APPENDIX 21:

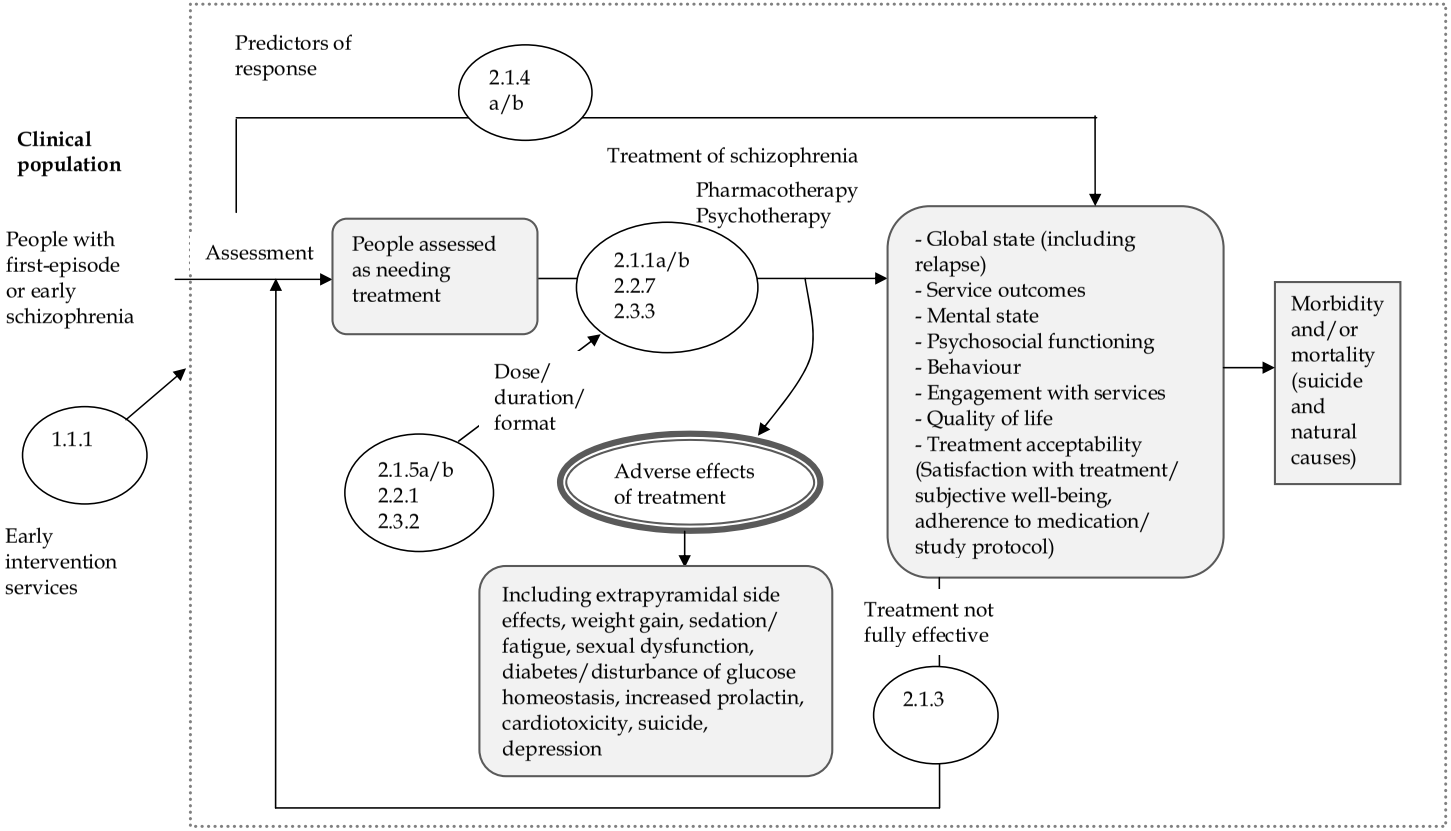
2009 ANALYTIC FRAMEWORK AND CLINICAL QUESTIONS

ACCESS AND ENGAGEMENT

No.	Primary clinical questions
1.1.1	For people with psychosis, do early intervention services improve outcomes when compared with standard care?
1.1.1a	For all people with psychosis, do early intervention services improve the number of people remaining in contact with services?
1.1.1b	For African–Caribbean people with psychosis, do early intervention services improve the number of people remaining in contact with services?
1.1.2	For all people from black and minority ethnic groups (particularly, African–Caribbean people) with psychosis, do services, such as assertive outreach teams, crisis teams, and home treatment teams improve the number of people remaining in contact with services?
1.1.3	For all people from black and minority ethnic groups with psychosis, do specialist ethnic mental health services (culturally specific or culturally skilled) improve the number of people remaining in contact with services?

