

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Centre for Clinical Practice – Surveillance Programme

### *Recommendation for Guidance Executive*

#### **Clinical guideline**

CG155: Psychosis and schizophrenia in children and young people

#### **Publication date**

January 2013

#### **Surveillance report for GE**

April 2015

#### **Surveillance recommendation**

The [Evidence Update on CG155](#): Psychosis and schizophrenia in children and young people identified 1 potential impact on the guideline.

Following further discussion of the impact at a Triage Panel, GE is asked to consider the proposal to update the following question in CG155 using the Standing Committee for Updates via the Clinical Guidelines Update Team:

- 'What is the adverse effects profile of olanzapine compared to other second-generation antipsychotics for treating children and young people with psychosis and schizophrenia?'

GE is asked to note that this 'yes to update' proposal will not be consulted on.

#### **Key findings**

			Potential impact on guidance	
			Yes	No
Evidence identified from Evidence Update			✓	
Anti-discrimination and equalities considerations				✓
Feedback from Triage Panel meeting			✓	
No update	<b>CGUT update</b>	Standard update	Transfer to static list	Change review cycle
	✓			

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Centre for Clinical Practice – Surveillance Programme

### Surveillance review of CG155: Psychosis and schizophrenia in children and young people

#### *Recommendation for Guidance Executive*

#### ***Background information***

Guideline issue date: 2013

2-year review: 2015

NCC: National Collaborating Centre for Mental Health

#### ***2-year Evidence Update***

1. The [Evidence Update on CG155](#): Psychosis and schizophrenia in children and young people was used as a source of evidence for this surveillance review and considered new evidence since the guideline was published. The search dates of the Evidence Update were 1 May 2012 to 25 September 2014. A summary of the evidence is provided in the Evidence Update.
2. The Evidence Update identified 1 area where there may be an impact on current guideline recommendations: Initial treatment with antipsychotic medication in children and young people with first episode psychosis. This area was considered by a Triage Panel.

#### ***Triage Panel recommendation***

3. The new evidence identified through the Evidence Update for CG155 which may potentially impact on guideline recommendations was considered by the Triage Panel to determine the most appropriate route to commission an update:

4. ***Clinical question: What is the adverse effects profile of olanzapine compared to other second-generation antipsychotics for treating children and young people with psychosis and schizophrenia?***

Three studies relevant to this question were identified in the Evidence Update. A cohort study<sup>1</sup> compared weight and other metabolic changes between young people and adults who had received olanzapine treatment for at least 24 weeks. Following treatment with olanzapine, the magnitude of changes in body weight and some blood lipid levels were greater in young people. A cross-sectional study<sup>2</sup> (examining baseline results of a cluster-randomised assessment of an integrated programme of drug treatment, psychotherapy and supported employment) assessed cardiometabolic risk and its moderators and mediators. Higher levels of triglycerides, insulin, and insulin resistance were associated with olanzapine therapy. A cohort study<sup>3</sup> aiming to identify single-nucleotide polymorphisms associated with antipsychotic-induced weight gain found that after 12 weeks of antipsychotic treatment, patients who had taken olanzapine gained substantially more weight than people taking other antipsychotics (quetiapine, risperidone and aripiprazole). These patients therefore had to be excluded from the study to maintain homogeneity of the phenotype. The Triage Panel felt that because of the adverse effects associated with olanzapine, particularly weight gain and metabolic effects, olanzapine may not be suitable for first-line treatment in children and young people with first episode psychosis. NICE CG155 does not specifically state that olanzapine should not be used first line, and the guideline should be updated to reflect evidence of its adverse effects.

**Decision:** NICE to update this clinical question using the Standing Committee for Updates via the Clinical Guidelines Update Team.

### ***Ongoing research***

5. No ongoing research was identified.

### ***Anti-discrimination and equalities considerations***

6. None identified.

### ***Implications for other NICE programmes***

7. This guideline relates to [CG178](#) Psychosis and schizophrenia in adults: treatment and management:
- a. Some recommendations in CG155 were taken directly from, or adapted from, the adult guideline 'Schizophrenia' (now replaced by 'Psychosis and schizophrenia in adults' [NICE CG178]). The following recommendations from CG178 have been incorporated into CG155 (some directly, some with adaptations) or are worded similarly/identically, and therefore may be affected by an update of CG155: 1.3.2.1, 1.3.4.1, 1.3.5.1, 1.3.6.1–1.3.6.11

8. This guideline relates to a quality standard in development: [Bipolar disorder, psychosis and schizophrenia in children and young people](#) (Anticipated publication date October 2015):
  - a. The draft quality standard includes a statement on monitoring antipsychotic medication (Children and young people with bipolar disorder, psychosis or schizophrenia prescribed antipsychotic medication have side effects monitored throughout treatment). If the guideline is updated to be more specific about the use of olanzapine, a definition of antipsychotic medication will be needed in the QS.

