National Institute for Health and Care Excellence

Draft for consultation

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

[C] Prevalence of comorbidity

NICE guideline TBC

Evidence review

January 2020

Draft for Consultation

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

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Review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

Introduction

People with complex psychosis may have comorbid mental health conditions and may be at high-risk of poor physical health outcomes. Such comorbid conditions will need to be taken into account when formulating rehabilitation plans.

Summary of the protocol

Please see Table 1 for a summary of the Population and Outcome (PO) characteristics of this review.

Table 1: Summary of the protocol (PO table)

Population	People with complex psychosis and related severe mental health conditions.
Outcome	Mental health (in addition to complex psychosis and related severe mental health conditions) • Anxiety • depression, • PTSD • Personality disorder • OCD Neurodevelopment: • Autism spectrum disorder, • ADHD • Borderline/mild learning disabilities • Cognitive impairments • Learning impairments • Executive impairments Acquired brain based disorders • Acquired cognitive injuries • Korsakoff (dementia, etc) • Acquired brain injury Substance misuse excluding tobacco Physical health: • respiratory disorders, • cardiovascular disorders, • Metabolic syndrome • Diabetes • Obesity • Osteoporosis • Kidney disease • Sexual dysfunction and reproductive health

	• Cancer • hepatitis • HIV • tuberculosis • Oral health problems Physical disabilities • Wheelchair users • Sensory impairments (vision + hearing)

ADHD: attention deficit hyperactivity disorder; HIV: human immunodeficiency virus; OCD: obsessive compulsive disorder; PTSD: posttraumatic stress disorder.

For further details see the review protocol in appendix A.

Clinical evidence

Included studies

Eighteen studies were identified for this review, 12 systematic reviews (Achim 2011, Ayano 2018, Correll 2017, Hunt 2016, Hunt 2018, Kincaid 2017, Kisely 2015, McEnery 2019, Preti 2018, Stubbs 2014, Vancampfort 2015 and Yapici-Eser 2018) and 6 observational studies (Gabilondo 2017, McDermid 2015, PHE 2018, Reilly 2015, Smith 2013 and Sylvia 2015).

The included studies are summarised in Table 2.

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

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

Table 2: Summary of included studies

Study	Population	Comorbidities
Achim 2011 Systematic review	Schizophrenia (N=4,032; 5 studies)	• Anxiety disorders
Ayano 2018 Systematic review	SMI (N=11,715; 18 studies)	• Hepatitis B • Hepatitis C • HIV infection
Correll 2017 Systematic review	SMI (N=3,211,768; 92 studies) Controls (N=113,383,368)	• Cardiovascular disease • Cardiovascular mortality
Gabilondo 2017 Cross-sectional study Spain	Schizophrenia (N=7,331) Controls (N=224,075)	• Dementia*
Hunt 2016 Systematic review	Bipolar syndrome (N=65,785; 78 studies)	• Alcohol misuse • Illicit drug misuse
Hunt 2018 Systematic review	Schizophrenia (N=165,811; 123 studies)	• Alcohol misuse • Illicit drug misuse
Kincaid 2017 Systematic review	Psychosis (N=800; 6 studies)	• Autism spectrum disorder

Study	Population	Comorbidities
Kisely 2015 Systematic review	SMI (N=3,316; 55 studies) Controls (N=29,906)	• Oral health
McDermid 2015 Longitudinal study USA	Bipolar disorder (N=1600)	• Borderline personality disorder
McEnery 2019 Systematic review	Psychosis (N= 92,522; 25 studies)	• Social anxiety
PHE 2018 UK	Schizophrenia (N= 9,357) Controls (N= 1,051,127)	• Stroke • COPD • Coronary heart disease • Hypertension • Diabetes • Obesity • Asthma • Cancer • Multiple comorbidities
Preti 2018 Systematic review	Bipolar disorder (N=3,391;15 studies)	• Panic disorder
Reilly 2015 Cross-sectional study UK	SMI (N=31,807) Controls (N=159,035)	• Learning disabilities*
Smith 2013 Cross-sectional study UK	Schizophrenia (N= 9,677) Controls (N= 1,414,701)	• Parkinson's disease* • Blindness • Hearing impairment
Stubbs 2014 Systematic review	Schizophrenia (N=3,038) Controls (N= 1,107)	• Osteoporosis
Sylvia 2015 Cross-sectional (as part of RCT) USA	Bipolar disorder (N=482)	• Head trauma*
Vancampfort 2015 Systematic review	SMI (N= 52,678;198 studies) Controls (N not reported)	• Metabolic syndrome • Obesity
Yapici-Eser 2018 Systematic review	Bipolar disorder (N not reported; 125 studies)	• Anxiety disorders

SMI: serious mental illness
**Other comorbidities were reported but are more completely covered elsewhere by systematic reviews*

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

GRADE methods were not used for this review question, however see appendix F for a summary of the evidence from the included studies.

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

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

Comorbid mental health conditions (in addition to complex psychosis and related severe mental conditions)

Anxiety

- Evidence from 1 systematic review (N=939; unclear risk of bias) indicated a prevalence of 11% of generalised anxiety disorder in people with schizophrenia.
- Evidence from 1 systematic review (N=92,522; unclear risk of bias) indicated a prevalence of 21% of social anxiety disorder in people with schizophrenia.
- Evidence from 1 systematic review (N=6,529; unclear risk of bias) indicated a prevalence of 13% of generalised anxiety disorder in people with bipolar disorder.

Depression

- No evidence was identified to inform this outcome.

PTSD

- Evidence from 1 systematic review (N=1,388; unclear risk of bias) indicated a prevalence of 12% of PTSD in people with schizophrenia.

Personality disorder

- Evidence from 1 cross-sectional study (N=1,600; low risk of bias) indicated a prevalence of 29% of borderline personality disorder in people with bipolar disorder.

OCD

- Evidence from 1 systematic review (N=3,007; unclear risk of bias) indicated a prevalence of 12% OCD in people with schizophrenia.
- Evidence from 1 systematic review (N=7,134; unclear risk of bias) indicated a prevalence of 10% of OCD in people with bipolar disorder.

Neurodevelopmental comorbidities

Autism spectrum disorder

- Evidence from 1 systematic review (N=800; unclear risk of bias) indicated a prevalence of 7% of autism spectrum disorder in people with psychosis.

ADHD

- No evidence was identified to inform this outcome.

Borderline/mild learning disabilities

- Evidence from 1 cross-sectional study (N=31,807; low risk of bias) indicated a prevalence of 2% of learning disability in people with SMI.

Cognitive impairments

- No evidence was identified to inform this outcome.

Learning impairments

- No evidence was identified to inform this outcome.

Executive impairments

- No evidence was identified to inform this outcome.

Acquired brain based disorders

Acquired cognitive injuries

- No evidence was identified to inform this outcome.

Korsakoff's syndrome (dementia, etc.)

- Evidence from 1 cross-sectional study (N=7,331; low risk of bias) indicated a prevalence of 6% of dementia in people with schizophrenia.

Acquired brain injury

- Evidence from 1 cross-sectional study (N=9,677; low risk of bias) indicated a prevalence of <1% of Parkinson's disease in people with schizophrenia.
- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 2% of stroke in people with SMI.
- Evidence from 1 cross-sectional study (N=482; unclear risk of bias) indicated a prevalence of 16% of prior head trauma in people with bipolar disorder.

Substance misuse - excluding tobacco

- Evidence from 1 systematic review (N=65,785; unclear risk of bias) indicated a prevalence of 37% of alcohol misuse in people with bipolar disorder.
- Evidence from 1 systematic review (N=165,811; unclear risk of bias) indicated a prevalence of 23% of alcohol misuse in people with schizophrenia.
- Evidence from 1 systematic review (N=65,785; unclear risk of bias) indicated a prevalence of 13% of illicit drug misuse in people with bipolar disorder.
- Evidence from 1 systematic review (N=165,811; unclear risk of bias) indicated a prevalence of 28% of illicit misuse in people with schizophrenia.

Physical health comorbidity

Respiratory disorders

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 3% of COPD in people with SMI.
- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 12% of asthma in people with SMI.

Cardiovascular disorders

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 3% of coronary heart disease in people with SMI.
- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 12% of hypertension in people with SMI.

Metabolic syndrome

- Evidence from 1 systematic review (N=52,678; unclear risk of bias) indicated a prevalence of 33% of metabolic syndrome in people with SMI.
- Evidence from 1 systematic review (N=29,596; unclear risk of bias) indicated a prevalence of 33% of metabolic syndrome in people with schizophrenia.
- Evidence from 1 systematic review (N=5,287; unclear risk of bias) indicated a prevalence of 32% of metabolic syndrome in people with bipolar syndrome.

Diabetes

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 9% of diabetes in people with SMI.

Obesity

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 13% of obesity in people with SMI.

Osteoporosis

- Evidence from 1 systematic review (N=3,038; unclear risk of bias) indicated a prevalence of 13% of osteoporosis in people with schizophrenia.

Kidney disease

- No evidence was identified to inform this outcome.

Sexual dysfunction and reproductive health

- No evidence was identified to inform this outcome.

Cancer

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 3% of cancer in people with SMI.

Hepatitis

- Evidence from 1 systematic review (N not reported; unclear risk of bias) indicated a prevalence of 18% of hepatitis B in people with SMI.
- Evidence from 1 systematic review (N not reported; unclear risk of bias) indicated a prevalence of 6% of hepatitis C in people with SMI.

HIV

- Evidence from 1 systematic review (N not reported; unclear risk of bias) indicated a prevalence of 8% of HIV in people with SMI.

Tuberculosis

- No evidence was identified to inform this outcome.

Oral health problems

- Evidence from 1 systematic review (N = 3,054; unclear risk of bias) indicated a prevalence of 65% of total loss of teeth in people with SMI, in a subgroup analysis of UK and Danish studies.
- Evidence from 1 systematic review (N = 3,054; unclear risk of bias) indicated a mean decayed, filled or missing teeth (DMFT) score of 30 in people with SMI, in a subgroup analysis of UK studies

Physical disabilities

Wheelchair users

- No evidence was identified to inform this outcome.

Sensory impairments (vision + hearing)

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 1% of blindness in people with SMI.
- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 5% of hearing loss in people with SMI.

Multiple comorbidities

Any physical health comorbidity

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 41% of any physical health comorbidity in people with SMI.

2 or more physical health comorbidities

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 16% of 2 or more physical health comorbidities in people with SMI.

3 or more physical health comorbidities

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 5% of 3 or more physical health comorbidities in people with SMI.

4 or more physical health comorbidities

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of 2% of 4 or more physical health comorbidities in people with SMI.

5 or more physical health comorbidities

- Evidence from 1 cross-sectional study (N=9,357; low risk of bias) indicated a prevalence of <1% of 5 or more physical health comorbidities in people with SMI.

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 committee were interested the prevalence of mental and physical health comorbidity in people with severe mental illness (SMI). They were aware of premature mortality in people with SMI and considered that this prevalence information could be used to focus on key areas for assessment and intervention in rehabilitation services to reduce premature mortality among people with SMI.

Although not included as an outcome in the review protocol, the committee also considered evidence about the relative rates of comorbidity in SMI compared to matched controls where this was reported. They acknowledged that even if prevalence of comorbidities was lower or no different in people with SMI compared to controls the absolute prevalence could still be high enough to justify routine assessment for that condition.

The quality of the evidence

GRADE methodology was not used for this review, instead evidence quality assessment for each outcome was based on the risk of bias of the individual study reporting that outcome. The risk of bias was either low or unclear: the uncertainty was usually when study populations were potentially not representative of the current UK population with SMI. For this reason, the committee prioritised recent population based UK studies and only considered other evidence when such studies were not available.

No evidence was identified for the outcomes of: depression, ADHD, cognitive impairments, learning impairments, executive impairments, acquired cognitive injuries, kidney disease, sexual dysfunction, reproductive health, tuberculosis and wheelchair use.

Where recommendations have been adopted or adapted from other NICE guidance, the evidence from those guidelines is presented in appendix M.

Benefits and harms

Working with other healthcare providers

The evidence indicated that people with severe mental illness are at increased risk of many comorbid conditions. The committee considered it crucial that lead commissioners develop local protocols with primary and secondary healthcare providers to ensure people in rehabilitation services receive appropriate physical healthcare, access to screening and health promotion. As part of this recommendation they highlighted the need for monitoring and reporting outcomes as a way of auditing the effectiveness of these local protocols, and the need for collaborative working among a number of different practitioners and services.

Assessment and care planning

The committee agreed that evidence about the rates of physical health conditions, mental health conditions and substance misuse in this population supported their recommendation to consider these as a part of a formal assessment which takes place within 4 weeks of entering the rehabilitation service. They were aware that such assessments are common practice, and take a range of needs into consideration. As part of this assessment they recommended an initial physical health check that combines elements of an ongoing annual health check (see below), and also health checks related to drug monitoring (see evidence report H for further details). As well as health needs, the committee included in the overall needs assessment other factors relevant to people with complex psychosis. Particular consideration was given to people with complex psychosis who have experienced abuse and trauma, either in a healthcare setting (for example detention, restraint, receiving medicines

against their will), and during their personal life. The committee agreed that identifying any comorbid health conditions, and assessing other common needs for people with complex psychosis, could contribute to a healthcare plan that would reduce morbidity and mortality, and improve people's function and quality of life. This underlined the recommendation to use the results of this initial assessment to develop a formulation to inform care plans jointly with the person, covering the identified areas of need.

The evidence about the prevalence of physical health comorbidity supported the committee's recommendation to be aware of multiple comorbidities and other physical health conditions including: COPD, cardiovascular disease, obesity, metabolic syndrome, diabetes, osteoporosis, dental problems and poor oral health and substance misuse. They agreed that these conditions may contribute to higher mortality in this group. They considered all people should be vigilant for them as there may be an opportunity for prevention or treatment and improvement in long term outcomes.

Responsibilities for healthcare providers

The committee made specific recommendations identifying who is responsible for delivering the physical health section of the care plans (primary care or rehabilitation). In their experience, access to physical health care services may be different depending on the setting of the rehabilitation service, and they thought it was crucial that people did not miss out on routine screening, monitoring or treatment of physical health. They outlined the role of inpatient rehabilitation in physical health, and adapted existing NICE guidance regarding GP responsibilities (see below). See also evidence report M for detail of co-ordinating physical healthcare by a nominated health professional.

Monitoring physical health

The committee recommended an annual physical health check (see details below). Evidence about the relatively high prevalence of hepatitis in inpatients with SMI led to the recommendation to be alert to the possibility of such infections. The committee agreed this may be related to homelessness, intravenous drug use or a history of sexually transmitted disease and that the NICE guideline on hepatitis B and C testing should be followed.

