National Institute for Health and Care Excellence

Final

Rehabilitation in adults with complex psychosis and related severe mental health conditions

[O] Effective interventions for improving engagement in addressing substance misuse

NICE guideline NG181

Evidence review

August 2020

Final

This evidence review was developed by the National Guideline Alliance which is part of the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

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Effective interventions for improving engagement in addressing substance misuse

Review question: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Introduction

Substance misuse is common among people with complex psychosis and related severe mental health conditions. However, it can be challenging to encourage this population to take-up and continue with services aiming to address this problematic misuse. The aim of this review is to compare the effectiveness of interventions specific to rehabilitation that aim to improve the engagement of people with complex psychosis and severe mental illness in addressing substance misuse when it is occurring.

The title of the guideline changed to “Rehabilitation for adults with complex psychosis” during development. The previous title of the guideline has been retained in the evidence reviews for consistency with the wording used in the review protocols.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Adults (aged 18 years and older) with complex psychosis and other severe mental health conditions (as defined in scope) who misuse substances (including alcohol) and are currently receiving rehabilitation in an inpatient rehabilitation unit or while living in supported accommodation or in the community.
Intervention	Individual service user interventions: • Motivational interviewing • Psychoeducation Mental health service: • Training for staff (e.g. how to identify, manage and address) • Health promotion and information/advice resources • Screening/available diagnosis • Making links with substance misuse services • Commissioning of support/payment for services • Dual pathways • Service culture/approach/policy to substance use Assertive community treatment Substance misuse service, e.g.: • Adaptations to services to facilitate people with serious mental illness

	• Collaboration with mental health staff and experts • Joint care planning regarding mixing treatments (e.g. opiate substitutes and use of benzodiazepines) Peer support interventions: • Presence of peer support, buddies, groups etc. • Presence of experts by experience
Comparison	Standard care No intervention
Outcomes	**Critical** Engagement with substance misuse intervention: • Dropout rate • Measure of transition • Sessions attended • Sustained healthy behaviour **Important** Substance use: • Knowledge and motivation • Antisocial behaviours – e.g. incidences of violence, arrests Psychiatric symptoms Mortality

For further details see the review protocol in appendix A.

Clinical evidence

Included studies

1 randomised trial reported in 2 publications (Hellerstein 1995) was identified for this review. The included study is summarised in Table 2.

The RCT compares an integrated outpatient treatment versus non-integrated treatment for dual psychiatric and addictive disorders.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Hellerstein 1995 RCT USA	N=47 M/F = 36/11 Age = 31.9 ±6.7 Diagnosis: Schizophrenia = 14, Schizoaffective = 33	A manualised program (COPAD) of twice-per-week group therapy - integrating psychiatric and substance use treatment, and	Comparable levels and hours of substance abuse and psychiatric service psycho-therapy at separate sites, and provided	• Dropout rate: ○ Treatment retention (numbers still in attendance) at 4 and 8 months

Study	Population	Intervention	Comparison	Outcomes
	Substances used: Cocaine = 87.2% (inc. Crack = 40.4%), Marijuana = 76.6%, Alcohol = 91.5%	coordinated communication amongst clinicians	without formal case coordination.	• Psychiatric symptoms: ○ Addiction severity index – psychological composite score

COPAD: The Combined Psychiatric and Addictive Disorder (COPAD) intervention; M/F: male/female; RCT: randomised controlled trial

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Quality assessment of clinical outcomes included in the evidence review

See the clinical evidence profiles in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Clinical evidence statements

Comparison 1. Integrated outpatient treatment versus non-integrated treatment

Critical outcomes

Engagement (retention) with substance misuse intervention: Dropout rate

- Very low quality evidence from 1 RCT (n=47) showed a clinically important increase in retention at 4 months between people with schizophrenia and psychoactive substance use disorder who received an integrated treatment program for psychiatric and addictive disorder compared to those who received non-integrated treatment.
- Very low quality evidence from 1 RCT (n=47) showed no statistically significant difference in retention at 8 months between people with schizophrenia and psychoactive substance use disorder who received an integrated treatment program for psychiatric and addictive disorder compared to those who received non-integrated treatment.

Engagement (retention) with substance misuse intervention: measure of transition

No evidence was identified to inform this outcome

Engagement (retention) with substance misuse intervention: sessions attended

No evidence was identified to inform this outcome

Engagement (retention) with substance misuse intervention: sustained healthy behaviour

No evidence was identified to inform this outcome

Important outcomes

Substance use: knowledge and motivation

No evidence was identified to inform this outcome

Substance use: antisocial behaviours

No evidence was identified to inform this outcome

Psychiatric symptoms

- Very low quality evidence from 1 RCT (n=47) showed no statistically significant difference in the change in psychiatric symptoms from baseline to 4 or 8 months between people with schizophrenia and psychoactive substance use disorder who received an integrated treatment program for psychiatric and addictive disorder compared to those who received non-integrated treatment.

Mortality

No evidence was identified to inform this outcome

Economic evidence statements

No economic evidence was identified which was applicable to this review question.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The objective of the evidence review was to find interventions that improved engagement with substance misuse services. The critical outcomes for this evidence review were engagement related – including the amount of sessions attended, levels of dropout, measures of transition (to indicate increased service uptake) and sustained healthy behaviour. The important outcomes were changes to psychiatric symptoms, mortality, changes in antisocial behaviour (e.g. arrests or violent incidents), knowledge about substance misuse, and level of motivation to change.

The quality of the evidence

The evidence review identified 1 randomised trial of a dual pathway intervention to improve engagement with substance use services in a rehabilitation setting. No evidence was identified for individual service user interventions, assertive community treatment, substance misuse services, peer support interventions, and all other mental health service interventions aside from dual pathways.

Evidence about engagement with the substance misuse intervention (using dropout rates) and psychiatric symptoms was assessed as very low quality using GRADE. The quality of the evidence was downgraded due to risk of bias (unclear methods used for randomisation or blinding and biased sampling methods) and for imprecision. There was no evidence about other measures of engagement with substance misuse interventions, substance use or mortality.

As a result, the recommendations were mostly based upon committee consensus and adapting recommendations from existing NICE guidelines. The quality of evidence underlying these guidelines was not appraised in detail by the committee. However, because the population concerned in this review are a direct subpopulation of those specified in the existing recommendations it was considered sufficient. The committee identified the most relevant existing recommendations and then used their collective experience to make adaptions to the wording in order to make them more applicable to this population without changing the underlying message.

The lack of evidence for most of the interventions to increase engagement with substance abuse services meant the guideline committee made a research recommendation (see Appendix L).

Benefits and harms

There was limited evidence that integrated treatment programs for psychiatric and substance misuse problems had better retention after 4 months than non-integrated services. The committee accepted these findings, confirming that specialist integrated support is far easier to make relevant to population-specific problems - such as interactions between substances and medication, or how substances exacerbate psychotic symptoms. Integrated services would mean less travel for service users and would make them less likely to 'fall between the gaps' between services. However, reorganising or creating integrated services would be a major overhaul for most services across the UK. The committee were reluctant to make a recommendation with huge financial and resource implications when there was only one very low quality study supporting it. As a result, they chose not to draft a recommendation based on this evidence.

The committee recommended asking people about their substance and alcohol use as a screening upon entry to rehabilitation services. Entry and initial assessment was considered

the best time because it will ensure the best service provision and care planning from the start. The committee discussed their experience that a very high number of people (believed by them to be as much as half or more) in rehabilitation services had a comorbid substance use problem, making it a large enough issue to justify recommending this be asked about routinely.

The recommendation about assessing people's readiness to address their substance abuse was based upon qualitative evidence identified in "Evidence Report J: Approaches valued by service users". One evidence statement suggested the therapeutic relationship built up between service users and rehabilitation staff was a powerful motivator for addressing substance misuse. Another evidence statement suggested that an element of 'choice' or 'self-determination' from the service user was needed before they could address their problem. With these statements in mind the committee drafted this recommendation to encourage staff to use their judgement based upon the therapeutic alliance they've built up when assessing the readiness of service users to engage with support.