### **Conclusion**

9. Through the Evidence Update of CG155, new evidence that may potentially impact guideline recommendations was identified in the following area of the guideline and discussed at the Triage Panel:
  - a. Initial treatment with antipsychotic medication in children and young people with first episode psychosis
10. This area was considered by the Triage Panel, where it was decided that this update could be achieved by updating the following question in the guideline:
  - a. What is the adverse effects profile of olanzapine compared to other second-generation antipsychotics for treating children and young people with psychosis and schizophrenia?
11. For all other areas of the guideline no evidence was identified which would impact on recommendations.

Mark Baker – Centre Director  
Philip Alderson – Consultant Clinical Adviser  
Patrick Langford – Technical Analyst

Centre for Clinical Practice  
April 2015

## Appendix 1 Decision matrix

Surveillance and identification of triggers for updating CG155. The table below provides summaries of the evidence that were identified and included in the Evidence Update.

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p>155-01 In children and young people, what are the specific behaviours and symptoms that are associated with an increased risk of developing psychosis and schizophrenia (at risk mental state)? Sub-questions:            a) What is the course of these behaviours and symptoms?            b) What are the specific behaviours and symptoms that prompt initial recognition of psychosis or prompt diagnosis of schizophrenia?</p>			
<p><b>Cognitive deficits in people at risk of psychosis</b>            A systematic review and meta-analysis<sup>4</sup> (44 studies, n=3861; mean age in the at-risk study population 15–29 years) examined the association between cognitive deficits and the risk of, and transition to, psychosis among people at risk of psychosis. Compared with controls, deficits were seen in every cognitive domain for people at clinical risk and familial risk of psychosis. People at clinical risk who went on to transition to psychosis had more severe cognitive deficits than those who did not transition in all cognitive domains (except sustained attention).</p>	<p>Not applicable</p>	<p>Not applicable</p>	<p>The Evidence Update concluded that cognitive deficits appear to be evident in people at familial or clinical risk of psychosis, and the level of deficit appears to have some correlation with eventual transition to psychosis. NICE CG155 does not currently recommend assessment or monitoring of cognitive deficits in children or young people at risk of psychosis, however cognitive assessment is recommended for children and young people with first episode psychosis. It may be that the same principles of assessing children and</p>

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
			young people with first episode psychosis should potentially also be applied to those with possible psychosis. Further studies are needed to investigate timing and development of cognitive deficits in psychosis, and to establish the utility of measuring cognitive deficits in the context of assessment, monitoring, prognosis and early intervention.
155-02 For children and young people who are at risk of developing psychosis and schizophrenia (at risk mental state), does the provision of pharmacological, psychological or psychosocial and/or dietary interventions improve outcomes?			
<p><b>Cognitive behavioural therapy (CBT) for people at risk of psychosis</b></p> <p>A multicentre RCT<sup>5</sup> (n=288; age 14–35, mean=20.74 years) in the UK examined the effect of CBT on transition to psychosis and psychotic symptoms among people at high risk of psychosis. The mean number of sessions received by the CBT group was 9. The number of patients transitioning to psychosis, and distress from psychotic symptoms, did not differ significantly between the CBT and the control group, but psychotic symptom severity was significantly lower in the CBT group.</p>	Not applicable	Not applicable	The Evidence Update concluded that in people at high risk of psychosis, a mean of 9 sessions of CBT plus monitoring of mental state does not appear to reduce transition to psychosis or distress from symptoms of psychosis, but does appear to reduce the severity of psychotic symptoms. This evidence was considered broadly consistent with