Care and treatment for physical health conditions

The committee agreed that risk factors and physical or mental health conditions identified during the initial health check should be managed according to existing NICE guidance (see below).

Although the evidence report identified a number of studies addressing the prevalence of comorbidities in people with complex psychosis and related conditions, the committee were aware that there was little data about the numbers of deaths caused by physical comorbidities in people with complex psychosis. The committee agreed that in the UK this data could be captured and recorded, and would contribute to the understanding of priority health needs in people with complex psychosis and related severe mental health conditions. The committee therefore suggested a research recommendation in this area.

Cost effectiveness and resource use

The committee noted that no relevant published economic evaluations had been identified for this topic.

The recommendation that a lead commissioner develop protocols and monitor outcomes for physical healthcare reflects current practice, and is a statutory obligation as outlined in Section 177 of the Mental Health Act 1983 (as amended).

The committee's recommendation for a comprehensive needs assessment reflects current practice. The committee recognised that comorbidity was a key issue within this population

and therefore recommended a formal initial physical health assessment and ongoing physical health checks. It was noted that the recommendations to offer physical health checks follows NICE guidance psychosis and schizophrenia in adults (CG178). If there is an increase in the amount of people who take part in these health checks, then there may be some additional resource impact. However, these costs may be offset in the longer term by the prevention of morbidity and future illness.

The recommendations relating to GPs monitoring the physical health of people and treating people with comorbid conditions is adapted from existing NICE guidance and reinforces best current practice. The recommendations for treatment should also be current practice.

Other factors the committee took into account

The committee had not originally planned to adapt recommendations from other guidelines for this evidence review and had intended to cross-refer to the recommendations about physical health and comorbidity from the NICE guidelines on psychosis and schizophrenia in adults and bipolar disorder. Although the committee were in general agreement with the content of these recommendations in some cases the wording was not appropriate for this guideline and for this reason some were adapted (see Appendix M).

Responsibilities for healthcare providers

Recommendations about primary healthcare from the NICE guideline on schizophrenia in adults were adapted (see appendix M). The committee considered they were consistent with the evidence about physical comorbidities, and would encourage GPs to keep case registers of people with SMI to monitor their physical and mental health, to perform regular health checks and to treat any health conditions identified.

Monitoring physical health

The committee agreed that in addition to an initial health assessment on entry to rehabilitation, there should be ongoing physical health checks. They recommended an annual health check, in line with other NICE guidance. They adapted consensus-based recommendations from the NICE guideline on psychosis and schizophrenia in adults and on bipolar disorder, using elements from the physical health checks in both guidelines, and also adding assessments of sexual health, vision, hearing and podiatry, smoking, alcohol and substance use, and thyroid function to the list checks, based on their clinical knowledge and experience and the evidence review. To increase the uptake of this health check, and to overcome access issues, they agreed it could be done either at the rehabilitation service by a nominated professional (see evidence report M) or at their GP practice. In line with other NICE guidance and best practice, the committee recommended sharing the results of the physical health check with the person and relevant practitioners. Additional physical health checks related to drug monitoring are reported in evidence report H.

The committee also adapted recommendations from the NICE guideline on schizophrenia in adults to routinely monitor for and treat other coexisting mental health conditions, including depression, anxiety and substance misuse, and adapted the recommendation by adding obsessive compulsive disorder, as it was identified as a common comorbidity.

Care and treatment for physical health conditions

The committee agreed that risk factors, and physical or mental health conditions identified during the initial health check, should be managed according to existing NICE guidance. For the treatment recommendation, the committee listed the same conditions as in the NICE schizophrenia and psychosis guideline, but added COPD to the list of conditions, given the high proportion of COPD in the population.

Equalities

The committee discussed that some comorbidities could be more common in certain ethnic groups, in those with substance abuse problems or in homeless people. They agreed, however, that their recommendations about monitoring and treating comorbidities would apply regardless of this and should not have an adverse impact on any specific group.

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Appendices

Appendix A – Review protocols

Review protocol for review question 1.3: What coexisting need to be considered when formulating a rehabilitation plan with people with complex psychosis

Table 3: Review protocol for prevalence of comorbidity

Field (based on PRISMA-P	Content
Review question	What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?
Type of review question	Prevalence
Objective of the review	
Eligibility criteria – population	People with complex psychosis and related severe mental health conditions. Studies with mixed populations should include at least 66% with complex psychosis and related severe mental health conditions. Mixed study population will be examined in a sensitivity analysis as a potential source of heterogeneity.
Eligibility criteria – predictive factor(s)	Mental health (in addition to complex psychosis and related severe mental health conditions) • Anxiety • depression, • PTSD, Personality disorder • OCD Neurodevelopment: • Autism spectrum disorder, • ADHD • Borderline/mild learning disabilities • Cognitive impairments • Learning impairments

Field (based on PRISMA-P	Content
	• Executive impairments Acquired brain based disorders • Acquired cognitive injuries • Korsakoff (dementia, etc.) • Acquired brain injury Substance misuse excluding tobacco Physical health: • respiratory disorders, • cardiovascular disorders, • Metabolic syndrome • Diabetes • Obesity • Osteoporosis • Kidney disease • Sexual dysfunction and reproductive health • Cancer • hepatitis • HIV • tuberculosis • Oral health problems Physical disabilities • Wheelchair users • Sensory impairments (vision + hearing)
Eligibility criteria – comparator(s)	Not applicable.
Outcomes and prioritisation	Prevalence of each characteristic or condition Point prevalence of each characteristic or condition in those currently in a rehabilitation service

Field (based on PRISMA-P	Content
Eligibility criteria – study design	Cross sectional studies, cohort studies
Other inclusion exclusion criteria	Date limit: 1990 Country limit: UK studies only. In the absence of UK evidence countries with similar baseline prevalence of complex psychosis and related severe mental health conditions within Australasia, Europe and Canada/USA. The GC 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.
Proposed sensitivity/sub-group analysis, or meta-regression	Sub-groups: • People in rehab versus not in rehab
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.
Information sources – databases and dates	Sources to be searched will include: Medline, Embase, PsycINFO, Cochrane library (CDSR and CENTRAL) and DARE and HTA (via CRD)
Identify if an update	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 supplementary document.
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 Dr 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 applicable

ADHD: attention deficit hyperactivity disorder; COPD: chronic obstructive pulmonary disease; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HIV: human immunodeficiency virus; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; OCD: obsessive compulsive disorder; PTSD: posttraumatic stress disorder; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Literature search strategies for review question 1.3: What coexisting need to be considered when formulating a rehabilitation plan with people with complex psychosis

Databases: Embase/Medline/PsycInfo

Date searched: 27/06/2019

#	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	*Anxiety/
27	(Anxiety disorder/ or *Depression/ or posttraumatic stress disorder/ or personality disorder/ or Autism/ or attention deficit disorder/ or *cognitive defect/ or acquired brain injury/ or Korsakoff psychosis/ or *dementia/) use emczd
28	(Anxiety Disorders/ or *Depression/ or Depressive Disorder, Major/ or Depressive Disorder/ or Stress Disorders, Post-Traumatic/ or personality disorders/ or exp Autism Spectrum Disorder/ or exp "Attention Deficit and Disruptive Behavior Disorders"/ or exp cognition disorders/ or exp Korsakoff Syndrome/ or dementia/) use ppez
29	(Anxiety Disorders/ or major depression/ or posttraumatic stress disorder/ or personality disorders/ or Autism Spectrum Disorders/ or exp Attention Deficit Disorder/ or cognitive impairment/ or Traumatic brain injury/ or korsakoffs psychosis/ or dementia/) use psyh
30	Obsessive Compulsive Disorder/
31	learning disorder/
32	(drug misuse/ or drug abuse/ or substance abuse/ or alcohol abuse/) use emczd
33	(exp Drug Misuse/ or alcoholism/) use ppez
34	(exp Drug abuse/ or exp alcohol abuse/) use psyh
35	(respiratory tract disease/ or *cardiovascular disease/ or *heart disease/ or metabolic disorder/ or *diabetes mellitus/ or Obesity/ or Osteoporosis/ or Kidney disease/ or Sexual dysfunction/ or Malignant neoplasm/ or Hepatitis/ or Human immunodeficiency virus/ or Tuberculosis/ or Mouth disease/ or Tooth disease/ or Physical disability/ or Wheelchair user/ or visual impairment/ or hearing impairment/) use emczd

#	Searches
36	(Respiratory Tract Diseases/ or cardiovascular diseases/ or heart diseases/ or Metabolic Diseases/ or diabetes mellitus/ or Obesity/ or Osteoporosis/ or Kidney diseases/ or Sexual Dysfunction, Physiological/ or Neoplasms/ or Hepatitis/ or HIV/ or Tuberculosis/ or Mouth diseases/ or Tooth diseases/ or Disabled persons/ or Visually impaired persons/ or hearing disorders/ or vision disorders/) use ppez
37	(Respiratory Tract Disorders/ or Cardiovascular Disorders/ or Heart Disorders/ or Metabolism Disorders/ or metabolic syndrome/ or exp diabetes/ or Obesity/ or Osteoporosis/ or Kidney diseases/ or exp Sexual Function Disturbances/ or Neoplasms/ or Hepatitis/ or HIV/ or Tuberculosis/ or Disabilities/ or exp Vision Disorders/ or exp hearing disorders/) use psyh
38	or/26-37
39	(*Comorbidity/ or multiple chronic conditions/) use emczd
40	(exp Comorbidity/ or multiple chronic conditions/) use ppez
41	(Comorbidity/ or Dual diagnosis/) use psyh
42	or/39-41
43	38 and 42
44	(anxiety or depression or ptsd or "posttraumatic stress" or "post-traumatic stress" or "personality disorder*" or "obsessive compulsive disorder" or autism or "Asperger* syndrome" or "attention deficit disorder*"" or ADHD or "learning disorder*" or "learning disabilit*" or "cognitive impairment*" or "learning impairment*" or "executive impairment*" or korsakoff* or dementia).tw.
45	(acquired adj (brain or cognitive) adj2 (disorder* or injury or injuries)).tw.
46	((drug* or alcohol or substance*) adj2 (misuse or abuse)).tw.
47	Alcoholism.tw.
48	((respiratory or cardio* or metabolic or heart or kidney* or lung*) adj2 (disease* or disorder*)).tw.
49	(Diabetes or obesity or osteoporosis or cancer* or neoplasm* or malignan* or hepatitis or HIV or tuberculosis or "Human immunodeficiency virus" or "Sexual dysfunction" or disability or "Wheelchair user*").tw.
50	((tooth or mouth) adj2 disease*).tw.
51	((visual* or hearing or vision) adj2 (impair* or disorder*)).tw.
52	or/44-51
53	(comorbid* or co-morbid* or multimorbid* or multi-morbid* or ((coexist* or co-exist*) adj2 (condition* or disease* or disorder* or illness*))).tw.
54	52 and 53
55	43 or 54
56	(*Epidemiology/ or *prevalence/ or *incidence/) use emczd
57	(Epidemiology/ or prevalence/ or incidence/) use ppez
58	epidemiology/ use psyh
59	(Epidemiology or prevalence or incidence).ti.
60	or/56-59
61	25 and 55 and 60
62	limit 61 to (yr="1990 - current" and english language)
63	Letter/ use ppez
64	letter.pt. or letter/ use emczd
65	note.pt.
66	editorial.pt.
67	Editorial/ use ppez
68	News/ use ppez
69	news media/ use psyh
70	exp Historical Article/ use ppez
71	Anecdotes as Topic/ use ppez
72	Comment/ use ppez
73	Case Report/ use ppez
74	case report/ or case study/ use emczd
75	Case report/ use psyh
76	(letter or comment*).ti.
77	or/63-76
78	randomized controlled trial/ use ppez
79	randomized controlled trial/ use emczd

#	Searches
80	random*.ti,ab.
81	cohort studies/ use ppez
82	cohort analysis/ use emczd
83	cohort analysis/ use psyh
84	case-control studies/ use ppez
85	case control study/ use emczd
86	or/78-85
87	77 not 86
88	animals/ not humans/ use ppez
89	animal/ not human/ use emczd
90	nonhuman/ use emczd
91	"primates (nonhuman)"/
92	exp Animals, Laboratory/ use ppez
93	exp Animal Experimentation/ use ppez
94	exp Animal Experiment/ use emczd
95	exp Experimental Animal/ use emczd
96	animal research/ use psyh
97	exp Models, Animal/ use ppez
98	animal model/ use emczd
99	animal models/ use psyh
100	exp Rodentia/ use ppez
101	exp Rodent/ use emczd
102	rodents/ use psyh
103	(rat or rats or mouse or mice).ti.
104	or/87-103
105	62 not 104

1 **Database: Cochrane Library**

2 Date searched: 27/06/2019

#	Searches
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: [Anxiety Disorders] this term only
15	MeSH descriptor: [Depression] this term only
16	MeSH descriptor: [Depressive Disorder, Major] this term only
17	MeSH descriptor: [Depressive Disorder] this term only
18	MeSH descriptor: [Stress Disorders, Post-Traumatic] this term only
19	MeSH descriptor: [Personality Disorders] this term only
20	MeSH descriptor: [Autism Spectrum Disorder] explode all trees
21	MeSH descriptor: [Attention Deficit and Disruptive Behavior Disorders] this term only