The committee made a recommendation to alert those in rehabilitation services to the three main related guidelines for the reader to find further information and guidance. These guidelines contain much more detailed recommendations on assessment, care planning, intervention and partnership between services with regards to substance misuse. Two of the existing guidelines relate specifically to all the population with psychosis and related conditions, and one related to alcohol misuse in all the general population. Although the focus of the current guideline is on rehabilitation and its specific subpopulation, the committee agreed that these existing guidelines should broadly still be applicable.

The committee agreed it was important to emphasise the responsibility of all rehabilitation services to consider and address substance use problems as an intrinsic part of their service. There is a high comorbidity of substance misuse amongst the rehabilitation service user population. Limited findings from the evidence search suggested that integrating substance misuse into mental health services is better than separate services, and although this evidence was not strong enough to make a strong recommendation about fully integrated services, this recommendation was intended to acknowledge the importance of some overlap between services. Qualitative evidence identified in "Evidence Report J: approaches valued by service users" suggested that a harm reduction approach is considered important by service users, rather than services being withheld until substance misuse is addressed. A lack of identified evidence on effectiveness meant that no specific interventions could be recommended, and so instead the committee listed what they believed were the most important targets for an effective service.

The recommendation about reasonable adjustments draws upon the Equalities Act 2010 which establishes the responsibility upon services to make reasonable adjustments to facilitate their use by groups with mental health disabilities. The committee formed this recommendation following a discussion that people with mental health difficulties often struggle with access to substance misuse services outside of mental health because they struggle to accommodate their extra needs.

A recommendation was made on training of all rehabilitation staff to recognise and care for people with coexisting substance use problems. This recommendation was adapted from 1.4.1 in CG120 "Healthcare professionals working within secondary care mental health services should ensure they are competent in the recognition, treatment and care of adults and young people with psychosis and coexisting substance misuse." It was adapted to focus on rehabilitation services rather than individual professionals, and also added a training component. The committee agreed these were the most relevant audience to target with the power and responsibility to implement changes.

A recommendation was also made which addressed an area that the committee thought was missing from existing recommendations and research. Commissioners were considered the people with most power to influence local services, and with a responsibility to make sure

they are working. This recommendation was made by consensus to encourage lead commissioners to make sure that local protocols and pathways are coherent and accessible, and that this is confirmed by monitoring and assessment.

Cost effectiveness and resource use

No relevant studies were identified in a systematic review of the economic evidence.

The committee considered the evidence relating to integrated treatment programs for psychiatric and substance misuse problems. Whilst noting the benefits of an integrated treatment program, the committee considered that the limitations pertaining to the clinical evidence, and the lack of evidence of cost effectiveness, meant that they could not justify recommendations that would entail the reorganisation of existing services which could have a large resource impact.

The recommendations to ask people with complex psychosis and severe mental illness about substance misuse upon entry to rehabilitation services was made by consensus and would be unlikely to warrant a high resource impact. Noting the limited included evidence in the accompanying clinical review, the committee made a recommendation to alert people in work in rehabilitation services to existing NICE guidance on coexisting severe mental illness and substance misuse. The committee did not believe this would entail an increase in resource use as the recommendations reflect standard practice, though, there may be some additional costs where staff training does not already cover recognition of substance misuse.

There may be some additional increase in costs for areas where there is under provision for people with complex psychosis with regards to access to existing available services. However, any increase in accessing such services is in accordance with providers' statutory obligations to make services accessible. Furthermore, due to the high comorbidity of substance misuse amongst the rehabilitation service user population, the health benefits of an uptake in existing services would offset any increase in costs from a wider NHS perspective.

Other factors the committee took into account

The current review question was focused on ways to increase engagement with substance misuse services. The committee noted that the identification of service users with substance use problems, approaches and interventions for addressing substance use problems, and care planning were also important areas for the current guideline's population. The committee highlighted that following existing guidance would be highly relevant:

- Coexisting severe mental illness (psychosis) and substance misuse: assessment and management in healthcare settings [NG58]
- Coexisting severe mental illness and substance misuse: community health and social care services [CG120]
- Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence [CG115]

The committee reviewed the identified evidence about integrating services to improve engagement however the strength of evidence was not enough to recommend a very substantial change to service organisation. Several recommendations were instead formed with reference to three existing guidelines identified above.

References

Hellerstein 1995

Hellerstein, D. J., Rosenthal, R. N., & Miner, C. R., A prospective study of integrated outpatient treatment for substance-abusing schizophrenic patients, The American Journal on Addictions, 4(1), 33-42, 1995

Hellerstein, D. J., Rosenthal, R. N., Miner, C. R., Integrating services for schizophrenia and substance abuse, Psychiatric Quarterly, 72(4), 291-306, 2001

Appendices

Appendix A – Review protocols

Review protocol for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Table 3: Review protocol for interventions that are effective in improving the engagement in addressing substance misuse

Field (based on PRISMA-P)	Content
Review question	What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?
Type of review question	Intervention review
Objective of the review	The aim of this review is to compare the effectiveness of interventions specific to rehabilitation that aim to improve the engagement of people with complex psychosis and severe mental illness in addressing substance misuse.
Eligibility criteria – population	Adults (aged 18 years and older) with complex psychosis and other severe mental health conditions (as defined in scope) who misuse substances (including alcohol) and are currently receiving rehabilitation in an inpatient rehabilitation unit or while living in supported accommodation or in the community.
Eligibility criteria – interventions	Individual service user interventions: • Motivational interviewing • Psychoeducation Mental health service: • Training for staff (e.g. how to identify, manage and address) • Health promotion and information/advice resources • Screening/available diagnosis • Making links with substance misuse services

Field (based on PRISMA-P)	Content
	• Commissioning of support/payment for services • Dual pathways • Service culture/approach/policy to substance use Assertive community treatment Substance misuse service, e.g.: • Adaptations to services to facilitate people with serious mental illness • Collaboration with mental health staff and experts • Joint care planning regarding mixing treatments (e.g. opiate substitutes and use of benzodiazepines) Peer support interventions: • Presence of peer support, buddies, groups etc. • Presence of experts by experience
Eligibility criteria – comparator	Standard care No intervention
Outcomes and prioritisation	**Critical** Engagement with substance misuse intervention: • Dropout rate • Measure of transition • Sessions attended • Sustained healthy behaviour **Important** Substance use: • Knowledge and motivation • Antisocial behaviours – e.g. incidences of violence, arrests Psychiatric symptoms Mortality

Field (based on PRISMA-P)	Content
Eligibility criteria – study design	Randomised controlled trials. If no RCTs are available for any of the interventions, comparative observational studies will be considered. Systematic review findings will be extracted from directly if the quality and detail of their synthesis is high – in the case of low quality syntheses (where important details are lost) the component studies will be extracted from individually.
Other inclusion exclusion criteria	Not focussed on smoking (comes under separate review question). Date limit: 1990 The date limit for studies after 1990 was suggested by the committee considering the change in provision of mental health services from institutionalised care in the 1970s to deinstitutionalises and community-based care from 1990s onwards. Country limit: UK, USA, Australasia, Europe, Canada. The committee limited to these countries because they have similar cultures to the UK, given the importance of the cultural setting in which mental health rehabilitation takes place. English language papers Complete peer reviewed papers only – abstracts, conferences papers and dissertations excluded.
Proposed sensitivity/sub-group analysis, or meta-regression	Interventions internal to rehabilitation services versus interventions external to rehabilitation services Other subgroups to be considered: • Service users' trait of 'risk taking' • Length of stay at service • Value based culture / social engagement (including therapeutic relationships – family, carers; team sports/activities) • Family involvement • Group therapy vs individual therapy • Inpatient vs supported accommodation

Field (based on PRISMA-P)	Content
	• Black and Asian ethnic minorities Observational studies should adjust for the following: • Age • Measure of clinical severity • Gender
Selection process – duplicate screening/selection/analysis	A random sample of the references identified in the search will be sifted by a second reviewer. This sample size of this pilot round will be at least 10% of the total, All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.
Data management (software)	NGA STAR software will be used for study sifting, data extraction, recording quality assessment using checklists and generating bibliographies/citations. RevMan will be used to generate plots and for any meta-analysis. 'GRADEpro' will be used to assess the quality of evidence for each outcome 'GRADEpro' was used to assess the quality of evidence for each outcome.
Information sources – databases and dates	Sources to be searched: Embase, Medline, PsycINFO, Cochrane library (CDSR and CENTRAL), DARE and HTA (via CRD) Limits (e.g. date, study design): Human studies /English language
Identify if an update	This review question is not an update
Author contacts	For details please see https://www.nice.org.uk/guidance/indevelopment/gid-ng10092
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).