Initial treatment

This is concerned with appropriate treatment and management when a person first comes to the attention of services with a clinical picture indicating a probable diagnosis of schizophrenia.



Initial treatment with antipsychotic medication

No.	Primary clinical question
2.1.1a	For people with first-episode or early schizophrenia, what are the benefits and downsides of continuous oral antipsychotic drug[43] treatment when compared with another oral antipsychotic drug at the initiation of treatment[44]?
	Secondary clinical questions
2.1.3	For people with first-episode or early schizophrenia in whom initial oral antipsychotic medication is not fully effective, what is the most effective treatment strategy and when do you decide to alter initial treatment?
2.1.4a	For people with first-episode or early schizophrenia, are there any relevant factors (including patient populations) which predict the nature and degree of response to initial antipsychotic medication?
2.1.5a	For people with first-episode or early schizophrenia, what should be the dose/duration (and where relevant frequency) of initial antipsychotic medication?
2.2.1	When antipsychotic-naïve patients are started on antipsychotic medication, are relatively low doses required for a therapeutic response?
2.2.5	For people with first-episode or early schizophrenia, what is the most appropriate treatment strategy to manage known side effects of antipsychotic medication?
2.2.6	For people with first-episode or early schizophrenia, what is the most appropriate treatment strategy if antipsychotic medication is effective but not tolerated?
2.2.7	For people with first-episode or early schizophrenia, what baseline measurements should be taken before initiating antipsychotic medication?

[43] The analysis will compare each of the SGAs (amisulpride, aripiprazole, olanzapine, paliperidone, quetiapine, sertindole and zotepine) with each other, as well as with haloperidol and any non-haloperidol FGA.

[44] When administered within the recommended dose range (BNF 54).

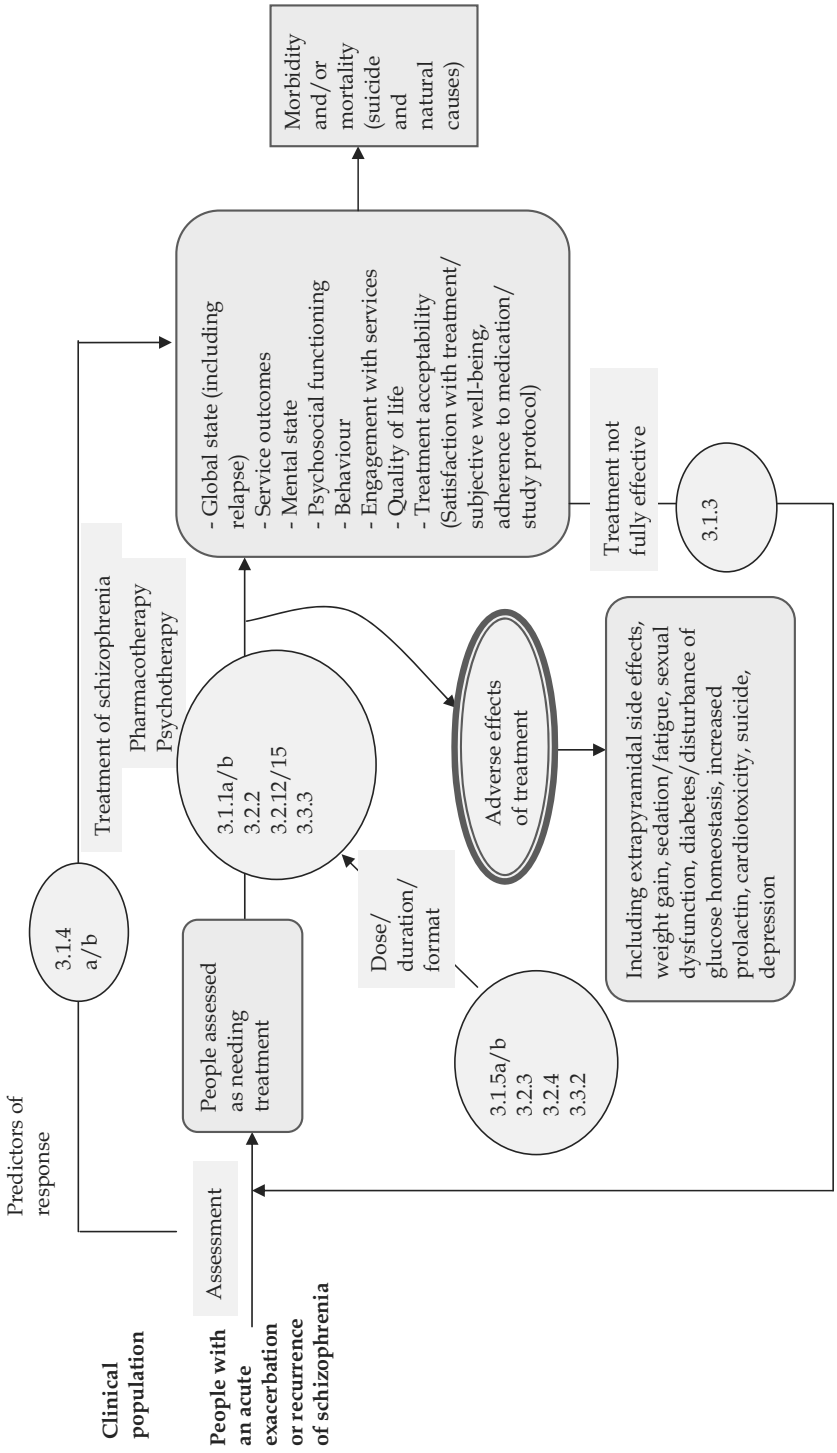
Initial treatment with a psychological/psychosocial intervention