#	Searches
22	MeSH descriptor: [Cognition Disorders] explode all trees
23	MeSH descriptor: [Korsakoff Syndrome] explode all trees
24	MeSH descriptor: [Dementia] this term only
25	MeSH descriptor: [Obsessive-Compulsive Disorder] this term only
26	MeSH descriptor: [Learning Disorders] this term only
27	MeSH descriptor: [Drug Misuse] explode all trees
28	MeSH descriptor: [Alcoholism] this term only
29	MeSH descriptor: [Respiratory Tract Diseases] this term only
30	MeSH descriptor: [Cardiovascular Diseases] this term only
31	MeSH descriptor: [Heart Diseases] this term only
32	MeSH descriptor: [Metabolic Diseases] this term only
33	MeSH descriptor: [Diabetes Mellitus] this term only
34	MeSH descriptor: [Obesity] this term only
35	MeSH descriptor: [Osteoporosis] this term only
36	MeSH descriptor: [Kidney Diseases] this term only
37	MeSH descriptor: [Sexual Dysfunction, Physiological] this term only
38	MeSH descriptor: [Neoplasms] this term only
39	MeSH descriptor: [Hepatitis] this term only
40	MeSH descriptor: [HIV] this term only
41	MeSH descriptor: [Tuberculosis] this term only
42	MeSH descriptor: [Mouth Diseases] this term only
43	MeSH descriptor: [Tooth Diseases] this term only
44	MeSH descriptor: [Disabled Persons] this term only
45	MeSH descriptor: [Visually Impaired Persons] this term only
46	MeSH descriptor: [Hearing Disorders] this term only
47	MeSH descriptor: [Vision Disorders] this term only
48	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47
49	MeSH descriptor: [Comorbidity] explode all trees
50	MeSH descriptor: [Multiple Chronic Conditions] this term only
51	#49 OR #50
52	#48 AND #51
53	(anxiety or depression or ptsd or posttraumatic stress or post-traumatic stress or personality disorder* or obsessive compulsive disorder or autism or Asperger* syndrome or attention deficit disorder* or ADHD or learning disorder* or learning disabilit* or cognitive impairment* or learning impairment* or executive impairment* or korsakoff* or dementia):ti,ab,kw
54	(acquired near (brain or cognitive) near/2 (disorder* or injury or injuries)):ti,ab,kw
55	((drug* or alcohol or substance*) near/2 (misuse or abuse)):ti,ab,kw
56	(Alcoholism):ti,ab,kw
57	((respiratory or cardio* or metabolic or heart or kidney* or lung*) near/2 (disease* or disorder*)):ti,ab,kw
58	(Diabetes or obesity or osteoporosis or cancer* or neoplasm* or malignan* or hepatitis or HIV or tuberculosis or "Human immunodeficiency virus" or "Sexual dysfunction" or disability or "Wheelchair user*"):ti,ab,kw
59	((tooth or mouth) near/2 disease*):ti,ab,kw
60	((visual* or hearing or vision) near/2 (impair* or disorder*)):ti,ab,kw
61	#53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60
62	(comorbid* or co-morbid* or multimorbid* or multi-morbid* or ((coexist* or co-exist*) near/2 (condition* or disease* or disorder* or illness*))):ti,ab,kw
63	#61 AND #62
64	#52 OR #63
65	#13 AND #64
66	MeSH descriptor: [Epidemiology] this term only
67	MeSH descriptor: [Prevalence] this term only
68	MeSH descriptor: [Incidence] this term only

#	Searches
69	(Epidemiology or prevalence or incidence):ti,ab,kw
70	#66 OR #67 OR #68 OR #69
71	#65 AND #70 with Cochrane Library publication date Between Jan 1990 and Jul 2019

1 **Database: CRD**

2 Date searched: 27/06/2019

#	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

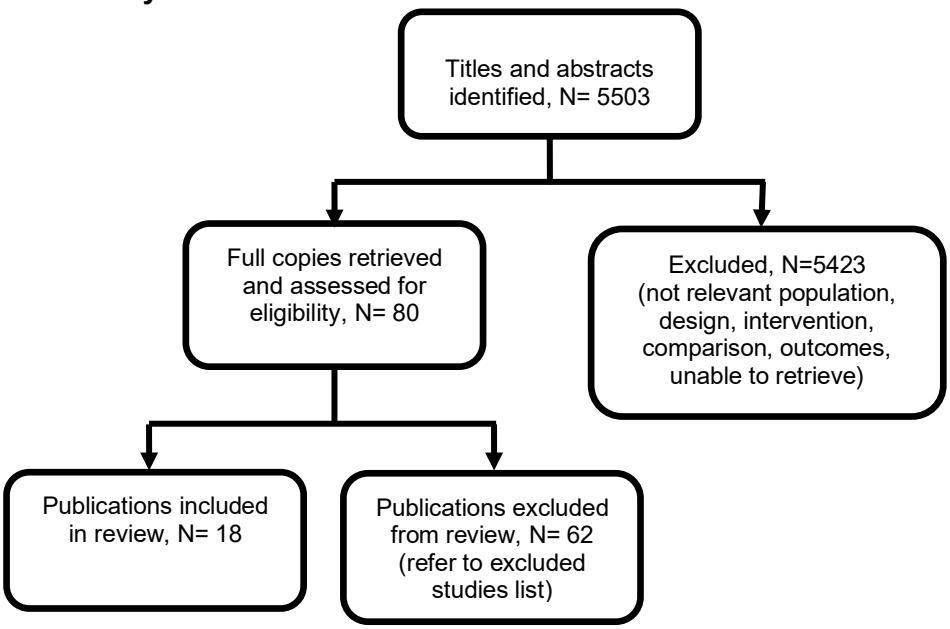
4

5

Appendix C – Clinical evidence study selection

Clinical study selection for 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

Table 4: Clinical Evidence Tables

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Full citation Achim, Amelie M., Maziade, Michel, Raymond, Eric, Olivier, David, Merette, Chantal, Roy, Marc-Andre, How prevalent are anxiety disorders in schizophrenia? A meta-analysis and critical review on a significant association, Schizophrenia bulletin, 37, 811-821, 2011 **Ref Id** 1068787 **Study type** Systematic review **Study dates** Search date 2009 **Country where the study was carried out** International **Source of funding**	**Inclusion criteria** Studies focusing on schizophrenia spectrum psychotic disorder diagnoses (including schizophrenia, schizoaffective, schizophreniform and delusional disorders, and psychosis not otherwise specified) according to standardized diagnostic criteria (e.g., DSM-IV); Use of standardized criteria to diagnose comorbid anxiety disorder (including obsessive-compulsive disorder [OCD], panic disorder [PD], agoraphobia [AGO], post-traumatic stress disorder [PTSD], social phobia [SP], simple phobia [SPP], and generalized anxiety disorder [GAD]); Sufficient data to extract the prevalence rate for at least one anxiety disorder. **Exclusion criteria** Studies were rejected if they included bipolar patients unless anxiety disorder prevalence was reported separately for patients with schizophrenia; studies reporting prevalence rates for anxiety symptoms instead of anxiety disorder or if the diagnoses were based on self-report measures and/or on a cut-off	**Comorbidity definition** Standardized criteria to diagnose comorbid anxiety disorder.	**Results** Prevalence (95% CI) Anxiety: GAD 10.9% (2.9 to 18.8%); N=939, 14 studies Anxiety: OCD 12.1% (7.0 to 17.1%); N=3,007, 34 studies Anxiety: panic disorder 9.8% (4.3 to 15.4%); N=1,393, 23 studies Anxiety: PTSD 12.4% (4.0 to 20.8%); N=1,388, 20 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – study characteristics not reported. Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Unclear concern Concerns about the synthesis. Low concern Risk of bias in the review Unclear concern.

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Canadian Institutes of Health Research (CIHR) (#MOP-77647)	score on a scale instead of diagnostic criteria. Abstracts were excluded **Participants with SMI** 4032 (52 studies) **Controls** none **Characteristics** Not reported			
Full citation Correll, Christoph U., Solmi, Marco, Veronese, Nicola, Bortolato, Beatrice, Rosson, Stella, Santonastaso, Paolo, Thapa-Chhetri, Nita, Fornaro, Michele, Gallicchio, Davide, Collantoni, Enrico, Pigato, Giorgio, Favaro, Angela, Monaco, Francesco, Kohler, Cristiano, Vancampfort, Davy, Ward, Philip B., Gaughran, Fiona, Carvalho, Andre F., Stubbs, Brendon, Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: A large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls, World Psychiatry, 16, 163-180, 2017 **Ref Id** 1069736 **Study type** Systematic review	**Inclusion criteria** Studies reporting on patients with schizophrenia, schizophrenia spectrum or schizoaffective disorder, bipolar disorder or bipolar spectrum disorders, major depressive disorder or depressive episodes, or SMI (defined as at least two among major depressive spectrum, bipolar spectrum and schizophrenia spectrum disorders) according to DSM-III, DSM-IV, DSM-5, ICD-8, ICD9 or ICD-10, or a medical record diagnosis based on a clinical interview) Having a cross-sectional or a retrospective/ prospective longitudinal design, either with or without a control group; Using a standardized definition of cardiovascular disease (CVD); Reporting RR, HR or odds ratio (OR) comparing patients with region-specific controls, percentage or number of events at baseline (data used for cross-sectional analysis prevalence) and/or follow-up (data	**Comorbidity definition** Standardized definition of cardiovascular disease (CVD) - not specified further	**Results** Prevalence of cardiovascular disease (95% CI) - from cross-sectional studies in SMI (in European studies): 9.7% (6.5 to 14.2%); N= 17,286, 6 studies In Schizophrenia: 11.8% (7.1 to 19.0%); N=191,982, 13 studies In Bipolar disorder: 8.4% (5.4 to 12.6%); N=66,911, 12 studies Compared to control group: in SMI: RR 1.17 (0.96-1.42) for incident disease In Schizophrenia: OR 1.23 (0.92 to 1.62) In Bipolar disorder: OR 1.73 (1.11 to 2.71)	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – many international studies – however European subgroup results reported. Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Low

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Study dates Search done in 2016 **Country where the study was carried out** International **Source of funding** The National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South London at King's College Hospital NHS Foundation Trust. Stanley Medical Research Institute.	used for longitudinal analysis cumulative incidence). **Exclusion criteria** Studies that investigated cardiovascular risk estimates and/or factors, subclinical CVD, or SMI rates in populations with CVD. **Participants with SMI** 3,211,768 **Controls** 113,383,368 **Characteristics** SMI: mean age 50 years, 49% male. 38 studies included patients with schizophrenia (of which 29 were longitudinal), 30 with bipolar disorder (21 longitudinal), 30 with major depressive disorder (22 longitudinal), and 14 with SMI (8 longitudinal) Controls: mean age 51 years, 49% male 27 studies (N=27,037,943) were cross-sectional and 65 studies (N=89,557,193) were longitudinal.			
Full citation Gabilondo, Andrea, Alonso-Moran, Edurne, Nuno-Solinis, Roberto, Orueta, Juan F., Iruin, Alvaro, Comorbidities with chronic physical conditions and gender profiles of illness in schizophrenia. Results from PREST, a new health dataset, Journal	**Inclusion criteria** The study population included every person who was covered by public health insurance in the Basque Country on 31st August 2011 and who had been covered for at least 6 months in the previous year, regardless of whether or not they had made any contact with or use of the Basque Health Service. This was the PREST database.	**Comorbidity definition** Dementia - not further defined. Other comorbidities were reported, but these were comprehensively covered in systematic reviews.	**Results** Dementia: Prevalence 5.6% (5.1 to 6.1%); OR 4.86 (4.37 to 5.40)	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? –Y 2.Were study participants sampled in an

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
of psychosomatic research, 93, 102-109, 2017 **Ref Id** 1070270 **Study type** Population based cross-sectional study **Study dates** 2007 to 2010 **Country where the study was carried out** Spain **Source of funding** No funding from agencies in the public, commercial, or not-for-profit sectors.	People registered in PREST who also had a diagnosis of schizophrenia (F20,ICD10) made by a mental health specialist were cases. The control group were people in PREST without a diagnosis of schizophrenia. **Exclusion criteria** Not reported **Participants with SMI** 7331 **Controls** 2248075 **Characteristics** Participants with schizophrenia			appropriate way? Exclusion criteria not reported 3.Was the sample size adequate? Y 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Unclear – used healthcare DB 8.Was there appropriate statistical analysis? Y 9.Was the response rate adequate, and if not, was the low response rate managed appropriately? Y Overall appraisal: include
Full citation Hunt, Glenn E., Large, Matthew M., Cleary, Michelle, Lai, Harry Man Xiong, Saunders, John B., Prevalence of comorbid substance use in	**Inclusion criteria** Studies with original research conducted in community (epidemiology studies), clinical populations (in- or out-patient settings or within mental health districts or catchment	**Comorbidity definition** Standardized diagnostic criteria for SUDs - such as the Structured Clinical Interview for Axes I or II DSM-IV Disorders	**Results** Prevalence (95% CI) in studies from Canada,	**ROBIS summary** Concerns about specification of study eligibility criteria. Results from Canada, Europe,

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
schizophrenia spectrum disorders in community and clinical settings, 1990-2017: Systematic review and meta-analysis, Drug and alcohol dependence, 191, 234-258, 2018 **Ref Id** 1070792 **Study type** Systematic review **Study dates** Studies published from 1990 to January 2018 **Country where the study was carried out** International **Source of funding** Nothing declared	areas) or longitudinal studies of cohorts or national/state case registries reporting substance misuse disorders (SUD) in schizophrenia or patients with first-episode psychosis (FEP). Studies were included if they reported on the prevalence of any substance use disorder (SUD), alcohol use disorder (AUD), any illicit drug use disorder (DUD), cannabis use disorder (CUD), stimulants (cocaine or amphetamine) or opioid use. **Exclusion criteria** Review papers, studies with fewer than 50 participants (or 100 participants for opioid studies), studies using non-standardized diagnostic criteria for SUDs. **Participants with SMI** 165,811 (123 studies) **Controls** none **Characteristics** 123 individual studies described comorbid rates of substance use in subjects with a schizophrenia spectrum disorder; 86 studies were conducted in clinical settings (in or out-patient units) and the rest of the 37 studies described schizophrenia populations that were part of epidemiological surveys (N = 6), case registry studies (N = 11) or large cohort or clinical trials (N = 20). 36 studies conducted in the USA, 53 in Europe, 8 in oriental Asia (Malaysia, Singapore, Taiwan, and Thailand) and the	(SCID), Schedules for Clinical Assessment in Neuropsychiatry (SCAN) or the Composite International Diagnostic Interview (CIDI).	Europe, Australia, New Zealand and Brazil Alcohol misuse: 22.6% (19.7% to 25.8%) Illicit drug misuse: 27.5% (22.9 to 32.6%)	Australia, New Zealand and Brazil combined Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review Unclear.

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
	rest of the studies were conducted in Australia (n = 11), Canada (n = 7), Israel (n = 2), and one each in Brazil, Costa Rica, Egypt, India, New Zealand and Zimbabwe.			
Full citation Hunt, G. E., Malhi, G. S., Cleary, M., Lai, H. M. X., Sitharthan, T., Prevalence of comorbid bipolar and substance use disorders in clinical settings, 1990-2015: Systematic review and meta-analysis, Journal of affective disorders, 206, 331-349, 2016 **Ref Id** 1070794 **Study type** Systematic review **Study dates** Studies published between 2009 and 2015 **Country where the study was carried out** International **Source of funding** No financial support was received.	**Inclusion criteria** Studies reporting original research on prevalence of substance misuse disorders (SUD) in clinical populations or bipolar registries, in patients with bipolar disorder (BD) diagnosed using structured diagnostic instruments (DSM-III-R to DSM-IV-TR, ICD-8 to ICD-10). **Exclusion criteria** Studies with less than 50 participants. Studies reporting prevalence rates for SUDs or BD separately were excluded as prevalence of comorbidity required both a psychiatric and SUD diagnosis within a defined population. Those excluding entry based on current or past history of a SUDs were excluded. Studies using non-standardised diagnostic criteria for substance use **Participants with SMI** 65,785 (78 studies) **Controls** None **Characteristics** 78 studies included. 56 individual studies describing comorbid rates of SUDs amongst community dwelling, consecutive admissions	**Comorbidity definition** Standardised diagnostic criteria for substance use	**Results** Prevalence (SEM) in studies from Canada, Europe, Australia, New Zealand and Brazil Alcohol misuse: 36.9% (SEM 34.1 to 39.7%) Illicit drug misuse: 13.3% (SEM 10.0 to 16.6%)	**ROBIS summary** Concerns about specification of study eligibility criteria. Results from Canada, Europe, Australia, New Zealand and Brazil combined Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review Unclear.