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
			recommendations in NICE CG155 to consider CBT when symptoms are not sufficient for a diagnosis of psychosis or schizophrenia. However, reduction in the severity of psychotic symptoms may be achievable in less than the 16 sessions of CBT currently recommended by the guideline, and further research is needed to examine the optimum number of sessions.
<p><b>CBT with or without an antipsychotic for people at risk of psychosis</b></p> <p>An RCT<sup>6</sup> (n=115; age 14–30, mean=18 years) in Australia compared the effect of CBT plus risperidone, CBT plus placebo, and supportive therapy plus placebo on transition to psychosis among people at high risk of psychosis. Rates of transition to psychosis did not differ significantly between the treatment groups.</p>	Not applicable	Not applicable	The Evidence Update concluded that rates of transition to psychosis in people at high risk of psychosis appear to be similar following CBT (with or without risperidone) and supportive therapy. This was considered consistent with NICE CG155 to consider CBT when symptoms are not sufficient for a diagnosis of psychosis or schizophrenia. The similar efficacy seen in the

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			study of CBT with or without risperidone is consistent with the recommendation not to offer antipsychotic medication when symptoms are not sufficient for a diagnosis of psychosis or schizophrenia. Further research is needed to establish the efficacy of CBT for young people at high risk of psychosis.
<p>155-03 Does the efficacy profile of continuous antipsychotic drug treatment, compared with alternative management strategies (placebo, another drug treatment, psychological interventions, psychosocial interventions) differ between children/young people and adults with psychosis and schizophrenia? The following subgroups should be considered:</p> <ul style="list-style-type: none"> <li>• Initial treatment (first episode psychosis)</li> <li>• Acute treatment (not first episode psychosis)</li> <li>• Treatment resistance</li> <li>• Remission</li> <li>• Maintaining and promoting recovery</li> </ul>			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
<p>155-04 Are children and young people with psychosis and schizophrenia more susceptible to side effects of antipsychotic medication, compared with adults with psychosis and schizophrenia (in particular, metabolic, neurological and cognitive impairments)? The following subgroups should be considered:</p> <ul style="list-style-type: none"> <li>• Initial treatment (first episode psychosis)</li> <li>• Acute treatment (not first episode psychosis)</li> <li>• Treatment resistance</li> <li>• Remission</li> <li>• Maintaining and promoting recovery</li> </ul>			
<p><b>Long-term safety and tolerability of quetiapine</b>  A 26-week open-label continuation study<sup>7</sup> (n=381; age 10–17 years) in Asia, Europe, South Africa and the USA evaluated the safety and tolerability of quetiapine monotherapy in young people with schizophrenia or bipolar disorder. 10-15% of patients experienced potentially clinically significant changes in high-density lipoprotein cholesterol and triglyceride levels, and clinically significant</p>	Not applicable	Not applicable	The Evidence Update concluded that in children and young people aged 10–17 years with schizophrenia or bipolar disorder, safety and tolerability of quetiapine over 26 weeks can be limited by a number of



Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p>weight gain was seen in 18% of patients. Overall, 85% of participants experienced adverse events.</p>			<p>adverse effects, including potentially clinically significant lipid disturbance, weight gain, and raised blood pressure. The full version of NICE CG155 noted the paucity and low quality of evidence for antipsychotic drug use in children and young people with first episode psychosis, and therefore also drew on evidence in adults from the NICE clinical guideline 'Schizophrenia' (now replaced by 'Psychosis and schizophrenia in adults' [NICE CG178]). The evidence was considered consistent with NICE CG155, particularly that weight, blood pressure and blood lipids should be monitored throughout treatment. It also adds to the evidence base for antipsychotic drugs in young people to aid clinicians in deciding on the most appropriate drug.</p>

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p><b>Long-term safety and tolerability of olanzapine</b></p> <p>A cohort study<sup>1</sup> (n=179 young people, age 12–18, mean age=15.8 years; n=4280 adults) compared weight and other metabolic changes between young people and adults who had received olanzapine treatment for at least 24 weeks. Data on people treated with olanzapine for at least 24 weeks were extracted from several studies (young people=6 studies; adults=86 studies) of patients with an array of mental health disorders including schizophrenia, schizoaffective disorder, borderline personality disorder, bipolar I disorder, prodromal psychosis, and depression. Following long-term (&gt;24 weeks) treatment with olanzapine, the types of metabolic changes seen in young people aged 12–18 years were similar to those seen in adults. However, the magnitude of changes in parameters such as body weight and some blood lipid levels were significantly greater in young people.</p>	Not applicable	Not applicable	The Evidence Update concluded that following long-term (>24 weeks) treatment with olanzapine, the types of metabolic changes seen in young people aged 12–18 years were similar to those seen in adults. However, the magnitude of changes in parameters such as body weight and some blood lipid levels were significantly greater in young people. NICE CG155 does not specifically state that olanzapine should not be used first line, therefore these data may have a potential impact on the guideline.
<p><b>Cardiometabolic risk in people with schizophrenia</b></p> <p>A cross-sectional study<sup>2</sup> (n=404; age 15–40, mean=23.6 years) in the USA assessed cardiometabolic risk and its moderators and mediators in people with first-episode schizophrenia spectrum disorders. The study examined baseline results of the Recovery After an Initial Schizophrenia Episode–Early Treatment Program (RAISE-ETP) – a cluster-randomised assessment of an integrated programme of drug treatment, psychotherapy and supported</p>	Not applicable	Not applicable	The evidence suggests that people with first episode schizophrenia spectrum disorders (with a mean lifetime antipsychotic treatment duration of less than 7 weeks) appear to have higher rates of smoking, metabolic