No.	Primary clinical question
2.1.1b	For people with first-episode or early schizophrenia, what are the benefits and downsides of psychological/psychosocial interventions[45] when compared with alternative management strategies at initiation of treatment?
	Secondary clinical questions
2.1.4b	For people with first-episode or early schizophrenia, are there any relevant factors (including patient populations) that predict the nature and degree of response to an initial psychological/psychosocial intervention?
2.1.5b	For people with first-episode or early schizophrenia, what should be the dose/duration (and where relevant frequency) of an initial psychological/psychosocial intervention?
2.3.2	For people with first-episode or early schizophrenia, what is the most effective format for particular psychological/psychosocial interventions (for example, group or individual)?
2.3.3	For people with first-episode or early schizophrenia, are there any advantages of combining particular psychological/psychosocial interventions with an antipsychotic, either concurrently or sequentially?

[45] The analysis will be conducted separately for each intervention (CBT, cognitive remediation, counselling and supportive psychotherapy, family intervention, psychodynamic psychotherapy and psychoanalysis, psychoeducation, social skills training and arts therapies).

Acute treatment

This is concerned with the management and treatment of any acute exacerbation or recurrence of schizophrenia.



Acute treatment with antipsychotic medication

No.	Primary clinical question
3.1.1a	For people with an acute exacerbation or recurrence of schizophrenia, what are the benefits and downsides of continuous oral antipsychotic drug[46] treatment when compared with another oral antipsychotic drug[47]?
	Secondary clinical questions
3.1.3	For people with an acute exacerbation or recurrence of schizophrenia who have an inadequate or no response to oral antipsychotic medication, what is the most effective treatment strategy and when do you decide to alter treatment?
3.1.4a	For people with an acute exacerbation or recurrence of schizophrenia, are there any relevant factors (including patient populations) which predict the nature and degree of response to initial antipsychotic treatment?
3.1.5a	For people with an acute exacerbation or recurrence of schizophrenia, what should be the dose/duration (and, where relevant, frequency) of initial antipsychotic treatment?
3.2.3	For people with an acute exacerbation or recurrence of schizophrenia, what is the optimal dose range for antipsychotic medication (for example, in chlorpromazine equivalents, milligrams per day for conventional antipsychotics and on a drug-by-drug basis for the SGAs)?
3.2.4	Does rapid escalation of dosage/relatively high dosage yield any advantage in terms of speed of onset or degree of therapeutic response?
3.2.13	For people with an acute exacerbation or recurrence of schizophrenia, what is the most appropriate treatment strategy to manage known side effects of antipsychotic medication?