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
	to in- or out-patients with a BD. The remaining articles described bipolar populations that were part of large cohorts or multi-site networks or national surveys of people with BD. Thirty-five studies (45%) were carried out in the USA, 27 (35%) in Europe, 9 (12%) in Oriental Asia (Korea, Taiwan and Malaysia) and the other eight (10%) in Australia, Brazil, Canada, Costa Rica and New Zealand. Prevalence rates for AUDs were reported in 64 (82%) of the included studies, followed by SUDs (42, 54%), cannabis use disorders (32, 41%) and illicit drug use (27, 35%).			
Full citation Kincaid, Debbie L., Doris, Michael, Shannon, Ciaran, Mulholland, Ciaran, What is the prevalence of autism spectrum disorder and ASD traits in psychosis? A systematic review, Psychiatry research, 250, 99-105, 2017 **Ref Id** 1071144 **Study type** Systematic review **Study dates** Search date 2015 **Country where the study was carried out** International	**Inclusion criteria** Studies in participants with a psychotic disorder (with provided details on diagnosis of psychotic disorder) and assessment of autism spectrum disorder (ASD) (or autistic like traits - ALTs) and outcomes; prevalence rates of ASD (or ALTs); and published in English, in a peer-reviewed journal. **Exclusion criteria** Studies were excluded if all participants were from either an ASD population or an Intellectual Disability (ID) population. **Participants with SMI** 800 (6 studies) **Controls** None **Characteristics**	**Comorbidity definition** Autism spectrum disorder (ASD) - not further defined.	**Results** Median prevalence (range) ASD: 6.7% (0.78 to 52%), N=800, 5 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. High concern – 1/6 studies from UK Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern – no quantitative synthesis Risk of bias in the review Unclear.

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Source of funding The Queen's University of Belfast, School of Psychology, Belfast, Northern Ireland.	6 studies reported prevalence of ASD one each from UK, Finland, USA, Sweden, Australia and Taiwan			
Full citation McDermid, Joanna, Sareen, Jitender, El-Gabalawy, Renee, Pagura, Jina, Spiwak, Rae, Enns, Murray W., Co-morbidity of bipolar disorder and borderline personality disorder: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions, Comprehensive psychiatry, 58, 18-28, 2015 **Ref Id** 1071706 **Study type** Longitudinal study **Study dates** Surveys conducted from 2001-2002 and from 2004-2005 **Country where the study was carried out** USA **Source of funding** National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse	**Inclusion criteria** Data came from waves 1 and 2 of the longitudinal National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), which was conducted by the United States Census Bureau under the direction of the National Institute on Alcohol Abuse and Alcoholism. Wave 1 interviews were conducted between 2001 and 2002 and designed form a nationally representative sample of the non-institutionalized, civilian population of the 50 United States including 43,093 respondents. Wave 2 interviews were conducted with 34,653 of the original wave 1 respondents approximately 3 years later (2004–2005). **Exclusion criteria** Not reported **Participants with SMI** 1600 **Controls** None **Characteristics** Not reported	**Comorbidity definition** Mood, anxiety, substance use and personality disorder diagnoses were assessed using the Alcohol Use Disorders and Associated Disabilities Interview (AUDADIS-IV) according to the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV).	**Results** Prevalence of BPD (95% CI) 28.8% (26.6 to 31.1%), N=1600	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? Y 2.Were study participants sampled in an appropriate way? Y 3.Was the sample size adequate? Y 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Y 8.Was there appropriate statistical analysis? Y

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
				9.Was the response rate adequate, and if not, was the low response rate managed appropriately? Overall appraisal: include but this is a US study
Full citation McEnery, C., Lim, M. H., Tremain, H., Knowles, A., Alvarez-Jimenez, M., Prevalence rate of social anxiety disorder in individuals with a psychotic disorder: A systematic review and meta-analysis, Schizophrenia research, 208, 25-33, 2019 **Ref Id** 1071720 **Study type** Systematic review **Study dates** Studies published between 1980 and May 31, 2018 **Country where the study was carried out** International **Source of funding** Funded by an Australian Government Research Training Program Scholarship.	**Inclusion criteria** Studies were included if (1) all participants were 15 years or older and had a psychotic disorder diagnosis (schizophrenia spectrum) and a diagnosis of social anxiety disorder, (2) prevalence rates were reported, (3) they used cohort, correlational, nonrandomised, randomised con- trolled trials (RCTS) and quasi-experimental studies; (4) published in English in a peer-reviewed journal; (5) they were published between 1980 and May 31, 2018; and (5) they had a minimum of 20 participants. **Exclusion criteria** Case studies, conference papers, review papers, or qualitative studies were excluded. **Participants with SMI** 92,522 **Controls** None **Characteristics** 25 studies were included. The studies were conducted in 13 different countries from 1998 to 2018 (most in USA, Canada, Australia and	**Comorbidity definition** Social anxiety disorder was defined according to the DSM-5 (American Psychiatric, 2013), DSM-IV (APA, 2000), DSM-III-R (APA, 1987), or ICD-10 (World Health Organization [WHO], 1992), criteria or a well-established, clinically validated measure of social anxiety.	**Results** Prevalence (95% CI) Social anxiety disorder: 21% (16 to 26%), N=92,522, 25 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no subgroup analysis for UK studies Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
	Europe), and over 90% of participants were male. Seventeen of the studies based their prevalence rates on outpatients, six on inpatients, and two studies relied on both inpatients and outpatients.			
Full citation Preti, A., Vrublevska, J., Veroniki, A. A., Huedo-Medina, T. B., Kyriazis, O., Fountoulakis, K. N., Prevalence and treatment of panic disorder in bipolar disorder: systematic review and meta-analysis, Evidence-Based Mental Health, 21, 53-60, 2018 **Ref Id** 1072351 **Study type** Systematic review **Study dates** Studies published before August 2017 **Country where the study was carried out** International **Source of funding** Banting Postdoctoral Fellowship Program from the Canadian Institutes of Health Research.	**Inclusion criteria** Studies that included primary data concerning the comorbidity of panic disorder (PD) in adults (over 18 years old) patients with bipolar disorder (BD): the number of patients with confirmed diagnosis of BD and with a comorbid diagnosis of PD. Studies published in the English language **Exclusion criteria** Not reported **Participants with SMI** 3391 (15 studies) **Controls** None **Characteristics** 15 studies reported on cross-sectional prevalence of PD in BD. The majority were in USA, Europe and Canada.	**Comorbidity definition** Panic disorder - criteria DSM-III(R) or DSM-IV; procedure for diagnosis SCID, SADS, SCID, DIGS, DIG, WMH-CIDI	**Results** Prevalence (95%CI) Panic disorder: 15.1% (7.9 to 24.0%), N=3,391, 15 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no subgroup analysis for UK Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Full citation Public Health England, Research and analysis, Severe mental illness (SMI) and physical health inequalities: briefing, 2018 **Ref Id** 1107397 **Study type** Cross-sectional study **Study dates** 2018 **Country where the study was carried out** **Source of funding**	**Inclusion criteria** The Health Improvement Network (THIN) database for over 780 GP practices in England. This includes approximately 6% of the English population. Patients were included if they had a complete registration date recorded in THIN, and their data had passed the internal validation checks, they were aged 15 to 74 years. SMI patients were defined as having schizophrenia, affective disorder (bipolar or unspecified affective disorder) or other types of psychoses using Quality and Outcomes Framework (QOF) business rules, using Read codes from THIN. **Exclusion criteria** Not reported **Participants with SMI** 9,357 **Controls** 1,051,127 **Characteristics** SMI: 52% male, most were in the age group 35-54 years (age histograms reported) Controls: 50% male, most were in the age group 35-54 years (age histograms reported) (comparisons were age and sex standardised)	**Comorbidity definition** 10 physical health conditions for SMI and all patients in THIN were identified using QOF business rules: asthma, atrial fibrillation, cancer, coronary heart disease, COPD, diabetes, heart failure, hypertension, obesity and stroke	**Results** Prevalence (%) in SMI patients (95% CIs) Obesity 12.82 (12.12-13.55) Asthma 12.35 (11.48-13.26) Hypertension 12.05 (11.41-12.72) Diabetes 9.51 (8.92-10.12) COPD 2.90 (2.59-3.24) Cancer 2.42 (2.13-2.73) CHD 2.42 (2.13-2.73) Stroke 1.59 (1.36-1.85) Atrial fibrillation 0.86 (0.70-1.06) Heart failure 0.82 (0.65-1.01) Rate ratio (prevalence in SMI / prevalence in all patients) Obesity 1.8 Asthma 1.2 Hypertension 1.0 Diabetes 1.9 COPD 2.1 Cancer 0.9 CHD 1.2 Stroke 1.6 Atrial fibrillation 0.9 Heart failure 1.5	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? Y 2.Were study participants sampled in an appropriate way? Y 3.Was the sample size adequate? Y 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Y 8.Was there appropriate statistical analysis? Y 9.Was the response rate adequate, and if not, was the low response rate managed appropriately? Y

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
				Overall appraisal: include
Full citation Reilly, Siobhan, Olier, Ivan, Planner, Claire, Doran, Tim, Reeves, David, Ashcroft, Darren M., Gask, Linda, Kontopantelis, Evangelos, Inequalities in physical comorbidity: a longitudinal comparative cohort study of people with severe mental illness in the UK, BMJ Open, 5, e009010, 2015 **Ref Id** 1107396 **Study type** Cohort study **Study dates** 2000 to 2012 (but only results from 2012 used in this evidence review) **Country where the study was carried out** UK **Source of funding** Supported by the National Institute for Health Research (NIHR) School for Primary Care Research (SPCR).	**Inclusion criteria** People with a diagnosis consistent with SMI (schizophrenia, bipolar disorder, affective disorder and other types of psychosis) were identified from the Clinical Practice Research Datalink (CPRD) - a large primary care database of anonymised longitudinal medical records which contains detailed information on diagnoses, referrals, prescribed treatments and test results. This data is collected from 627 UK primary care practices. Results were collected in yearly bins from 1 April 2000 to 31 March 2012. **Exclusion criteria** People with drug/alcohol-induced psychoses, organic psychoses, dementia, unipolar depression, personality disorders and psychotic disorders in childhood/adolescence. **Participants with SMI** 31, 807 **Controls** 159,035 **Characteristics** People with SMI: 49% male, mean age 51.6 years Controls: 49% male, mean age 51.6 years	**Comorbidity definition** 16 chronic conditions were selected from the extended list of the Quality and Outcomes Framework (QOF) financial incentive scheme. These were: hypertension, diabetes (type I and II), asthma, hypothyroidism, osteoarthritis, chronic kidney disease (CKD), learning disability, coronary heart disease, epilepsy, chronic obstructive pulmonary disease (COPD), cancer, stroke, heart failure, rheumatoid arthritis, dementia and psoriasis. These were discussed and agreed a priori by all authors, and read codes associated with these conditions were agreed with clinical experts so they could be identified from the CPRD database.	**Results** Prevalence of learning disability 1.9% (1.7 to 2.0%); RR 8.45 (CI not reported) compared to control group. More recent data were available from other studies for the other chronic conditions, and so was not extracted from the study.	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? Y 2.Were study participants sampled in an appropriate way? Y 3.Was the sample size adequate? 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Y 8.Was there appropriate statistical analysis? Y 9.Was the response rate adequate, and if not, was the low response rate

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
				managed appropriately? Y Overall appraisal: include
Full citation Sylvia, L. G., Shelton, R. C., Kemp, D. E., Bernstein, E. E., Friedman, E. S., Brody, B. D., McElroy, S. L., Singh, V., Tohen, M., Bowden, C. L., et al.,, Medical burden in bipolar disorder: findings from the Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder study (Bipolar CHOICE), Bipolar disorders, 17, 212-223, 2015 **Ref Id** 1073121 **Study type** Randomised trial **Study dates** 2013 **Country where the study was carried out** USA **Source of funding** Funded by the Agency for Healthcare Research & Quality Grant R01 HS019371-01	**Inclusion criteria** Age 18 or older, with a DSM-IV-TR bipolar I or bipolar II diagnosis and at least mildly symptomatic [Clinical Global Impression Scale for Bipolar Disorder (CGI-BP) ≥ 3] at study entry. **Exclusion criteria** Not reported **Participants with SMI** 482 **Controls** None **Characteristics** Mean age 38.9 years, 41.3% male, 72.2% white, 68.3% bipolar I disorder	**Comorbidity definition** Clinical interviews obtained demographic information, psychiatric/medical history (e.g., asthma, myocardial infarction, and hepatitis). Medical comorbidities were divided into two groups to understand specific trends in the conditions associated with bipolar disorder:(Group 1) cardiometabolic disturbances (coronary artery dis- ease, myocardial infarction, diabetes, hyperglycemia, hyperlipidemia, hypercholesterolemia, triglyceridemia, and metabolic syndrome); (Group 2) non-cardiovascular conditions (kidney disease, seizures, thyroid disease, asthma, migraines, cancer, hepatitis, and head trauma). Comorbid substance use (smoking, alcohol and drug abuse/ dependence) was also included in the analyses.	**Results** Prevalence (95% CI) Head trauma: 16.2% (13.2 to 19.7%), N=482 This study reported other comorbidities but these are more comprehensively covered in systematic reviews	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? Y 2.Were study participants sampled in an appropriate way? No – RCT so sample is likely to be biased 3.Was the sample size adequate? Unclear 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Y 8.Was there appropriate statistical analysis? Y