Field (based on PRISMA-P)	Content
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/.
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual 2014
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods chapter of the guideline
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Gillian Baird in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods see supplementary document C.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England
PROSPERO registration number	Not registered

GRADE: Grading of Recommendations Assessment, Development and Evaluation; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NHS: National Health Service; UK: United Kingdom; USA: United States of America

Appendix B – Literature search strategies

Literature search strategies for review question: 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Databases: Embase/Medline/PsycINFO

Date searched: 12/12/2018

#	Searches
1	exp psychosis/ use emczd
2	Psychotic disorders/ use ppez
3	exp psychosis/ use psyh
4	(psychos?s or psychotic).tw.
5	exp schizophrenia/ use emczd
6	exp schizophrenia/ or exp "schizophrenia spectrum and other psychotic disorders"/ use ppez
7	(exp schizophrenia/ or "fragmentation (schizophrenia)"/) use psyh
8	schizoaffective psychosis/ use emczd
9	schizoaffective disorder/ use psyh
10	(schizophren* or schizoaffective*).tw.
11	exp bipolar disorder/ use emczd
12	exp "Bipolar and Related Disorders"/ use ppez
13	exp bipolar disorder/ use psyh
14	((bipolar or bipolar type) adj2 (disorder* or disease or spectrum)).tw.
15	Depressive psychosis/ use emczd
16	Delusional disorder/ use emczd
17	delusions/ use psyh
18	(delusion* adj3 (disorder* or disease)).tw.
19	mental disease/ use emczd
20	mental disorders/ use ppez
21	mental disorders/ use psyh
22	(psychiatric adj2 (illness* or disease* or disorder* or disabilit* or problem*)).tw.
23	((severe or serious) adj3 (mental adj2 (illness* or disease* or disorder* or disabilit* or problem*))).tw.
24	(complex adj2 (mental adj2 (illness* or disease* or disorder* or disabilit* or problem*))).tw.
25	or/1-24
26	(Rehabilitation/ or cognitive rehabilitation/ or community based rehabilitation/ or psychosocial rehabilitation/ or rehabilitation care/ or rehabilitation center/) use emczd
27	(exp rehabilitation/ or exp rehabilitation centers/) use ppez
28	(Rehabilitation/ or cognitive rehabilitation/ or neuropsychological rehabilitation/ or psychosocial rehabilitation/ or independent living programs/ or rehabilitation centers/ or rehabilitation counselling/) use psyh
29	residential care/ use emczd
30	(residential facilities/ or assisted living facilities/ or halfway houses/) use ppez
31	(residential care institutions/ or halfway houses/ or assisted living/) use psyh
32	(resident* adj (care or centre or center)).tw.
33	(halfway house* or assist* living).tw.
34	((inpatient or in-patient or long-stay) adj3 (psychiatric or mental health)).tw.
35	(Support* adj (hous* or accommodat* or living)).tw.
36	(rehabilitation or rehabilitative or rehabilitate).tw.
37	rehabilitation.fs.
38	or/26-37
39	Substance abuse/ use emczd

#	Searches
40	exp Substance-Related Disorders/ use ppez
41	exp Drug abuse/ use psyh
42	exp Drug abuse/ use emczd
43	exp Drug misuse/ use ppez
44	Drug Addiction/ use psyh
45	exp Drug dependence/ use emczd
46	"Substance Use Disorder"/ use psyh
47	alcoholism/ use ppez
48	alcoholism/ use psyh
49	((alcohol or cannabis or cocaine or drug or drugs or opioid or substance*) adj2 (abuse or abuser* or abusing or addict* or dependen* or misuse or overuse or overuser or problem* or "use" or user*)).tw.
50	alcoholism.tw.
51	(addict* adj2 (disorder* or disease*)).tw.
52	or/39-51
53	25 and 38 and 52
54	psychoeducation/ use emczd
55	psychoeducation/ use psyh
56	Psychoeducat*.tw.
57	motivational interviewing/
58	Motivational interview*.tw.
59	or/54-58
60	Staff training/ use emczd
61	Personnel training/ use psyh
62	((staff* or personnel or worker* or employee*) adj2 (train* or educat*)).tw.
63	or/60-62
64	health promotion/
65	(health* adj3 (promot* or advice)).tw.
66	64 or 65
67	"Diagnosis, Dual (Psychiatry)"/ use ppez
68	Dual diagnosis/ use psyh
69	((screen* or recognis* or available) adj2 diagnos*).tw.
70	(dual* adj (diagnosis or disorder*)).tw.
71	((comorbid* or co morbid* or coexist* or co exist* or cooccur* or co occur*) and ((alcohol or substance*) adj2 disorder*)).tw.
72	or/67-71
73	Drug dependence treatment/ use emczd
74	Substance abuse treatment centers/ use ppez
75	Drug rehabilitation/ use psyh
76	((drug or substance) adj (misuse or abuse or dependen* or rehabilitation or "use") adj2 (center* or centre* or facilit* or service* or program* or treat* or therap* or workshop* or work shop*)).tw.
77	or/73-76
78	Assertive community treatment/ use psyh
79	Assertive community treatment.tw.
80	78 or 79
81	peer group/ use emczd
82	exp peer group/ use ppez
83	exp social support/
84	(Peer adj3 (buddy or buddies or group* or support*)).tw.
85	or/81-84
86	Drug interaction/ use emczd
87	Drug interactions/ use ppez
88	Drug interactions/ use psyh
89	((drug* or medication) adj2 interact*).tw.

#	Searches
90	((adjunct* or mix* or combin*) adj2 (treat* or drug* or prescription* or medication*)).tw.
91	((collab* or joint or integrate* or combin*) adj2 (care or treat*)).tw.
92	or/86-91
93	59 or 63 or 66 or 72 or 77 or 80 or 85 or 92
94	53 and 93
95	limit 94 to (yr="1990 - current" and english language)
96	remove duplicates from 95
97	Letter/ use ppez
98	letter.pt. or letter/ use emczd
99	note.pt.
100	editorial.pt.
101	Editorial/ use ppez
102	News/ use ppez
103	news media/ use psyh
104	exp Historical Article/ use ppez
105	Anecdotes as Topic/ use ppez
106	Comment/ use ppez
107	Case Report/ use ppez
108	case report/ or case study/ use emczd
109	Case report/ use psyh
110	(letter or comment*).ti.
111	or/97-110
112	randomized controlled trial/ use ppez
113	randomized controlled trial/ use emczd
114	random*.ti,ab.
115	cohort studies/ use ppez
116	cohort analysis/ use emczd
117	cohort analysis/ use psyh
118	case-control studies/ use ppez
119	case control study/ use emczd
120	or/112-119
121	111 not 120
122	animals/ not humans/ use ppez
123	animal/ not human/ use emczd
124	nonhuman/ use emczd
125	"primates (nonhuman)"/
126	exp Animals, Laboratory/ use ppez
127	exp Animal Experimentation/ use ppez
128	exp Animal Experiment/ use emczd
129	exp Experimental Animal/ use emczd
130	animal research/ use psyh
131	exp Models, Animal/ use ppez
132	animal model/ use emczd
133	animal models/ use psyh
134	exp Rodentia/ use ppez
135	exp Rodent/ use emczd
136	rodents/ use psyh
137	(rat or rats or mouse or mice).ti.
138	or/121-137
139	96 not 138