[46] The analysis will be compare each of the SGAs (amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, sertindole and zotepine) with each other, as well as with haloperidol and any non-haloperidol FGA.

[47] When administered within the recommended dose range (BNF 54). *Note*. Clozapine is only licensed in the UK for people with treatment-resistant schizophrenia and in people with schizophrenia who have severe, untreatable neurological adverse reactions to other antipsychotic agents, including atypical antipsychotics. Treatment-resistance is defined as a lack of satisfactory clinical improvement despite the use of adequate doses of at least two different antipsychotic agents, including an atypical antipsychotic agent, prescribed for adequate duration.

	Secondary clinical questions
3.2.14	For people with an acute exacerbation or recurrence of schizophrenia, what is the most appropriate treatment strategy if antipsychotic medication is effective but not tolerated?
3.2.15	For people with an acute exacerbation or recurrence of schizophrenia, what baseline measurements should be taken before initiating antipsychotic medication?

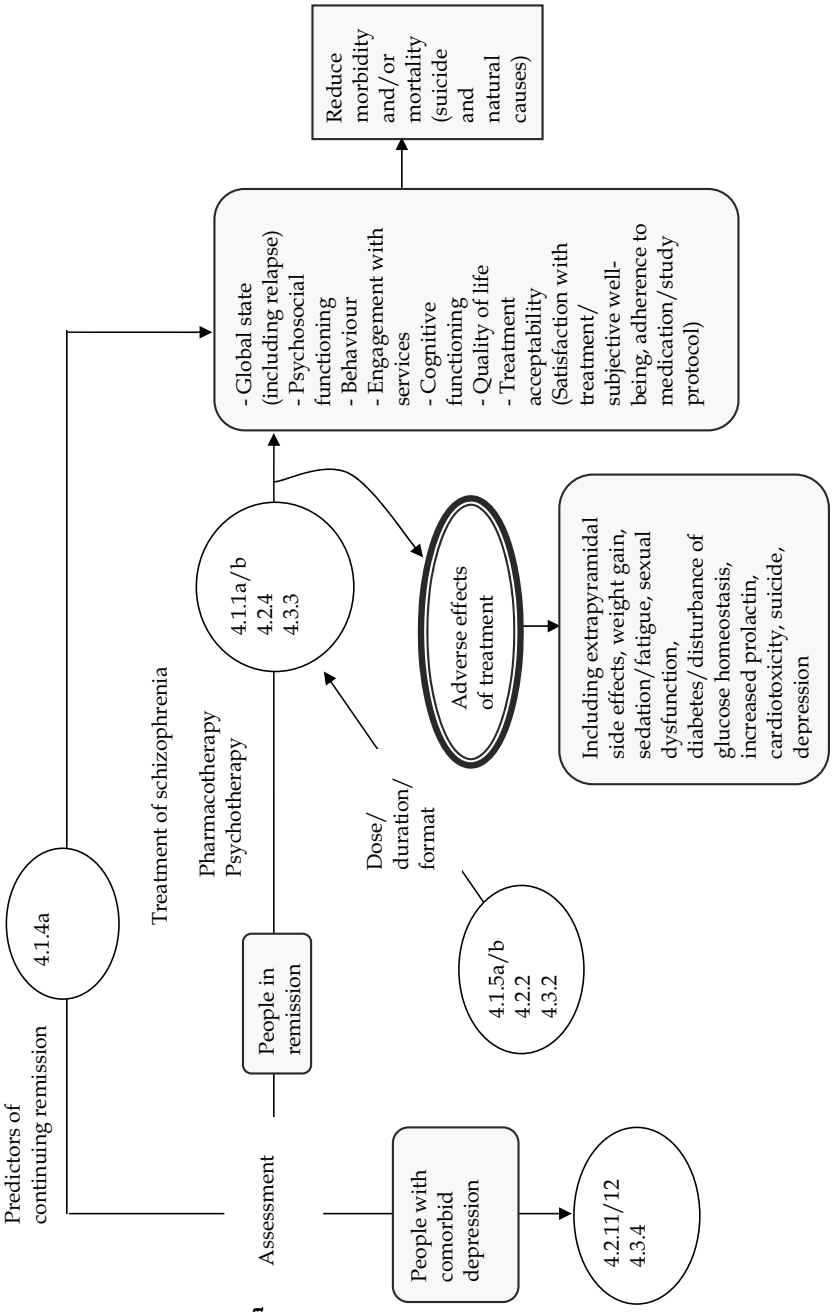
Acute treatment with a psychological/ psychosocial intervention

