability in the following sections this will not be mentioned when describing comparisons). Barrowclough et al., 2010) reported 81-100% treatment fidelity for the intervention and Nagel et al. (2009) reported only minor variations to fidelity. Key characteristics of included studies are summarised in Table 4.

Mental health

A meta-analysis of 3 RCTs (n=466; Barrowclough et al. (2001); Barrowclough et al. (2010); Hjorthøj et al. (2013)) which compared an integrated psychosocial intervention with TAU, reported overall psychotic symptoms (assessed with the PANSS). At follow-ups ranging from 43 to 104 weeks, there was no difference in symptoms between integrated treatment and TAU (SMD=0.03; 95% CI, −0.27 to 0.33; p=0.83; I^2=44%) (see appendix 11, forest plot 1.2.2).

One RCT (n=62) also included participants with schizophrenia spectrum disorders and cannabis dependence (Bonsack et al., 2011) but reported the positive and negative subscales[6] of the PANSS separately so it was not possible to add outcomes to the meta-analysis described above. . At 52 weeks' follow-up, there was a small reduction in positive symptoms (SMD=−0.22; 95% CI, −0.72 to 0.27; p=0.38) and negative symptoms (SMD=−0.30, 95% CI, −0.80 to 0.21; p=0.25), in the integrated treatment group compared with TAU,; however the difference was not significant (see appendix 11, forest plot 1.2.3 and 1.2.4).

One RCT (n=31), which included participants with a schizophrenia spectrum disorder and an alcohol- or cannabis-use disorder (Eack et al., 2015), found a small increase in the severity of mental health symptoms (based on a composite score from the following scales: Brief Psychiatric Rating Scale, Wing Negative Symptom

[6] The positive and negative subscales of the PANSS measure positive and negative symptoms of schizophrenia spectrum disorders or psychosis. Positive symptoms refer to changes in thoughts, feelings and behaviour that are added on to a persons experiences (for instance, hallucinations or delusions). Negative symptoms refer to changes in thoughts, feelings and behaviour which can be described as being reduced (for instance, emotional apathy, lack of drive, poverty of speech, social withdrawal and self-neglect).

Scale, Raskin Depression Scale, and Covi Anxiety Scale) at 78 weeks' follow-up in participants who received cognitive enhancement therapy compared with those who received TAU (SMD=0.20, 95% CI, −0.57 to 0.98; p=0.61), however this difference was not significant (see appendix 11, forest plot 1.2.1).

Three RCTs (n=425) reported the number of participants who relapsed during the study period: Barrowclough et al. (2001), Barrowclough et al. (2010) and Bonsack et al. (2011). In Barrowclough et al. (2001) a relapse was defined as a hospital admission or an exacerbation of symptoms lasting for 2 or more weeks. In Barrowclough et al. (2010) a relapse was defined as an exacerbation of symptoms lasting for 2 or more weeks, with the number of participants requiring hospital admission reported separately. Bonsack et al. (2011) only reported the number of participants who required hospital admission during the study period. At 78 weeks' follow-up, there was evidence from 1 RCT (Barrowclough et al., 2001) suggesting that the integrated treatment programme reduced the risk of relapse (RR=0.58, 95% CI, 0.30 to 1.13; p=0.11; 7/18 [39%] versus 12/18 [67%]), but this was not significant (see appendix 11, forest plot 1.2.5). At 104 weeks' follow-up, there was evidence from 1 RCT (Barrowclough et al. 2010) suggesting no difference between groups in the risk of relapse (RR=1.03, 95% CI, 0.78 to 1.36; p=0.82; 63/161 [39%] versus 61/161 [38%]) (see appendix 11, forest plot 1.2.6). A meta-analysis of 2 RCTs (n=388; Barrowclough et al., 2010; Bonsack et al., 2011) suggested no difference in the risk of hospital admission (RR=1.08, 95% CI, 0.75 to 1.54; p=0.69; event rate ranging from 20% to 34% in the TAU group) at follow-ups ranging from 52 to 104 weeks (see appendix 11, forest plot 1.2.7).

Substance use

Substance use was reported differently across included studies and could not be combined in a meta-analysis.

One RCT (Barrowclough et al., 2010), which included participants with schizophrenia spectrum and substance-use disorders, found no difference between intervention groups for the proportion of days participants were abstinent from their main substance at 104 weeks' follow-up (SMD=0.06, 95% CI, −0.19 to 0.31; p=0.62) (see appendix 11, forest plot 1.2.8).

One RCT (Hjorthøj et al., 2013) which included participants with schizophrenia spectrum and cannabis misuse, found no difference between intervention groups for the proportion of days participants used cannabis during a 1 month period at 43 weeks' follow-up (IRR=0.80, 95% CI 0.21–3.10; p=0.75).

One RCT (Bonsack et al., 2011), which included participants with schizophrenia spectrum disorders and cannabis dependence, found a significant reduction in cannabis use between motivational interviewing and TAU at 24 weeks' follow-up (Mann-Whitney U=308.0; p=0.015)), but this did not hold at 52 weeks' follow-up (Mann-Whitney U=378.5 (not significant, p-value not reported).).

Three RCTs reported substance use outcomes but due to a lack of data it was not possible to calculate effect sizes. At 26 weeks' follow-up, Barrowclough et al. (2001) reported a larger increase in the proportion of days abstinent from the most frequently used substance in the intervention group (change from baseline (median, range): 15.22, −35 to 98) than in TAU (change from baseline (median, range): 8.08,

−25 to 50), however the difference between groups was not significant (Mann-Whitney U=90.50, p-value not reported).. There was also no significant difference between groups in the severity of substance misuse, however change scores and p-values were not reported. Eack et al. (2015) reported no significant difference (p=0.347) between cognitive enhancement therapy and TAU in the number of participants who were abstinent from drugs or alcohol by the end of their participation in the study. Nagel et al. (2009) measured the substance use with the Severity of Dependence Scale at 24 weeks' follow-up, however results were unclear.

Adaptive functioning

A meta-analysis of 3 RCTs (n=425; Barrowclough et al. (2001), Barrowclough et al. (2010) and Bonsack et al. (2011)) showed no difference in general functioning (assessed with the Global Assessment of Functioning scale), between integrated treatment and TAU (SMD=−0.03; 95% CI, −0.24 to 0.18; p=0.81) at follow-ups ranging from 52 to 104 weeks (see appendix 11, forest plot 1.2.11).

Three RCTs (Barrowclough et al. (2001), Bonsack et al. (2011), Eack et al., (2015)) reported participants' social functioning but different outcome measures were used therefore it was not possible to combine results in a meta-analysis. In 1 RCT (Eack et al., 2015) comparing cognitive enhancement therapy with TAU, there was a small increase in social functioning (based on a composite score of the following measures: Social Adjustment Scale-II, Major Role Adjustment Inventory and the Global Assessment Scale) at 78 weeks' follow-up in favour of the intervention group (SMD=0.22; 95% CI, −0.56 to 0.99; p=0.59), however this was not significant (see appendix 11, forest plot 1.2.13). Barrowclough et al. (2001) also showed a small effect in favour of the integrated treatment group at 78 weeks' follow-up for social functioning (assessed with the Social Functioning Scale), but this was not significant (SMD=0.19; 95% CI, −0.54 to 0.92; p=0.61) (see appendix 11, forest plot 1.2.14). Bonsack et al. (2011) reported social and occupational functioning (assess with the Social and Occupational Functioning Assessment Scale) at 52 weeks' follow-up and found a small effect in favour of TAU (SMD=−0.16; 95% CI, −0.66 to 0.33; p=0.52), however this was not significant (see appendix 11, forest plot 1.2.15).

One RCT (n=49) included participants with a severe mental illness and cannabis or alcohol-use disorders from indigenous communities in Australia (Nagel et al., 2009) and reported no significant difference (p=0.068) between treatment groups at 24 weeks' follow-up in levels of health and social functioning (assessed with the HoNOS).

In 1 RCT (n=103) comparing an integrated treatment programme with TAU (Hjorthøj et al., 2013), there was a small increase in quality of life (assessed with the Manchester Short Assessment of Quality of Life scale) in favour of TAU at 43 weeks' follow-up (SMD=−0.21, 95% CI, −0.60 to 0.18; p=0.29), however this was not significant (see appendix 11, forest plot 1.2.12).

Observational evidence

One before-and-after study (n=173) carried out in the UK (Copello et al., 2013) assessed the effect of a consultation-liaison service delivered by staff from a dual diagnosis service (COMPASS). The intervention included assessment, motivational work and follow-up. Staff from COMPASS delivered the intervention alongside the service users' care co-ordinator. The care coordinator was involved to help facilitate integrated treatment and to increase their ability to continue the work upon completion of the intervention. All people who presented to the service within a 3-year period were included in the study, which meant that not all participants had a dual diagnosis. Although the exact proportion of participants with a dual diagnosis is unclear it is likely to be high as the service was developed to cater for this population. At 156 weeks' follow-up, the authors reported a significant improvement in alcohol use, drug use and overall substance use for clinician-rated measures. For self-report measures there was a significant improvement in alcohol use but not for the severity of substance use dependence. Results should be considered with caution due to the lack of a control group and high rate of attrition (47%).

Evidence statement 3.2: Integrated treatment[7] compared with TAU

There is moderate evidence from 6 RCTs (4[+][1,2,5,6] and 2[–][3,4]) comparing integrated treatment in combination with TAU with TAU alone for mental health, substance use and adaptive functioning outcomes. One before-and-after study (1[–][7]) assessed the effectiveness of integrated treatment in combination with TAU on substance use outcomes. One RCT[2] reported 81-100% fidelity to the intervention and another RCT[6] reported only 'minor variations' to the intervention.

Mental health

There is evidence from a meta-analysis and 4 RCTs on the effectiveness of integrated treatment on mental health symptoms. There was inconsistent evidence from a meta-analysis (n=466) of 2[+][1,2] UK RCTs and 1[+][5] Danish RCT which overall indicated no significant difference in psychotic symptoms between the integrated treatment and TAU (SMD=0.03; 95% CI, −0.27 to 0.33; p=0.83; I^2=44%) at follow-ups ranging from 43 to 104 weeks. There was also evidence from 2 RCTs: 1[−][3] RCT (n=62) conducted in Switzerland indicated a small reduction in severity of positive symptoms (SMD=−0.22; 95% CI, −0.72 to 0.27; p=0.38) and negative symptoms (SMD=−0.30, 95% CI, −0.80 to 0.21; p=0.25) in the integrated treatment group compared with TAU at 52 weeks' follow-up however the difference was not significant, and 1[−][4] US RCT (n=31) showed lower levels of mental health symptoms in the cognitive enhancement therapy group compared with TAU at 78 weeks' follow-up (SMD=0.20, 95% CI, −0.57 to 0.98; p=0.61), however this difference was not significant.

There is consistent evidence from 3 RCTs on relapse due to mental health problems. At 78 weeks' follow-up 1[+][1] UK RCT (n=36) suggested that an integrated treatment may reduce the risk of relapse (defined as a hospital admission or an exacerbation of symptoms lasting 2 or more weeks) (RR=0.58,

[7] Integrated treatment here refers to any intervention which was delivered in the context of a multidisciplinary team in combination with usual care

95% CI, 0.30 to 1.13; p=0.11; 7/18 [39%] versus 12/18 [67%]), but this was not significant. One UK RCT 1[+][2] (n=327) suggested no difference between groups in the risk of relapse (defined as an exacerbation of symptoms lasting 2 or more weeks) (RR=1.03, 95% CI, 0.78 to 1.36; p=0.82; 63/161 [39%] versus 61/161 [38%])) at 104 weeks' follow-up. Consistent evidence from a meta-analysis of 2 RCTs (1[+][2] and 1[–][3]; n=388) suggested no difference in the risk of hospital admission between groups at follow-ups ranging from 52 to 104 weeks (RR=1.08, 95% CI, 0.75 to 1.54; p=0.69; event rate ranging from 20% to 34% in the TAU group).

Substance use

There is consistent evidence from 3 RCTs on substance use outcomes. One UK RCT (1[+][2]) suggested no significant difference between intervention groups for abstinence from the participants' main substance at 104 weeks' follow-up (SMD=0.06, 95% CI, −0.19 to 0.31; p=0.62). One RCT conducted in Switzerland (1[–][3]) suggested a reduction in cannabis use with motivational interviewing compared with TAU at 24 weeks' follow-up (Mann-Whitney U=308.0; p=0.015), but at 52 weeks' follow-up there was no evidence of a significant difference (Mann-Whitney U=378.5 (not significant, p-value not reported). One US RCT (1[−][4]) reported no significant difference between cognitive enhancement therapy and TAU in the number of participants who were abstinent from drugs or alcohol by study completion (p=0.347).One UK RCT (1[+][1]) reported a larger increase in the proportion of days abstinent from the most frequently used substance in the intervention group (change from baseline (median, range): 15.22, −35 to 98) than in TAU (change from baseline (median, range): 8.08, −25 to 50) but this was not significant (Mann-Whitney U=90.50, p-value not reported). There was also no significant difference between groups in the severity of substance misuse (p-values not reported). One RCT conducted in Denmark (1[+][5]) suggested no significant difference between intervention groups in the proportion of days using cannabis during a 1 month period at 43 weeks' follow-up (IRR=0.80, 95% CI 0.21–3.10; p=0.75).

Adaptive functioning

There is evidence from a meta-analysis and 4 RCTs on the effectiveness of integrated treatment on adaptive functioning outcomes. Consistent evidence from a meta-analysis (n=425) of 2[+][1,2] UK RCTs and 1[–][3] RCT conducted in Switzerland suggested no difference in general functioning between integrated treatment and TAU (SMD=−0.03; 95% CI, −0.24 to 0.18; p=0.81) at follow-ups ranging from 52 to 104 weeks. There was also evidence from 4 RCTS. One UK RCT (1[+][1]) and 1[−][4] US RCT suggested a small increase in social functioning with the integrated treatment compared with TAU, however these were not significant (SMD=0.19; 95% CI, −0.54 to 0.92; p=0.61[1]; SMD=0.22; 95% CI, −0.56 to 0.99; p=0.59[4]). One RCT conducted in Australia (1[+][6]; n=49) reported no significant difference between treatment groups in levels of health and social functioning (p=0.068).One RCT conducted in Switzerland 1[−][3] indicated a small increase in social and occupational functioning at 52 weeks' follow-up but this was not significant (SMD=−0.16; 95% CI, −0.66 to 0.33; p=0.52). In 1[+][5] RCT conducted in Denmark there was a small increase in quality of life at 43 weeks' follow-up in favour of TAU compared with integrated treatment, however this was not significant (SMD=−0.21,95% CI, −0.60 to 0.18; p=0.29).

Observational evidence
One UK before-and-after study (1[−][7]; n=173) reported a significant improvement in alcohol use ($p<0.001$), drug use ($p<0.05$) and overall substance use ($p<0.001$) for clinician-rated measures following a consultation-liaison service. For self-report measures there was a significant improvement in alcohol use ($p<0.05$) but not for the severity of substance use dependence.

Applicability to the UK:
This evidence is only partially applicable to the UK. This is because 4 out of the 7 studies were conducted in the Australia, Denmark, Switzerland and the US where TAU is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Also, for the study conducted in Australia this included people from indigenous communities so there is limited applicability to UK populations. Most of the interventions that comprise the integrated treatment components assessed in this question are available in the UK but cognitive enhancement therapy[4] (or its equivalent) is not widely available in the UK, with its use restricted to a small number of specialist centres concerned with its development and evaluation.

[1]Barrowclough et al. (2001) [+]
[2]Barrowclough et al. (2010) [+]
[3]Bonsack et al. (2011) [–]
[4]Eack et al. (2015) [–]
[5]Hjorthøj et al. (2013) [+]
[6]Nagel et al. (2009) [+]
[7]Copello et al. (2013) [–]

4.4.2 Integrated treatment compared with an active comparator

Table 5: Summary of characteristics of studies contributing to the comparison: integrated treatment compared with an active control

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Wenze et al. (2015) RCT Quality: [+]	US, Providence, NR	Bipolar disorder and substance abuse disorder (n=30)	Integrated treatment adherence programme	Enhanced assessment and monitoring	NR

Narrative summary

One RCT (Wenze et al. (2015) [+]) compared integrated treatment (n=14) with an active control, enhanced assessment and monitoring (n=16). The authors reported a high level of treatment integrity. Integrated treatment included assistance with transition from acute care to maintenance treatment, treatment engagement, support with post-discharge sobriety and helping patients monitor symptoms and get support from family and providers. The comparator was enhanced treatment as usual intervention which involved enhanced assessment and monitoring. It was not possible to calculate effect sizes with the data provided, so results are reported narratively as described by the authors. The authors reported average to high fidelity to the intervention across specific components of the protocol, in-person sessions, patient telephone sessions, and significant other sessions. Key characteristics of the included study are summarised in Table 5.

Mental health

In a small US-based RCT (n=30), Wenze et al. (2015) compared integrated treatment with enhanced assessment and monitoring in participants with bipolar disorder and substance-use disorder. At 24 weeks' follow-up, the authors reported significantly greater improvements in depressive (b^8=−0.92, SE=0.39, p<0.05) and manic symptoms (b=−1.19, SE=0.45, p<0.05) in the integrated treatment group compared with active control. The integrated treatment group also had fewer emergency room visits, however the difference was not significant (b=0.16, SE=0.08, p<0.10). The authors reported no significant difference between groups in the number of hospital admissions (b=0.02, SE=0.13, p-value not reported).