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p>employment across 34 community mental health centres. Smoking, metabolic syndrome, dyslipidemia and prehypertension were all higher than in the general population. Body composition outcomes (such as higher BMI) correlated with psychiatric illness duration, and metabolic issues correlated with antipsychotic treatment duration. Higher levels of triglycerides, insulin and insulin resistance were associated with olanzapine therapy.</p>			<p>syndrome, dyslipidemia and prehypertension than the general population. Body composition issues (such as higher BMI) appear to correlate with duration of psychiatric illness, and metabolic issues (such as higher triglycerides) appear to correlate with antipsychotic treatment duration. This was considered consistent with NICE CG155 recommendations to regularly monitor weight, blood pressure, fasting blood glucose, HbA1c and blood lipids throughout antipsychotic treatment, and to provide information about smoking, diet and exercise to children and young people with first episode psychosis in the early treatment phase.</p>
<p><b>Risk of diabetes with antipsychotics</b> A retrospective case-control study<sup>8</sup> (n=43,287; age 6–24, mean=14.5 years) in the USA compared the risk of type 2 diabetes in people taking antipsychotic drugs with matched</p>	Not applicable	Not applicable	The Evidence Update concluded that children and young people aged 6–17 years prescribed

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p>controls taking another psychotropic drug. Antipsychotic users were at significantly greater risk of type 2 diabetes than controls. This risk was apparent within the first year of follow-up and remained for up to 1 year after stopping antipsychotics. The increased risk was also present when the analysis was restricted to children and young people aged 6 to 17 years.</p>			<p>antipsychotics appear to have an increased risk of type 2 diabetes. This risk can remain for up to 1 year after stopping antipsychotics. These data were considered consistent with NICE CG155 recommendations to discuss possible side effects when choosing an antipsychotic drug, including metabolic issues (such as diabetes), and to monitor and record fasting blood glucose and HbA1c throughout treatment.</p>
<p><b>Risk of neutropenia with clozapine</b>  A retrospective cohort study<sup>9</sup> (n=87; age 6–18, mean age at first admission=13.4 years) in the USA analysed rates of and risk factors for neutropenia in hospitalised children and young people with schizophrenia treated with clozapine. Mild neutropenia was seen in 31% of patients and moderate neutropenia in 20% of patients (versus 3% reported among adults). Younger, male, and African-American children were at greater risk of neutropenia.</p>	<p>Not applicable</p>	<p>Not applicable</p>	<p>The Evidence Update concluded that in children and young people aged 6–18 years with schizophrenia treated with clozapine, mild neutropenia appears to develop in about one-third of patients and moderate neutropenia in about one-fifth (higher rates than adult populations). There appears to be no evidence of serious adverse events (such as</p>

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
			agranulocytosis or serious infection), although younger, male, and African-American children appear to be at greater risk of neutropenia. This evidence is consistent with NICE CG155 to offer clozapine to children and young people with schizophrenia whose illness has not responded adequately to pharmacological treatment, and reinforces the need for long-term monitoring of blood counts.
<p>155-05 Do clinicians manage and monitor side effects of antipsychotic treatment differently in children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered:  • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery</p>			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
<p>155-06 For initial treatment in children and young people with psychosis and schizophrenia:  a) Should the dose/duration (and, where relevant, frequency) be different compared with adults?  b) Are there any different factors (including patient population, age, and so on) that predict the nature and degree of response to medication, which should be considered in children and young people with psychosis and schizophrenia that it is not necessary to consider in adults with psychosis and schizophrenia?</p>			
<p><b>Short-term efficacy and safety of quetiapine</b>  A 6-week multicentre RCT<sup>10</sup> (n=222; age 13–17, mean=15.4 years) in Asia, Europe, South Africa and the USA evaluated the efficacy and safety of quetiapine monotherapy in young people with schizophrenia. By</p>	Not applicable	Not applicable	The Evidence Update concluded that after 6 weeks, quetiapine appears to improve schizophrenia symptoms in