No.	**Updated clinical question**
3.1.1b	For people with an acute exacerbation or recurrence of schizophrenia, what are the benefits and downsides of psychological/psychosocial interventions[48] when compared with alternative management strategies?
	Secondary clinical questions
3.1.4b	For people with an acute exacerbation or recurrence of schizophrenia, are there any relevant factors (including patient populations) that predict the nature and degree of response to an initial psychological/psychosocial intervention?
3.1.5b	For people with an acute exacerbation or recurrence of schizophrenia, what should be the dose/duration (and, where relevant, frequency) of an initial intervention?
3.3.2	For people with an acute exacerbation or recurrence of schizophrenia, what are the most effective formats for psychological/psychosocial interventions (for example, group or individual)?
3.3.3	For people with an acute exacerbation or recurrence of schizophrenia, are there any advantages of combining a psychological/psychosocial intervention with an antipsychotic, either concurrently or sequentially?

[48] The analysis will be conducted separately for each intervention (CBT, cognitive remediation, counselling and supportive psychotherapy, family interventions, psychodynamic psychotherapy and psychoanalysis, psychoeducation, social skills training and arts therapies).

Promoting recovery in people with schizophrenia that is in remission

This is concerned with the continuing management and treatment of schizophrenia.



Promoting recovery with antipsychotic medication in people with schizophrenia that is in remission[49]

No.	Primary clinical questions
4.1.1a	For people with schizophrenia that is in remission, what are the benefits and downsides of continuous oral antipsychotic drug[50] treatment when compared with another oral antipsychotic drug[51]?
4.2.4	For people with schizophrenia that is in remission, is any depot or long-acting antipsychotic medication associated with improved relapse prevention over time?
	Secondary clinical questions
4.1.4a	For people with schizophrenia that is in remission, are there any relevant factors (including patient populations) that predict continuing remission?
4.1.5a	For people with schizophrenia that is in remission, what should be the dose/duration (and, where relevant, frequency) of antipsychotic medication?
4.1.6a	For people with schizophrenia that is in remission, is antipsychotic medication acceptable to the person being treated?
4.2.2	For people with schizophrenia that is in remission, how long should antipsychotic medication be continued for prevention of relapse?
4.2.6	For people with schizophrenia that is in remission, who have had long-term antipsychotic drug treatment, is there any evidence that patients have a preference for either depot/long-acting or oral preparations?
4.2.11	For people with schizophrenia that is in remission and comorbid depressive features, is antipsychotic medication associated with an enhanced therapeutic response?
4.2.15	For people with schizophrenia that is in remission, is any antipsychotic medication associated with improved cognitive function in relevant domains?

[49] For the purposes of the guideline, the definition of remission includes people who have responded fully or partially to treatment.

[50] The analysis will compare each of the SGAs (amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, sertindole and zotepine) with each other, as well as with placebo, haloperidol and any non-haloperidol FGA. *Note*. Clozapine is only licensed in the UK for people with treatment-resistant schizophrenia and in people with schizophrenia who have severe, untreatable neurological adverse reactions to other antipsychotic agents, including atypical antipsychotics. Treatment resistance is defined as a lack of satisfactory clinical improvement despite the use of adequate doses of at least two different antipsychotic agents, including an atypical antipsychotic agent, prescribed for adequate duration.

[51] When administered within the recommended dose range (BNF 54).

	Secondary clinical questions
4.2.17	For people with schizophrenia that is in remission, is there any evidence that switching to a particular antipsychotic medication is associated with a lower liability for tardive dyskinesia?
4.2.18	For people with schizophrenia that is in remission, is augmentation of antipsychotic medication with another antipsychotic associated with an increased risk of/severity of treatment-emergent adverse events?
4.2.19	For people with schizophrenia that is in remission, what is the most appropriate treatment strategy to manage known side effects of antipsychotic medication?
4.2.20	For people with schizophrenia that is in remission, what is the most appropriate treatment strategy if antipsychotic medication is effective but not tolerated?