1

Database: Cochrane Library

Date searched: 12/12/2018

ID	Search
#1	MeSH descriptor: [Psychotic Disorders] explode all trees
#2	(psychos?s or psychotic):ti,ab,kw
#3	MeSH descriptor: [Schizophrenia] explode all trees
#4	(schizophren* or schizoaffective*):ti,ab,kw
#5	MeSH descriptor: [Bipolar Disorder] explode all trees
#6	(((bipolar or bipolar type) near/2 (disorder* or disease or spectrum))):ti,ab,kw
#7	MeSH descriptor: [Delusions] this term only
#8	((delusion* near/3 (disorder* or disease))):ti,ab,kw
#9	MeSH descriptor: [Mental Disorders] this term only
#10	((psychiatric near/2 (illness* or disease* or disorder* or disabilit* or problem*))):ti,ab,kw
#11	(((severe or serious) near/3 (mental adj2 (illness* or disease* or disorder* or disabilit* or problem*)))):ti,ab,kw
#12	((complex near/2 (mental adj2 (illness* or disease* or disorder* or disabilit* or problem*)))):ti,ab,kw
#13	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14	MeSH descriptor: [Rehabilitation] this term only
#15	MeSH descriptor: [Rehabilitation, Vocational] this term only
#16	MeSH descriptor: [Residential Facilities] this term only
#17	MeSH descriptor: [Assisted Living Facilities] this term only
#18	MeSH descriptor: [Halfway Houses] this term only
#19	((resident* near (care or centre or center))):ti,ab,kw
#20	(((inpatient or in-patient or long-stay) near/3 (psychiatric or mental health))):ti,ab,kw
#21	(((Support*) near (hous* or accommodat* or living))):ti,ab,kw
#22	((halfway house* or assist* living)):ti,ab,kw
#23	(rehabilitation or rehabilitative or rehabilitate):ti,ab,kw
#24	(#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25	#13 and #24
#26	MeSH descriptor: [Substance-Related Disorders] explode all trees
#27	MeSH descriptor: [Drug Misuse] explode all trees
#28	MeSH descriptor: [Alcoholism] this term only
#29	((alcohol or cannabis or cocaine or drug or drugs or opioid or substance*) near/2 (abuse or abuser* or addict* or dependen* or misuse or overuse or overuser or problem* or "use" or user)):ti,ab,kw
#30	alcoholism:kw,ti,ab
#31	(addict* near/2 (disorder* or disease*)):ti,ab,kw
#32	#26 or #27 or #28 or #29 or #30 or #31
#33	#25 and #32
#34	psychoeducat*:kw,ti,ab
#35	MeSH descriptor: [Motivational Interviewing] this term only
#36	Motivational interview*:kw,ti,ab
#37	((staff* or personnel or worker* or employee*) near/2 (train* or educat*)):kw,ti,ab
#38	MeSH descriptor: [Health Promotion] this term only
#39	(health* near/3 (promot* or advice)):kw,ti,ab
#40	MeSH descriptor: [Diagnosis, Dual (Psychiatry)] this term only
#41	((screen* or recognis* or available) near/2 diagnos*):kw,ti,ab
#42	(dual* near (diagnosis or disorder*)):kw,ti,ab
#43	((comorbid* or co morbid* or coexist* or co exist* or cooccur* or co occur*) and ((alcohol or substance*) near/2 disorder*)):ti,ab,kw
#44	MeSH descriptor: [Substance Abuse Treatment Centers] this term only
#45	((drug or substance) near (misuse or abuse or dependen* or rehabilitation) near/2 (center* or centre* or facilit* or service* or program* or treat* or therap* or workshop* or work shop*)):kw,ti,ab

ID	Search
#46	(Assertive community treatment):kw,ti,ab
#47	MeSH descriptor: [Peer Group] explode all trees
#48	MeSH descriptor: [Social Support] explode all trees
#49	(Peer near/3 (buddy or buddies or group* or support*)):kw,ti,ab
#50	MeSH descriptor: [Drug Interactions] this term only
#51	((drug* or medication) near/2 interact*):kw,ti,ab
#52	((adjunct* or mix* or combin*) near/2 (treat* or drug* or prescription* or medication*)):kw,ti,ab
#53	((collab* or joint or integrate* or combin*) near/2 (care or treat*)):kw,ti,ab
#54	#34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53
#55	#33 and #54 with Cochrane Library publication date Between Jan 1990 and Dec 2018

1 **Database: CRD**

2 Date searched: 12/12/2018

#	Searches
1	MeSH DESCRIPTOR Psychotic Disorders EXPLODE ALL TREES IN DARE,HTA
2	(psychos*s or psychotic) IN DARE, HTA
3	MeSH DESCRIPTOR Schizophrenia EXPLODE ALL TREES IN DARE,HTA
4	(schizophren* or schizoaffective*) IN DARE, HTA
5	MeSH DESCRIPTOR Bipolar Disorder EXPLODE ALL TREES IN DARE,HTA
6	(((bipolar or bipolar type) NEAR2 (disorder* or disease or spectrum))) IN DARE, HTA
7	MeSH DESCRIPTOR Delusions IN DARE,HTA
8	(delusion* NEAR3 (disorder* or disease)) IN DARE, HTA
9	MeSH DESCRIPTOR Mental Disorders IN DARE,HTA
10	(psychiatric NEAR2 (illness* or disease* or disorder* or disabilit* or problem*)) IN DARE, HTA
11	((severe or serious) NEAR3 (mental NEAR2 (illness* or disease* or disorder* or disabilit* or problem*))) IN DARE, HTA
12	(complex NEAR2 (mental NEAR2 (illness* or disease* or disorder* or disabilit* or problem*))) IN DARE, HTA
13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
14	MeSH DESCRIPTOR Rehabilitation IN DARE,HTA
15	MeSH DESCRIPTOR Rehabilitation, Vocational IN DARE,HTA
16	MeSH DESCRIPTOR Residential Facilities IN DARE,HTA
17	MeSH DESCRIPTOR Assisted Living Facilities IN DARE,HTA
18	MeSH DESCRIPTOR Halfway Houses IN DARE,HTA
19	(resident* NEAR (care or centre or center)) IN DARE, HTA
20	((inpatient or in-patient or long-stay) NEAR3 (psychiatric or mental health)) IN DARE, HTA
21	((Support*) NEAR (hous* or accommodat* or living)) IN DARE, HTA
22	(halfway house* or assist* living) IN DARE, HTA
23	(rehabilitation or rehabilitative or rehabilitate) IN DARE, HTA
24	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
25	#13 AND #24

3

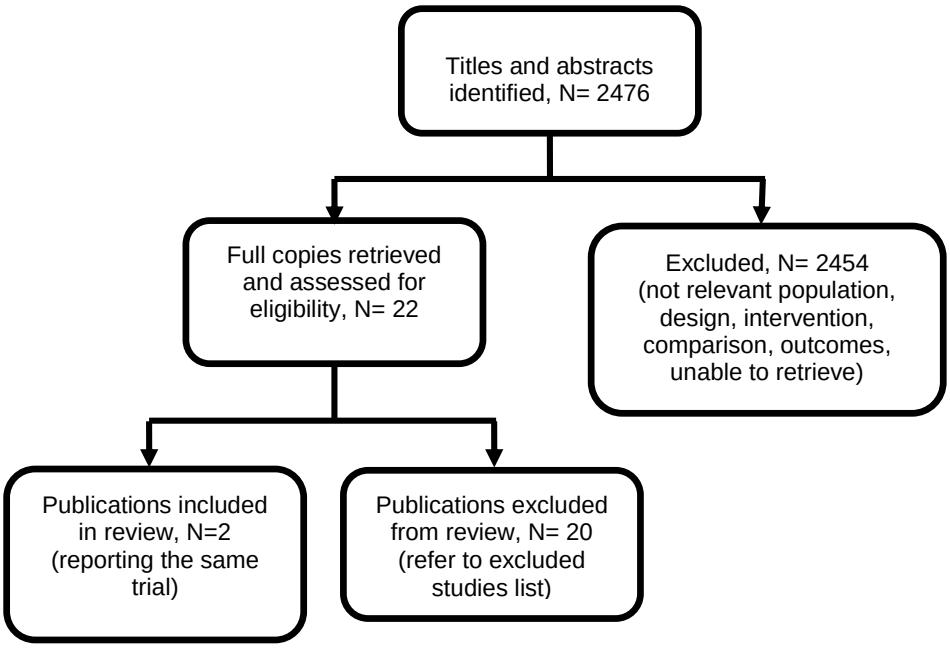
4

5

Appendix C – Clinical evidence study selection

Clinical study selection for review question: 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Table 4: Clinical evidence tables