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
				9.Was the response rate adequate, and if not, was the low response rate managed appropriately? Y Overall appraisal: include but acknowledge risk of bias
Full citation Yapici Eser, H., Kacar, A. S., Kilciksiz, C. M., Yalcinay-Inan, M., Ongur, D., Prevalence and Associated Features of Anxiety Disorder Comorbidity in Bipolar Disorder: A Meta-Analysis and Meta-Regression Study, Frontiers in psychiatry Frontiers Research Foundation, 9, 229, 2018 **Ref Id** 1073661 **Study type** Systematic review **Study dates** Studies published before September 2015 **Country where the study was carried out** International **Source of funding**	**Inclusion criteria** Original articles that diagnosed anxiety disorders in people with bipolar disorder (BD) were included. **Exclusion criteria** Studies that did not present conclusive data about BD—anxiety disorder comorbidity, review articles, studies on child and adolescent bipolar disorder patient samples, studies that were performed on data from health records/registries or hospital charts, studies that did not use structured clinical interviews for the diagnosis of anxiety disorders and diagnosed anxiety disorders based on scales, studies that reported data about the prevalence of “any anxiety disorder diagnosis” but did not define or clarify which disorders were concluded as “any anxiety disorder” were excluded. Studies that presented data of comorbidity in a heterogeneous sample of psychotic disorders (i.e., schizophrenia, schizoaffective disorder and bipolar disorder) were excluded, however, studies that included less than 5% of patients with schizoaffective disorder in addition to BD were included because of potential overlap in DSM-III criteria.	**Comorbidity definition** Anxiety disorders: based on structured interviews [SCID, SADS- Schedule for Affective Disorders for Schizophrenia, DIGS (Diagnostic interview for genetic studies), CIDI or MINI] or on selected diagnostic criteria (both DSM-III and DSM-IV)	**Results** Prevalence (95% CI) GAD: 13.3% (10.7 to 16.5%), N= 6,529, 28 studies OCD: 9.7% (7.9 to 11.9%), N= 7,134, 32 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no subgroup analysis for UK Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Funded by the Republic of Turkey Ministry of Development.	**Participants with SMI** 125 studies (total N not reported) **Controls** None **Characteristics** Overall patient characteristics not summarised			
Full citation Vancampfort, D., Stubbs, B., Mitchell, A. J., De Hert, M., Wampers, M., Ward, P. B., Rosenbaum, S., Correll, C. U., Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis, World Psychiatry, 14, 339-47, 2015 **Ref Id** 1096302 **Study type** Systematic review **Study dates** Studies published before 2015	**Inclusion criteria** Observational studies (cross-sectional, retrospective and prospective studies) in adults that fulfilled the following criteria: a) a diagnosis of schizophrenia or a related psychotic disorder, bipolar disorder or major depressive disorder according to the DSM-IV or ICD-10, irrespective of clinical setting (inpatient, outpatient or mixed); and b) a metabolic syndrome (MetS) diagnosis. For a randomized control trial, the variables of interest were extracted at baseline. There were no language or time restrictions. **Exclusion criteria** Studies with: a) non-standardized diagnoses, b) non-standardized definitions of MetS, c) insufficient data for extraction of MetS frequencies, d) restriction to patients at risk for or without cardiovascular diseases, and e) restriction to children and/or adolescents. **Participants with SMI**	**Comorbidity definition** Metabolic syndrome: diagnosed according to non-modified ATP-III, ATP-III-A, IDF or World Health Organization standards. Obesity: defined as waist circumference >102 cm in males and >88 cm in females (ATP-III or ATP-III-A)	**Results** Prevalence (95% CI) Metabolic syndrome in SMI: 32.6% (30.8 to 34.4%), N=52,678, 198 studies Obesity in SMI: Median 40.6% (range 26 to 55%), N=20,210, 65 studies (using ATP definition) Metabolic syndrome in schizophrenia: 33.4% (30.8 to 36.0%), N=29,596, 93 studies Metabolic syndrome in bipolar disorder: 31.7% (27.3 to 36.3%), N= 5,827, 6 studies Relative risk (95% CI) Obesity in SMI: RR 1.43 (1.23 to 1.66) Metabolic syndrome in schizophrenia: RR 1.86 (1.53 to 2.29) Metabolic syndrome in bipolar disorder: RR 1.58 (1.24 to 2.03)	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no subgroup analysis for UK Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Country where the study was carried out International **Source of funding** Not reported	52,678 (198 studies) **Controls** Included but N not reported **Characteristics** Mean age was 41.3 years (range 22.2-73.2), and mean illness duration was 12.4 years.			
Full citation Kisely, S., Baghaie, H., Lalloo, R., Siskind, D., Johnson, N. W., A systematic review and meta-analysis of the association between poor oral health and severe mental illness, Psychosomatic Medicine, 77, 83-92, 2015 **Ref Id** 935225 **Study type** Systematic review **Study dates** Studies published from 1988 to 2013. **Country where the study was carried out** International **Source of funding** University of Queensland Summer Research program.	**Inclusion criteria** Studies with a focus edentulism in SMI (primary diagnosis of dementia, schizophrenia, bipolar affective disorder, and other affective disorders), using clinical diagnoses or diagnostic criteria. **Exclusion criteria** Studies of eating disorder, PTSD, substance misuse or learning disability. Studies focused on less severe dental outcomes (e.g. dental hygiene). **Participants with SMI** 3,316 **Controls** 29,906 **Characteristics** 55 articles were included. Thirteen were from Europe. The remainder were from India (n = 2), Taiwan (n = 2), Australia (n = 4), Israel (n = 1), Hong Kong (n = 1), Ethiopia (n = 1), and the United States (n = 1). The most common diagnosis was psychosis, usually	**Comorbidity definition** Oral health problems: Edentulism defined as total loss of teeth Decayed, filled or missing tooth: DMFT score	**Results** Prevalence (95% CI) Edentulism: Around 65% (in UK & Danish studies) Odds ratio Edentulism: OR 2.81 (1.73 to 4.57), 16 studies Mean difference DMFT score: Mean difference 4.96 (2.53 to 7.39) (favours no SMI)	**ROBIS summary** Concerns about specification of study eligibility criteria. Low concern Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Unclear concern – results not well reported (e.g no CIs) for the UK subgroup Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
	schizophrenia. Other diagnoses (in descending order) included dementia, bipolar affective disorder, mood disorder, anxiety, and personality disorder. Ages ranged from 18 to 96 years.			
Full citation Stubbs, B., De Hert, M., Sepehry, A. A., Correll, C. U., Mitchell, A. J., Soundy, A., Detraux, J., Vancampfort, D., A meta-analysis of prevalence estimates and moderators of low bone mass in people with schizophrenia, 130, 470-86, 2014 **Ref Id** 1096303 **Study type** Systematic review **Study dates** Studies published before December 2013 **Country where the study was carried out** International **Source of funding** Authors declared funding or honoraria from: AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen-Cilag, Lundbeck JA, Pfizer, Sanofi-Aventis. Actelion, Alexza; Bristol-Myers Squibb, Cephalon, Eli Lilly,	**Inclusion criteria** Observational studies published in any language that measured skeletal status or bone mineral density (BMD) and reported prevalence of osteoporosis or osteopaenia in patients with a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual [DSM IV] or International Classification of Disease [ICD 10] criteria. **Exclusion criteria** Studies that did not (i) provide the prevalence of osteopaenia or osteoporosis according to a T- or Z-score in line with the WHO-criteria; (ii) confirm a diagnosis of schizophrenia with DSM-IV or ICD-10 criteria; (iii) had insufficient data and/or the authors did not provide sufficient information in response to requests for prevalence data. **Participants with SMI** 3,038 **Controls** 1,107 **Characteristics** In total, the dataset included 3038 patients with schizophrenia. The sample size in each study ranged from 10 to 965. The mean age	**Comorbidity definition** Osteoporosis (T-scores of <2.5 or Z-score < 2) or osteopenia (T-scores of 1 to 2.5 or Z-score < 1) according to the World Health Organization criteria	**Results** Prevalence (95% CI) Osteoporosis: 13.2% (7.8 to 21.6%), N=3,038, 19 studies Odds ratio (95% CI) Osteoporosis: OR 2.86 (1.27 to 6.42)	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no UK subgroups analysis. Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review. Unclear

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Genentech, GersonLehrman Group, IntraCellular Therapies, Lundbeck, Medavante, Medscape, Merck, Otsuka, ProPhase, Roche, Sunovion, Takeda, Teva, Vanda.BMS, Janssen/J&J, Novo Nordisk, A/Sand.	of participants was 42.7 years and the mean percentage of males was 59.2%. Eight studies were conducted in Asia, seven in Europe, and four in North America. Eight studies (n = 1883) were conducted in in-patient settings, six included out-patients (n = 525), four studies included participants from mixed settings (n 545), and the setting was unclear in one study (n = 85).			
Full citation Ayano, G., Tulu, M., Haile, K., Assefa, D., Habtamu, Y., Araya, G., Yohannis, Z., A systematic review and meta-analysis of gender difference in epidemiology of HIV, hepatitis B, and hepatitis C infections in people with severe mental illness, Ann Gen Psychiatry, 17, 16, 2018 **Ref Id** 1096304 **Study type** Systematic review **Study dates** Studies published from 1993 to 2017 **Country where the study was carried out** International **Source of funding** No funding received.	**Inclusion criteria** Studies in people with severe mental illness (SMI: schizophrenia, bipolar disorder or psychotic depression), with observational design reporting the prevalence of HIV, HBV and HCV. **Exclusion criteria** Non English language, editorials, reviews, studies with nonhuman subjects. **Participants with SMI** 11,715 (18 studies) **Controls** **Characteristics** Nine studies were conducted in the USA, two in Uganda, and one in China, India, Lebanon, South Africa, Italy, Mexico and Jordan.	**Comorbidity definition** Hepatitis B, Hepatitis C and HIV infection - diagnostic criteria not reported.	**Results** Prevalence (95%CI) in developed countries Hepatitis B: 19.7% (8.8 to 37.3%), 3 studies Hepatitis C: 6.2% (3.6 to 10.6%), 4 studies HIV: 7.5% (3.8 to 14.3%), 15 studies	**ROBIS summary** Concerns about specification of study eligibility criteria. Unclear concern – no UK subgroup analysis – developed countries used Concerns about methods used to identify and or select studies. Low concern Concerns about methods used to collect data and appraise studies. Low concern Concerns about the synthesis. Low concern Risk of bias in the review Unclear.

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
Full citation Smith, D. J., Langan, J., McLean, G., Guthrie, B., Mercer, S. W., Schizophrenia is associated with excess multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary care: cross-sectional study, BMJ Open, 3, 2013 **Ref Id** 1096305 **Study type** Cross-sectional study **Study dates** 2007 **Country where the study was carried out** UK **Source of funding** The Chief Scientist Office of the Scottish Government Health Directorates (Applied Research Programme Grant ARPG/07/1); the Scottish School of Primary Care	**Inclusion criteria** The study used a dataset from the Primary Care Clinical Informatics Unit at the University of Aberdeen which consists of all 1,751,841 registered patients who were alive and permanently registered with 314 general practices on 31 March 2007. People were identified as having 'schizophrenia or related non-organic psychosis' based on the recording ever of any of the following primary care read codes (where % is noted, this means 'this code and any below it in the code hierarchy'): E10% schizophrenic disorders; E121 chronic paranoid psychosis; E12z paranoid psychosis NOS; E13% other non-organic psychoses; E13z non-organic psychosis/psychotic episode; NOS E1z non-organic psychosis NOS; Eu20% schizophrenia; Eu22% persistent delusional disorder or the recording in the last 12 months of Eu23% acute/transient psychotic disorder. Differences between those with schizophrenia (cases), all other individuals (controls) and between female and male individuals with schizophrenia were calculated by age, deprivation and number of physical conditions. **Exclusion criteria** None reported **Participants with SMI** 9,677 **Controls** 1,414,701 **Characteristics**	**Comorbidity definition** Physical health comorbidities as recorded in the dataset from the Primary Care Clinical Informatics Unit at the University of Aberdeen	**Results** Prevalence (95% CI) Parkinson's disease: 0.8% (0.6 to 0.9%), N=9,677 Blindness: 1.1% (0.9 to 1.3%), N=9,677 Hearing impairment: 5.1% (4.7 to 5.6%), N=9,677 Odds ratios (95% CI) Parkinson's disease: OR 3.07 (2.42 to 3.88), N=1,424,378 Blindness: OR 1.44 (1.18 to 1.75), N=1,424,378 Hearing impairment: OR 1.14 (1.04 to 1.25), N=1,424,378 Other comorbidities were reported, but these were more comprehensively covered in systematic reviews.	**JBI critical appraisal checklist for prevalence studies** 1.Was the sample frame appropriate to address the target population? Y 2.Were study participants sampled in an appropriate way? Y 3.Was the sample size adequate? Y 4.Were the study subjects and the setting described in detail? Y 5.Was the data analysis conducted with sufficient coverage of the identified sample? Y 6.Were valid methods used for the identification of the condition? Y 7.Was the condition measured in a standard, reliable way for all participants? Y 8.Was there appropriate statistical analysis? Y 9.Was the response rate adequate, and if not, was the low response rate managed appropriately? Y

Study details	Participants	Comorbidity definitions	Prevalence	Limitations
	Those with schizophrenia were more likely to be male (schizophrenia 51.5% men vs controls 49.1% men) and tended to be older than controls (schizophrenia mean age 51.6 years vs controls mean age 48 years). Individuals with schizophrenia were more socially deprived on average (schizophrenia Carstairs score 0.34 vs controls −0.17), with2 3.3% living in the most deprived quintile of postcodes versus 17.8% of controls.			Overall appraisal: include

JBI: Joanna Briggs Institute

Appendix E – Forest plots

Forest plots for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

No meta-analysis was done for this review question.

Appendix F – GRADE tables

GRADE tables for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

GRADE methods were not used for this review question, however see Table 5 for a summary of the prevalence results.