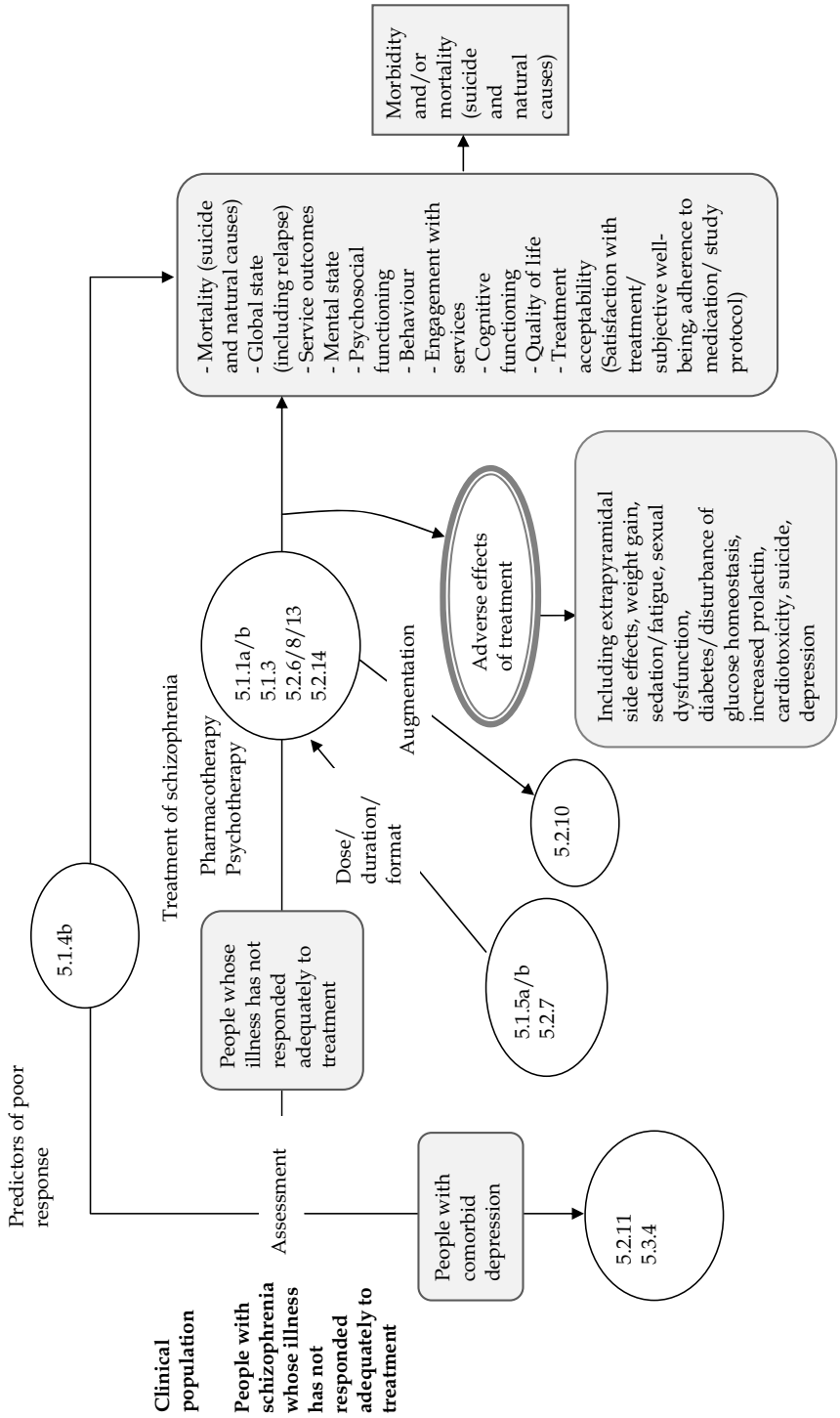
Promoting recovery with a psychological/psychosocial intervention in people with schizophrenia that is in remission

No.	**Primary clinical question**
4.1.1b	For people with schizophrenia that is in remission, what are the benefits and downsides of psychological/psychosocial interventions[52] when compared with alternative management strategies?
	Secondary clinical questions
4.1.5b	For people with schizophrenia that is in remission, what should be the dose/duration (and, where relevant, frequency) of a psychological/psychosocial intervention?
4.3.2	For people with schizophrenia that is in remission, what is the most effective format for psychological/psychosocial interventions (for example, group or individual)?
4.3.3	For people with schizophrenia that is in remission, is there any advantage in terms of preventing relapse of combining psychological/psychosocial interventions with an antipsychotic drug, either concurrently or sequentially?
4.3.4	For people with schizophrenia that is in remission and comorbid depressive features, is any psychological/psychosocial intervention associated with an enhanced therapeutic response?