Substance use

Wenze et al. (2015) reported no significant differences between integrated treatment and enhanced assessment and monitoring in the number of standard drinks (b=7.19, SE=8.11, p-value not reported), number of days drinking (b=0.64,

[8] 'b' here refers to multi-level regression coefficients which reflect change in the relationship between scores and time for the average participant in the Integrated Treatment Adherence Program (vs. Enhanced Assessment and Monitoring)

SE=0.94, p-value not reported), number of heavy drinking days (b=0.81, SE=1.04, p-value not reported) or number of days using drugs (b=−1.67, SE=0.83, p<0.10), in the 3 months preceding 24 weeks' follow-up.

Adaptive functioning

At 24 weeks' follow-up, Wenze et al. (2015) reported significant improvements in psychosocial and physical disability (b=−1.84, SE=0.86, p<0.05) and daily activities (b=4.82, SE=2.09, p<0.05) in the integrated treatment group compared with enhanced assessment and monitoring.

Service utilisation

Wenze et al. (2015) reported no significant difference between groups in the number of intervention sessions attended (b=−1.34, SE=1.20, p-value not reported).

Evidence statement 3.3: Integrated treatment compared with an active comparator

There is weak evidence from 1[+][1] RCT, comparing integrated treatment with an active comparator (enhanced assessment and monitoring), on mental health and substance use outcomes, adaptive functioning and service utilisation. Fidelity to intervention was reported to be average to high.

In 1[+][1] US RCT (n=30) of participants with bipolar disorder and a substance-use disorder, the authors reported significant improvements in the integrated treatment group (n=14) compared with the active control (n=16) in manic symptoms (b[9]=−1.19, SE=0.45, p<0.05) and depressive symptoms (b=−0.92, SE=0.39, p<0.05), as well as psychosocial and physical disability (b=−1.84, SE=0.86, p<0.05) and daily activities (b=4.82, SE=2.09, p<0.05) at 24 weeks' follow-up. The authors reported no significant differences between groups in the number of standard drinks (b=7.19, SE=8.11, p-value not reported), number of days drinking (b=0.64, SE=0.94, p-value not reported), number of heavy drinking days (b=0.81, SE=1.04, p-value not reported), number of days using drugs (b=−1.67, SE=0.83, p<0.10), number of hospital admissions (b=0.02, SE=0.13, p-value not reported), emergency department visits (b=0.16, SE=0.08, p<0.10) or in the number of intervention sessions attended (b=−1.34, SE=1.20, p-value not reported).

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. There has been a decline in the number of integrated services in the UK.

[1]Wenze et al. (2015) [+]

[9] b here refers to multi-level regression coefficients which reflect change in the relationship between scores and time for the average participant in the Integrated Treatment Adherence Program (vs. Enhanced Assessment and Monitoring)

4.5 OTHER INTERVENTIONS

4.5.1 Brokerage case management compared with an active comparator

Table 6: Summary of characteristics of studies contributing to the comparison: brokerage case management compared with an active control

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Havassy et al. (2000) RCT Quality: [–]	US, San Francisco, Urban	Severe mental illness* and substance dependence (n=142)	Intensive clinical (brokerage) case management	Expanded brokerage case management	Community or hospital based
**5% of participants had an adjustment disorder, 2% had an anxiety disorder*					

Narrative summary

One RCT (Havassy et al. (2000) [–]) compared brokerage case management (n=134) with an active comparator (expanded brokerage case management) (n=134) in people with severe mental illness. Although the authors referred to the intervention group as 'intensive clinical case management', it is referred here as 'brokerage case management' as we wanted to highlight the added element of brokerage which differentiated this intervention to those in the ACT group (see section 4.3). The intensive clinical case management programme consisted in psychotherapy and a wide array of integrated services, including brokerage and placement, for an unlimited time which were community based. The active comparator (expanded brokerage case management) programme provided hospital-based case managers who provided intensive support during post-discharge from hospital and worked assertively toward linking service users with comprehensive community services. Participants were recruited while receiving inpatient treatment, however the study started at discharge from hospital after baseline assessments. Substance dependence was not a requirement for inclusion in the trial and only 47% of the sample had the additional dual diagnosis. The authors stratified randomisation by substance dependence so it was possible to include the findings in this review, however it was not possible to calculate effect sizes because the data were not reported separately for the dual diagnosis sub-group. Key characteristics of the included study are summarised in Table 6.

Mental health

One RCT (n=142) based in the US included participants with severe mental illness and substance dependence. At 24 weeks' follow-up the authors reported no significant difference between groups in symptoms of depression or in the number of days the participant was an inpatient in a psychiatric hospital (p-values not provided).

Substance use

Havassy et al. (2000) reported no significant difference in the number of days using alcohol or other substances during a 30-day period between the brokerage case management group and the active comparator at 24 weeks' follow-up (p-values not provided).

Adaptive functioning

Havassy et al. (2000) reported no significant difference between brokerage case management and the active comparator for quality of life at 24 weeks' follow-up (p-values not provided).

Service utilisation

Havassy et al. (2000) reported no significant differences between brokerage case management and the active comparator in the number of outpatient services used, in addition to those provided by both interventions (p-values not provided) or in the number of emergency psychiatric visits during the study period (p-value not provided).

Evidence statement 3.4: Brokerage case management compared with an active comparator

There is weak evidence from 1[–][1] RCT, comparing brokerage case management with an active comparator (expanded brokerage case management), on mental health and substance use outcomes, adaptive functioning and service utilisation.

One 1[–][1] US RCT (n=268) included participants with severe mental illness and substance dependence who were discharged from inpatient care at the start of the trial. At 24 weeks' follow-up the authors reported no significant differences between brokerage case management and an active comparator for: depressive symptoms, use of inpatient care, substance use, quality of life, number of outpatient services used or emergency psychiatric visits (p-values not reported).

Applicability to the UK:

This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Brokerage case management is compatible with the personalised budget approach to care in the UK.

[1]Havassy et al. (2015) [–]

4.5.2 Contingency management combined with compensated work therapy compared with compensated work therapy alone

Table 7: Summary of characteristics of studies contributing to the comparison: contingency management combined with compensated work therapy compared with compensated work therapy alone

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Drebing et al. (2005) RCT Quality: [–]	US, Bedford (Massachusetts), NR	Veterans with a severe mental illness* and substance dependence (n=19)	Contingency management and compensated work therapy	Compensated work therapy	NR
Drebing et al. (2007) RCT Quality: [–]	US, Bedford (Massachusetts), NR	Veterans with a severe mental illness** and substance dependence (n=101)	Contingency management and compensated work therapy	Compensated work therapy	NR
** 74% affective disorder (bipolar disorder or major depression), 58% anxiety disorder, 11% psychosis* *** Participant group also had post-traumatic stress disorder (53%) and anxiety disorders (50%)*					

Narrative summary

Two RCTs (Drebing et al. (2005) [–], Drebing et al. (2007) [–]) compared contingency management combined with compensated work therapy with compensated work therapy alone in veterans with a dual diagnosis. Drebing et al (2005) was the pilot study of a bigger trial of the same intervention by Drebing et al. (2007). In both studies the compensated work therapy programme includes a supported employment component that helps participants maintain employment in their own competitive jobs through structured support and management. Participants are placed in structured work settings and compensated for their work. Staff also help participants negotiate and resolve difficulties on the job and prepare for obtaining their own competitive job. Participants are encouraged to perform job-search tasks, abstain from drugs and/or alcohol, and obtain and then maintain competitive employment. The intervention group additionally received contingency management which consisted of incentives for taking steps toward obtaining and maintaining competitive employment and for abstinence from substance use. Dual diagnosis was defined as drug or alcohol dependence and a diagnosis of one of the following mental health problems: schizophrenia, bipolar disorder, major depression, post-traumatic stress disorder or other anxiety disorder. Although only people with a severe mental illness were included in this review, Drebing et al. (2007) was included because 79% of participants had major depression and 21% had bipolar disorder. This suggested that the diagnoses of post-traumatic stress disorder (53%) and anxiety disorder (50%) were additional coexisting disorders. In Drebing et al (2005) 74% had an affective disorder (bipolar disorder or major depression), 11% had psychosis, and 58% had an anxiety disorder, suggesting that only a small proportion (15%) did not have a dual diagnosis. To improve readability

in the following sections the combined treatment group will be referred to as contingency management. Key characteristics of included studies are summarised in Table 7.

Substance use

At 16 weeks' follow-up, 1 US-based RCT (n=101) found a reduced risk of substance use relapse with contingency management compared with compensated work therapy alone (RR=0.69; 95% CI, 0.50 to 0.96; p=0.03; 25/50 [50%] versus 36/50 [72%]) (see appendix 11, forest plot 1.3.1). At 39 weeks' follow-up, there was still a reduced risk of relapse with contingency management, however this was not significant (RR=0.89; 95% CI, 0.70 to 1.14; p=0.38; 34/50 [68%] versus 38/50 [76%]) (see appendix 11, forest plot 1.3.2).

Adaptive functioning

At 16 weeks' follow-up, 1 RCT (Drebing et al., 2005) found that participants in the contingency management group had significantly higher wage earnings compared with those who received compensated work therapy along (Mann-Whitney U=20; p<0.05; $4,701 vs. $2,796). The contingency management group had a significantly shorter time to first job interview compared with the compensated group therapy group (Hazard ratio=6.23, 95% CI, 1.31 to 29.64, p<0.05), and had more weeks of competitive employment during the study period, however this was not significant (Mann-Whitney U=31; p<0.28; 4.2 weeks vs. 0.8 weeks).

At 39 weeks' follow-up, 1 RCT (Drebing et al., 2007) found increased employment with contingency management compared with compensated work therapy alone (RR=1.79; 95% CI, 1.06 to 3.02; p=0.03; 25/50 [50%] versus 14/50 [28%]) (see appendix 11, forest plot 1.3.3).

Evidence statement 3.5: Contingency management combined with compensated work therapy compared with compensated work therapy alone

There is weak evidence from 2[–][1,2] RCTs comparing contingency management in combination with compensated work therapy with compensated work therapy alone on substance use and adaptive functioning outcomes.

Substance use

One US RCT (1[–][2]; n=101), which included veterans with a severe mental illness and substance-use disorder, suggested a reduced risk of substance use relapse with contingency management at 16 weeks' follow up (RR=0.69; 95% CI, 0.50 to 0.96; p=0.03; 25/50 [50%] versus 36/50 [72%]) and at 39 weeks' follow-up (RR=0.89; 95% CI, 0.70 to 1.14; p=0.38; 34/50 [68%] versus 38/50 [76%]), although for the later time-point this was not significant.

Adaptive functioning

There is evidence from 2 US RCTs on the effectiveness of contingency management on improved adaptive functioning.

One US pilot RCT (1[–][1]; n=19) which included veterans with a severe mental illness and substance-use disorder, suggested higher wage earnings with contingency management at 16 weeks' follow-up compared with compensated work therapy (Mann-Whitney U=20; p<0.05; $4,701 vs. $2,796). The contingency management group also showed a significantly shorter time to first job interview (Hazard ratio=6.23, 95% CI, 1.31 to 29.64, p<0.05), and had more weeks of competitive employment during the study period, however this was not significant (Mann-Whitney U=31; p<0.28; 4.2 weeks vs. 0.8 weeks).

In 1[-][2] RCT, at 39 weeks' follow-up, there was increased employment with contingency management compared with compensated work therapy alone (RR=1.79; 95% CI, 1.06 to 3.02; p=0.03; 25/50 [50%] versus 14/50 [28%]).

Applicability to the UK:

This evidence is only partially applicable to the UK because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. There is an increasing use of contingency management in UK health services however the service style changes and training required to support its implementation are limited. There are also ethical and social concerns about incentivising people to take up health care interventions.

[1]Drebing et al. (2005) [–]
[2]Drebing et al. (2007) [–]

4.5.3 Time-limited care co-ordination compared with a matched attention control

Table 8: Summary of characteristics of studies contributing to the comparison: time-limited care co-ordination compared with a matched attention control

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Smelson et al. (2012) RCT Quality: [–]	US, New Jersey, NR	Veterans with schizophrenia spectrum disorders or bipolar I disorder and substance dependence/abuse (n=102)	Time-limited care co-ordination	Matched attention control	NR

Narrative summary

One RCT (n=102) compared time-limited care co-ordination (n=55) with a matched attention control (n=47) in veterans with schizophrenia spectrum disorders or bipolar I disorder and a substance-use disorder (Smelson et al. (2012) [–]). Time-limited care co-ordination (TLC) integrates mental health and substance use disorder treatment and assertive community treatment. The TLC program also includes peer specialists who served as role models, providing participants with emotional support during the transition from inpatient to outpatient care. The matched attention control consisted in health education delivered in group sessions. Both groups also received treatment as usual which consisted in psychoeducation and psychotherapy, skills training, medication management and relapse prevention treatment. Participants were recruited while receiving inpatient treatment, however the study started at discharge from hospital after baseline assessments. For mental health outcomes the authors did not provide sufficient data to calculate effects sizes, so these are summarised here as reported by the authors. Key characteristics of the included study are summarised in Table 8.

Mental health

At 24 weeks' follow-up, Smelson et al. (2012) reported modest declines in both groups in the number of days (during the previous 30 days) in which participants experienced depression, anxiety and hallucinations, but no significant difference between groups (p-values not reported).

Substance use

One RCT (n=102) reported a reduced risk of alcohol use (assessed with the Addiction Severity Scale) at 24 weeks' follow-up with time-limited care co-ordination compared with a matched attention control (RR=0.60, 95% CI, 0.34 to 1.07 p=0.08; 13/40 [33%] versus 14/26 [54%]), although there was no significant difference between groups (see appendix 11, forest plot 1.4.1). Other drug use was also measured but the difference between groups at follow-up was not reported.

Service utilisation

One RCT (n=102) reported an increased attendance of outpatient appointments with time-limited care co-ordination compared with a matched control (RR=2.08, 95% CI, 1.14 to 3.80; p=0.02; 29/39 [69%] versus 8/24 [33%]) at 24 weeks' follow-up (see appendix 11, forest plot 1.4.2).

Evidence statement 3.6: Time-limited care co-ordination compared with a matched attention control

There is weak evidence from 1[–][1] RCT comparing time-limited care co-ordination with a matched attention control on mental health and substance use outcomes.

One US study 1[–][1], which included 102 veterans with schizophrenia spectrum disorders or bipolar I disorder and a substance-use disorder, reported no significant difference between groups in the number of days experiencing depression, anxiety and hallucinations in the previous 30 days at 24 weeks' follow-up (p-values not reported). For substance use outcomes, there was a reduced risk of alcohol use with time-limited care co-ordination at 24 weeks' follow-up (RR=0.60, 95% CI, 0.34 to 1.07; p=0.08), however this was not significant. Other drug use was also measured but the difference between groups at follow-up was not reported. Significantly more participants in the time-limited care co-ordination group attended an outpatient appointment compared with those in the matched attention control group (RR=2.08, 95% CI, 1.14 to 3.80; p=0.02; 29/39 [69%] versus 8/24 [33%]).

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. A time-limited care co-ordination approach is compatible with current standard models of care in the UK.

[1]Smelson et al. (2012) [–]

4.5.4 Shelter-based psychiatric clinic compared with treatment as usual

Table 9: Summary of characteristics of studies contributing to the comparison: shelter-based psychiatric clinic compared with TAU

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Bradford et al. (2005) RCT Quality: [–]	US, NR	Mental illness and substance misuse disorder* (72%) (n=102)	Shelter-based psychiatric clinic	Routine shelter care	Shelter
**Mood disorder (60%), psychotic disorder (6%), anxiety disorder (6%), other (18%). Only 72% of participants had a substance-use disorder.*					

Narrative summary

One US-based RCT (n=102) compared a shelter-based psychiatric clinic with usual shelter care in homeless people with a mental health problem (Bradford et al. (2005) [–]).The shelter-based psychiatric intervention programme (n=51) included continuity of care, case management services, collaboration between psychiatrist and social worker with assertive follow-up. In the usual care group (n=51) there was little continuity of care, participants scheduled their own appointments, and there was no systematic follow-up of missed appointments. It was unclear how many participants had a severe mental illness as the authors reported that 60% had a mood disorder, 6% had a psychotic disorder, 6% had an anxiety disorder and 18% had other mental health problems. Although substance use was not a requirement for study entry, the trial was included in this review as a large proportion of the sample had a diagnosis of a substance-use disorder (72%). Key characteristics of the included study are summarised in Table 9.

Adaptive functioning

Bradford et al. (2005) showed a higher rate of participants who had stable housing at shelter exit in the psychiatric clinic group compared with the usual shelter care group (RR=1.17, 95% CI, 0.73 to 1.89; p=0.51; 22/49 [45%] versus 18/47 [38%]), however the difference was not significant (see appendix 11, forest plot 1.5.2). The psychiatric clinic group also showed a higher rate of employment at shelter exit compared with usual shelter care (RR=1.67, 95% CI, 0.85 to 3.27; p=0.14; 17/50 [34%] versus 10/49 [20%]), but the difference was not significant (see appendix 11, forest plot 1.5.1). For both findings it was unclear at what time point outcomes were measured.