Table 5: Prevalence of comorbidities

Comorbidity	Prevalence in SMI (95% CI)	Prevalence in controls (95% CI)	RR / OR (95% CI) ‡	Population	N SMI	N controls	N studies	References	Risk of bias
MENTAL HEALTH									
Anxiety: GAD	10.9% (2.9 to 18.8%)	-	-	Schizophrenia	939	-	14	Achim 2011	Unclear
	13.3% (10.7 to 16.5%)	-	-	Bipolar disorder	6,529	-	28	Yaipici 2018	Unclear
Anxiety: OCD	12.1% (7.0 to 17.1%)	-	-	Schizophrenia	3,007	-	34	Achim 2011	Unclear
	9.7% (7.9 to 11.9%)	-	-	Bipolar disorder	7,134	-	32	Yaipici 2018	Unclear
Anxiety: social anxiety disorder	21% (16 to 26%)	-	-	Schizophrenia	92,522	-	25	McEnery 2019	Unclear
Anxiety: panic disorder	9.8% (4.3 to 15.4%)	-	-	Schizophrenia	1,393	-	23	Achim 2011	Unclear
	15.1% (7.9 to 24.0%)	-	-	Bipolar disorder	3,391	-	15	Preti 2018	Unclear
Anxiety: PTSD	12.4% (4.0 to 20.8%)	-	-	Schizophrenia	1,388	-	20	Achim 2011	Unclear
Depression	Not reported	-	-	-	-	-	-	-	-
Borderline personality disorder	28.8% (26.6 to 31.1%)	-	-	Bipolar disorder	1,600	-	1	McDermid 2015	Low
NEURODEVELOPMENTAL									

Comorbidity	Prevalence in SMI (95% CI)	Prevalence in controls (95% CI)	RR / OR (95% CI) ‡	Population	N SMI	N controls	N studies	References	Risk of bias
Autism spectrum disorder	Median 6.7% (0.78 to 52%)	-	-	Psychosis	800	-	5	Kincaid 2017	Unclear
ADHD	Not reported	-	-	-	-	-	-	-	-
Learning disabilities	1.9% (1.7 to 2.0%)	0.22% (0.20 to 0.24%)	RR 8.45 (CI not reported)	SMI	31,807	159,035	1	Reilly 2015	Low
Cognitive impairments	Not reported	-	-	-	-	-	-	-	-
Learning impairments	Not reported	-	-	-	-	-	-	-	-
Executive impairments	Not reported	-	-	-	-	-	-	-	-
ACQUIRED BRAIN DISORDERS									
Parkinson's disease	0.8% (0.6 to 0.9%)	0.19% (0.18 to 0.20%)	**OR 3.07 (2.42 to 3.88)**	Schizophrenia	9,677	1,414,701	1	Smith 2013	Low
Dementia	5.6% (5.1 to 6.1%)	3.0% (2.9 to 3.0%)	**OR 4.86 (4.37 to 5.40)**	Schizophrenia	7,331	2,248,075	1	Gabilondo 2017	Low
Head trauma	16.2% (13.2 to 19.7%)	-	-	Bipolar disorder	482	-	1	Sylvia 2014	Unclear
Stroke	1.7% (1.4 to 2.1%)	1.0% (CI not reported)	**RR 1.8**	SMI	9,357	1,051,127	1	PHE 2018	Low
SUBSTANCE MISUSE (EXCLUDING TOBACCO)									
Alcohol misuse	36.9% (SEM 34.1 to 39.7%)*		-	Bipolar disorder	65,785	-	78	Hunt 2016	Unclear
	22.6% (19.7% to 25.8%)*		-	Schizophrenia	165,811	-	123	Hunt 2018	Unclear
Illicit drug misuse	13.3% (SEM 10.0 to 16.6%)*		-	Bipolar disorder	65,785	-	78	Hunt 2016	Unclear
	27.5% (22.9 to 32.6%)		-	Schizophrenia	165,811	-	123	Hunt 2018	Unclear
PHYSICAL HEALTH									

Comorbidity	Prevalence in SMI (95% CI)	Prevalence in controls (95% CI)	RR / OR (95% CI) ‡	Population	N SMI	N controls	N studies	References	Risk of bias
COPD	2.6% (2.3 to 3.0%)	1.4% (CI not reported)	**RR 1.9**	SMI	9,357	1,051,127	1	PHE 2018	Low
Coronary heart disease	2.7% (2.3 to 3.1%)	2.0% (CI not reported)	**RR 1.3**	SMI	9,357	1,051,127	1	PHE 2018	Low
Hypertension	12.0% (11.2 to 12.9%)	11.5% (CI not reported)	RR 1.0	SMI	9,357	1,051,127	1	PHE 2018	Low
Cardiovascular mortality	-		**HR 1.78 (1.60 to 1.98**	SMI	671,384	14,335,203	31	Correll 2017	Low
Metabolic syndrome	32.6% (30.8 to 34.4%)	-	-	SMI	52,678	-	198	Vancampfort 2015	Unclear
	33.4% (30.8 to 36.0%)		**RR 1.86 (1.53 to 2.29)**	Schizophrenia	29,596	Not reported	93	Vancampfort 2015	Unclear
	31.7% (27.3 to 36.3%)		**RR 1.58 (1.24 to 2.03)**	Bipolar disorder	5,827	Not reported	6	Vancampfort 2015	Unclear
Diabetes	9.4% (8.7 to 10.1%)	4.9% (CI not reported)	**RR 1.9**	SMI	9,357	1,051,127	1	PHE 2018	Low
Obesity	12.9% (12.0 to 13.8%)	7.0% (CI not reported)	**RR 1.8**	SMI	9,357	1,051,127	1	PHE 2018	Low
Asthma	12.0% (11.1 to 13.0%)	10.0% (CI not reported)	**RR 1.2**	SMI	9,357	1,051,127	1	PHE 2018	Low
Osteoporosis	13.2% (7.8 to 21.6%)		**OR 2.86 (1.27 to 6.42)**	Schizophrenia	3,038	1,107	19	Stubbs 2014	Unclear
Sexual dysfunction and reproductive health	Not reported	-	-	-	-	-	-	-	-
Cancer	2.9% (2.6 to 3.3%)	2.7% (CI not reported)	RR 1.1	SMI	9,357	1,051,127	1	PHE 2018	Low
Hepatitis B	19.7% (8.8 to 37.3%)§	-	-	SMI	Not reported	-	3	Ayano 2018	Unclear
Hepatitis C	6.2% (3.6 to 10.6%)§	-	-	SMI	Not reported	-	4	Ayano 2018	Unclear

Comorbidity	Prevalence in SMI (95% CI)	Prevalence in controls (95% CI)	RR / OR (95% CI) ‡	Population	N SMI	N controls	N studies	References	Risk of bias
HIV	7.5% (3.8 to 14.3%) §	-	-	SMI	Not reported	-	15	Ayano 2018	Unclear
Tuberculosis	Not reported	-	-	-	-	-	-	-	-
Oral health problems: total loss of teeth	Around 65% (in UK & Danish studies)		**OR 2.81 (1.73 to 4.57)**	SMI	3,316	29,906	16	Kisely 2014	Unclear
Oral health problems: decayed, filled or missing teeth (DMFT score)	DMFT 30.0 for UK studies		**Mean difference 4.96 (2.53 to 7.39)**	SMI	3,054	11,880	11	Kisely 2014	Unclear
PHYSICAL DISABILITIES									
Wheelchair users	Not reported	-	-	-	-	-	-	-	-
Blindness	1.1% (0.9 to 1.3%)		**OR 1.44 (1.18 to 1.75)**	Schizophrenia	9,677	1,414,701	1	Smith 2013	Low
Hearing loss	5.1% (4.7 to 5.6%)		**OR 1.14 (1.04 to 1.25)**	Schizophrenia	9,677	1,414,701	1	Smith 2013	Low
MULTIPLE COMORBIDITIES									
Any physical health comorbidity	41.4% (40.5-42.5%)	29.5% (CI not reported)	**RR 1.4**	SMI	9,357	1,051,127	1	PHE 2018	Low
2 or more comorbidities	15.6% (14.9-16.3%)	8.7% (CI not reported)	**RR 1.8**	SMI	9,357	1,051,127	1	PHE 2018	Low
3 or more comorbidities	5.1% (4.6-5.5%)	2.7% (CI not reported)	**RR 1.8**	SMI	9,357	1,051,127	1	PHE 2018	Low
4 or more comorbidities	1.6% (1.4 - 1.9%)	0.8% (CI not reported)	**RR 2.0**	SMI	9,357	1,051,127	1	PHE 2018	Low
5 or more comorbidities	0.4% (0.3 to 0.6%)	0.2% (CI not reported)	**RR 1.9**	SMI	9,357	1,051,127	1	PHE 2018	Low

COPD: chronic obstructive pulmonary disease; DMFT: decayed filled or missing teeth; GAD: generalised anxiety disorder; HIV: human immunodeficiency virus; OCD: obsessive compulsive disorder; OR: odds ratio; PTSD: posttraumatic stress disorder; RR: rate ratio; SEM: standard error of the mean; SMI: serious mental illness

** Studies from Canada, Europe, Australia, New Zealand and Brazil*

† Studies from Europe

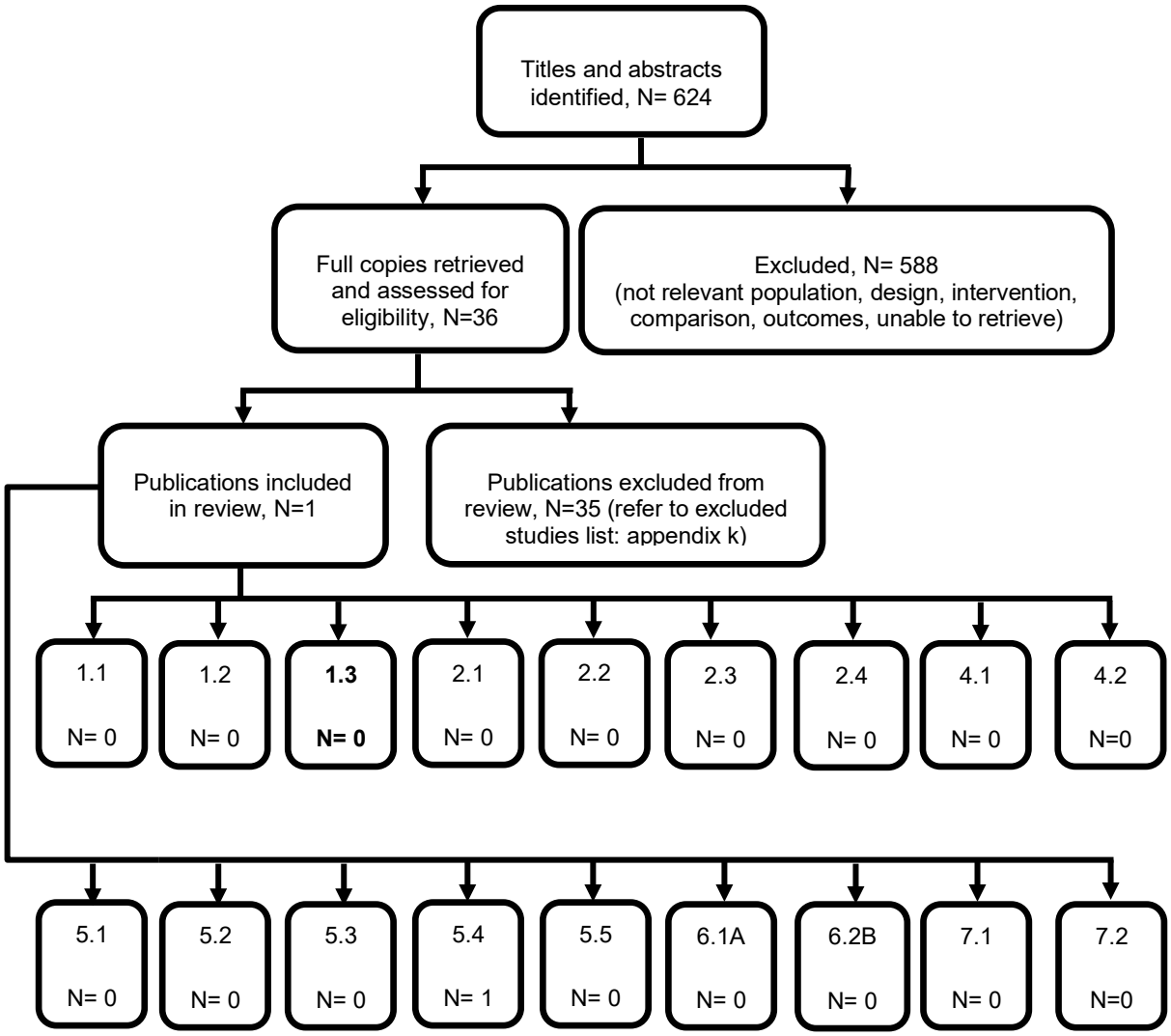
‡ RR or OR greater than 1 indicates increased risk of comorbidity in the population with SMI. Numbers in bold indicate a statistically significant higher prevalence in SMI.
§ Studies from developed countries ratio; SEM: standard error of the mean; SMI: serious mental illness

Appendix G – Economic evidence study selection

Economic evidence study selection for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

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 to review 1.3

Figure 2: Health economic study selection flow chart



Appendix H – Economic evidence tables

Economic evidence tables for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

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

Appendix I – Economic evidence profiles

Economic evidence profiles for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

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

Appendix J – Economic analysis

Economic evidence analysis for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

No economic analysis was conducted for this review question.

1 Appendix K – Excluded studies

2 Excluded clinical and economic studies for review question 1.3: What coexisting 3 conditions (neurodevelopmental, cognitive, mental/physical health disorders) 4 need to be considered when formulating a rehabilitation plan with people with 5 complex psychosis?

6 Clinical studies

7 **Table 6: Excluded studies and reasons for their exclusion**

Study	Reason for Exclusion
Abou Kassm, Sandra, Hoertel, Nicolas, Naja, Wadih, McMahon, Kibby, Barriere, Sarah, Blumenstock, Yvonne, Portefaix, Christophe, Raucher-Chene, Delphine, Bera-Potelle, Celine, Cuervo-Lombard, Christine, Guerin-Langlois, Christophe, Lemogne, Cedric, Peyre, Hugo, Kaladjian, Arthur, Limosin, Frederic, Metabolic syndrome among older adults with schizophrenia spectrum disorder: Prevalence and associated factors in a multicenter study, Psychiatry research, 275, 238-246, 2019	Older age group only
Allison, D. B., Newcomer, J. W., Dunn, A. L., Blumenthal, J. A., Fabricatore, A. N., Daumit, G. L., Cope, M. B., Riley, W. T., Vreeland, B., Hibbeln, J. R., Alpert, J. E., Obesity among those with mental disorders: a National Institute of Mental Health meeting report, American Journal of Preventive Medicine, 36, 341-50, 2009	Expert review
Altamura, A. C., Serati, M., Albano, A., Paoli, R. A., Glick, I. D., Dell'Osso, B., An epidemiologic and clinical overview of medical and psychopathological comorbidities in major psychoses, European Archives of Psychiatry & Clinical Neuroscience, 261, 489-508, 2011	Expert review
Amann, Benedikt L., Radua, Joaquim, Wunsch, Christian, Konig, Barbara, Simhandl, Christian, Psychiatric and physical comorbidities and their impact on the course of bipolar disorder: A prospective, naturalistic 4-year follow-up study, Bipolar disorders, 19, 225-234, 2017	Cohort included in Hunt 2016 systematic review
Amerio, A., Stubbs, B., Odone, A., Tonna, M., Marchesi, C., Ghaemi, S. N., The prevalence and predictors of comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review and meta-analysis, Journal of affective disorders, 186, 99-109, 2015	Systematic review - covers the same studies as Yapici 2018 - but with an older search date
Berkol, T. D., Yargic, I., Ozyildirim, I., Yazici, O., Comorbidity of adult attention deficit and hyperactivity disorder in bipolar patients: Prevalence, sociodemographic and clinical correlates, Noropsikiyatri Arsivi, 51, 97-102, 2014	Turkish study
Bernardo, M., Canas, F., Banegas, J. R., Casademont, J., Riesgo, Y., Varela, C., Ricava Study Group, Prevalence and awareness of cardiovascular risk factors in patients with schizophrenia: a cross-sectional study in a low cardiovascular disease risk geographical area, European Psychiatry: the Journal of the Association of European Psychiatrists, 24, 431-41, 2009	Included in Mitchell 2013 SR
Boke,O., Aker,S., Sarisoy,G., Saricicek,E.B., Sahin,A.R., Prevalence of metabolic syndrome among inpatients with schizophrenia, International Journal of Psychiatry in Medicine, 38, 103-112, 2008	Included in Mitchell 2013 SR
Bolton, James M., Robinson, Jennifer, Sareen, Jitender, Self-medication of mood disorders with alcohol and drugs in the National Epidemiologic Survey on Alcohol and Related Conditions, Journal of affective disorders, 115, 367-375, 2009	Does not report prevalence