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Hellerstein, D. J., Rosenthal, R. N., & Miner, C. R., A prospective study of integrated outpatient treatment for substance-abusing schizophrenic patients, The American Journal on Addictions, 4(1), 33-42, 1995 **Ref Id** 193105 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial	**Sample size** n= 47 randomised (n= 23 intervention; n=24 control) **Characteristics** M/F = 36/11 Age = 31.9 ±6.7 Mental health diagnosis: Schizophrenia = 14 Schizoaffective = 33 Mean duration of psychiatric illness: 7.5 (±6.7) years Substances used: Cocaine = 87.2%, (inc. Crack = 40.4%), Marijuana = 76.6%, Alcohol = 91.5% **Inclusion criteria**	**Interventions** The Combined Psychiatric and Addictive Disorder (COPAD) intervention which is a manualised program of twice-per-week group therapy integrating psychiatric and substance use treatment. Groups consist of 8-12 patients, and sessions last approximately 75mins. Components include supportive group substance abuse counselling, psychoeducation about mental illness and medication, psychoeducation about alcohol and drugs use and HIV, assessment and management of substance abuse issues, encouragement to attend and apply	**Details** Methods: Randomised Controlled trial. Non-starters were those that failed to attend at least two initial sessions, and the results were analysed with this group included (intention-to-treat analysis) and also without. **Outcomes measures** Treatment retention: The number of patients still in regular attendance of treatment sessions measured at 4 and 8 months. Psychiatric status: Addiction severity index – psychiatric composite score (ASI-PCS)	**Results** 18 of the 47 randomised participants were considered non-starters for not attending two or more sessions – 7 from the COPAD group and 11 from the control group. Retention (ITT - including non-starters): Of the 23 patients randomised to COPAD 16 (69.6%) were retained in treatment at 4 months and 11 (47.8%) were retained at 8 months. Of the 24 patients randomised to the control condition 9 (37.5%) were retained in treatment at 4 months and 6 (25%) were retained at 8 months.	**Limitations (assessed using Cochrane risk of bias tool)** Random sequence generation: unclear risk. Methods of randomisation not described. Allocation concealment: unclear risk. Allocation concealment not described. Blinding of participants and personnel: unclear risk. Blinding not described. Blinding of outcome assessors: unclear risk. Blinding not described. Incomplete outcome data (attrition bias): low risk. The key outcome was focused on recording dropouts.

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Aim of the study Test the hypothesis that for a population of patients with comorbid schizophrenia and PSUD, integrated treatment will lead to better outcome than non-integrated treatment, as defined by engagement and retention in treatment, rehospitalisation, and level of psychiatric and substance abuse severity. **Study dates** Not specified **Source of funding** Supported by UPHS grant R01 MH46327 from the National Institute of Mental Health.	Long-term outpatients aged 18-50. Diagnosis of schizophrenia-continuum disorder and DSM-III psychoactive substance abuse/dependence (PSUD). Had expressed a desire for substance misuse treatment. **Exclusion criteria** Life threatening illness. Antisocial personality disorder diagnosis. Global Assessment of Functioning (GAF) score <30 and Mini-Mental State Examination (MMSE) score <24. Need for long-term inpatient hospitalisation.	approaches, monthly medication management, and coordinated communication amongst clinicians. **Control group:** Comparable levels and hours of substance abuse and psychiatric service psychotherapy at separate sites, provided without a formal method of case coordination.	measured at baseline as well as 4 and 8 months. Higher scores indicate worse symptom severity.	The difference at 4 months was reported statistically significant (*P* =0.041; Fisher's exact test [two tailed]) while the difference at 8 months (*P*=0.012; Fisher's exact test [two tailed]) was not. The correlation between experimental group status and retention in treatment (ϕ = 0.32; df = 45) suggest a moderate effect size. Psychiatric symptoms: The ASI-PCS showed no significant differences between groups at baseline-to-4 months, baseline-to-8 months, or 4-8 months. A significant overall effect was shown for within subjects differences (Wilks' λ= 0.56; F[2, 14]=5.55; *P*=0.017), suggesting psychiatric symptoms improved over time for participants in general.	Selective reporting: high risk. *P*-values and significance tests not consistently reported.
Full citation Hellerstein, D. J., Rosenthal, R. N., Miner, C. R.,	***(For study details see Hellerstein et al. 1995)***				

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Integrating services for schizophrenia and substance abuse, Psychiatric Quarterly, 72(4), 291-306, 2001					

ASI-PCS: Addiction Severity Index – psychological composite score;; GAF: Global Assessment of Functioning; ITT: intention to treat; MMSE: Mini-Mental State Examination; PSUD: psychoactive substance misuse disorder;

Appendix E – Forest plots

Forest plots for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessment for these outcomes is provided in the GRADE profiles in appendix F.

Appendix F – GRADE tables

GRADE tables for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Table 5: Clinical evidence profile for comparison integrated outpatient treatment versus non-integrated treatment (ITT analysis)

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Integrated treatment**	**Non-integrated treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Treatment retention as measured by number of participants still in treatment at 4 months compared to baseline (Better indicated by higher numbers)												
1	randomised trial	very serious[1]	no serious inconsistency	no serious indirectness	Serious imprecision[2]	none	16/23 (69.6%)	9/24 (37.5%)	RR 1.86 (1.04 to 3.32)	322 more per 1000 (from 15 more to 870 more)	VERY LOW	CRITICAL
Treatment retention as measured by number of participants still in treatment at 8 months compared to baseline (Better indicated by higher numbers)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	Serious imprecision[2]	none	11/23 (47.8%)	6/24 (25.0%)	RR 1.91 (0.85 to 4.32)	227 more per 1000 (from 37 fewer to 830 more)	VERY LOW	CRITICAL
Improvement in psychiatric symptoms as measured by difference in mean ASI-PCS score at 4 months compared to baseline (Better indicated by bigger decrease in score)												
1	randomised trial	very serious[1]	no serious inconsistency	no serious indirectness	Very serious imprecision[3]	none	23	24	-	MD 0.11 more (-0.69 to 0.47)	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Integrated treatment**	**Non-integrated treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Improvement in psychiatric symptoms as measured by difference in mean ASI-PCS score at 8 months compared to baseline (Better indicated by bigger decrease in score)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	Very serious imprecision[3]	none	23	24	-	MD 0.01 less (-0.69 to 0.71)	VERY LOW	IMPORTANT

ASI-PCS: Addiction Severity Index – psychological composite score; CI: confidence interval; MD: mean difference; RR: relative risk