Service utilisation

During the study period, a higher proportion of participants in the psychiatric clinic group compared with the usual shelter care group attended 1 or more community mental health centre appointments (RR=1.74; 95% CI, 1.15 to 2.62; p=0.008; 33/51 [65%] versus 19/51 [37%]) (see appendix 11, forest plot 1.5.3), 2 or more community mental health centre appointments (RR=1.89; 95% CI, 0.93 to 3.84; p=0.08; 17/51 [33%] versus 9/51 [18%]) (see appendix 11, forest plot 1.5.4) and 3

or more community mental health centre appointments (RR=1.43; 95% CI, 0.59 to 3.46; p=0.43; 10/51 [20%] versus 7/51 [14%]) (see appendix 11, forest plot 1.5.5), although for the latter two this was not significant. Considering only the sub-sample of participants who had a substance-use disorder (n=69), there was a higher proportion of participants in the psychiatric clinic group compared with the usual shelter care group who attended a substance use programme (RR=4.11; 95% CI, 1.56 to 10.82; p=0.004; 19/37 [51%] versus 4/32 [12.5%]) (see appendix 11, forest plot 1.5.6). Attending a substance use programme was defined as 'attending an inpatient/residential substance abuse facility or an intake and screening appointment and ≥1 substance abuse class at the community mental health centre' during the study period.

Evidence statement 3.7: Shelter-based psychiatric clinic compared with TAU

There is weak evidence from 1[–][1] RCT comparing a shelter-based psychiatric clinic with usual shelter care on adaptive functioning outcomes and service utilisation.

One US study 1[–][1] which included 102 homeless people with a mental health problem (of whom 72% had a substance-use disorder) suggested a higher rate of participants who had stable housing (RR=1.17, 95% CI, 0.73 to 1.89; p=0.51) and a higher rate of employment (RR=1.67, 95% CI, 0.85 to 3.27; p=0.14) in the shelter-based psychiatric clinic group at shelter exit, however both findings were not significant. There was a significantly higher proportion of participants who attended 1 or more community mental health centre appointments (RR=1.74; 95% CI, 1.15 to 2.62; p=0.008; 33/51 [65%] versus 19/51 [37%]), however this was not significant when those who attended 2 or more (RR=1.89; 95% CI, 0.93 to 3.84; p=0.08; 17/51 [33%] versus 9/51 [18%]) and 3 or more appointments were considered (RR=1.43; 95% CI, 0.59 to 3.46; p=0.43; 10/51 [20%] versus 7/51 [14%]). Considering only the sub-sample of participants with a substance-use disorder (n=69), a higher proportion of participants in the psychiatric clinic group compared with the usual shelter care group attended a substance use programme (RR=4.11; 95% CI, 1.56 to 10.82; p=0.004; 19/37 [51%] versus 4/32 [12.5%]) during the study period.

Applicability to the UK:
This evidence is only partially applicable to the UK, because the study was conducted in the US where usual care is likely to differ from that provided in the UK, specifically to offer less well co-ordinated services for severe mental illness. Such models of care have already been developed in the UK with a focus on homelessness, many of whom would meet criteria for dual diagnosis although these are not currently widely developed.

[1]Bradford et al. (2005) [–]

4.5.5 Staff training compared with no training

Table 10: Summary of characteristics of studies contributing to the comparison: staff training compared with no training

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Johnson et al. (2007) Cluster RCT Quality: [–]	UK, London, Urban	Severe mental illness and substance-use disorder (n=232)	Training community staff	No training	South London and Maudsley NHS Trust (now Foundation Trust)
Graham et al. (2006) Non-randomised controlled trial Quality: [–]	UK, Birmingham, Urban	Severe mental illness and substance-use disorder (n=58)	Training	Delayed training control group	Northern Birmingham Mental Health NHS Trust

Narrative summary

One UK-based RCT (n=232) (Johnson et al., (2007) [–]) and 1 UK-based non-randomised controlled trial (n=58) (Graham et al. (2006) [–]) compared a training intervention for staff with a control group. In Johnson et al. (2007), the training community staff group (n=128) received a 5-day training course in assessment and management of dual diagnosis, and subsequent monthly supervision whereas the 'no training' group (n=105) received CMHT management as usual with no specific dual diagnosis intervention. Although 84% of participants received the control intervention as intended, only 35% received training as intended. In Graham et al (2006), the training group received the intervention immediately (n=37) whereas the delayed training group (n=21) received the intervention after 18 months. Training was delivered to all members of the assertive outreach team at the same time over a 6-day period. This included a 'product champion' from the COMPASS programme who provided on-going training, co-working alongside the team and keyworkers and facilitated case discussion/supervision sessions. Although staff members were the target of the intervention, outcomes were measured for the service users with a dual diagnosis under the care of the staff who took part in the study. Key characteristics of the included studies are summarised in Table 10.

Mental health

One RCT (Johnson et al., 2007) delivered a training intervention to case managers from community mental health teams in London. At 78 weeks' follow-up, the intervention group showed a small to moderate reduction in the severity of psychiatric symptoms (assessed with the BPRS-24) (SMD=−0.44, 95% CI, −0.71 to −0.16; p=0.002), compared with a mean score of 41.6 (SD=11.6) in the no training group (see appendix 11, forest plot 1.6.1). There was a reduced risk of hospital

admission in the training group compared with no training at 78 weeks' follow-up (RR=0.89, 95% CI, 0.67 to 1.20; p=0.46; 49/113 [43%] versus 47/97 [48%]), however this was not significant (see appendix 11, forest plot 1.6.3). There was no difference between the groups in hospital bed use during the 78-week study period (SMD=0.02, 95% CI, −0.25 to 0.29; p=0.87) (see appendix 11, forest plot 1.6.2).

One non-randomised controlled trial (Graham et al., 2006) delivered a brief training intervention to assertive outreach teams either immediately or with a delay of 78 weeks. At 78 weeks' follow-up, when the delayed training group had not yet received training, the authors reported no significant difference between the service user groups in psychiatric symptoms (assessed with the BPRS-24) (p-value not reported).

Substance use

One RCT (Johnson et al., 2007) reported outcomes for alcohol use, cannabis use and other drug use both continuously and dichotomously. At 78 weeks' follow-up the intervention group showed lower levels of alcohol use (SMD=−0.13; 95% CI, −0.45 to 0.19; p=0.43) and a small reduction in drug use (SMD=−0.26; 95% CI, −0.58 to 0.06; p=0.11), although the difference was not significant (see appendix 11, forest plots 1.6.4 and 1.6.8). There was no difference between the intervention and control group for cannabis use (SMD=0.03; 95% CI, −0.29 to 0.35; p=0.86) (see appendix 11, forest plot 1.6.6). There was a reduced risk of using cannabis (RR=0.89, 95% CI, 0.57 to 1.39; p=0.61; 24/76 [32%] versus 27/76 [36%]) and other drugs (RR=0.92, 95% CI, 0.45 to 1.89; p=0.83; 12/76 [16%] versus 13/76 [17%]) in the intervention group in the month before the follow-up assessment, but the difference between groups was not significant (see appendix 11, forest plots 1.6.7 and 1.6.9). There was no difference between groups in the risk of using alcohol in the month preceding follow-up assessment (RR=1.04, 95% CI, 0.85 to 1.26; p=0.72; 56/76 [74%] versus 54/76 [71%]) (see appendix 11, forest plot 1.6.5).

One non-randomised controlled trial (Graham et al., 2006) reported no significant difference between groups in service user engagement with substance use treatment (assessed with the SATS) or in substance-related beliefs. The authors did report significantly less alcohol consumed by participants within the immediately trained group compared with those within the delayed training group (p-value not reported). Due to the small number of participants who used cannabis the authors were unable to investigate the effect of training on cannabis use.

Acceptability of services

One RCT (Johnson et al., 2007) indicated no difference in service user satisfaction (assessed with the CSQ) between the intervention and control group at 78 weeks' follow-up (SMD=0.02, 95% CI, −0.26 to 0.29; p=0.91), although there was moderate improvement in satisfaction with treatment (assessed with the TPQ) for the intervention group compared with the control group at 78 weeks' follow-up (SMD=0.51, 95% CI, 0.23 to 0.79; 0.0003) (see appendix 11, forest plots 1.6.12 and 1.6.13). When adjusting for baseline scores, the authors reported no significant difference between groups for satisfaction with treatment (adjusted difference=0.68, 95% CI, −2.1 to 3.5).

Adaptive functioning

One RCT (Johnson et al., 2007) indicated no difference in social functioning (assessed with the LSP) at 78 weeks' follow-up between the intervention and control group (SMD=0.03, 95% CI, −0.24 to 0.30; p=0.82) (see appendix 11, forest plot 1.6.10). Although there was a small significant effect in favour of the intervention group for quality of life (assessed with the MANSA) (SMD=0.27; 95% CI, −0.00 to 0.55; p=0.05) (see appendix 11, forest plot 1.6.11), when adjusting for baseline scores the authors reported no significant difference at 78 weeks' follow-up (adjusted difference=0.62; 95% CI, −3.8 to 2.9).

Evidence statement 3.8: Staff training compared with no training

There is weak evidence from 1[–][1] non-randomised controlled trial and 1[–][2] RCT comparing staff training with no training on mental health and substance use outcomes, the acceptability of services, adaptive functioning outcomes and service utilisation. One RCT[2] reported that fidelity to the training intervention was low, with 35% of the intervention group receiving the intervention as intended.

Mental health

There is inconsistent evidence from 1 RCT and 1 non-randomised controlled study on the effectiveness of training on mental health outcomes. One UK RCT (1[–][2]; n=232) suggested a small to moderate reduction in the severity of mental health symptoms at 78 weeks' follow-up in the intervention group (SMD=−0.44, 95% CI, −0.71 to −0.16; p=0.002) but no significant difference between groups in the risk of hospital admission (RR=0.89, 95% CI, 0.67 to 1.20; p=0.46; 49/113 [43%] versus 47/97 [48%]), or the use of hospital beds (SMD=0.02, 95% CI, −0.25 to 0.29; p=0.87). One UK non-randomised controlled study (1[–][1]; n=58) indicated no significant difference between groups in mental health symptoms at 78 weeks' follow-up (p-value not reported).

Substance use

There is inconsistent evidence from 1 RCT and 1 non-randomised controlled trial on the effectiveness of training on substance use outcomes. One UK RCT 1[–][2] suggested no significant difference between groups in alcohol use (SMD=−0.13; 95% CI, −0.45 to 0.19; p=0.43; RR=1.04, 95% CI, 0.85 to 1.26; p=0.72; 56/76 [74%] versus 54/76 [71%]), cannabis use (SMD=0.03; 95% CI, −0.29 to 0.35; p=0.86; RR=0.89, 95% CI, 0.57 to 1.39; p=0.61; 24/76 [32%] versus 27/76 [36%]) or other drug use (SMD=−0.26; 95% CI, −0.58 to 0.06; p=0.11; RR=0.92, 95% CI, 0.45 to 1.89; p=0.83; 12/76 [16%] versus 13/76 [17%]) at 78 weeks' follow-up. One UK non-randomised controlled study 1[–][1] indicated no significant difference between groups in service user engagement with substance use treatment or in substance-related beliefs (p-values not reported). The authors did report significantly less alcohol consumed by participants in the intervention group compared with control at 78 weeks' follow-up (p-value not reported).

Acceptability of services

One UK RCT 1[–][2] suggested no difference in service user satisfaction in the intervention group at 78 weeks' follow-up (SMD=0.02, 95% CI, −0.26 to 0.29; p=0.91), and greater satisfaction with treatment for the intervention group, which was not significant when controlling for baseline scores (adjusted difference=0.68, 95% CI, −2.1 to 3.5).

Adaptive functioning

One UK RCT 1[–][2] suggested no difference in social functioning at 78 weeks' follow-up between the intervention and control group (SMD=0.03, 95% CI, −0.24 to 0.30; p=0.82), and greater quality of life in the intervention group, which was not significant when adjusting for baseline scores (adjusted difference=0.62; 95% CI, −3.8 to 2.9).

Applicability to the UK:

The evidence is directly applicable to the UK as both included studies were

conducted in the UK. This model has been implemented in a number of UK services but resources for this have been reduced significantly in recent years.

[1]Graham et al. (2006) [–]
[2]Johnson et al. (2007) [–]

4.5.6 Supportive housing compared with treatment as usual

Table 11: Summary of characteristics of studies contributing to the comparison: supportive housing compared with TAU

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Aubry et al. (2015) RCT Quality: [+]	Canada, Vancouver, Winnipeg, Toronto, Montreal and Moncton, Mixed	Homeless people with bipolar disorder or psychotic disorder and substance related problem* (n=950)	Supportive housing	TAU	NR
**Only 73% of participants had a substance-related problem.*					

Narrative summary

One large RCT (n=950) based in Canada compared a supportive housing intervention with TAU for homeless people with bipolar disorder or a psychotic disorder (Aubry et al. (2015) [+]). The supportive housing intervention (n=469) provided service users with assistance in finding and moving into housing, rent supplements and support services using ACT, a multidisciplinary team approach with a 10:1 client to staff ratio. Access to housing and community support is immediate without requiring participation in treatment or sobriety as a precondition. The TAU group (n=481) had access existing programmes such as outreach, drop-in centres, shelters and general medical health, addiction, and social services. They could also receive any housing and support services other than the supportive housing intervention. Only 73% of the sample had a substance-related problem, however because of the size of the trial and the limited RCT evidence for housing interventions it was deemed important to include this study in the review. An assessment of fidelity found that the intervention was delivered on average with a high level of fidelity. Key characteristics of the included study are summarised in Table 11.

Mental health

One RCT (Aubry et al., 2015) comparing a supportive housing intervention with TAU in homeless people found improved mental health symptoms (assessed with the CSI) in the intervention group compared with TAU at 52 weeks' follow-up (SMD=−0.10; 95% CI, −0.23 to 0.02; p=0.11), however the difference was not significant (see appendix 11, forest plot 1.7.1).

Substance use

One RCT (Aubry et al., 2015) suggested no difference between groups in the number of participants who had 2 or more substance use problems in the previous month at 52 weeks' follow-up (RR=1.00, 95% CI, 0.86 to 1.17; p=0.96; 188/469 [40%] versus 192/481 [40%]) (see appendix 11, forest plot 1.7.2).

Adaptive functioning

One RCT (Aubry et al., 2015) found evidence for an increased rate of participants in stable housing at 52 weeks' follow-up in the intervention group compared with TAU (RR=2.35, 95% CI, 2.01 to 2.75; p<0.00001; 316/433 [73%] versus 124/400 [31%]) (see appendix 11, forest plot 1.7.3). The study also suggested a small to moderate improvement in quality of life (SMD=0.42, 95% CI, 0.29 to 0.55; p<0.00001) and a small improvement in general functioning (SMD=0.24, 95% CI, 0.11 to 0.37; p=0.0002) in the intervention group compared with the control group at 52 weeks' follow-up (see appendix 11, forest plots 1.7.4 and 1.7.5).

Evidence statement 3.9: Supportive housing compared with treatment as usual

There is moderate evidence from 1[+][1] RCT, comparing a supportive housing intervention with TAU, on mental health and substance use outcomes and adaptive functioning. The study reported that the intervention was delivered on average with a 'high level' of fidelity.

One study 1[+][1] conducted in Canada, which included 950 homeless people with a mental health problem (of whom 73% had a substance use problem), suggested improved mental health symptoms in the intervention group compared with TAU at 52 weeks' follow-up (SMD=−0.10; 95% CI, −0.23 to 0.02; p=0.11), however the difference was not significant. There was no difference between groups in levels of substance use (RR=1.00, 95% CI, 0.86 to 1.17; p=0.96; 188/469 [40%] versus 192/481 [40%]). At 52 weeks' follow-up the evidence suggested a higher rate of housing (RR=2.35, 95% CI, 2.01 to 2.75; p<0.00001; 316/433 [73%] versus 124/400 [31%]), a small to moderate improvement in quality of life (SMD=0.42, 95% CI, 0.29 to 0.55; p<0.00001) and a small improvement in general functioning (SMD=0.24, 95% CI, 0.11 to 0.37; p=0.0002) in favour of the supportive housing group.

Applicability to the UK:
The evidence is only partially applicable to the UK because the study is conducted in Canada where policies regarding access to supported housing are likely to differ from those provided in the UK. A number of community services provide housing support in the UK; these services are often located in the third sector and are linked to statutory mental health services. Such services could provide the basis for an extension for this work to support people with dual diagnosis.

[1]Aubry et al. (2015) [+]

4.5.7 Supportive text messaging compared with control messages

Table 12: Summary of characteristics of studies contributing to the comparison: supportive text messaging compared with control text messaging

Author (year); study design; quality	Country, region, location	Population (N)	Intervention	Comparator	Service setting
Agyapong et al. (2013) RCT Quality: [+]	Ireland, Dublin, Urban	Major depressive disorder and alcohol dependency syndrome/alcohol misuse (n=54)	Supportive text messaging	Control text messaging	N/A

Narrative summary

One RCT (n=54) compared supportive text messaging with control text messaging in people with major depressive disorder and an alcohol-use disorder (Agyapong et al. (2013) [+]). Participants in the intervention group (n=26) received supportive text messages twice daily for 3 months. The themes of the messages included dealing with stress, maintaining good mental wellbeing, promoting abstinence from alcohol, dealing with cravings, promoting adherence with medication, and providing general support. The control group (n=28) also received messages but these were delivered once fortnightly and thanked the participant for taking part in the study. Participants were recruited while receiving inpatient treatment, however the study started at discharge from hospital after baseline assessments. Key characteristics of the included study are summarised in Table 12.