[52] The analysis will be conducted separately for each intervention (CBT, cognitive remediation, counselling and supportive psychotherapy, family interventions, psychodynamic psychotherapy and psychoanalysis, psychoeducation, social skills training and arts therapies).

Promoting recovery in people with schizophrenia whose illness has not responded adequately to treatment

This is concerned with the continuing management and treatment of schizophrenia.



Promoting recovery with antipsychotic medication in people with schizophrenia whose illness has not responded adequately to treatment

No.	Primary clinical questions
5.1.1a	For people with schizophrenia whose illness has not responded adequately to treatment, what are the benefits and downsides of continuous oral antipsychotic drug[53] treatment when compared with another oral antipsychotic drug[54]?
5.2.6	For people with schizophrenia whose illness has not responded adequately to treatment and who have had long-term antipsychotic drug treatment, is there any evidence that patients have a preference for either depot/long-acting or oral preparations?
5.2.10	For people with schizophrenia whose illness has not responded adequately to clozapine treatment, is augmentation of clozapine with another antipsychotic medication associated with an enhanced therapeutic response?
	Secondary clinical questions
5.1.3	For people with schizophrenia whose illness has not responded adequately to treatment, when do you decide to change antipsychotic medication?
5.1.4a	For people with schizophrenia whose illness has not responded adequately to treatment, are there any relevant factors (including patient populations) that predict poor response to antipsychotic medication?
5.1.5a	For people with schizophrenia whose illness has not responded adequately to treatment, what should be the dose/duration (and, where relevant, frequency) of antipsychotic medication?
5.2.7	For people with schizophrenia whose illness has not responded adequately to treatment, do high (mega) doses of antipsychotic medication offer any therapeutic advantage over standard (recommended) dosage?
5.2.8	For people with schizophrenia whose illness has not responded adequately to treatment, is clozapine more effective than other antipsychotic medications?

[53] The analysis will be compare each of the SGAs (amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, sertindole and zotepine) with each other, as well as with placebo, haloperidol and any non-haloperidol FGA.
[54] When administered within the recommended dose range (BNF 54).

	Secondary clinical questions
5.2.11	For people with schizophrenia and comorbid depressive features whose illness has not responded adequately to treatment, is antipsychotic medication associated with an enhanced therapeutic response?
5.2.13	For people with schizophrenia with persistent negative symptoms, is any antipsychotic medication (including adjunctive treatments) associated with an enhanced therapeutic response?
5.2.14	For people with schizophrenia with persistent symptoms of irritability, hostility and aggression, is any antipsychotic medication (including adjunctive treatments) associated with an enhanced therapeutic response?
5.2.15	For people with schizophrenia whose illness has not responded adequately to treatment, is any antipsychotic medication associated with improved cognitive function in relevant domains?
5.2.18	For people with schizophrenia whose illness has not responded adequately to treatment, is augmentation of antipsychotic medication with another antipsychotic associated with an increased risk of/severity of treatment-emergent adverse events?

Promoting recovery with a psychological/psychosocial intervention in people with schizophrenia whose illness has not responded adequately to treatment

No.	Primary clinical question
5.1.1b	For people with schizophrenia whose illness has not responded adequately to treatment, what are the benefits and downsides of psychological/psychosocial interventions[55] when compared with alternative management strategies?
	Secondary clinical questions
5.1.5b	For people with schizophrenia whose illness has not responded adequately to treatment, what should be the dose/duration (and where relevant frequency) of a psychological/psychosocial intervention?
5.3.4	For people with schizophrenia and comorbid depressive features whose illness has not responded adequately to treatment, are psychological/psychosocial interventions associated with an enhanced therapeutic response?

[55] The analysis will be conducted separately for each intervention (CBT, cognitive remediation, counselling and supportive psychotherapy, family interventions, psychodynamic psychotherapy and psychoanalysis, psychoeducation, social skills training and arts therapies).