Study	Reason for Exclusion
Bresee, Lauren C., Majumdar, Sumit R., Patten, Scott B., Johnson, Jeffrey A., Prevalence of cardiovascular risk factors and disease in people with schizophrenia: A population-based study, Schizophrenia research, 117, 75-82, 2010	Included in Corell 2017 SR
Carney, C. P., Jones, L., Woolson, R. F., Medical comorbidity in women and men with schizophrenia: a population-based controlled study, Journal of general internal medicine, 21, 1133â□□1137, 2006	Included in Janssen 2015
Catala-Lopez, F., Suarez-Pinilla, M., Suarez-Pinilla, P., Valderas, J. M., Gomez-Beneyto, M., Martinez, S., Balanza-Martinez, V., Climent, J., Valencia, A., McGrath, J., Crespo-Facorro, B., Sanchez-Moreno, J., Vieta, E., Tabares-Seisdedos, R., Inverse and direct cancer comorbidity in people with central nervous system disorders: A meta-analysis of cancer incidence in 577,013 participants of 50 observational studies, Psychotherapy and psychosomatics, 83, 89-105, 2014	Does not report prevalence - compares incidence of cancers in those with and without schizophrenia
Cerullo, Michael A., Strakowski, Stephen M., The prevalence and significance of substance use disorders in bipolar type I and II disorder, Substance Abuse Treatment, Prevention, and Policy Vol 2 2007, ArtID 29, 2, 2007	Unclear whether this is a systematic review, methods not fully reported
Compton, W. M., Thomas, Y. F., Stinson, F. S., Grant, B. F., Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: Results from the national epidemiologic survey on alcohol and related conditions, Archives of general psychiatry, 64, 566-576, 2007	Does not report prevalence in our groups of interest
Daumit, G. L., Goff, D. C., Meyer, J. M., Davis, V. G., Nasrallah, H. A., McEvoy, J. P., Rosenheck, R., Davis, S. M., Hsiao, J. K., Stroup, T. S., et al.,, Antipsychotic effects on estimated 10-year coronary heart disease risk in the CATIE schizophrenia study, Schizophrenia research, 105, 175â□□187, 2008	Prevalence not reported.
Di Florio, A., Craddock, N., van den Bree, M., Alcohol misuse in bipolar disorder. A systematic review and meta-analysis of comorbidity rates, European psychiatry, 29, 117-124, 2014	Systematic review - superceeded by Hunt 2016 systematic review
Dixon, L., Weiden, P., Delahanty, J., Goldberg, R., Postrado, L., Lucksted, A., Lehman, A., Prevalence and correlates of diabetes in national schizophrenia samples, Schizophrenia bulletin, 26, 903-912, 2000	Included in Stubbs 2015 SR
Dixon, Lisa, Postrado, Leticia, Delahanty, Janine, Fischer, Pamela J., Lehman, Anthony, The association of medical comorbidity in schizophrenia with poor physical and mental health, Journal of nervous and mental disease, 187, 496-502, 1999	Included in systematic reviews
Duke, Peter J., Pantelis, Christos, McPhillips, Michael A., Barnes, Thomas R., Comorbid non-alcohol substance misuse among people with schizophrenia: Epidemiological study in central London, The British Journal of Psychiatry, 179, 509-513, 2001	Included in Hunt 2018 systematic review
Eisner, L. R., Johnson, S. L., Youngstrom, E. A., Pearlstein, J. G., Simplifying profiles of comorbidity in bipolar disorder, Journal of affective disorders, 220, 102-107, 2017	Does not report prevalence
Ferreiro Fernandez, B., Garcia Mahia, M. C., Vidal Millares, M., Prevalence of metabolic syndrome in psychotic patients treated with antipsychotics, European Neuropsychopharmacology, 24, S513, 2014	Subgroup treated with antipsychotics (N=126)
Flensborg-Madsen, T., Mortensen, E. L., Knop, J., Becker, U., Sher, L., Gronbaek, M., Comorbidity and temporal ordering of alcohol use disorders and other psychiatric disorders: results from a Danish register-based study, Comprehensive psychiatry, 50, 307-14, 2009	Prevalence not reported in our population of interest

Study	Reason for Exclusion
Forman-Hoffman, V. L., Batts, K. R., Hedden, S. L., Spagnola, K., Bose, J., Comorbid mental disorders among adults in the mental health surveillance survey, Annals of Epidemiology, 28, 468-474, 2018	Does not report prevalence in our groups of interest
Gadermann, Anne M., Alonso, Jordi, Vilagut, Gemma, Zaslavsky, Alan M., Kessler, Ronald C., Comorbidity and disease burden in the National Comorbidity Survey Replication (NCS-R), Depression and anxiety, 29, 797-806, 2012	Does not report prevalence in our groups of interest
Godin, O., Etain, B., Henry, C., Bougerol, T., Courtet, P., Mayliss, L., Passerieux, C., Azorin, J. M., Kahn, J. P., Gard, S., Costagliola, D., Leboyer, M., FondaMental Advanced Centers of Expertise in Bipolar Disorders, Collaborators, Metabolic syndrome in a French cohort of patients with bipolar disorder: results from the FACE-BD cohort, Journal of clinical psychiatry, 75, 1078-85; quiz 1085, 2014	Included in Vancampfort 2015 systematic review
Goldstein, Benjamin I., Liu, Shang-Min, Zivkovic, Nevena, Schaffer, Ayal, Chien, Lung-Chang, Blanco, Carlos, The burden of obesity among adults with bipolar disorder in the United States, Bipolar disorders, 13, 387-395, 2011	Cohort included in Vancampfort 2015 systematic review
Grant, Bridget F., Stinson, Frederick S., Dawson, Deborah A., Chou, S., Dufour, Mary C., Compton, Wilson, Pickering, Roger P., Kaplan, Kenneth, Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions, Alcohol Research & Health, 29, 107-120, 2006	Included in Nabavi 2015 systematic review
Grinshpoon, A., Barchana, M., Ponizovsky, A., Lipshitz, I., Nahon, D., Tal, O., Weizman, A., Levav, I., Cancer in schizophrenia: is the risk higher or lower?, Schizophrenia research, 73, 333-41, 2005	Does not report prevalence
Gunewardene, Ranil, Lampe, Lisa, Ilchef, Ralf, Prevalence of hepatitis C in two inpatient psychiatry populations, Australasian psychiatry, 18, 330-334, 2010	Unclear whether the included population matches our protocol
Hasin, D. S., Stinson, F. S., Ogburn, E., Grant, B. F., Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions, Archives of general psychiatry, 64, 830-42, 2007	Does not report prevalence in our groups of interest
Hasin, Deborah S., Grant, Bridget F., The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: Review and summary of findings, Social Psychiatry and Psychiatric Epidemiology, 50, 2015	Overview of publications and findings from The National Epidemiologic Survey on Alcohol and Related Conditions
Henry, C., Den Bulke, D. V., Bellivier, F., Etain, B., Rouillon, F., Leboyer, M., Anxiety disorders in 318 bipolar patients: Prevalence and impact on illness severity and response to mood stabilizer, Journal of clinical psychiatry, 64, 331-335, 2003	Included in Nabavi 2015 systematic review
Huang, Boji, Dawson, Deborah A., Stinson, Frederick S., Hasin, Deborah S., Ruan, W., Saha, Tulshi D., Smith, Sharon M., Goldstein, Rise B., Grant, Bridget F., Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: Results of the National Epidemiologic Survey on Alcohol and Related Conditions, The Journal of clinical psychiatry, 67, 1062-1073, 2006	Prevalence not reported in our groups of interest
Janssen, Ellen M., McGinty, Emma E., Azrin, Susan T., Juliano-Bult, Denise, Daumit, Gail L., Review of the evidence: Prevalence of medical conditions in the United States population with serious mental illness, General hospital psychiatry, 37, 199-222, 2015	USA only. More relevant UK prevalence data found in PHE 2018

Study	Reason for Exclusion
Jerrell,J.M., McIntyre,R.S., Tripathi,A., Incidence and costs of cardiometabolic conditions in patients with schizophrenia treated with antipsychotic medications, Clinical Schizophrenia and Related Psychoses, 4, 161-168, 2010	Population selected by treatment received
Kilbourne, A. M., Cornelius, J. R., Han, X., Pincus, H. A., Shad, M., Salloum, I., Conigliaro, J., Haas, G. L., Burden of general medical conditions among individuals with bipolar disorder, Bipolar disorders, 6, 368-73, 2004	Included in Janssen 2015 systematic review
Kuo, S. C., Chen, Y. T., Li, S. Y., Lee, Y. T., Yang, A. C., Chen, T. L., Liu, C. J., Chen, T. J., Su, I. J., Fung, C. P., Incidence and outcome of newly-diagnosed tuberculosis in schizophrenics: A 12-year, nationwide, retrospective longitudinal study, BMC Infectious Diseases, 13 (1) (no pagination), 2013	Does not report prevalence
Kuppili, P. P., Nebhinani, N., Deciphering the paradoxical incidence of cancer in schizophrenia, Australasian psychiatry, 26, 624-627, 2018	Incidence not prevalence
Lazareck, S., Robinson, J. A., Crum, R. M., Mojtabai, R., Sareen, J., Bolton, J. M., A longitudinal investigation of the role of self-medication in the development of comorbid mood and drug use disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), Journal of clinical psychiatry, 73, e588-93, 2012	Prevalence not reported in our groups of interest
Leucht, S., Burkard, T., Henderson, J., Maj, M., Sartorius, N., Physical illness and schizophrenia: A review of the literature, Acta psychiatrica scandinavica, 116, 317-333, 2007	Expert review
Limosin, F., Gasquet, I., Leguay, D., Azorin, J. M., Rouillon, F., Body mass index and prevalence of obesity in a French cohort of patients with schizophrenia, Acta Psychiatrica Scandinavica, 118, 19-25, 2008	Obesity in schizophrenia covered by Mitchell 2013 systematic review
Margolese, Howard C., Malchy, Leslie, Negrete, Juan Carlos, Tempier, Raymond, Gill, Kathryn, Drug and alcohol use among patients with schizophrenia and related psychoses: Levels and consequences, Schizophrenia research, 67, 157-166, 2004	Included in Hunt 2018 systematic review
Merikangas, K. R., Jin, R., He, J. P., Kessler, R. C., Lee, S., Sampson, N. A., Viana, M. C., Andrade, L. H., Hu, C., Karam, E. G., Ladea, M., Medina-Mora, M. E., Ono, Y., Posada-Villa, J., Sagar, R., Wells, J. E., Zarkov, Z., Prevalence and correlates of bipolar spectrum disorder in the World Mental Health Survey Initiative, Archives of general psychiatry, 68, 241-251, 2011	International study - includes many countries not in our protocol
Mitchell, Alex J., Vancampfort, Davy, Sweers, Kim, van Winkel, Ruud, Yu, Weiping, De Hert, Marc, Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders-A systematic review and meta-analysis, Schizophrenia bulletin, 39, 306-318, 2013	Systematic review - updated by Vancampfort 2015
Nabavi, B., Mitchell, A. J., Nutt, D., A Lifetime Prevalence of Comorbidity Between Bipolar Affective Disorder and Anxiety Disorders: A Meta-analysis of 52 Interview-based Studies of Psychiatric Population, EBioMedicine, 2, 1405-1419, 2015	Systematic review includes the same studies as Pavlova 2015
Nuevo, R., Chatterji, S., Fraguas, D., Verdes, E., Naidoo, N., Arango, C., Ayuso-Mateos, J. L., Increased risk of diabetes mellitus among persons with psychotic symptoms: results from the WHO World Health Survey, Journal of clinical psychiatry, 72, 1592â□□1599, 2011	Included in Stubbs 2015 SR
Osborn, David P., Limburg, Heather, Walters, Kate, Petersen, Irene, King, Michael, Green, Jane, Watson, Jo, Nazareth, Irwin, Relative incidence of common cancers in people with severe mental illness. Cohort study in the United Kingdom THIN primary care database, Schizophrenia research, 143, 44-49, 2013	Incidence not prevalence