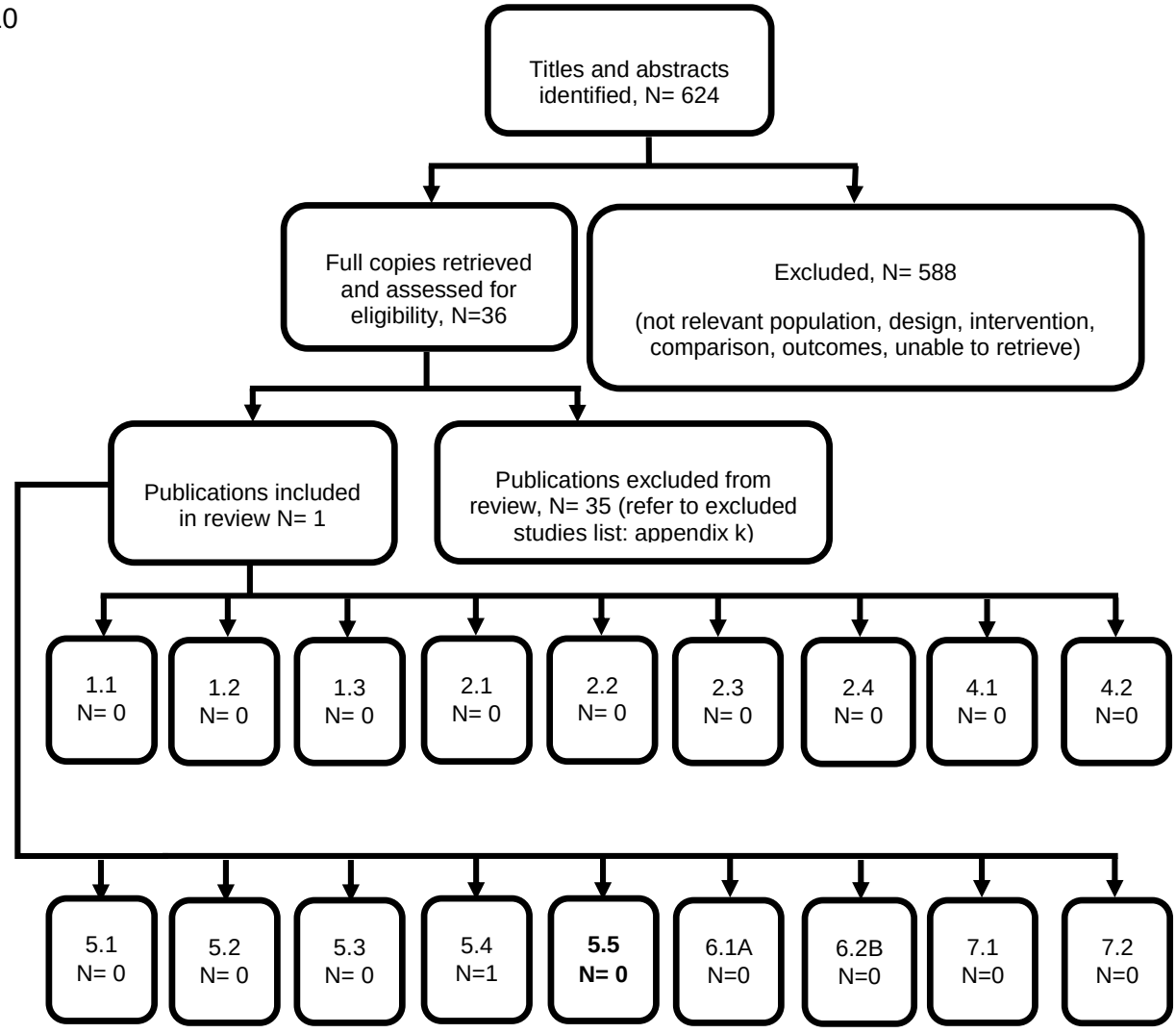
1 Evidence downgraded by 2 due to very serious risk of bias owing to unclear risk of detection bias as assessors were not reported as blind to treatment; and selection bias as participant sampling and randomisation methods were not clear.
2 Evidence downgraded by 1 due to risk of serious imprecision, 95% confidence intervals crosses one default MID.
3 Evidence downgraded by 2 due to risk of very serious imprecision, 95% confidence intervals cross both default MID for continuous outcomes, calculated as 0.5 of SD of baseline control (0.35).

Appendix G – Economic evidence study selection

Economic evidence study selection for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

A global health economic literature search was undertaken, covering all review questions in this guideline. However, as shown in Figure 2, no evidence was identified which was applicable for review question 5.5.

Figure 2: Health economic study selection flow chart



Appendix H – Economic evidence tables

Economic evidence tables for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

No evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

No evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Clinical studies

Table 6: Excluded clinical studies and reasons for their exclusion

Study	Reason for Exclusion
Brooner, R. K., Kidorf, M. S., King, V. L., Peirce, J., Neufeld, K., Stoller, K., Kolodner, K., Managing psychiatric comorbidity within versus outside of methadone treatment settings: a randomized and controlled evaluation, Addiction, 108, 1942-51, 2013	Did not meet inclusion criteria of >2/3rds population of interest
Brown, Clayton H., Bennett, Melanie E., Li, Lan, Bellack, Alan S., Predictors of initiation and engagement in substance abuse treatment among individuals with co-occurring serious mental illness and substance use disorders, Addictive Behaviors, 36, 439-447, 2011	Did not meet inclusion criteria of >2/3rds population of interest
Clark, R. E., Teague, G. B., Ricketts, S. K., Bush, P. W., Xie, H., McGuire, T. G., Drake, R. E., McHugo, G. J., Keller, A. M., Zubkoff, M., Cost-effectiveness of assertive community treatment versus standard case management for persons with co-occurring severe mental illness and substance use disorders, Health Services ResearchHealth Serv Res, 33, 1285-308, 1998	Outcome of interest not given
DeMarce, J. M., Lash, S. J., Stephens, R. S., Grambow, S. C., Burden, J. L., Promoting continuing care adherence among substance abusers with co-occurring psychiatric disorders following residential treatment, Addictive Behaviors, 33, 1104-1112, 2008	Mental health condition of participants not specified.
Drake, R. E., McHugo, G. J., Clark, R. E., Teague, G. B., Xie, H., Miles, K., Ackerson, T. H., Assertive community treatment for patients with co-occurring severe mental illness and substance use disorder: a clinical trial, American Journal of Orthopsychiatry, 68, 201-215, 1998	Service utilisation measured at baseline but not measured again as an outcome
Drebing, C. E., Van Ormer, E. A., Krebs, C., Rosenheck, R., Rounsaville, B., Herz, L., Penk, W., The impact of enhanced incentives on vocational rehabilitation outcomes for dually diagnosed veterans, Journal of Applied Behavior Analysis, 38, 359-72, 2005	Did not meet inclusion criteria of >2/3rds population of interest
Fletcher, T. D., Cunningham, J. L., Calsyn, R. J., Morse, G. A., Klinkenberg, W. D., Evaluation of treatment programs for dual disorder individuals: modeling longitudinal and mediation effects, Administration and policy in mental health, 35, 319â€• 336, 2008	Mental health condition of participants not specified.
Graham, H. L., Copello, A., Griffith, E., Freemantle, N., McCrone, P., Clarke, L., Walsh, K., Stefanidou, C. A., Rana, A., Birchwood, M., Pilot randomised trial of a brief intervention for comorbid substance misuse in psychiatric in-patient settings, Acta Psychiatrica Scandinavica, 133, 298-309, 2016	Only first-episode psychosis
Herman, S. E., BootsMiller, B., Jordan, L., Mowbray, C. T., Brown, W. G., Deiz, N., Bandla, H., Solomon, M., Green, P., Immediate outcomes of substance use treatment within a state psychiatric hospital, Journal of Mental Health Administration, 24, 126-138, 1997	Did not meet inclusion criteria of >2/3rds population of interest
Kidorf, M., Brooner, R. K., Gandotra, N., Antoine, D., King, V. L., Peirce, J., Ghazarian, S., Reinforcing integrated psychiatric service attendance in an opioid-agonist program: a randomized and controlled trial, Drug & Alcohol Dependence, 133, 30-6, 2013	Did not meet inclusion criteria of >2/3rds population of interest