Mental health

At 24 weeks' follow-up, 1 RCT (Agyapong et al., 2013) indicated reduced severity in symptoms of depression (assessed with the BDI-II) in the intervention group compared with the control group (SMD=−0.17, 95% CI, −0.71 to 0.36, p=0.52), however the difference was not significant (see appendix 11, forest plot 1.8.1).

Substance use

At 24 weeks' follow-up, 1 RCT (Agyapong et al., 2013) indicated a moderate effect in favour of the intervention group for preoccupation with alcohol (assessed with the OCDS) (SMD=−0.45, 95% CI, −1.00 to 0.09; p=0.10) and mean number of days abstinent from alcohol (SMD=0.42, 95% CI, −0.12 to 0.97; p=0.12), as well as a small to moderate effect in favour of the intervention group for confidence in abstaining from alcohol (assessed with the AASE) (SMD=0.35; 95% CI, −0.19 to 0.89; p=0.20). However none of these effects were significant (see appendix 11, forest plots 1.8.2, 1.8.3 and 1.8.4).

Adaptive functioning

One RCT (Agyapong et al., 2013) reported a moderate effect in favour of the intervention group for participants' general functioning (assessed with the GAF) at 24 weeks' follow-up (SMD=0.53; 95% CI, −0.01 to 1.08; p=0.05) (see appendix 11, forest plot 1.8.5).

Evidence statement 3.10: Supportive text messaging compared with control text messaging

There is moderate evidence from 1[+][1] RCT, comparing supportive text messaging with control text messaging, on mental health and substance use outcomes and adaptive functioning.

One RCT 1 [+][1] (n=54) conducted in Ireland compared 3 months of supportive text messaging with control text messaging in people with major depressive disorder and an alcohol-use disorder who had been discharged from an inpatient unit. At 24 weeks' follow-up, there were lower levels of depression in the intervention group compared with the control group (SMD=−0.17, 95% CI, −0.71 to 0.36, p=0.10), however the difference was not significant. The evidence suggested small to moderate effects in favour of the intervention group for preoccupation with alcohol (SMD=−0.45, 95% CI, −1.00 to 0.09; p=0.10), mean number of days abstinent from alcohol (SMD=0.42, 95% CI, −0.12 to 0.97; p=0.12) and confidence in abstaining from alcohol (SMD=0.35; 95% CI, −0.19 to 0.89; p=0.20), however these were not significant. A moderate effect in favour of the intervention group was found at 24 weeks' follow-up for participants' general functioning (SMD=0.53; 95% CI, −0.01 to 1.08; p=0.05).

Applicability to the UK:
Although the study was conducted in Ireland, the findings are directly applicable to a UK setting as the effect of receiving supportive text messages on peoples' behaviour is not likely to differ between countries.

[1]Agyapong et al. (2013) [+]

4.6 DISCUSSION

Overall, there was little evidence to support any service delivery model over another. Based on weak evidence from the US, ACT showed no evidence of benefit when compared with usual care for mental health, substance use, housing, employment or quality of life outcomes, although there was evidence from 1 study of increased contact with the delivered programme The evidence for integrated treatment which looked at the effect of integrating an additional intervention with usual care was moderate in quality and included 2 RCTs and a before-and-after study that were based in the UK however no effects were found for mental health, substance use, quality of life and general functioning outcomes. This is generally in line with recent systematic reviews, which found no evidence of benefit for integrated treatment on mental health, substance use and general functioning outcomes for studies conducted in the US (Chow et al., 2012) or for psychosocial interventions delivered either as standalone interventions or in the context of a specialist team (Hunt et al., 2013).

For all other comparisons, only 1 or 2 studies were included in each. The most compelling evidence came from a Canadian RCT, which included 950 homeless people and compared a supportive housing intervention with usual care. Although there were no improvements in mental health and substance use outcomes, participants were twice as likely to have stable housing at 1 year, as well as showing improvements in quality of life and general functioning. There was some suggestion from 2 trials from the US (one of which was a small pilot trial) that contingency management may improve employment for people receiving vocational rehabilitation, although there were no lasting improvements in substance use outcomes. A study from Ireland reported improved general functioning for people recently discharged from inpatient care after receiving supportive text messages, however no improvements in alcohol use or symptoms of depression were found. One UK based study which looked at the effect of a staff training intervention for case managers based in community mental health teams, found improvements in their patients' mental health symptoms, however, other patient related outcomes such as substance use, adaptive functioning and the acceptability of services showed no change. These findings should nonetheless be viewed with caution as there was a high rate if attrition and fidelity to the training intervention was low (35% of the intervention group received the intervention as intended).

4.6.1 Applicability of findings

The majority of the studies in this review were undertaken in North America. This limits the applicability of the results. There is evidence from UK studies to show that ACT (which is effective in the US) is not effective in the UK. This has been explained as being due to better standard care in the UK compared with the US; in studies where the comparator group performs better, it is less likely that the additional benefit of the intervention will translate to a difference in outcomes between intervention groups (Killaspy et al., 2006). The 3 studies that provide some

evidence of benefit for supportive housing and contingency management were all conducted in North America and this, again, limits applicability.

4.6.2 Limitations and gaps in evidence

Out of 22 included studies, only 5 were based in the UK, whereas 12 were based in the US. Poor reporting of outcomes limited analysis and the pooling of results. The overall quality of included evidence was low to moderate, with no studies rated as high quality [++]. This was partly due to the fact that it was not possible to blind participants and providers from intervention allocation, so there was a high risk of performance bias. Many trials were not registered, which meant it was not possible to assess whether outcomes had been selectively reported. Other common limitations were mainly a lack of information provided by the authors about the process of allocating participants to the intervention group and whether outcome assessors were aware of which intervention group participants were in.

The main gap in the evidence was the limited number of UK studies. Although the inclusion criteria of the review were expanded to include UK observational studies, only 2 additional studies were identified from a database search of over 8,000 records. Although an important factor when judging the effectiveness of service delivery models, fidelity to the intervention was only reported in 7 studies. Reported outcomes focused more on mental health and substance use and there were limited outcomes on housing and other social outcomes. There was also an absence of studies investigating physical health outcomes. The accessibility of services (for example, waiting times) was also not reported in any included studies. Although there were some studies that reported service utilisation outcomes (for example the number of contacts with services or treatment adherence), this evidence was limited. Also, whether increased contact with a service signifies a positive outcome for people with a dual diagnosis is debatable. In 2 studies the mean age of participants was 26 to 27 years, however no evidence specifically including young people was identified. There was little evidence of the role of consultation or dual diagnosis specialists in community mental health services and no evidence on measures for practical help was identified. Finally, although consideration was given to the needs of vulnerable groups, as detailed in section 2.4, when identifying studies and extracting data, only 2 studies included people who were homeless and 1 study included people from a minority ethnic group, however these were people from Indigenous communities in Australia so there is limited applicability to UK ethnic minority populations.

5 CONCLUSIONS

This review has failed to find little, if any convincing, evidence for the effectiveness of interventions focused on delivering integrated treatments or enhancing service delivery systems for people with a dual diagnosis. There was some suggestion from a single trial that contingency management may improve outcomes for people in a specialist work programme and a trial of supportive housing suggested that providing housing assistance and supportive services may lead to the sustainability of stable housing and improved quality of life and community functioning. A single trial based in the UK also suggested that mental health outcomes may improve following staff training, however, the finding should be viewed with caution due to methodological limitations in the study.

It is worth noting that for a number of important interventions, for example ACT and integrated psychological treatment, there have been a number of trials, mainly based in the US, that have consistently failed to show any evidence of effect. In these areas it seems reasonable to conclude that these interventions are likely to be of little benefit for people with dual diagnosis in the English NHS and related services.

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APPENDICES

APPENDIX 1 Search strategy

RQ 3: Which service models for health, social care and voluntary and community sector organisations are effective and efficient at meeting the needs of people with a severe mental illness who also misuse substances?

Database(s): **Ovid MEDLINE (r)** 1946 to July week 4 2015

Search strategy:

#	Searches
1	affective disorders, psychotic/ or exp bipolar disorder/ or depressive disorder/ or depressive disorder, major/ or depressive disorder, treatment resistant/ or exp psychotic disorders/ or exp schizophrenia/ or "schizophrenia and disorders with psychotic features"/ or schizophrenic psychology/
2	emergency services, psychiatric/ or hospitals, psychiatric/ or psychiatric department, hospital/ or (mentally ill persons/ and (inpatients/ or hospitalization/))
3	((bipolar* adj (depres* or disorder*)) or ((cyclothymi* or rapid or ultradian) adj2 cycl*) or rcbd or mania* or manic*).ti,ab.
4	(delusional disorder* or psychos* or psychotic* or schizophren*).ti,ab.
5	(psychiatric adj2 (admission* or admit* or comorbid* or co morbid* or emerg* or hospital* or inpatient* or in*1 patient* or morbid* or outpatient* or patient* or population*)).ti,ab.
6	depres*.ti,ab.
7	(((acute or chronic* or serious* or severe) adj (mental* or psychiatric* or psychological*) adj (condition* or disease* or disorder* or disturbanc* or ill*)) or smi*1).ti,ab.
8	(comorbidity/ and exp mental disorders/) or ((comorbid* or co morbid* or coexist* or co exist* or concur* or cooccur* or co occur*) adj2 (mental* or psychiatric* or psychological*) adj2 (condition* or disease* or disorder* or disturbanc* or ill*)).ti,ab.
9	or/1-8
10	exp alcohol-related disorders/ or alcoholics/ or amphetamine related disorders/ or cocaine related disorders/ or drug overdose/ or inhalant abuse/ or marijuana abuse/ or exp opioid related disorders/ or phencyclidine abuse/ or psychosis, substance induced/ or substance abuse, intravenous/ or substance related disorders/ or exp substance withdrawal syndrome/
11	designer drugs/ or drug overdose/ or needle exchange programs/ or needle sharing/ or exp street drugs/ or substance abuse detection/ or substance abuse treatment centers/
12	(alcohol* adj2 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or nonprescri* or non prescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.

13	((amphetamin* or crystal meth* or desoxyn or dexamfetamin* or dexedrine or dextroamphetamin* or methamphetamin* or psychostimulant* or stimulant* or uppers) adj2 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or nonprescri* or non prescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.
14	((amphetamin* or crystal meth* or desoxyn or dexamfetamin* or dexedrine or dextroamphetamin* or methamphetamin* or psychostimulant* or stimulant* or uppers) adj2 (usage* or use or user* or uses or using or utiliz* or utilis*)).ti,ab.
15	((benzoylmethyl ecgonine or cocain* or crack*1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj2 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or nonprescri* or non prescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.
16	((benzoylmethyl ecgonine or cocain* or crack*1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj2 (usage* or use or user* or uses or using or utiliz* or utilis*)).ti,ab.
17	((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj2 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or nonprescri* or non prescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.
18	((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj2 (usage* or use or user* or uses or using or utiliz* or utilis*)).ti,ab.
19	((acetomorphine or anpec or diacephine or diacetylmorphin* or diacetylmorphine* or diagesil or diagesil or diamorf* or diamorf* or diamorphin* or diamorphin* 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 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or nonprescri* or non prescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.
20	((acetomorphine or anpec or diacephine or diacetylmorphin* or diacetylmorphine* or diagesil or diagesil or diamorf* or diamorf* or diamorphin* or diamorphin* 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 (usage* or use or user* or uses or using or utiliz* or utilis*)).ti,ab.
21	or/10-20
22	abus* product*.ti,ab.
23	((drug*1 or polydrug* or psychotropic* or substance*) adj2 (abstain* or abstinen* or abus* or addict* or banned or excessive us* or criminal or depend* or habit* or illegal* or illicit* or intoxicat* or misus* or non prescri* or nonprescri* or overdos* or over dos* or recreation* or rehab* or unlawful* or withdraw*)).ti,ab.
24	(((alcohol* or drug*1 or polydrug* or recreation* or substance*) adj use*1) or alcoholi*).ti,ab.
25	((club or designer or street) adj (drug* or substance*)).ti,ab.
26	((crav* adj2 (alcohol* or inject*)) or hard drug* or needle fixation or soft drug*

	or vsa*1).ti,ab.
27	or/22-26
28	or/21,27
29	"diagnosis, dual (psychiatry)"/
30	(chemical* adj (user or addict*) adj3 ((mental* or psychiatric or psychological*) adj (condition* or disease* or disorder* or disturbanc* or ill*))).ti,ab.
31	((comorbid* or co morbid* or coexist* or co exist* or concur* or cooccur* or co occur*) adj5 (addict* or ((drug or substance*) adj5 (abus* or misus))) adj3 ((mental* or psychiatric or psychological*) adj (condition* or disease* or disorder* or disturbanc* or ill*))).ti,ab.
32	((dual* or tripl*) adj2 diagnos*).ti,ab.
33	or/29-32
34	(9 and 28) or 33
35	exp general practice/ or general practitioners/ or physicians/ or physicians, family/ or physician's practice patterns/ or physicians, primary care/ or physicians, women/ or primary health care/
36	(clinician* or ((general or family) adj practic*) or ((family or primary) adj (care or healthcare or medical care or medicine)) or family doctor* or gp*1 or physician* or practitioner*).ti,ab.
37	or/35-36
38	community care/ or community based rehabilitation/ or community health centers/ or exp community health nursing/ or community health services/ or community integration/ or community medicine/ or community mental health centers/ or community mental health services/ or community networks/ or community pharmacy services/ or community program/ or community psychiatry/ or emergency shelter/ or home care agencies/ or home care services/ or home care services, hospital-based/ or home health nursing/ or exp home nursing/ or house calls/
39	((exp rehabilitation/ or exp rehabilitation centers/ or rehab*.ti,ab. or rh.fs.) and communit*.sh,ti,ab.)
40	(((communit* or home*) adj3 (agenc* or care or center* or centre* or clinic* or consultant* or doctor* or employee* or expert* or facilitator* or healthcare or instructor* or leader* or manager* or mentor* or nurs* or personnel* or pharmacy or pharmacist* or psychiatrist* or psychologist* or psychotherapist* or specialist* or staff* or team* or therapist* or tutor* or visit* or worker*)) or care management team* or domiciliary care* or homecare or linkworker* or link worker*).ti,ab.
41	(camhs or cmht*1).ti,ab.
42	(((communit* or home*) adj2 (assessment or evaluation or monitor*)) or (needs assessment and communit*)).ti,ab.
43	((communit* or home*) adj (based or deliver* or interact* or led or maintenance or mediat* or operated or provides or provider* or run or setting*)).ti,ab.
44	((communit* or home*) adj2 group*).ti,ab.
45	((communit* or home*) adj3 (advice* or advis* or aftercare or assist* or casework* or case work* or counsel* or educat* or help* or integrat* or liaison* or mentor* or network* or reinforc* or reintegrat* or sector* or setting* or support* or visit*)).ti,ab.
46	((communit* or home*) adj3 (intervention* or program* or rehab* or therap* or

	service* or skill* or treat*)).ti,ab.
47	(communit* adj5 (advocacy or apprenticeship* or awareness campaign* or development group* or empower* or employ* or inclusi* or individual support* or personal assistan* or selfadvocacy or selfemploy* or self advocacy or self employ* or support* or train*)).ti,ab.
48	(health adj (cent* or visit*)).ti,ab.
49	independent sector*.ti,ab.
50	((non institutional* or noninstitution*) adj2 (sector* or setting*)).ti,ab.
51	or/38-50
52	((pharmacist* or pharmacies or pharmacy) adj3 (advice* or care* or communit* or counsel* or educat* or intervention* or liaison* or program* or rehab* or service*)).ti,ab.
53	(pharmacist* adj3 (frontline or front line or face to face or one to one)).ti,ab.
54	or/52-53
55	foster home care/ or exp rehabilitation centers/ or social support/ or social work/ or social work, psychiatric/ or social welfare/
56	((child adj2 protect*) or (child* adj3 (foster* or in*1 care or looked after or residential care)) or foster care).ti,ab.
57	(social* adj2 (care or security or welfare or work*)).ti,ab.
58	((social* or welfare) adj3 (advice* or advis* or aftercare or assist* or casework* or case work* or counsel* or educat* or help* or integrat* or liaison* or mentor* or network* or reintegrate* or setting* or support* or visit*)).ti,ab.
59	(social* adj3 (intervention* or program* or rehab* or service* or therap* or treat*)).ti,ab.
60	or/55-59
61	ambulatory care/ or exp ambulatory care facilities/ or case management/ or day care/ or hospitals, rural/ or rural populations/ or exp outpatient clinics, hospital/ or rural health services/
62	((act adj (model* or team*)) or (assertive adj1 community adj1 treatment) or ((care or case) adj management) or (care adj1 program* adj1 approach) or cap or (madison adj4 model*) or (training adj2 (community adj1 living)) or pact or tcl).ti,ab.
63	((ambulatory or outreach* or out reach*) adj3 (advice* or advis* or aftercare or assist* or casework* or case work* or counsel* or educat* or help* or integrat* or liaison* or mentor* or network* or reintegrate* or sector* or setting* or support* or visit*)).ti,ab.
64	((ambulatory or outpatient* or out patient*) adj (based or deliver* or interact* or led or mediat* or operated or provides or provider* or run or setting*)).ti,ab.
65	((ambulatory or outpatient* or out patient*) adj3 (intervention* or program* or rehab* or service* or treat*)).ti,ab.
66	((outreach* or out reach* or remote or rural* or (social* adj2 (exclus* or isolat*)) or suburban* or urban*) adj3 (assist* or intervention* or program* or service* or treat*)).ti,ab.
67	(care program* or daily living program* or ((ambulatory or day or posthospital* or post hospital*) adj2 (care or center* or centre* or clinic* or facilit* or hosp* or intervention* or treatment* or unit*)) or daycare or day case or dropin* or drop in* or dispensar* or domiciliar* or (home adj2 (care or treatment)) or (partial* adj2 hosp*)).ti,ab.
68	mobile support* team*.ti,ab.
69	(visit* adj2 (clinic* or consultant* or consultation* or service* or special*)).ti,ab.