Main findings and conclusion of the 2-year Evidence Update (March 2015)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2015) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
<p>6 weeks, change in Positive and Negative Syndrome Scale total scores was greater for quetiapine 400 and 800 mg/day than placebo. Rates of medication-related adverse events and adverse events potentially associated with extrapyramidal symptoms were numerically higher with quetiapine than placebo, but serious adverse event rates were similar. The authors stated that differences in biochemical markers between the groups were not clinically significant.</p>			<p>young people aged 13–17 years, with a safety profile similar to that in adult populations. CG155 noted the paucity and low quality of evidence for antipsychotic drug use in children and young people with first episode psychosis, and therefore also drew on evidence in adults from the NICE clinical guideline ‘Schizophrenia’ (now replaced by ‘Psychosis and schizophrenia in adults’ [NICE CG178]). The evidence is consistent with NICE CG155 to offer oral antipsychotic medication for children and young people with first episode psychosis, and also adds to the evidence base for antipsychotic drugs in young people to aid clinicians in deciding on the most appropriate drug.</p>

<p><b>Genetic basis of weight gain associated with antipsychotic drugs</b></p> <p>A cohort study<sup>3</sup> (discovery cohort n=139; validation cohorts n=205) in the USA aimed to identify single-nucleotide polymorphisms associated with antipsychotic-induced weight gain. The single nucleotide polymorphism rs489693 demonstrated consistent recessive effects, and meta-analysis of the discovery and validation cohorts together revealed a genome-wide significant effect. Additionally, rs489693 was also significantly related to increases in several metabolic indices, including triglycerides, leptin, and insulin levels.</p>	Not applicable	Not applicable	<p>The Evidence Update concluded that a genetic locus near the melanocortin 4 receptor gene (mutations of which are linked to extreme obesity in children and young people) appears to be associated with weight gain and other adverse metabolic effects in response to antipsychotic drugs. Although NICE CG155 does not discuss genetic predisposition to weight gain associated with antipsychotics, the preliminary nature of the evidence and its limitations mean that these data are currently unlikely to affect the guideline. Further research is needed.</p>
<p>155-07 Are the same baseline measurements/ monitoring procedures undertaken before initiating antipsychotic medication used in children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery</p>			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
<p>155-08 For children and young people whose illness has not responded to pharmacological treatment, what is the next most effective treatment strategy and when do you decide to change treatment? Does this differ from adults with psychosis and schizophrenia?</p>			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable

155-09 Does the most appropriate treatment strategy in people where antipsychotic medication is effective but not tolerated differ between children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-10 Does the length of antipsychotic medication that is continued for prevention of relapse (maintaining and promoting recovery) differ between children and young people with psychosis and schizophrenia and adults with psychosis and schizophrenia?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-11 Does the risk of adverse effects associated with antipsychotic augmentation differ between children/young people and adults with psychosis and schizophrenia that is in remission?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-12 Do the advantages and disadvantages of psychological or psychosocial interventions, compared with alternative management, differ between children/young people and adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-13 Are the advantages and disadvantages of combining particular psychological/ psychosocial interventions with an antipsychotic, either concurrently or sequentially, different for children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-14 Should the duration (and, where relevant, frequency) of an initial psychological/ psychosocial intervention be different in children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable



<p>155-15 Is the most effective format for particular psychological/psychosocial interventions (for example, group or individual) the same for children and young people with psychosis and schizophrenia compared with adults with psychosis and schizophrenia? The following subgroups should be considered:          • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery</p>			
<p><b>Group psychoeducation for young people with psychosis and their families</b>          An RCT<sup>11</sup> (n=55; age 14–18 years) in Spain assessed a structured psychoeducational group intervention for young people with early-onset psychosis and their families. At the end of the intervention, fewer patients had visited the emergency department in the psychoeducational group than in the non-structured group. However, no significant differences were seen between the psychoeducational group and the non-structured group for number of patients hospitalised or days of hospitalisation.</p>	Not applicable	Not applicable	<p>The Evidence Update concluded that a structured psychoeducational group intervention for young people with psychosis and their parents or carers, comprising problem solving activities and provision of written materials, appears to reduce visits to the emergency department. This is consistent with recommendations in NICE CG155 for family-based psychological interventions. However, these recommendations were extrapolated from the NICE clinical guideline 'Schizophrenia' (now replaced by 'Psychosis and schizophrenia in adults' [NICE CG178]), and were therefore drawn from an evidence base among adult populations. The current evidence provides some data to confirm the efficacy of family-based interventions among young-</p>