Study	Reason for Exclusion
Pavlova, B., Perlis, R. H., Alda, M., Uher, R., Lifetime prevalence of anxiety disorders in people with bipolar disorder: A systematic review and meta-analysis, The Lancet Psychiatry, 2, 710-717, 2015	Reports lifetime prevalence only
Perugi, G., Quaranta, G., Belletti, S., Casalini, F., Mosti, N., Toni, C., Dell'Osso, L., General medical conditions in 347 bipolar disorder patients: clinical correlates of metabolic and autoimmune-allergic diseases, Journal of affective disorders, 170, 95-103, 2015	Lifetime prevalence only
Petry, N. M., Barry, D., Pietrzak, R. H., Wagner, J. A., Overweight and obesity are associated with psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions, Psychosomatic medicine, 70, 288-97, 2008	Prevalence not reported in our population of interest
Rapsey, C. M., Lim, C. C., Al-Hamzawi, A., Alonso, J., Bruffaerts, R., Caldas-de-Almeida, J. M., Florescu, S., de Girolamo, G., Hu, C., Kessler, R. C., Kovess-Masfety, V., Levinson, D., Medina-Mora, M. E., Murphy, S., Ono, Y., Piazza, M., Posada-Villa, J., ten Have, M., Wojtyniak, B., Scott, K. M., Associations between DSM-IV mental disorders and subsequent COPD diagnosis, Journal of psychosomatic research, 79, 333-9, 2015	International study which includes many countries not in our protocol
Saari, Kaisa M., Lindeman, Sari M., Viilo, Kaisa M., Isohanni, Matti K., Jarvelin, Marjo-Riitta, Lauren, Liisa H., Savolainen, Markku J., Koponen, Hannu J., A 4-Fold Risk of Metabolic Syndrome in Patients With Schizophrenia: The Northern Finland 1966 Birth Cohort Study, The Journal of clinical psychiatry, 66, 559-563, 2005	Included in Mitchell 2015 SR
Salvi, V., D'Ambrosio, V., Rosso, G., Bogetto, F., Maina, G., Age-specific prevalence of metabolic syndrome in Italian patients with bipolar disorder, Psychiatry and Clinical Neurosciences, 65, 47-54, 2011	Included in Vancampfort 2015 systematic review
Schoepf, D., Potluri, R., Uppal, H., Natalwala, A., Narendran, P., Heun, R., Type-2 diabetes mellitus in schizophrenia: Increased prevalence and major risk factor of excess mortality in a naturalistic 7-year follow-up, European psychiatry, 27, 33-42, 2012	Included in Stubbs 2015 SR
Shashidhara, M., Sushma, B. R., Viswanath, B., Math, S. B., Janardhan Reddy, Y. C., Comorbid obsessive compulsive disorder in patients with bipolar-I disorder, Journal of affective disorders, 174, 367-71, 2015	Included in Amerio 2015 SR
Simhandl, C., Radua, J., Konig, B., Amann, B. L., Prevalence and impact of comorbid alcohol use disorder in bipolar disorder: A prospective follow-up study, Australian and New Zealand journal of psychiatry, 50, 345-351, 2016	Included in Hunt 2016 systematic review
Sokal, J., Messias, E., Dickerson, F. B., Kreyenbuhl, J., Brown, C. H., Goldberg, R. W., Dixon, L. B., Comorbidity of medical illnesses among adults with serious mental illness who are receiving community psychiatric services, Journal of Nervous & Mental Disease, 192, 421-7, 2004	Prevalence not reported in our group of interest
Soyka, M., Albus, M., Kathmann, N., Finelli, A., Hofstetter, S., Holzbach, R., Immler, B., Sand, P., Prevalence of alcohol and drug abuse in schizophrenic inpatients, European Archives of Psychiatry & Clinical Neuroscience, 242, 362-72, 1993	Included in Hunt 2018 systematic review
Stubbs, B., Vancampfort, D., De Hert, M., Mitchell, A., The prevalence and predictors of type two diabetes mellitus in people with schizophrenia: A systematic review and comparative meta-analysis, Acta psychiatrica scandinavica, 132, 144-157, 2015	More relevant UK prevalence data found in PHE 2018
Toftdahl, N. G., Nordentoft, M., Hjorthoj, C., Prevalence of substance use disorders in psychiatric patients: a nationwide Danish population-	Included in Hunt 2018 systematic review

Study	Reason for Exclusion
based study, Social psychiatry and psychiatric epidemiology, 51, 129-140, 2016	
Varo, C., Murru, A., Salagre, E., Jimenez, E., Sole, B., Montejo, L., Carvalho, A., Stubbs, B., Grande, I., Martinez-Aran, A., Vieta, E., Reinares, M., Behavioral addictions in bipolar disorders: A systematic review, European neuropsychopharmacology, 29, 76-97, 2019	Behavioural addictions not relevant to protocol
Woodhead, C., Ashworth, M., Schofield, P., Henderson, M., Patterns of physical co-/multi-morbidity among patients with serious mental illness: a London borough-based cross-sectional study, BMC family practice, 15, 117, 2014	More relevant UK prevalence data found in PHE 2018

Economic studies

A global economic literature search was undertaken for this guideline, covering all review questions. 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 studies from the economic component of the review

Study	Reason for Exclusion
Aitchison, K J, Kerwin, R W, Cost-effectiveness of clozapine: a UK clinic-based study (Structured abstract), British Journal of PsychiatryBr J Psychiatry, 171, 125-130, 1997	Available as abstract only.
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	Available as abstract only.

Study	Reason for Exclusion
hospital patients (Structured abstract), Journal of Mental HealthJ Ment Health, 5, 379-94, 1996	
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 for patients with chronic schizophrenia, Archives of Psychiatric NursingArch Psychiatr Nurs, 14, 98-104, 2000	Study conducted in Hong Kong. A costing analysis.
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	Cost effectiveness study, but population of interest is not focussed on rehabilitation for people with complex psychosis.

Study	Reason for Exclusion
and cost-utility analysis, Psychiatry ResearchPsychiatry Res, 254, 198-204, 2017	
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 ScandinavicaActa Psychiatr Scand, 92, 199-201, 1995	Costing analysis which predates year 2000.
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	Structured abstract. Does not match any review question considered in this guideline.

Study	Reason for Exclusion
management of schizophrenia: a decision-analytic model (Structured abstract), Journal of Clinical Psychopharmacology, 25, 427-434, 2005	
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.
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, 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.

Study	Reason for Exclusion
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 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

Research question

What coexisting neurodevelopmental and mental health conditions need to be considered when forming a rehabilitation plan for people with complex psychosis and related severe mental health problems?

Why this is important

Although the evidence report identified a number of studies addressing the prevalence of comorbidities in people with complex psychosis and related conditions, the committee were aware that there was little data about the numbers of deaths caused by physical comorbidities in people with complex psychosis. The committee agreed that in the UK this data could easily be captured and recorded, and would contribute to the understanding of priority health needs in people with complex psychosis and related severe mental health conditions.

Table 8: Research recommendation rationale

Research question	What structured group activities are effective at improving interpersonal functioning (social skills) for people with complex psychosis and related SMI?
Why is this needed	
Importance to 'patients' or the population	People with complex psychosis and related severe mental health conditions have increased levels of comorbidity, but the numbers of deaths caused by these physical comorbidities is unknown. This information could help inform priority health needs and interventions, and reduce deaths.
Relevance to NICE guidance	This information could strengthen guidance on priority health needs and interventions.
Relevance to the NHS	This information could lead to fewer deaths.
National priorities	Improvement in mortality.
Current evidence base	This information is not routinely captured in the UK.
Equality	All patients with complex psychosis and related severe mental health conditions.
Feasibility	The committee thought this would be achievable.
Other comments	None.

Table 9: Research recommendation modified PICO table

Criterion	Explanation
Population	Patients aged 18+ with complex psychosis and related severe mental health conditions.
Intervention	Not applicable

Criterion	Explanation
Comparator	Not applicable
Outcomes	Mortality associated with comorbidities
Study design	Observational cohort study (register)
Timeframe	Decades
Additional information	The first step in the research would be to conduct a registry of people with complex psychosis and related severe mental health conditions, recording their comorbidities and causes of death.

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Appendix M – evidence for adapted recommendations

Evidence for adapted questions for review question 1.3: What coexisting conditions (neurodevelopmental, cognitive, mental/physical health disorders) need to be considered when formulating a rehabilitation plan with people with complex psychosis?

Recommendation	Original Recommendation	Supporting evidence statements	Committee's discussion – rationale and impact
Responsibilities for healthcare providers			
GPs should develop and use practice case registers to monitor the physical and mental health of people with complex psychosis and related severe mental health conditions in primary care.	CG178 1.5.3.1 Develop and use practice case registers to monitor the physical and mental health of people with psychosis or schizophrenia in primary care.	"The GDG for the 2014 guideline reconsidered the 2002 and 2009 guidelines in the area of primary care and the primary and secondary care interface. It was agreed that although there is no robust evidence to guide recommendations in this area, the GDG for the 2014 guideline concurred with its predecessors that consensus-based recommendations (based on the considerations above but not restricted to them) should be developed to help guide primary and secondary care health and social care professionals in these area"	The committee agreed with the existing guidance about the development and use of practice case registers. They adapted the wording to make it clear whose responsibility it was to develop and use these registers, and while this would typically be done by GPs it could also be done by other primary healthcare professionals. They also reworded the population to align with the current guideline.
For people having community rehabilitation, GPs should assume lead responsibility for the person's physical health needs, including health checks and treatment of physical health conditions, working collaboratively with the community mental health	CG178 1.5.3.2 GPs and other primary healthcare professionals should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and	"The GDG for the 2014 guideline reconsidered the 2002 and 2009 guidelines in the area of primary care and the primary and secondary care interface. It was agreed that although there is no robust evidence to guide recommendations in this area, the GDG for the 2014 guideline concurred with its	The committee agreed with the existing guidance about continuing physical health checks when people are in transition between healthcare settings. They adapted the wording because the original recommendation concerns transfer from secondary care to primary care, whereas the committee

Recommendation	Original Recommendation	Supporting evidence statements	Committee's discussion – rationale and impact
rehabilitation team and other services as relevant.	then at least annually. The health check should be comprehensive, focusing on physical health problems that are common in people with psychosis and schizophrenia. Include all the checks recommended in 1.3.6.1 and refer to relevant NICE guidance on monitoring for cardiovascular disease, diabetes, obesity and respiratory disease. A copy of the results should be sent to the care coordinator and psychiatrist, and put in the secondary care note	predecessors that consensus-based recommendations (based on the considerations above but not restricted to them) should be developed to help guide primary and secondary care health and social care professionals in these area"	acknowledged that health checks for people moving from inpatient to community rehabilitation would require collaboration between primary care healthcare professionals, the community mental health rehab team and other services. Given the increased prevalence of physical health problems, many associated with potentially modifiable risk factors, the committee also thought that the recommendation should emphasise preventative health care and treatment of physical health problems.
Healthy living			
Offer people in rehabilitation services a routine physical health check at least annually. The physical health check should include: • BMI • waist circumference • pulse and blood pressure • glycosylated haemoglobin (HbA1c), blood lipid profile, liver function tests and thyroid function • ECG if indicated • assessment of smoking, alcohol or substance use	CG178 1.3.6.1 Before starting antipsychotic medication, undertake and record the following baseline investigations: • weight (plotted on a chart) • waist circumference • pulse and blood pressure • fasting blood glucose, glycosylated haemoglobin (HbA1c), blood lipid profile and prolactin levels • assessment of any movement disorders	CG178 "Antipsychotic medications may cause metabolic/endocrine abnormalities (for example, weight gain, diabetes, lipid abnormalities and galactorrhoea)" "The GDG for the 2014 guideline reconsidered the 2002 and 2009 guidelines in the area of primary care and the primary and secondary care interface. It was agreed that although there is no robust evidence to guide recommendations in this area, the GDG for the 2014 guideline concurred with its predecessors that consensus-based recommendations (based on the	The committee agreed that the baseline investigations before starting antipsychotic medication recommended in CG178 should form the core of the annual physical health check for people in rehabilitation services as most would be receiving antipsychotic medication. The committee thought, based partly on evidence of the prevalence of comorbidities, that additional investigations should be done in the health check including: assessment of smoking, alcohol or substance use, sexual health and vision, hearing and podiatry.

Recommendation	Original Recommendation	Supporting evidence statements	Committee's discussion – rationale and impact
• assessment of nutritional status, diet and level of physical activity • assessment of any movement disorders • assessment of sexual health • vision, hearing and podiatry.	• assessment of nutritional status, diet and level of physical activity CG185 1.2.12 Ensure that the physical health check for people with bipolar disorder, performed at least annually, includes: • weight or BMI, diet, nutritional status and level of physical activity • cardiovascular status, including pulse and blood pressure • metabolic status, including fasting blood glucose, glycosylated haemoglobin (HbA1c) and blood lipid profile • liver function • renal and thyroid function, and calcium levels, for people taking long-term lithium.	considerations above but not restricted to them) should be developed to help guide primary and secondary care health and social care professionals in these area" CG185 "The GDG went beyond the evidence of clinical benefit to consider other important issues that can affect the physical health of an adult with severe mental illness. These issues relate to when physical health problems should be assessed, how they should be monitored and which should be responsibility for both physical and mental health."	They also reworded the recommendation (in line with the recommendation from CG185) to indicate a regular health check (at least once a year), rather than just before starting antipsychotic medication, because they thought it was crucial to monitor changes in physical health to inform and update care plans .
Ensure a copy of the results of the physical health check is available to the rehabilitation service, primary care, secondary mental healthcare and secondary physical healthcare as appropriate, and record them in the case notes. Discuss	CG178 1.5.3.2 GPs and other primary healthcare professionals should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and	"The GDG for the 2014 guideline reconsidered the 2002 and 2009 guidelines in the area of primary care and the primary and secondary care interface. It was agreed that although there is no robust evidence to guide recommendations in this area, the GDG for the 2014 guideline concurred with its	The committee adapted this recommendation because the results of the physical health check would need be made available to a different group of healthcare professionals, beyond the care-coordinator and psychiatrist listed in the original recommendation from CG178.

Recommendation	Original Recommendation	Supporting evidence statements	Committee's discussion – rationale and impact
any important findings with the person.	then at least annually. The health check should be comprehensive, focusing on physical health problems that are common in people with psychosis and schizophrenia. Include all the checks recommended in 1.3.6.1 and refer to relevant NICE guidance on monitoring for cardiovascular disease, diabetes, obesity and respiratory disease. A copy of the results should be sent to the care coordinator and psychiatrist, and put in the secondary care note	predecessors that consensus-based recommendations (based on the considerations above but not restricted to them) should be developed to help guide primary and secondary care health and social care professionals in these area"	
Care and treatment for physical health conditions			
Use the physical health check in recommendation 1.10.13 to identify at the earliest opportunity people who: • have hypertension • have abnormal lipid levels • are obese or at risk of obesity • have diabetes or are at risk of diabetes • have cardiovascular disease • are physically inactive • have chronic obstructive pulmonary disease (COPD).	CG178 1.5.3.3 Identify people with psychosis or schizophrenia who have high blood pressure, have abnormal lipid levels, are obese or at risk of obesity, have diabetes or are at risk of diabetes (as indicated by abnormal blood glucose levels), or are physically inactive, at the earliest opportunity following relevant NICE guidance (see cardiovascular disease: risk assessment and reduction, including lipid modification,	"The GDG for the 2014 guideline reconsidered the 2002 and 2009 guidelines in the area of primary care and the primary and secondary care interface. It was agreed that although there is no robust evidence to guide recommendations in this area, the GDG for the 2014 guideline concurred with its predecessors that consensus-based recommendations (based on the considerations above but not restricted to them) should be developed to help guide primary and secondary care health and social care professionals in these area"	The committee adapted this recommendation to align it with their recommendation about regular physical health checks, to indicate specific physical health problems that should be identified. These were listed in the original recommendation from CG178, but the committee thought that COPD should also be added to the list of important physical health problems and risk factors this population.

Recommendation	Original Recommendation	Supporting evidence statements	Committee's discussion – rationale and impact
Offer treatment in line with NICE guidance, ideally in primary care	preventing type 2 diabetes, obesity, hypertension, prevention of cardiovascular disease and physical activity).		

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