70	or/61-69
71	schools/ or exp students/
72	((mentor* or school* or teacher*) adj (based or deliver* or led or mediat* or operated or run or sector* or setting*)).ti,ab.
73	((mentor* or school* or teacher*) adj3 (intervention* or program* or rehab* or therap* or service* or skill* or treat*)).ti,ab.
74	((mentor* or pupil* or school* or teacher*) adj3 (advice* or advis* or aftercare or assist* or casework* or case work* or counsel* or educat* or integrat* or liaison* or mentor* or network* or reinforc* or reintegrat* or setting* or support* or visit*)).ti,ab.
75	or/71-74
76	charities/ or education, nonprofessional/ or friends/ or group processes/ or hotlines/ or peer group/ or exp psychotherapy, group/ or rehabilitation, vocational/ or self-help groups/ or voluntary workers/
77	(befriend* or be*1 friend* or buddy or buddies or ((community or lay or paid or support) adj (person or worker*))).ti,ab.
78	charit*.ti,ab.
79	((consumer* or famil* or friend* or lay or mutual* or peer* or social* or voluntary or volunteer*) adj3 (advice* or advis* or counsel* or educat* or forum* or help* or mentor* or network* or support* or visit*)).ti,ab.
80	((consumer* or famil* or peer* or self help or social* or support* or voluntary or volunteer*) adj2 group*).ti,ab.
81	((consumer* or famil* or friend* or lay or mutual* or peer* or self help or social* or voluntary or volunteer*) adj3 (intervention* or program* or rehab* or therap* or service* or skill* or treat*)).ti,ab.
82	(((consumer* or famil* or friend* or lay* or peer* or user* or voluntary or volunteer*) adj (based or counsel* or deliver* or interact* or led or mediat* or operated or provides or provider* or run*)) or voluntary work*).ti,ab.
83	((consumer* or famil* or friend* or lay* or peer* or relation* or support*) adj3 trust*).ti,ab.
84	(coping adj (behavio* or skill*)).ti,ab.
85	((emotion* adj (focus* or friend* or relation*)) or ((dyadic or loneliness or psychosocial* or psycho social*) adj2 (assist* or counsel* or intervention* or program* or support* or therap* or treat*)) or ((emotion* or one to one or transition*) adj support*) or (lay adj (led or run))).ti,ab.
86	((emotion* or network* or organi?ation* or peer*) adj2 support*).ti,ab.
87	(group*1 adj2 (advocacy or approach* or assist* or coach* or counsel* or educat* or help* or instruct* or learn* or module* or network* or participat* or program* or psychotherap* or rehab* or skill* or strateg* or support* or teach* or train* or workshop* or work shop*)).ti,ab.
88	((group* or network* or peer*1) adj2 (discuss* or exchang* or interact* or meeting*)).ti,ab.
89	(groupwork or (group adj2 work)).ti,ab.
90	(helpline or help line or ((phone* or telephone*) adj3 (help* or instruct* or interact* or interven* or mediat* or program* or rehab* or strateg* or support* or teach* or therap* or train* or treat* or workshop*)) or ((phone or telephone*) adj2 (assist* or based or driven or led or mediat*))).ti,ab.
91	(helpseek* or ((search* or seek*) adj4 (care or assistance or counsel* or healthcare or help* or support* or therap* or treat*))).ti,ab.
92	(((lay or peer*) adj3 (advis* or consultant or educator* or expert* or facilitator*

	or instructor* or leader* or mentor* or person* or tutor* or worker*)) or expert patient* or mutual aid).ti,ab.
93	(peer* adj3 (assist* or counsel* or educat* or program* or rehab* or service* or supervis*)).ti,ab.
94	((psychoeducat* or psycho educat*) adj3 (group or network* or service*)).ti,ab.
95	((social or psychosocial) adj (adapt* or reintegrat* or support*)).ti,ab.
96	(support* adj3 (approach* or educat* or instruct* or interven* or learn* or module* or network* or program* or psychotherap* or strateg* or technique* or therap* or train* or workshop* or work shop*)).ti,ab.
97	supportive treatment*.ti,ab.
98	(alcohol* anonymous or cocaine anonymous or narcotic* anonymous or recover inc or smart recovery or social interaction program* or (self management adj2 recovery training) or support* listening or supportive relationship* or schizophrenic* anonymous or visit* service* or (volunt* adj3 (aid* or support* or trained or work*))).ti,ab.
99	or/76-98
100	social skills/
101	(((psychosocial or social) adj3 skill*) or ((psychosocial or social) adj2 learn*) or ((psychosocial or social) adj3 competen*) or roleplay* or role play* or ((peer* or social* or psychosocial or support*) adj2 (group* or network*)) or ((group* or peer* or social* or psychosocial) adj2 (network* or support*))).ti,ab.
102	or/100-101
103	assisted living facilities/ or group homes/ or halfway houses/ or homeless persons/ or residential facilities/ or residential treatment/ or therapeutic community/
104	(((accommod* or bedsit* or bed sit* or flats or flatlets or homeless* or hous* or home* or hostel* or hous* or landlord* or lodge* or rent or rents or rented or renting or residen* or room* or runaway* or tenant*) adj3 (appointment* or care or cluster* or coach* or communit* or healthcare or integrat* or independen* or intervention* or model* or outreach or place* or program* or rehab* or reintegrat* or satellite or scheme* or service* or staffed or supervis* or support* or therap* or treatment* or warden* or visit*)) or ((rent or rents or rented or renting) adj3 (accommod* or bedsit* or bed sit* or flats or flatlets or homeless* or hous* or home* or hostel* or hous* or landlord* or lodge* or residen* or room* or runaway* or tenant*)) or shelter*).ti,ab.
105	((24 hour or day time or daytime or live in*1 or out of*1 hour*) adj (care or cover or healthcare or staff*)).ti,ab.
106	(((assist* or cooperative or co operative or independen* or staffed or supportive) adj2 (care or living)) or staff* model*).ti,ab.
107	(board* adj2 care).ti,ab.
108	((concept or support) adj house).ti,ab.
109	((communit* or mental health) adj2 (living or place* or resettl* or residence*)).ti,ab.
110	floating support.ti,ab.
111	(group adj (dwelling* or home*)).ti,ab.
112	(hous* adj2 (association* or officer* or resident*)).ti,ab.
113	(place* adj3 (adult* or famil* or person*)).ti,ab.
114	(resident* adj3 (continuum or facilit* or independen* or setting* or status)).ti,ab.
115	psychosocial therap*.ti,ab.

116	single room.ti,ab.
117	supporting people program*.ti,ab.
118	((therapeutic adj2 community) or modified tc).ti,ab.
119	or/103-118
120	employment, supported/ or occupational health/ or occupational medicine/ or occupational therapy/ or rehabilitation, vocational/ or return to work/ or vocational education/ or work/ or (employment/ and rh.fs.)
121	(club house* or clubhouse* or fountain house* or work therap*).ti,ab.
122	((employ* or job*1 or occupat* or reemploy* or vocation* or work*) adj3 (advice or advis* or assist* or coach* or counsel* or educat* or experience or integrat* or interven* or liaison* or placement* or program* or rehab* or reintegrat* or retrain* or scheme* or support* or service* or skill* or teach* or therap* or train* or transitional* or vocat*)).ti,ab.
123	((individual placement adj2 support) or ips model).ti,ab.
124	((permitted or voluntary or rehab*) adj3 work*).ti,ab.
125	((psychiatric or psychosocial or psycho social or social) adj2 rehab*).ti,ab.
126	rehabilitation counsel*.ti,ab.
127	(vocat* adj3 (advice* or advis* or assist* or casework* or case work* or counsel* or educat* or integrat* or interven* or liaison* or mentor* or network* or program* or rehab* or reintegrat* or service* or setting* or skill* or support* or retrain* or teach* or therap* or train* or treat* or specialist*)).ti,ab.
128	vocational outcome*.ti,ab.
129	or/120-128
130	crisis intervention/
131	(alternative* adj3 (hospital* or psychiatric care or ward*)).ti,ab.
132	((crisis or crises or recover*) adj3 (hous* or lodge* or shelter*)).ti,ab.
133	((crisis or residential) adj2 alternative*).ti,ab.
134	((crisis resolution adj2 home treatment team*)).ti,ab.
135	crht*1.ti,ab.
136	(resident* and crisis).ti,ab.
137	or/130-136
138	exp *activities of daily living/ or exp self care/ or exp *daily life activity/
139	(assertiveness training or communication skills training).ti,ab.
140	((benefits* or bills or budget* or computer* or diet* or financ* or money or nutrition* or relationship*) adj3 (advice* or assist* or coach* or educat* or interven* or program* or skill* or support* or service* or teach* or tool*)).ti,ab.
141	((healthy living adj (intervention* or program*)) or exercise program* or harm reduction program*).ti,ab.
142	((advice* or assist* or coach* or educat* or interven* or program* or skill* or support* or service* or teach* or tool*) adj2 (living or life or social or self care or independen* or survival)).ti,ab.
143	(transition* adj2 (adult* or support* or service*)).ti,ab.
144	(independen* adj2 (live* or living)).ti,ab.
145	or/138-144
146	"early intervention (education)"/
147	(early adj (intervent* or treat* or recogni* or detect*)).ti,ab.
148	or/146-147
149	exp hepatitis/ or exp hiv/ or exp hiv infections/ or exp tuberculosis/

150	((((acquired immunodeficiency or acquired immuno deficiency or human immuno deficiency or human immune deficiency or human immunodeficiency or immunodeficiency or lymphadenopathy) adj2 (retrovirus or syndrome* or virus)) or aids or (blood adj2 borne) or drtb or hepatitis or hiv or mdrtb or tuberculosis or xdrtb) adj3 (referral* or screen* or test*)).ti,ab.
151	exp mass screening/ or exp population surveillance/ or "referral and consultation"/
152	((((acquired immunodeficiency or acquired immuno deficiency or human immuno deficiency or human immune deficiency or human immunodeficiency or immunodeficiency or lymphadenopathy) adj2 (retrovirus or syndrome* or virus)) or aids or (blood adj2 borne) or drtb or hepatitis or hiv or mdrtb or tuberculosis or xdrtb) adj3 (educat* or disinfect* or empower* or knowledge or information* or instruct* or intervention* or promot* or psychoeducat* or psycho educat* or teach* or train* or book*1 or booklet* or brochure* or leaflet* or manual*1 or material* or multimedia or multi media or pamphlet* or poster* or program* or resource or service or scheme* or sterilis* or steriliz* or system* or workbook* or ((oral or printed or written) adj3 inform*) or video* or screen* or test* or diagnos* or prevent* or detect* or referral*)).ti,ab.
153	needle exchange programs/
154	(((needle* or syring*) adj2 exchang* adj2 program*) or (supervis* adj2 inject* adj2 (cent* or facilit* or service* or setting* or unit*))).ti,ab.
155	(149 and 151) or (or/150,152-154)
156	(addiction health service or (addiction adj (team* or unit*)) or community drugs service or daat or (drug adj2 (alcohol treatment agenc* or drug treatment cent*)) or ((liaison or local or rehab*) adj (program* or service* or worker*)) or ((rehabilitation or treatment*) adj (center* or centre* or clinic* or facility* or organi?ation* or program* or service*)) or mobile clinic*).ti,ab.
157	(dual diagnosis adj2 (agenc* or care or center* or centre* or clinic* or intervention* or program* or service* or team* or treatment* or worker*)).ti,ab.
158	((augment* or collaborat* or coordinat* or co ordinat* or enhanc* or holistic* or integrat* or interdisciplin* or inter disciplin* or interagenc* or inter agenc* or interorganis* or inter organis* or interprofessional* or inter professional* or intraprofessional* or intra professional* or multiagenc* or multi agenc* or multidimension* or multi dimension* or multidisciplin* or multi disciplin* or multifacet* or multi facet* or multiprofessional* or multi professional* or multiple or shared or stepped or tiered or transdisciplin* or trans discliplin*) adj3 (approach* or care or healthcare or intervention* or manag* or model* or program* or psychotherap* or service* or system* or team* or therap* or treatment* or work*)).ti,ab.
159	or/37,51,54,60,70,75,99,102,119,129,137,145,148,155-158
160	case management/
161	cooperative behavior/
162	"continuity of patient care"/
163	delivery of health care/ or delivery of health care, integrated/
164	interprofessional relations/
165	interinstitutional relations/ or multi-institutional systems/
166	models, organizational/
167	patient care team/
168	patient centered care/
169	community health planning/ or decision making, organizational/ or health care reform/ or health facility administration/ or health facility planning/ or health

	planning/ or health planning guidelines/ or health plan implementation/ or health resources/ or health services administration/ or exp health planning organizations/ or health systems plans/ or institutional management teams/ or national health programs/ or organizational innovation/ or patient care planning/ or planning techniques/ or program development/ or public health administration/ or regional health planning/ or regional medical programs/ or resource allocation/ or state health plans/
170	(algorithm* or pathway* or (treatment adj (delivery or guideline* or program* or protocol*))).ti,ab.
171	(((assertive or proassertive) adj2 (communit* or outreach or treatment*)) or act model*).ti,ab.
172	((augment* or collaborat* or coordinat* or co ordinat* or enhanc* or holistic* or integrat* or interdisciplin* or inter disciplin* or interagenc* or inter agenc* or interorganis* or inter organis* or interprofessional* or inter professional* or intraprofessional* or intra professional* or multiagenc* or multi agenc* or multidimension* or multi dimension* or multidisciplin* or multi disciplin* or multifacet* or multi facet* or multiprofessional* or multi professional* or multiple or shared or stepped or tiered or transdisciplin* or trans discliplin*) adj3 (approach* or care or healthcare or intervention* or manag* or model* or program* or psychotherap* or service* or system* or team* or therap* or treatment* or work*)).ti,ab.
173	(((care or case*) adj manag*) or managed care program* or (patient care adj (plan* or team*))).ti,ab.
174	(cluster adj3 health* adj3 social*).ti,ab.
175	((complex or organi?ational) adj intervention*).ti,ab.
176	((comprehensive adj2 (care or management or service or treatment)) or (managed adj (behavioral or behavioural) adj health) or (model* adj2 (approach* or care or consultation or integrated or service* or team* or treatment*))).ti,ab.
177	(co located team or co location or (joint service adj3 development) or linkwork* or multidisciplinary assessment or one stop shop or (pool* adj3 budget) or single assessment or strategic collaboration).ti,ab.
178	consultation liaison.ti,ab.
179	((contin* or coordinated or co ordinated or joint* or joined up or progression or seamless* or structured or uninterrupted) adj3 (care or healthcare or service*)).ti,ab.
180	(((continuous or integrated or joint or overlapping) adj commission*) or provider partnership*).ti,ab.
181	(continuity adj2 (care or healthcare)).ti,ab.
182	(((cooperative or co operative) adj behav*) or ((interpersonal or inter personal or interprofession* or inter profession* or interinstitution* or inter institution*) adj (work* or relation*))).ti,ab.
183	(flexible partnership* or (joint* adj3 working) or joined up partnership* or (partnership* adj3 working) or partnership project*).ti,ab.
184	(((horizontal or vertical) adj integrat*) or horizontal communication*).ti,ab.
185	(imhc or integrated psychiatry).ti,ab.
186	(integrat* adj3 health*).ti,ab.
187	((model* or pathway*) adj3 (approach* or care or healthcare or program* or psychotherap* or service* or specialit* or therap* or treatment*)).ti,ab.
188	((parallel or serial) adj2 (care or healthcare or model* or service* or therap* or treatment*)).ti,ab.