Study	Reason for Exclusion
Kidorf, M., King, V. L., Peirce, J., Gandotra, N., Ghazarian, S., Brooner, R. K., Substance use and response to psychiatric treatment in methadone-treated outpatients with comorbid psychiatric disorder, Journal of Substance Abuse Treatment, 51, 64-9, 2015	Did not meet inclusion criteria of >2/3rds population of interest
Lee, M. T., Acevedo, A., Garnick, D. W., Horgan, C. M., Panas, L., Ritter, G. A., Campbell, K. M., Impact of agency receipt of incentives and reminders on engagement and continuity of care for clients with co-occurring disorders, Psychiatric Services, 69, 804-811, 2018	Mental health condition of participants not specified.
Lehman, A. F., Herron, J. D., Schwartz, R. P., Myers, C. P., Rehabilitation for adults with severe mental illness and substance use disorders. A clinical trial, Journal of Nervous and Mental Disease, 181, 86-90, 1993	Not measuring outcome of interest (engagement) in both groups
Pantalon, M. V., Swanson, A. J., Use of the University of Rhode Island Change Assessment to measure motivational readiness to change in psychiatric and dually diagnosed individuals, Psychology of Addictive Behaviors, 17, 91-7, 2003	Did not meet inclusion criteria of >2/3rds population of interest
Quinlivan, R., Hough, R., Crowell, A., Beach, C., Hofstetter, R., Kenworthy, K., Service utilization and costs of care for severely mentally ill clients in an intensive case management program, Psychiatric ServicesPsychiatr Serv, 46, 365-71, 1995	Not focused on substance misuse
Rush, B. R., Dennis, M. L., Scott, C. K., Castel, S., Funk, R. R., The interaction of co-occurring mental disorders and recovery management checkups on substance abuse treatment participation and recovery, Evaluation Review, 32, 7-38, 2008	Did not meet inclusion criteria of >2/3rds population of interest
Smelson, D., Kalman, D., Losonczy, M. F., Kline, A., Sambamoorthi, U., Hill, L. S., Castles-Fonseca, K., Ziedonis, D., 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, 48, 127-132, 2012	Only first-episode psychosis
Timko, C., Chen, S., Sempel, J., Barnett, P., Dual diagnosis patients in community or hospital care: One-year outcomes and health care utilization and costs, Journal of Mental Health, 15, 163-177, 2006	Did not meet inclusion criteria of >2/3rds population of interest
Tracy, K., Burton, M., Nich, C., Rounsaville, B., Utilizing peer mentorship to engage high recidivism substance-abusing patients in treatment, American Journal of Drug & Alcohol Abuse, 37, 525-31, 2011	Did not meet inclusion criteria of >2/3rds population of interest
Tsemberis, S., Gulcur, L., Nakae, M., Housing First, Consumer Choice, and Harm Reduction for Homeless Individuals with a Dual Diagnosis, American Journal of Public Health, 94, 651-656, 2004	Not an eligible intervention type

Economic studies

A global economic literature search was undertaken for this guideline, covering all 18 review questions in this guideline. The table below is a list of excluded studies across the entire guideline and studies listed were not necessarily identified for this review question.

Table 7: Excluded economic studies and reasons for their exclusion

Table 8: Excluded studies from the economic component of the reviewStudy	Reason for Exclusion
Aitchison, K J, Kerwin, R W, Cost-effectiveness of clozapine: a UK clinic-based study (Structured	Available as abstract only.

Table 8: Excluded studies from the economic component of the reviewStudy	Reason for Exclusion
abstract), British Journal of PsychiatryBr J Psychiatry, 171, 125-130, 1997	
Barnes, T. R., Leeson, V. C., Paton, C., Costelloe, C., Simon, J., Kiss, N., Osborn, D., Killaspy, H., Craig, T. K., Lewis, S., Keown, P., Ismail, S., Crawford, M., Baldwin, D., Lewis, G., Geddes, J., Kumar, M., Pathak, R., Taylor, S., Antidepressant Controlled Trial For Negative Symptoms In Schizophrenia (ACTIONS): a double-blind, placebo-controlled, randomised clinical trial, Health Technology Assessment (Winchester, England)Health Technol Assess, 20, 1-46, 2016	Does not match any review questions considered in the guideline.
Barton, Gr, Hodgekins, J, Mugford, M, Jones, Pb, Croudace, T, Fowler, D, Cognitive behaviour therapy for improving social recovery in psychosis: cost-effectiveness analysis (Structured abstract), Schizophrenia ResearchSchizophr Res, 112, 158-163, 2009	Available as abstract only.
Becker, T., Kilian, R., Psychiatric services for people with severe mental illness across western Europe: what can be generalized from current knowledge about differences in provision, costs and outcomes of mental health care?, Acta Psychiatrica Scandinavica, SupplementumActa Psychiatr Scand Suppl, 9-16, 2006	Not an economic evaluation.
Beecham, J, Knapp, M, McGilloway, S, Kavanagh, S, Fenyo, A, Donnelly, M, Mays, N, Leaving hospital II: the cost-effectiveness of community care for former long-stay psychiatric hospital patients (Structured abstract), Journal of Mental HealthJ Ment Health, 5, 379-94, 1996	Available as abstract only.
Beecham, J., Knapp, M., Fenyo, A., Costs, needs, and outcomes, Schizophrenia BulletinSchizophr Bull, 17, 427-39, 1991	Costing analysis prior to year 2000
Burns, T., Raftery, J., Cost of schizophrenia in a randomized trial of home-based treatment, Schizophrenia BulletinSchizophr Bull, 17, 407-10, 1991	Not an economic evaluation. Date is prior to 2000
Bush, P. W., Drake, R. E., Xie, H., McHugo, G. J., Haslett, W. R., The long-term impact of employment on mental health service use and costs for persons with severe mental illness, Psychiatric ServicesPsychiatr Serv, 60, 1024-31, 2009	A United States costing analysis. Outcomes which relate to the Welfare system differs in substantial ways to a UK context.
Chalamat, M., Mihalopoulos, C., Carter, R., Vos, T., Assessing cost-effectiveness in mental health: vocational rehabilitation for schizophrenia and related conditions, Australian & New Zealand Journal of PsychiatryAust N Z J Psychiatry, 39, 693-700, 2005	Australian cost-benefit analysis - welfare system differs from UK context.
Chan, S., Mackenzie, A., Jacobs, P., Cost-effectiveness analysis of case management versus a routine community care organization	Study conducted in Hong Kong. A costing analysis.

Table 8: Excluded studies from the economic component of the reviewStudy	Reason for Exclusion
for patients with chronic schizophrenia, Archives of Psychiatric NursingArch Psychiatr Nurs, 14, 98-104, 2000	
Clark, R. E., Teague, G. B., Ricketts, S. K., Bush, P. W., Xie, H., McGuire, T. G., Drake, R. E., McHugo, G. J., Keller, A. M., Zubkoff, M., Cost-effectiveness of assertive community treatment versus standard case management for persons with co-occurring severe mental illness and substance use disorders, Health Services ResearchHealth Serv Res, 33, 1285-308, 1998	Not cost-utility analysis. Cost-effectiveness analysis but does not consider UK setting. Date of study is prior to year 2000.
Crawford, M. J., Killaspy, H., Barnes, T. R., Barrett, B., Byford, S., Clayton, K., Dinsmore, J., Floyd, S., Hoadley, A., Johnson, T., Kalaitzaki, E., King, M., Leurent, B., Maratos, A., O'Neill, F. A., Osborn, D., Patterson, S., Soteriou, T., Tyrer, P., Waller, D., Matisse project team, Group art therapy as an adjunctive treatment for people with schizophrenia: a randomised controlled trial (MATISSE), Health Technology Assessment (Winchester, England)Health Technol Assess, 16, iii-iv, 1-76, 2012	Study not an economic evaluation.
Dauwalder, J. P., Ciompi, L., Cost-effectiveness over 10 years. A study of community-based social psychiatric care in the 1980s, Social Psychiatry & Psychiatric EpidemiologySoc Psychiatry Psychiatr Epidemiol, 30, 171-84, 1995	Practice has changed somewhat since 1980s - not a cost effectiveness study.
Garrido, G., Penades, R., Barrios, M., Aragay, N., Ramos, I., Valles, V., Faixa, C., Vendrell, J. M., Computer-assisted cognitive remediation therapy in schizophrenia: Durability of the effects and cost-utility analysis, Psychiatry ResearchPsychiatry Res, 254, 198-204, 2017	Cost effectiveness study, but population of interest is not focussed on rehabilitation for people with complex psychosis.
Hallam, A., Beecham, J., Knapp, M., Fenyo, A., The costs of accommodation and care. Community provision for former long-stay psychiatric hospital patients, European Archives of Psychiatry & Clinical NeuroscienceEur Arch Psychiatry Clin Neurosci, 243, 304-10, 1994	Economic evaluation predates 2000. Organisation and provision of care may have changed by some degree.
Hu, T. W., Jerrell, J., Cost-effectiveness of alternative approaches in treating severely mentally ill in California, Schizophrenia BulletinSchizophr Bull, 17, 461-8, 1991	A United States costing analysis. Outcomes which relate to the Welfare system differs in substantial ways to a UK context.
Jaeger, J., Berns, S., Douglas, E., Creech, B., Glick, B., Kane, J., Community-based vocational rehabilitation: effectiveness and cost impact of a proposed program model.[Erratum appears in Aust N Z J Psychiatry. 2006 Jun-Jul;40(6-7):611], Australian & New Zealand Journal of PsychiatryAust N Z J Psychiatry, 40, 452-61, 2006	Study is a New Zealand based costing analysis of limited applicability to the UK.
Jonsson, D., Walinder, J., Cost-effectiveness of clozapine treatment in therapy-refractory schizophrenia, Acta Psychiatrica	Costing analysis which predates year 2000.