189	((premobile or pre mobile) adj3 (approach* or care or communit* or healthcare or program* or service* or therap* or treatment or work*)).ti,ab.
190	(system* adj2 care).ti,ab.
191	((deliver* or implement* or needs or organi* or plan* or utili*) adj3 (care or healthcare or model* or program* or service* or system*)).ti,ab.
192	or/160-191
193	34 and 159 and 192
194	(comment* or editorial* or historical article or letter).pt.
195	exp animals/ not humans/
196	or/194-195
197	193 not 196
198	limit 197 to english language
199	limit 198 to yr="2000 -current"
200	exp clinical trial/ or exp "clinical trials as topic"/ or cross-over studies/ or double-blind method/ or placebos/ or random allocation/ or single-blind method/
201	(clinical adj2 trial*).ti,ab.
202	(crossover or cross over).ti,ab.
203	(((single* or doubl* or trebl* or tripl*) adj2 blind*) or dummy or doubleblind* or mask* or singleblind* or trebleblind* or tripleblind*).ti,ab.
204	(placebo* or random*).ti,ab.
205	or/200-204
206	meta analysis.sh,pt. or "meta-analysis as topic"/ or "review literature as topic"/
207	(exp databases, bibliographic/ or (((electronic or computer* or online) adj database*) or bids or cochrane or embase or index medicus or isi citation or medline or psyclit or psychlit or scisearch or science citation or (web adj2 science)).ti,ab.) and (review*.ti,ab,sh,pt. or systematic*.ti,ab.)
208	((analy* or assessment* or evidence* or methodol* or quantativ* or systematic*) adj2 (overview* or review*)).tw. or ((analy* or assessment* or evidence* or methodol* or quantativ* or systematic*).ti. and review*.ti,pt.) or (systematic* adj2 search*).ti,ab.
209	(metaanal* or meta anal*).ti,ab.
210	(research adj (review* or integration)).ti,ab.
211	reference list*.ab.
212	bibliograph*.ab.
213	published studies.ab.
214	relevant journals.ab.
215	selection criteria.ab.
216	(data adj (extraction or synthesis)).ab.
217	(handsearch* or ((hand or manual) adj search*)).ti,ab.
218	(mantel haenszel or peto or dersimonian or der simonian).ti,ab.
219	(fixed effect* or random effect*).ti,ab.
220	((pool* or combined or combining) adj2 (data or trials or studies or results)).ti,ab.
221	or/206-220
222	199 and (or/205,221)
223	199 not 222

APPENDIX 2 Example quality checklist for RCTs

Study identification: Aubry T, Tsemberis S, Adair CE, Veldhuizen S, Streiner D, Latimer E. One-year outcomes of a randomized controlled trial of Housing First with ACT in five Canadian cities. Psychiatric Services. 2015;66(5):463-469.		
Checklist completed by: EM		
	High/Low/Unclear	**Supporting evidence**
1. Sequence generation		
1.1 How was the randomisation sequence generated?	Low	Participants were randomly assigned to treatment conditions at the end of the baseline interview by using a computer-generated algorithm programmed into the central data collection system.
2. Allocation concealment		
2.1 Was allocation adequately concealed?	Unclear	Not reported
3. Blinding		
3.1 Were patients and providers aware of allocation to intervention?	High	It was not possible to hide the treatment condition of participants from interviewers or from themselves
3.2 Were outcome assessors aware of participants' intervention allocation?	High	The study design was non-blind
4. Missing outcome data		
4.1 Were incomplete outcome data adequately addressed?	Low	"We conducted the analysis on the principle of intention to treat". A total of 856 (90%) participants completed the 12-month follow-up, including 406 of 481 (84%) participants in treatment as usual and 450 of 469 (96%) participants in Housing First
5. Selective outcome reporting		
5.1 Are reports of the study free	Low	Reported outcomes match protocol

of suggestion of selective outcome reporting?		
6. Other bias		
6. 1 Was the study free of other bias?	Low	Appears to be free of other bias

APPENDIX 3 Example quality checklist for observational studies

Study identification Copello A, Walsh K, Graham H, Tobin D, Griffith E, Day E, Birchwood M. A consultation-liaison service on integrated treatment: a program description. Journal of Dual Diagnosis. 2013;9(2):149-157.		
Checklist completed by: EM		
	Yes/Partly /No/Unclear /NA	**Comments**
1. Objectives		
1.1 Are the objectives of the study clearly stated?	Yes	Service evaluation
1.2 Was the study ethical?	Yes	Clients were informed that anonymous data would be used for an evaluation of the service, as specified by the UK Department of Health guidance for ethical conduct of research.
2. Sampling		
2.1 Were all members of the cohort entered at the beginning?	Yes	Participant entered over a 3 year period
2.2 Did the sampling scheme allow a representative sample?	Yes	All clients referred to service part of the cohort
3. Participation		
3.1 Was loss to follow-up low – i.e. less than 20%?	No	Data available only for participants who completed the intervention (53%)
3.2 Was completion rate on individual items of the assessment instrument high?	No	
4. Measurement		
4.1 Were valid measures of disease (case definition) and risks used?	Yes	All measures used have been previously validated

4.2 Were the data gathered using the best-accepted techniques? (e.g. trained telephone interviewers or examiners, mail questionnaire)	Partly	5/8 measures were self-report
4.3 Were the data tested for accuracy and reliability?	No	
Other comments: No control group		

APPENDIX 4 Completed quality appraisal checklist for RCTs

Study ID	Sequence generation	Allocation concealment	Blinding of providers and participants	Blinding of outcome assessors	Missing outcome data	Selective outcome reporting	Other bias	Overall quality rating (++, +, –)
Agyapong et al. (2013)	Low	Unclear	High	High	Low	Low†	Low	+
Aubry et al. (2015)	Low	Unclear	High	High	Low	Low†	Low	+
Barrowclough et al. (2001)	Low	Low	High	Low	Low	Unclear	Low	+
Barrowclough et al. (2010)	Low	Low	High	Low	Low	Low†	Low	+
Bonsack et al. (2011)	Low	Unclear	High	Unclear	Low	Unclear	Low	-
Bradford et al. (2005)	Low	High	High	Low	Unclear	Unclear	Low	–
Drake et al. (2004)	Unclear	Unclear	High	Low	Low	Unclear	Low	–
Drebing et al. (2005)	Unclear	Unclear	High	Unclear	Low	Unclear	Low	–
Drebing et al. (2007)	Unclear	Unclear	High	Unclear	Low	Unclear	Low	–
Eack et al. (2015)	Unclear	Unclear	High	Low	High	High	Low	–
Essock et al. (2006)	Low	Low	High	Low	Low	Unclear	Low	+
Fletcher et al. (2008)	Unclear	Unclear	High	Unclear	High	Unclear	Low	–
Havassy et al. (2000)	Low	Unclear	High	Unclear	High	Unclear	Low	–
Hjorthøj et al. (2013)	Low	Low	High	Low	High	Low†	Low	+
Johnson et al. (2007)	Low	Unclear	High	Unclear	High	Unclear	Low	–
Nagel et al. (2009)	Low	Unclear	High	Unclear	Low	Low†	Low	+

Study ID	Sequence generation	Allocation concealment	Blinding of providers and participants	Blinding of outcome assessors	Missing outcome data	Selective outcome reporting	Other bias	Overall quality rating (++, +, –)
Smelson et al. (2012)	Unclear	Unclear	High	Unclear	High	Unclear	Low	–
Striley et al. (2013)	Low	Low	High	Unclear	Low	Unclear	Low	+
Wenze et al. (2015)	Low	Unclear	High	Low	Low	Unclear	Low	+
Xie et al. (2005)	Unclear	Unclear	High	Low	Low	Unclear	Low	–
† Low indicates that the study protocol is available and all of the study's pre-specified outcomes that are of interest in the review have been reported in the pre-specified way								

APPENDIX 5 Completed quality appraisal checklist for observational studies

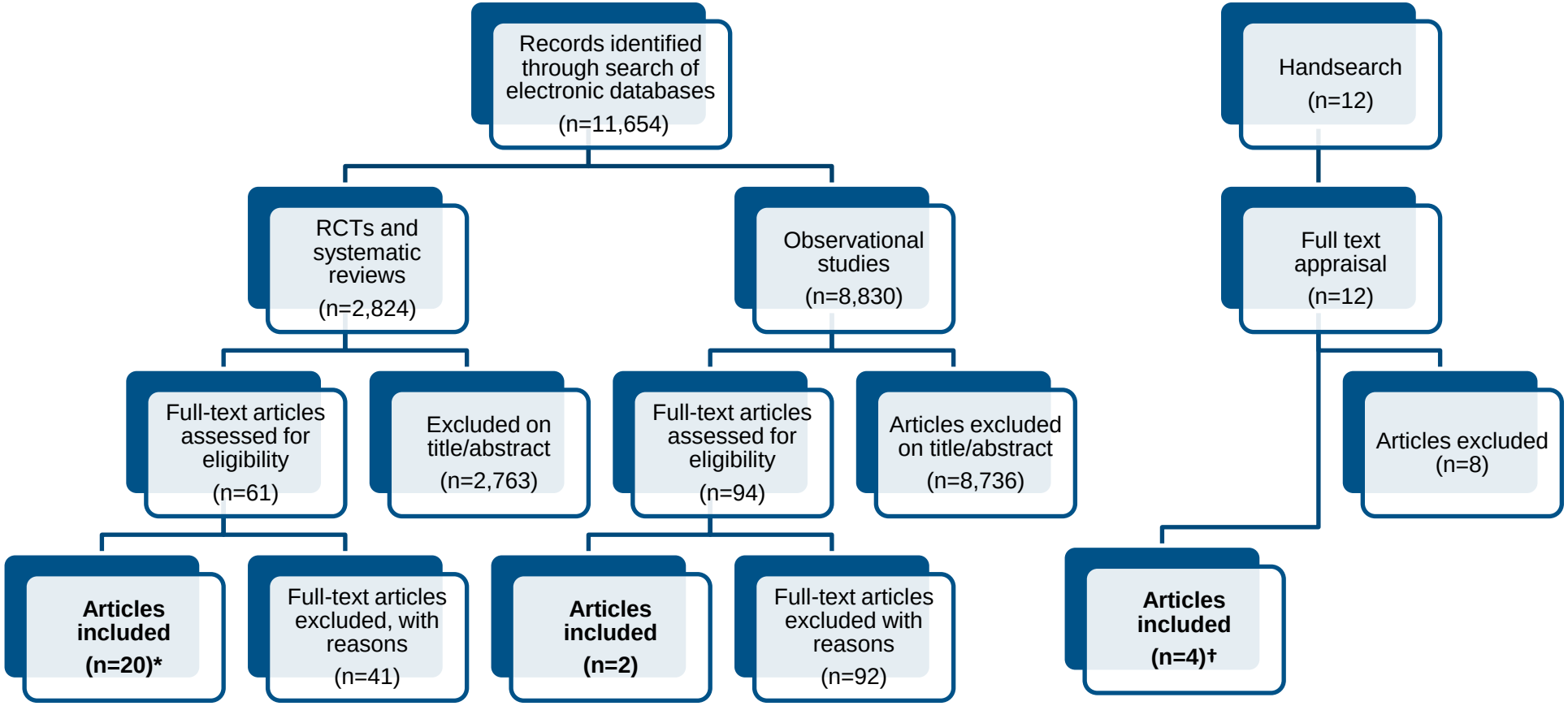
1. Checklist to Assess Evidence of Prevalence and Incidence, Descriptive or Longitudinal Studies

Study ID	Objectives		Sampling		Participation		Measurement			Overall quality rating (++, +, -)
	1.1	1.2	2.1	2.2	3.1	3.2	4.1	4.2	4.3	
Copello et al. (2013)	Yes	Yes	No	Yes	No	No	Yes	Partly	No	–

2. Effective Practice and Organisation of Care (EPOC) Risk of Bias Tool

Study ID	Sequence generation	Allocation concealment	Baseline outcome	Baseline characteri-stics	Incomplete outcome data	Blinding	Contami-nation	Selective outcome reporting	Other Bias	Overall quality rating (++, +, -)
Graham et al. (2006)	No	No	Unclear	Yes	No	Unclear	Unclear	Yes	Yes	–

APPENDIX 6 PRISMA diagram



*19 studies in total; 2 articles included the same study [Barrowclough et al. (2001) and Haddock et al. (2003)]
†All three studies ([a] Aubry et al., 2015; [b] Hjorthøj et al., 2013; [c] Johnson et al., 2007) had already been located in the RCT search in the following articles: [a] Hwang et al. 2010 (baseline data only), [b] Hjorthøj et al., 2010 (conference abstract), and [c] Craig et al. 2008 (same study reporting different outcomes).

APPENDIX 7 Bibliography for included studies

Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: single-blind randomised trial. Journal of Affective Disorders. 2012;141(2):168-76.

Aubry T, Tsemberis S, Adair CE, Veldhuizen S, Streiner D, Latimer E. One-year outcomes of a randomized controlled trial of Housing First with ACT in five Canadian cities. Psychiatric Services. 2015;66(5):463-469.

Barrowclough C, Haddock G, Tarrier N, Lewis SW, Moring J, O'Brien R, et al. Randomized controlled trial of motivational interviewing, cognitive behavior therapy, and family intervention for patients with comorbid schizophrenia and substance use disorders. American Journal of Psychiatry. 2001;158(10):1706-13.

Barrowclough C, Haddock G, Wykes T, Beardmore R, Conrod P, Craig T, et al. Integrated motivational interviewing and cognitive behavioural therapy for people with psychosis and comorbid substance misuse: randomised controlled trial. BMJ. 2010;341.

Bonsack C, Gibellini Manetti S, Favrod J, Montagrin Y, Besson J, Bovet P, et al. Motivational intervention to reduce cannabis use in young people with psychosis: a randomized controlled trial. Psychotherapy and Psychosomatics. 2011;80(5):287-97.

Bradford DW, Gaynes BN, Kim MM, Kaufman JS, Weinberger M. Can shelter-based interventions improve treatment engagement in homeless individuals with psychiatric and/or substance misuse disorders?: a randomized controlled trial. Medical Care. 2005;43(8):763-8.

Copello A, Walsh K, Graham H, Tobin D, Griffith E, Day E, et al. A consultation-liaison service on integrated treatment: a program description. Journal of Dual Diagnosis. 2013;9(2):149-57.

Craig TK, Johnson S, McCrone P, Afuwape S, Hughes E, Gournay K. et al. Integrated care for co-occurring disorders: psychiatric symptoms, social functioning, and service costs at 18 months. Psychiatric Services. 2008;59(3):276-82.

Drake RE, Xie H, McHugo GJ, Shumway M. Three-year outcomes of long-term patients with co-occurring bipolar and substance use disorders. Biological Psychiatry. 2004;56(10):749-56.

Drebing CE, Van Ormer EA, Krebs C, Rosenheck R, Rounsaville B, Herz L, et al. The impact of enhanced incentives on vocational rehabilitation outcomes for dually diagnosed veterans. Journal of Applied Behavior Analysis. 2005;38:359-372.

Drebing CE, Van Ormer EA, Mueller L, Hebert M, Penk WE, Petry NM, et al. Adding contingency management intervention to vocational rehabilitation: outcomes for

dually diagnosed veterans. Journal of Rehabilitation Research and Development. 2007;44(6):851-65.

Eack SM, Hogarty SS, Greenwald DP, Litschge MY, McKnight SA, Bangalore SS, et al. Cognitive enhancement therapy in substance misusing schizophrenia: Results of an 18-month feasibility trial. Schizophrenia Research. 2015;161(2):478-83.

Essock SM, Mueser KT, Drake RE, Covell NH, McHugo GJ, Frisman LK, et al. Comparison of ACT and standard case management for delivering integrated treatment for co-occurring disorders. Psychiatric Services. 2006;57(2):185-96.

Fletcher TD, Cunningham JL, Calsyn RJ, Morse GA, Klinkenberg WD. Evaluation of treatment programs for dual disorder individuals: modeling longitudinal and mediation effects. Administration and Policy in Mental Health and Mental Health Services Research. 2008;35(4):319-36.

Graham HL, Copello A, Birchwood M, Orford J, McGovern D, Mueser KT, et al. A preliminary evaluation of integrated treatment for co-existing substance use and severe mental health problems: impact on teams and service users. Journal of Mental Health. 2006;15(5):577-91.

Haddock G, BarrowClough C, Tarrier N, Moring J, O'Brien R, Schofield N, et al. Cognitive–behavioural therapy and motivational intervention for schizophrenia and substance misuse. The British Journal of Psychiatry. 2003;183(5):418-26.

Havassy BE, Shopshire MS, Quigley LA. Effects of substance dependence on outcomes of patients in a randomized trial of two case management models. Psychiatric Services. 2000;51(5):639-44.

Hjorthøj R, Fohlmann A, Larsen AM, Gluud C, Arendt M, Nordentoft M. Specialized psychosocial treatment plus treatment as usual (TAU) versus TAU for patients with cannabis use disorder and psychosis: the CapOpus randomized trialC. Psychological Medicine. 2013;43(7):1499-510.

Hwang SW, Stergiopoulos V, O'Campo P, Gozdzik A. Ending homelessness among people with mental illness: the At Home/Chez Soi randomized trial of a Housing First intervention in Toronto. BMC Public Health. 2012;12(1):787.

Johnson S, Thornicroft G, Afuwape S, Leese M, White IR, Hughes E, et al. Effects of training community staff in interventions for substance misuse in dual diagnosis patients with psychosis (COMO study): cluster randomised trial. British Journal of Psychiatry. 2007;191:451-2.

Morse GA, Calsyn RJ, Dean Klinkenberg W, Helminiak TW, Wolff N, Drake RE et al. Treating homeless clients with severe mental illness and substance use disorders: costs and outcomes. Community Mental Health Journal. 2006;42(4):377-404.

Nagel T, Robinson G, Condon J, Trauer T. Approach to treatment of mental illness and substance dependence in remote indigenous communities: results of a mixed methods study. The Australian Journal of Rural Health. 2009;17(4):174-82.

Smelson D, Kalman D, Losonczy MF, Kline A, Sambamoorthi U, Hill LS, et al. A brief treatment engagement intervention for individuals with co-occurring mental

illness and substance use disorders: results of a randomized clinical trial. Community Mental Health Journal. 2012;48(2):127-32.

Striley CW, Nattala P, Ben Abdallah A, Dennis ML, Cottler LB. Enhanced case management versus substance abuse treatment alone among substance abusers with depression. Social Work Research. 2013.

Wenze SJ, Gaudiano BA, Weinstock LM, Tezanos KM, Miller IW. Adjunctive psychosocial intervention following hospital discharge for patients with bipolar disorder and comorbid substance use: a pilot randomized controlled trial. Psychiatry Research. 2015;228(3):516-25.

Xie H, McHugo GJ, Helmstetter BS, Drake RE. Three-year recovery outcomes for long-term patients with co-occurring schizophrenic and substance use disorders. Schizophrenia Research. 2005;75(2):337-48.

APPENDIX 8 Bibliography for excluded RCT evidence

	Study	Reason for exclusion
1.	Abebe KZ. A study of treatment by site interaction in multisite clinical trials. Pittsburgh, PA USA: University of Pittsburgh; 2009.	Conference abstract
2.	Adamson SJ, Sellman JD, Foulds JA, Frampton CM, Deering D, Dunn A, et al. A randomized trial of combined citalopram and naltrexone for nonabstinent outpatients with co-occurring alcohol dependence and major depression. Journal of Clinical Psychopharmacology. 2015;35(2):143-9.	Population not relevant - not severe mental illness
3.	Baker AL, Kavanagh DJ, Kay-Lambkin FJ, Hunt SA, Lewin TJ, Carr VJ, et al. Randomized controlled trial of MICBT for co-existing alcohol misuse and depression: outcomes to 36-months. Journal of Substance Abuse Treatment. 2014;46(3):281-90.	Intervention not delivered in the context of a multidisciplinary/specialist team
4.	Bartels SJ, Coakley EH, Zubritsky C, Ware JH, Miles KM, Areán PA, et al. Improving access to geriatric mental health services: a randomized trial comparing treatment engagement with integrated versus enhanced referral care for depression, anxiety, and at-risk alcohol use. American Journal of Psychiatry. 2004;161(8):1455-62.	Population not relevant: not dual diagnosis
5.	Battersby MW, Beattie J, Pols RG, Smith DP, Condon J, Blunden S. A randomised controlled trial of the Flinders Program™ of chronic condition management in Vietnam veterans with co-morbid alcohol misuse, and psychiatric and medical conditions. Australian and New Zealand Journal of Psychiatry. 2013;47(5):451-62.	Population not relevant: not dual diagnosis
6.	Bechdolf A, Pohlmann B, Güttgemanns J, Geyer C, Lindner K, Ferber C, et al. [State-dependent motivational interviewing for people with schizophrenia and substance use: results of a randomised controlled trial]. Der Nervenarzt. 2012;83(7):888-96	Foreign language paper
7.	Bellack AS1, Bennett ME, Gearon JS, Brown CH, Yang Y. Bellack AS, Bennett ME, Gearon JS, Brown CH, Yang Y. A randomized clinical trial of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. Archives of General Psychiatry. 2006;63(4):426-32	Intervention not delivered in the context of a multidisciplinary team

8.	Brown SA, Glasner-Edwards SV, Tate SR, McQuaid JR, Chalekian J, Granholm E. Integrated cognitive behavioral therapy versus twelve-step facilitation therapy for substance-dependent adults with depressive disorders. Journal of Psychoactive Drugs. 2006;38(4):449-60.	Not an RCT: quasi-randomised
9.	Calsyn RJ, Yonker RD, Lemming MR, Morse GA, Klinkenberg WD. Impact of assertive community treatment and client characteristics on criminal justice outcomes in dual disorder homeless individuals. Criminal Behaviour and Mental Health. 2005;15(4):236-48.	Outcomes not relevant
10.	Daughters SB, Braun AR, Sargeant MN, Reynolds EK, Hopko DR, Blanco C, et al. Effectiveness of a brief behavioral treatment for inner-city illicit drug users with elevated depressive symptoms: the life enhancement treatment for substance use (LETS Act!). Journal of Clinical Psychiatry. 2008;69(1):122.	Intervention and population not relevant
11.	DeMarce JM, Lash SJ, Stephens RS, Grambow SC, Burden JL. Promoting continuing care adherence among substance abusers with co-occurring psychiatric disorders following residential treatment. Addictive Behaviors. 2008;33(9):1104-12.	Not an RCT: quasi-randomised
12.	DiNitto DM, Webb DK, Rubin A. The effectiveness of an integrated treatment approach for clients with dual diagnoses. Research on Social Work Practice. 2002;12(5):621-41.	Intervention not delivered in the context of a multidisciplinary team
13.	Esposito-Smythers C, Spirito A, Kahler CW, Hunt J, Monti P. Treatment of co-occurring substance abuse and suicidality among adolescents: a randomized trial. Journal of Consulting and Clinical Psychology. 2011;79(6):728.	Population not relevant - not severe mental illness
14.	Gálvez Flórez JF, Rincón Salazar DA. Clinical management of dually diagnosed patients: treatment for drug abusing and dependent patients with major psychiatric comorbidities. Revista Colombiana de Psiquiatría. 2009;38(1):143-76.	Foreign language paper
15.	Goti J, Diaz R, Serrano L, Gonzalez L, Calvo R, Gual A, et al. Brief intervention in substance-use among adolescent psychiatric patients: a randomized controlled trial. European Child & Adolescent Psychiatry. 2010;19(6):503-11.	Population not relevant - not severe mental illness
16.	Gouzoulis-Mayfrank E, Koenig S, Schmitz-Buhl M, Daumann J. Schizophrenia and comorbid substance use disorder: integrated psychosocial treatment in a community psychiatric hospital: results from an RCT with 12 months follow-up. European Psychiatry. 2015;30:392.	Conference abstract
17.	Graham HL, Copello A, Birchwood M, Orford J, McGovern D, Mueser KT, et al. A preliminary evaluation of integrated treatment for co-existing substance use and severe mental health problems: Impact on teams and service users. Journal of	Not an RCT

	Mental Health. 2006;15(5):577-91.	
18.	Happell B, Stanton R, Hoey W, Scott D. Cardiometabolic health nursing to improve health and primary care access in community mental health consumers: protocol for a randomised controlled trial. International Journal of Nursing Studies. 2014;51(2):236-42	Study protocol
19.	Henderson CE. A Study of Competing Treatment Models for the Dually Diagnosed: Chemical Dependency Programs Versus Mental Health: Alliant International University, California School of Professional Psychology, Los Angeles; 2006.	Dissertation: full text not available
20.	Hides L, Carroll S, Catania L, Cotton SM, Baker A, Scaffidi A, et al. Outcomes of an integrated cognitive behaviour therapy (CBT) treatment program for co-occurring depression and substance misuse in young people. Journal of Affective Disorders. 2010;121(1):169-74.	Not an RCT
21.	Hjorthøj C, Fohlmann A, Larsen A, Madsen M, Vesterager L, Gluud C, et al. Interim Analysis of the CapOpus trial: a randomized, parallel-group, observer-blinded clinical trial of specialized addiction treatment versus treatment as usual for young patients with cannabis abuse and psychosis. Schizophrenia Research; 2010;117:190.	Conference abstract
22.	Hughes E, Wanigaratne S, Gournay K, Johnson S, Thornicroft G, Finch E, et al. Training in dual diagnosis interventions (the COMO Study): randomised controlled trial. BMC Psychiatry. 2008;8(1):12.	Study already included, outcome reported not relevant (staff attitudes, self-efficacy and knowledge)
23.	Hunter SB, Watkins KE, Hepner KA, Paddock SM, Ewing BA, Osilla KC, et al. Treating depression and substance use: a randomized controlled trial. Journal of Substance Abuse Treatment. 2012;43(2):137-51.	Population not relevant - not severe mental illness
24.	Kilbourne AM, Biswas K, Pirraglia PA, Sajatovic M, Williford WO, Bauer MS. Is the collaborative chronic care model effective for patients with bipolar disorder and co-occurring conditions? Journal of Affective Disorders. 2009;112(1):256-61.	Comparison not relevant; outcomes for participants with bipolar disorder were compared with outcomes for those with bipolar disorder and substance use disorders
25.	Latimer E, Rabouin D. The At Home/Chez Soi Canadian Study of Housing First for people who are homeless and mentally ill: study design and baseline data for the Montreal site. Psychiatrische Praxis. 2011;38(S 01):OP21_EC.	Conference abstract
26.	Lydecker KP, Tate SR, Cummins KM, McQuaid J, Granholm E, Brown SA. Clinical outcomes of an integrated treatment for depression and substance use disorders. Psychology of Addictive Behaviors. 2010;24(3):453.	Population not relevant - not severe mental illness
27.	Mangrum LF, Spence RT, Lopez M. Integrated versus parallel treatment of co-	No data available: only 66% of participants

	occurring psychiatric and substance use disorders. Journal of Substance Abuse Treatment. 2006;30(1):79-84.	were randomised and no disaggregated data is available
28.	Meister K, Rietschel L, Burlon M, Jannsen H, Bock T, Wegscheider K, et al. A cluster-randomized, parallel group, observer blind trial of a group based motivational-behavioural therapy for young people with psychosis and substance use disorder. Early Intervention in Psychiatry. 2010;4(s1):38-187.	Conference abstract
29.	Nuijten M, Blanken P, van der Hoorn B, van den Brink W, Hendriks V. A randomised controlled trial of outpatient versus inpatient integrated treatment of dual diagnosis patients: a failed but informative study. Mental Health and Substance Use. 2012;5(2):132-47.	Setting not relevant
30.	Odom AE. A Randomized Study of Integrated Outpatient Treatment and Assertive Community Treatment for Patients with Comorbid Mental Illness and Substance Use Disorders: Comparing Treatment Outcome for Domiciled and Homeless Patients. New School for Social Research; 2005.	Dissertation: full text not available
31.	Park T, Cheng D, Samet J, Winter M, Saitz R, editors. Effectiveness of chronic disease management for co-occurring substance and mental health disorders. Alcoholism-Clinical and Experimental Research. 2012: Wiley-Blackwell, New Jersey, USA.	Full text not available
32.	Park TW, Cheng DM, Samet JH, Winter MR, Saitz R. Chronic Care Management for Substance Dependence in Primary Care Among Patients With Co-Occurring Disorders. Psychiatric Services. 2015.	Full text not available
33.	Petersen L, Jeppesen P, Thorup A, Øhlenschlæger J, Krarup G, Østergård T, et al. Substance abuse and first-episode schizophrenia-spectrum disorders. The Danish OPUS trial. Early Intervention in Psychiatry. 2007;1(1):88-96.	Population not relevant - not dual diagnosis
34.	Rohde P, Waldron HB, Turner CW, Brody J, Jorgensen J. Sequenced versus coordinated treatment for adolescents with comorbid depressive and substance use disorders. Journal of Consulting and Clinical Psychology. 2014;82(2):342	Population not relevant - not severe mental illness
35.	Salloum I, Douaihy A, Daley D, Kelly T, Cornelius J, Kirisci L, editors. Integrated individual therapy for bipolar disorder and alcoholism: results from a randomized pilot study. Bipolar Disorders. 2009. Wiley-Blackwell Publishing, Malden, USA.	Conference abstract
36.	Schmitz JM, Averill P, Sayre S, McCleary P, Moeller FG, Swann A. Cognitive–behavioral treatment of bipolar disorder and substance abuse: a preliminary randomized study. Addictive Disorders & Their Treatment. 2002;1(1):17-24.	Intervention not delivered in the context of a multidisciplinary team
37.	Timko C, Chen S, Sempel J, Barnett P. Dual diagnosis patients in community or	Comparison not relevant

	hospital care: one-year outcomes and health care utilization and costs. Journal of Mental Health. 2006;15(2):163-77.	
38.	Weiss R, Griffin M, editors. Integrated group therapy for patients with bipolar disorder and substance dependence. Alcoholism-Clinical and Experimental Research. 2010. Wiley-Blackwell Publishing, Malden, USA.	Conference abstract
39.	Weiss RD, Griffin ML, Jaffee WB, Bender RE, Graff FS, Gallop RJ, Fitzmaurice GM. A "community-friendly" version of integrated group therapy for patients with bipolar disorder and substance dependence: a randomized controlled trial. Drug and Alcohol Dependence. 2009;104(3):212-9.	Intervention not delivered in the context of a multidisciplinary team
40.	Worley MJ, Tate SR, Brown SA. Mediational relations between 12-Step attendance, depression and substance use in patients with comorbid substance dependence and major depression. Addiction. 2012;107(11):1974-83.	Not an RCT: quasi-randomised
41.	Wüsthoff LE, Waal H, Gråwe RW. The effectiveness of integrated treatment in patients with substance use disorders co-occurring with anxiety and/or depression-a group randomized trial. BMC Psychiatry. 2014;14: 67.	Not severe mental illness

APPENDIX 9 Bibliography for excluded observational studies

	Study	Reason for exclusion
1.	Dau W, Schmidt A, Schmidt AF, Banger M. Is it reasonable to have the same treatment programme for party-drug and cannabis users? Results from the inpatient treatment model Bonn Model: Youth Addiction. Sucht. 2009;55(6):339-46.	Non-UK (Germany)
2.	Bayney R, St John-Smith P, Conhye A. MIDAS: a new service for the mentally ill with comorbid drug and alcohol misuse. The Psychiatrist. 2002;26(7):251-4.	No relevant data
3.	Battrick T, Hilbery O, Holloway S. Findings from the Making Every Adult Matter (MEAM) service pilots: a summary paper. Advances in Dual Diagnosis. 2013;6(2):66-75.	Population not relevant: not dual diagnosis
4.	Chilton J, Parrish M, Crone D. A preliminary review of an outpatient dual diagnosis recovery group programme. Groupwork. 2012;21(3):71-84.	No relevant data
5.	Dye S, Dannaram S, Loynes B, Dickenson R. Supervised community treatment: 2-year follow-up study in Suffolk. The Psychiatrist. 2012;36(8):298-302.	Not an intervention study
6.	Fakhoury W, Priebe S. An unholy alliance: substance abuse and social exclusion among assertive outreach patients. Acta Psychiatrica Scandinavica. 2006;114(2):124-31.	Not an intervention study
7.	Farren CK, Snee L, McElroy S. Gender differences in outcome at 2-year follow-up of treated bipolar and depressed alcoholics. Journal of Studies on Alcohol and Drugs. 2011;72(5):872-80.	Setting not relevant
8.	Gomes K, Hart KE. Adherence to recovery practices prescribed by Alcoholics Anonymous: benefits to sustained abstinence and subjective quality of life. Alcoholism Treatment Quarterly. 2009;27(2):223-35.	Intervention not relevant
9.	Thekiso TB, Murphy P, Milnes J, Lambe K, Curtin A, Farren CK. Acceptance and commitment therapy in the treatment of alcohol use disorder and comorbid affective disorder: a pilot matched control trial. Behavior Therapy. 2015.	Setting not relevant
10.	Davis KE, Devitt T, Rollins A, O'Neill S, Pavick D, Harding B. Integrated residential treatment for persons with severe and persistent mental illness: lessons in recovery.	Non-UK (USA)

	Journal of Psychoactive Drugs. 2006;38(3):263-72.	
11.	De Leon G. The addiction therapeutic communities for psychiatric disorders. Therapeutic Communities-London-Association of Therapeutic Communities. 2005;26(4):405.	Book
12.	Deady M, Kay-Lambkin F, Teesson M, Mills K. Developing an integrated, Internet-based self-help programme for young people with depression and alcohol use problems. Internet Interventions. 2014;1(3):118-31.	Non-UK (Australia)
13.	Deranja E, Manring J, Gregory R, J. Selected Posters from the 2012 Poster Session of the American Psychoanalytic Association: A Manual-Based Treatment Approach for. Journal of the American Psychoanalytic Association. 2012;60(3):591-8.	Conference abstract
14.	DiNitto DM, Webb DK, Rubin A, Morrison-Orton D, Wambach KG. Self-help group meeting attendance among clients with dual diagnoses. Journal of Psychoactive Drugs. 2001;33(3):263-72.	Non-UK (USA)
15.	Dugmore L. Partnership working in dual diagnosis. Nursing Times. 2010;107(7):20-1.	No relevant data
16.	Egelko S, Galanter M, Dermatis H, Jurewicz E, Jamison A, Dingle S, et al. Improved psychological status in a modified therapeutic community for homeless MICA men. Journal of Addictive Diseases. 2002;21(2):75-92.	Non-UK (USA)
17.	Filia S, Lee S, Sinclair K, Wheelhouse A, Wilkins S, de Castella A, et al. Demonstrating the effectiveness of less restrictive care pathways for the management of patients treated with clozapine. Australasian Psychiatry. 2013;21(5):449-55.	Non-UK (USA)
18.	Finnell DS, Osborne FH. Stages of change for psychotropic medication adherence and substance cessation. Archives of Psychiatric Nursing. 2006;20(4):166-74.	Non-UK (USA)
19.	Fleischmann H. Chronic Alcoholics with Multiple Impairments and Alcoholics in Rehabilitation-Two Different Groups of Alcoholics in a Psychiatric Hospital. Sucht. 2001;47(5):321-30.	Non-UK (German)
20.	Friedmann PD, Hendrickson JC, Gerstein DR, Zhang Z. Designated case managers as facilitators of medical and psychosocial service delivery in addiction treatment programs. The Journal of Behavioral Health Services & Research. 2004;31(1):86-97.	Non-UK (USA)
21.	Gardstrom SC, Bartkowski J, Willenbrink J, Diestelkamp WS. The impact of group music therapy on negative affect of people with co-occurring substance use disorders and mental illnesses. Music Therapy Perspectives. 2013;31(2):116-26.	Non-UK (USA)