Table 8: Excluded studies from the economic component of the reviewStudy	Reason for Exclusion
ScandinavicaActa Psychiatr Scand, 92, 199-201, 1995	
Knapp, M, Patel, A, Curran, C, Latimer, E, Catty, J, Becker, T, Drake, Re, Fioritti, A, Kilian, R, Lauber, C, Rossler, W, Tomov, T, Busschbach, J, Comas-Herrera, A, White, S, Wiersma, D, Burns, T, Supported employment: cost-effectiveness across six European sites (Structured abstract), World Psychiatry, 12, 60-68, 2013	Available as abstract only.
Lazar, S. G., The cost-effectiveness of psychotherapy for the major psychiatric diagnoses, Psychodynamic psychiatry, 42, 2014	Review of clinical and cost studies on psychotherapy. Studies cited do not match population for relevant review question.
Leff, J, Sharpley, M, Chisholm, D, Bell, R, Gamble, C, Training community psychiatric nurses in schizophrenia family work: a study of clinical and economic outcomes for patients and relatives (Structured abstract), Journal of Mental HealthJ Ment Health, 10, 189-197, 2001	Structured abstract. Not a cost effectiveness study.
Liffick, E., Mehdiyoun, N. F., Vohs, J. L., Francis, M. M., Breier, A., Utilization and Cost of Health Care Services During the First Episode of Psychosis, Psychiatric ServicesPsychiatr Serv, 68, 131-136, 2017	A United States costing analysis. Outcomes which relate to the Welfare system differs in substantial ways to a UK context.
Mihalopoulos, C., Harris, M., Henry, L., Harrigan, S., McGorry, P., Is early intervention in psychosis cost-effective over the long term?, Schizophrenia BulletinSchizophr Bull, 35, 909-18, 2009	Not a cost utility analysis. Australian costing analysis.
Perlis, R H, Ganz, D A, Avorn, J, Schneeweiss, S, Glynn, R J, Smoller, J W, Wang, P S, Pharmacogenetic testing in the clinical management of schizophrenia: a decision-analytic model (Structured abstract), Journal of Clinical Psychopharmacology, 25, 427-434, 2005	Structured abstract. Does not match any review question considered in this guideline.
Quinlivan, R., Hough, R., Crowell, A., Beach, C., Hofstetter, R., Kenworthy, K., Service utilization and costs of care for severely mentally ill clients in an intensive case management program, Psychiatric ServicesPsychiatr Serv, 46, 365-71, 1995	A United States costing analysis. Outcomes which relate to the Welfare system differs in substantial ways to a UK context.
Roine, E., Roine, R. P., Rasanen, P., Vuori, I., Sintonen, H., Saarto, T., Cost-effectiveness of interventions based on physical exercise in the treatment of various diseases: a systematic literature review, International Journal of Technology Assessment in Health CareInt J Technol Assess Health Care, 25, 427-54, 2009	Literature review on cost effectiveness studies based on physical exercise for various diseases and population groups - none of which are for complex psychosis.
Rosenheck, R A, Evaluating the cost-effectiveness of reduced tardive dyskinesia with second-generation antipsychotics (Structured abstract), British Journal of PsychiatryBr J Psychiatry, 191, 238-245, 2007	Structured abstract. Does not match any review question considered in this guideline.

Table 8: Excluded studies from the economic component of the reviewStudy	Reason for Exclusion
Rund, B. R., Moe, L., Sollien, T., Fjell, A., Borchgrevink, T., Hallert, M., Naess, P. O., The Psychosis Project: outcome and cost-effectiveness of a psychoeducational treatment programme for schizophrenic adolescents, Acta Psychiatrica ScandinavicaActa Psychiatr Scand, 89, 211-8, 1994	Not an economic evaluation. Cost effectiveness discussed in narrative only, with a few short sentences.
Sacristan, J A, Gomez, J C, Salvador-Carulla, L, Cost effectiveness analysis of olanzapine versus haloperidol in the treatment of schizophrenia in Spain (Structured abstract), Actas Luso-espanolas de Neurologia, Psiquiatria y Ciencias Afines, 25, 225-234, 1997	Available as abstract only.
Torres-Carbajo, A, Olivares, J M, Merino, H, Vazquez, H, Diaz, A, Cruz, E, Efficacy and effectiveness of an exercise program as community support for schizophrenic patients (Structured abstract), American Journal of Recreation Therapy, 4, 41-47, 2005	Available as abstract only
Wang, P S, Ganz, D A, Benner, J S, Glynn, R J, Avorn, J, Should clozapine continue to be restricted to third-line status for schizophrenia: a decision-analytic model (Structured abstract), Journal of Mental Health Policy and Economics, 7, 77-85, 2004	Available as abstract only.
Yang, Y K, Tarn, Y H, Wang, T Y, Liu, C Y, Laio, Y C, Chou, Y H, Lee, S M, Chen, C C, Pharmacoeconomic evaluation of schizophrenia in Taiwan: model comparison of long-acting risperidone versus olanzapine versus depot haloperidol based on estimated costs (Structured abstract), Psychiatry and Clinical Neurosciences, 59, 385-394, 2005	Taiwan is not an OECD country.
Zhu, B., Ascher-Svanum, H., Faries, D. E., Peng, X., Salkever, D., Slade, E. P., Costs of treating patients with schizophrenia who have illness-related crisis events, BMC Psychiatry, 8, 2008	USA costing analysis. The structure of the US health system means that costs do not translate well into a UK context.

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Appendix L – Research recommendations

Research recommendations for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

No research recommendations were made for this review question.

Appendix M – Evidence behind the reference recommendations

Supporting evidence and rationale/impact for adopted & adapted recommendations for review question 5.5: What interventions specific to rehabilitation are effective in improving the engagement of people with complex psychosis and other related severe mental health conditions in addressing substance misuse?

Table 9: Evidence behind the reference recommendations

Recommendation	Original rec	Supporting evidence	Committee's discussion – rationale and impact
1.6.14 Rehabilitation services should ensure that their healthcare staff are competent to recognise and care for people with psychosis and coexisting substance misuse	Adapted – CG120 1.4.1 Healthcare professionals working within secondary care mental health services should ensure they are competent in the recognition, treatment and care of adults and young people with psychosis and coexisting substance misuse.	CG120: Coexisting severe mental illness (psychosis) and substance misuse: assessment and management in healthcare settings (November 2011) This recommendation was formed by consensus: • The guideline development group felt there was a need to recommend that healthcare professionals should ensure they are competent in the recognition, treatment and care of people with psychosis and coexisting substance misuse. • Little research was available to determine how healthcare professionals should work together to provide the most appropriate care and treatment for people with psychosis and coexisting substance misuse.	The committed felt the need for a recommendation on training of all rehabilitation staff to recognise and care for people with coexisting substance use problems. It was adapted from CG120 to focus on rehabilitation services rather than individual professionals, and added a training component. The committee agreed these were the most relevant audience to target with the power and responsibility to implement changes.

Recommendation	Original rec	Supporting evidence	Committee's discussion – rationale and impact
		• Where evidence existed, it was often collected in different countries, such as the US, where the interventions, training and competence of professionals, the configuration of the healthcare system, and in particular, what counts as 'standard care', may be very different. • The recommendation was developed through an iterative process, synthesising the collective experience of the GDG to develop a framework of good practice recommendations that it is hoped will support healthcare professionals develop services in mental health and, in particular substance misuse, services so that people with psychosis and coexisting substance misuse can receive the care and treatment most likely to bring benefit and improve their lives and those of their families, carers or significant others	

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