22.	Garland AF, Aarons GA, Brown SA, Wood PA, Hough RL. Diagnostic profiles associated with use of mental health and substance abuse services among high-risk youths. Psychiatric Services. 2003;54(4):562-4.	Non-UK (USA)
23.	Gilbert AR, Domino ME, Morrissey JP, Gaynes BN. Differential service utilization associated with trauma-informed integrated treatment for women with co-occurring disorders. Administration and Policy in Mental Health and Mental Health Services Research. 2012;39(6):426-39.	Non-UK (USA)
24.	Gobbart S. 'Changing Habits': an evaluation of a dual diagnosis focused, integrated, multimodal, psychosocial education and skill building group programme delivered in a community-based setting. Mental Health and Substance Use. 2013;6(1):29-46.	Non UK (Australia)
25.	Goldstein BI, Goldstein TR, Collinger KA, Axelson DA, Bukstein OG, Birmaher B, et al. Treatment development and feasibility study of family-focused treatment for adolescents with bipolar disorder and comorbid substance use disorders. Journal of Psychiatric Practice. 2014;20(3):237.	Non-UK (USA)
26.	Grella CE, Joshi V, Hser Y-I. Effects of comorbidity on treatment processes and outcomes among adolescents in drug treatment programs. Journal of Child & Adolescent Substance Abuse. 2004;13(4):13-31.	Non-UK (USA)
27.	Guo S, Biegel DE, Johnsen JA, Dyches H. Assessing the impact of community-based mobile crisis services on preventing hospitalization. Psychiatric Services. 2014.	Non-UK (USA)
28.	Helmus TC, Saules KK, Schoener EP, Roll JM. Reinforcement of counseling attendance and alcohol abstinence in a community-based dual-diagnosis treatment program: A feasibility study. Psychology of Addictive Behaviors. 2003;17(3):249.	Non-UK (USA)
29.	Hesse M, Pedersen MU. Easy-access services in low-threshold opiate agonist maintenance. International Journal of Mental Health and Addiction. 2008;6(3):316-24.	Non-UK (Denmark)
30.	Humphreys K, Moos R. Can encouraging substance abuse patients to participate in self-help groups reduce demand for health care? a quasi-experimental study. Alcoholism: Clinical and Experimental Research. 2001;25(5):711-6.	Non-UK (USA)
31.	Hunt GE, Bergen J, Bashir M. Medication compliance and comorbid substance abuse in schizophrenia: impact on community survival 4 years after a relapse. Schizophrenia Research. 2002;54(3):253-64.	Non-UK (Australia)
32.	Karper L, Kaufmann M, Millspaugh G, Vega E, Stern G, Stern G, et al. Coordination of care for homeless individuals with comorbid severe mental disorders and	Non-UK (USA)

	substance-related disorders. Journal of Dual Diagnosis. 2008;4(2):142-57.	
33.	King R, Jordan A, Mazurek E, Earle K, Earle E, Runham A. Assertive community treatment--dually diagnosed: the hyphen was the easy part. Mental Health Aspects of Developmental Disabilities. 2009;12(1):1.	Non UK (Canada)
34.	Klag SML, O'Callaghan FV, Creed PA, Zimmer-Gembeck M. Motivating young people towards success: evaluation of a motivational interviewing-integrated treatment program for COD clients in a residential therapeutic community. Therapeutic Communities. 2009;30(4):366-386.	Non-UK (Australia)
35.	Kortrijk HE, Mulder C, van Vliet D, van Leeuwen C, Jochems E, Staring A. Changes in motivation for treatment in precontemplating dually diagnosed patients receiving assertive community treatment. Community Mental Health Journal. 2013;49(6):733-41.	Non-UK (Netherlands)
36.	Kortrijk HE, Mulder CL, Drukker M, Wiersma D, Duivenvoorden HJ. Duration of assertive community treatment and the interpretation of routine outcome data. Australian and New Zealand Journal of Psychiatry. 2012;46(3):240-8.	Non-UK (Netherlands)
37.	Kuehn BM. Bipolar Disorder and Addiction. JAMA. 2010;303(20):2022	Non-UK (USA)
38.	Kuehn BM. Integrated care key for patients with both addiction and mental illness. JAMA. 2010;303(19):1905-7.	Non-UK (USA)
39.	Küfner H, Hackmann K, Nees S, Storz S, Shaw R, Reuter B, et al. Motivation of drug addicts not responding to treatment. Development and trial of a motivational programme for drug addicts not responding to treatment. Suchtmedizin. 2007;9(4):208-17.	Non-UK (Germany)
40.	Lambert M, Conus P, Lubman D, Wade D, Yuen H, Moritz S, et al. The impact of substance use disorders on clinical outcome in 643 patients with first-episode psychosis. Acta Psychiatrica Scandinavica. 2005;112(2):141-8.	Non-UK (Australia)
41.	Levin S, Madover S, Wilson S. A recovery approach to bring about 'CHANGES'. Behavioral Healthcare. 2006;26(7):36-7, 9.	Non-UK (USA)
42.	Lin W-F. The treatment of substance abuse disorders by the psychological forgiveness. Educational Psychology. 2010;41(4):859-84.	Non-UK (China)
43.	MacDonald EM, Luxmoore M, Pica S, Tanti C, Blackman J-M, Catford N, et al. Social networks of people with dual diagnosis: the quantity and quality of relationships at different stages of substance use treatment. Community Mental Health Journal. 2004;40(5):451-64.	Non-UK (Australia)

44.	Magura S, Laudet AB, Mahmood D, Rosenblum A, Knight E. Adherence to medication regimens and participation in dual-focus self-help groups. Psychiatric Services. 2002;53(3):310-6.	Non-UK (USA)
45.	Magura S, Rosenblum A, Betzler T. Substance use and mental health outcomes for comorbid patients in psychiatric day treatment. Substance Abuse: Research and Treatment. 2009;3:71.	Non-UK (USA)
46.	Malet L, Reynaud M, Llorca P-M, Falissard B. Impact of practitioner's training in the management of alcohol dependence: a quasi-experimental 18-month follow-up study. Substance Abuse Treatment, Prevention, and Policy. 2006;1(1):18.	Non-UK (France)
47.	Maremmani AGI, Rovai L, Bacciardi S, Rugani F, Pacini M, Pani PP, et al. The long-term outcomes of heroin dependent-treatment-resistant patients with bipolar 1 comorbidity after admission to enhanced methadone maintenance. Journal of Affective Disorders. 2013;151(2):582-9.	Non-UK (Italy)
48.	Maremmani I, Pacini M, Lazzeri A, Perugi G, Deltito J. Concurrent abuse of cannabis is associated with a shorter duration of hospitalization in treatment-resistant psychotic bipolar inpatients treated with clozapine. Addictive Disorders & Their Treatment. 2006;5(1):1-7.	Non-UK (Italy)
49.	Maremmani I, Pacini M, Lubrano S, Perugi G, Tagliamonte A, Pani PP, et al. Long-term outcomes of treatment-resistant heroin addicts with and without DSM-IV Axis 1 psychiatric comorbidity (dual diagnosis). European Addiction Research. 2008;14(3):134-42.	Non-UK (Italy)
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51.	Maybery D, Reupert A, Goodyear M. Goal setting in recovery: families where a parent has a mental illness or a dual diagnosis. Child & Family Social Work. 2015;20(3):354-363.	Non-UK (Australia)
52.	McCoy ML, Devitt T, Clay R, Davis KE, Dincin J, Pavick D, et al. Gaining insight: who benefits from residential, integrated treatment for people with dual diagnoses? Psychiatric Rehabilitation Journal. 2003;27(2):140.	Non-UK (USA)
53.	McHugh G, Mueser KT, Drake RE. Treatment of substance abuse in persons with severe mental illness. The Treatment of Schizophrenia: Status and Emerging Trends. 2001:137-52.	Non-UK (USA)
54.	Min S-Y, Whitecraft J, Rothbard AB, Salzer MS. Peer support for persons with co-	Non-UK (USA)

	occurring disorders and community tenure: a survival analysis. Psychiatric Rehabilitation Journal. 2007;30(3):207.	
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56.	Moos R, Schaefer J, Andrassy J, Moos B. Outpatient mental health care, self-help groups, and patients' one-year treatment outcomes. Journal of Clinical Psychology. 2001;57(3):273-87.	Non-UK (USA)
57.	Mueser KT, Fox L. A family intervention program for dual disorders. Community Mental Health Journal. 2002;38(3):253-70.	Non-UK (USA)
58.	Neighbors CJ, Zywiak WH, Stout RL, Hoffmann NG. Psychobehavioral risk factors, substance treatment engagement and clinical outcomes as predictors of emergency department use and medical hospitalization. Journal of Studies on Alcohol. 2005;66(2):295-304.	Non-UK (USA)
59.	Ostacher MJ, Perlis RH, Nierenberg AA, Calabrese J, Stange JP, Salloum I, et al. Impact of substance use disorders on recovery from episodes of depression in bipolar disorder patients: prospective data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). The American Journal of Psychiatry. 2010;167(3):289-97.	Non-UK (USA)
60.	Padgett DK, Stanhope V, Henwood BF, Stefancic A. Substance use outcomes among homeless clients with serious mental illness: comparing Housing First with treatment first programs. Community Mental Health Journal. 2011;47(2):227-32.	Non-UK (USA)
61.	Penn PE, Brooks AJ. Five years, twelve steps, and REBT in the treatment of dual diagnosis. Journal of Rational-Emotive and Cognitive-Behavior Therapy. 2000;18(4):197-208.	Non-UK (USA)
62.	Pressman M, Brook DW, Maidman P, Orlowski B. Clinical improvement in adolescents comorbid for substance abuse and psychiatric diagnoses through multiple group psychotherapy. Group. 2001;25(4):321-32	Non-UK (USA)
63.	Primm AB, Gomez MB, Tzolova-Iontchev I, Perry W, Vu HT, Crum RM. Severely mentally ill patients with and without substance use disorders: Characteristics associated with treatment attrition. Community Mental Health Journal. 2000;36(3):235-46.	Non-UK (USA)
64.	Pringle JL, Edmondston LA, Holland CL, Kirisci L, Emptage NP, Balavage VK, et al. The role of wrap around services in retention and outcome in substance abuse	Non-UK (USA)

	treatment: findings from the Wrap Around Services Impact Study. Addictive Disorders & Their Treatment. 2002;1(4):109-18.	
65.	Rao R. Outcomes from liaison psychiatry referrals for older people with alcohol use disorders in the UK. Mental Health and Substance Use. 2013;6(4):362-8.	Full text not available
66.	Ribeiro MS, Alves MJM, Guirro ÚBdP, Baldi BG. Alcoholism: the influence of the recognition of comorbidity on the adherence of patients to the therapeutic program. Revista Brasileira de Psiquiatria. 2004;53(2):124-32.	Non-UK (USA)
67.	Ribeiro MS, Ribeiro LC, Ferreira RA, De Souza GF. Characteristics of alcoholics to prolonged membership in an outpatient program. Revista de Exemplo. 2010;23(6):965-72.	Non-UK (Portugal)
68.	Ritsher JB, McKellar JD, Finney JW, Otilingam PG, Moos RH. Psychiatric comorbidity, continuing care and mutual help as predictors of five-year remission from substance use disorders. Journal of Studies on Alcohol. 2002;63(6):709-15.	Non-UK (USA)
69.	Rogers N, Lubman D, Allen N. Therapeutic alliance and change in psychiatric symptoms in adolescents and young adults receiving drug treatment. Journal of Substance Use. 2008;13(5):325-39.	Non-UK (Australia)
70.	Roozen H, Kerkhof A, Van den Brink W. Experiences with an outpatient relapse program (community reinforcement approach) combined with naltrexone in the treatment of opioid-dependence: effect on addictive behaviors and the predictive value of psychiatric comorbidity. European Addiction Research. 2003;9(2):53-8.	Non-UK (Spain)
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72.	Rus-Makovec M, Cebasek-Travnik Z. Co-occurring mental and somatic diagnoses of alcohol dependent patients in relation to long-term aftercare alcohol abstinence and well-being. Psychiatria Danubina. 2008;20(2):194-207.	Non-UK (Slovenia)
73.	Schulte S, Holland M. Report of the evaluation study of the Manchester Dual Diagnosis network. Unpublished report.	No relevant data
74.	Shane PA, Jasiukaitis P, Green RS. Treatment outcomes among adolescents with substance abuse problems: the relationship between comorbidities and post-treatment substance involvement. Evaluation and Program Planning. 2003;26(4):393-402.	Non-UK (USA)
75.	Shippee ND, Rosen BH, Angstman KB, Fuentes ME, DeJesus RS, Bruce SM, et al. Baseline screening tools as indicators for symptom outcomes and health services	Non-UK (USA)

	utilization in a collaborative care model for depression in primary care: a practice-based observational study. General Hospital Psychiatry. 2014;36(6):563-9.	
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77.	Stapleton R, Comiskey C. Anxiety and depression among opiate users who misuse substances during treatment. Irish Journal of Psychological Medicine. 2011;28(1):6.	Population not relevant: not dual diagnosis
78.	Ströhle A, Höfler M, Pfister H, Müller A-G, Hoyer J, Wittchen H-U, et al. Physical activity and prevalence and incidence of mental disorders in adolescents and young adults. Psychological Medicine. 2007;37(11):1657-66.	Non-UK (German)
79.	Stuyt EB, Meeker JL. Benefits of auricular acupuncture in tobacco-free inpatient dual-diagnosis treatment. Journal of Dual Diagnosis. 2006;2(4):41-52.	Non-UK (USA)
80.	Suzuki J, Zinser J, Klaiber B, Hannon M, Grassi H, Spinosa M, et al. Feasibility of implementing share medical appointments (SMAs) for office-based opioid treatment with buprenorphine: a pilot study. Substance Abuse. 2015;36(2):166-9.	Non-UK (USA)
81.	Sylvestre DL, Zweben JE. Integrating HCV services for drug users: a model to improve engagement and outcomes. International Journal of Drug Policy. 2007;18(5):406-10.	Non-UK (USA)
82.	Timko C, Sutkowi A, Cronkite RC, Makin-Byrd K, Moos RH. Intensive referral to 12-step dual-focused mutual-help groups. Drug and Alcohol Dependence. 2011;118(2):194-201.	Non-UK (USA)
83.	Tomlinson KL, Brown SA, Abrantes A. Psychiatric comorbidity and substance use treatment outcomes of adolescents. Psychology of Addictive Behaviors. 2004;18(2):160.	Non-UK (USA)
84.	Van Dorn RA, Kosterman R, Williams JH, Chandler K, Young MS, Catalano RF, et al. The relationship between outpatient mental health treatment and subsequent mental health symptoms and disorders in young adults. Administration and Policy in Mental Health and Mental Health Services Research. 2010;37(6):484-96.	Non-UK (USA)
85.	Van Vugt MD, Kroon H, Delespaul PA, Mulder CL. Assertive community treatment and associations with substance abuse problems. Community Mental Health Journal. 2014;50(4):460-5.	Non-UK (Netherlands)
86.	Vannoy SD, Mauer B, Kern J, Girn K, Ingoglia C, Campbell J, et al. A learning collaborative of CMHCs and CHCs to support integration of behavioral health and general medical care. Psychiatric Services. 2014.	Non-UK (USA)

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88.	White AR. Characteristics of three consumer cohorts in vocational rehabilitation: A comparison of consumers with dual-diagnosis, psychiatric, or substance use related disorders. Journal of Applied Rehabilitation Counseling. 2011;42(1):15.	Non-UK (USA)
89.	Witbeck G, Hornfeld S, Dalack GW. Emergency room outreach to chronically addicted individuals: A pilot study. Journal of Substance Abuse Treatment. 2000;19(1):39-43.	Non-UK (USA)
90.	Wornson BE. Impact of recovery high schools on student academic success, continued sobriety, and treatment outcome. Humanities and Social Sciences, 2014;74(9).	Dissertation: full text not available
91.	Young MS, Barrett B, Engelhardt MA, Moore KA. Six-month outcomes of an integrated assertive community treatment team serving adults with complex behavioral health and housing needs. Community Mental Health Journal. 2014;50(4):474-9.	Non-UK (USA)
92.	Ziedonis DM, Stern R. Dual recovery therapy for schizophrenia and substance abuse. Psychiatric Annals. 2001;31(4):255.	Non-UK (USA)
93.	Zubritsky C, Rothbard AB, Dettwyler S, Kramer S, Chhatre S. Evaluating the effectiveness of an integrated community continuum of care program for individuals with serious mental illness. Journal of Mental Health. 2013;22(1):12-21.	Population not relevant: not dual diagnosis
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95.	Zweben A. Integrating pharmacotherapy and psychosocial interventions in the treatment of individuals with alcohol problems. Journal of Social Work Practice in the Addictions. 2001;1(3):65-80.	Population not relevant: not dual diagnosis

APPENDIX 10 Evidence tables

These are presented in a separate file.

APPENDIX 11 Forest plots

These are presented in a separate file.