			people with psychosis. However, the study compared a psychoeducational group intervention with a non-structured group intervention, and was not a comparison between young people and adults, therefore applicability of the study to the guideline question is reduced. Further research is needed.
155-16 Do the competencies or training requirements for practitioners to be able to deliver psychological/psychosocial interventions differ for those working with children and young people with psychosis and schizophrenia compared with those working with adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-17 Are there any different factors (including patient population, age, and so on) that predict the nature and degree of response to psychological/psychosocial interventions, which should be considered in children and young people with psychosis and schizophrenia that it is not necessary to consider in adults with psychosis and schizophrenia? The following subgroups should be considered: • Initial treatment (first episode psychosis) • Acute treatment (not first episode psychosis) • Treatment resistance • Remission • Maintaining and promoting recovery			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-18 For children and young people with psychosis and schizophrenia: a) Are there any psychological or psychosocial interventions (CRT) that enhance cognition and/or improve engagement with education/occupational activities? b) What are the competencies or training requirements for practitioners to be able to deliver such interventions?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-19 For children and young people with psychosis and schizophrenia (particularly from black and minority ethnic groups), do specialised intensive services (EIP services; specialist CAMHS) improve access and engagement with mental health services?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable

155-20 What is the best way of providing educational opportunities to integrate/coordinate access to education/employment opportunities for children and young people with schizophrenia: school, or a classroom in a CAMHS unit?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
155-21 For children and young people with psychosis and schizophrenia, what can be done to improve their experience of care?			
<p><b>Long-term outcomes of early-onset schizophrenia</b></p> <p>A systematic review and meta-analysis<sup>12</sup> (21 studies, n=716; mean follow-up=14.4 years) analysed the long-term outcome and prognosis of early-onset schizophrenia in study participants with a mean age of ≤18 years. Most patients with early-onset schizophrenia had a poor outcome.</p>	Not applicable	Not applicable	The Evidence Update concluded that the evidence on early onset of schizophrenia in children and young people appears to be associated with poor long-term outcomes. This is consistent with NICE CG155 which states that long-term care strategies should be in place for children and young people with psychosis, including continuity of services, management of transition between services, long-term monitoring, and support for education and employment needs.

## References

1. Kryzhanovskaya LA, Xu W, Millen BA et al. (2012) Comparison of long-term (at least 24 weeks) weight gain and metabolic changes between adolescents and adults treated with olanzapine. *Journal of Child and Adolescent Psychopharmacology* 22: 157–65
2. Correll CU, Robinson DG, Schooler NR et al. (2014) Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders: baseline results from the RAISE-ETP study. *JAMA Psychiatry* 71: 1350–63
3. Malhotra AK, Correll CU, Chowdhury NI et al. (2012) Association between common variants near the melanocortin 4 receptor gene and severe antipsychotic drug-induced weight gain. *Archives of General Psychiatry* 69: 904–12
4. Bora E, Lin A, Wood SJ et al. (2014) Cognitive deficits in youth with familial and clinical high risk to psychosis: a systematic review and meta-analysis. *Acta Psychiatrica Scandinavica* 130: 1–15
5. Morrison AP, French P, Stewart SL et al. (2012) Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *BMJ* 344: e2233
6. McGorry PD, Nelson B, Phillips LJ et al. (2013) Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: twelve-month outcome. *Journal of Clinical Psychiatry* 74: 349–56
7. Findling RL, Pathak S, Earley WR et al. (2013) Safety, tolerability, and efficacy of quetiapine in youth with schizophrenia or bipolar I disorder: a 26-week, open-label, continuation study. *Journal of Child and Adolescent Psychopharmacology* 23: 490–501
8. Bobo WV, Cooper WO, Stein CM et al. (2013) Antipsychotics and the risk of type 2 diabetes mellitus in children and youth. *JAMA Psychiatry* 70: 1067–75
9. Maher KN, Tan M, Tossell JW et al. (2013) Risk factors for neutropenia in clozapine-treated children and adolescents with childhood-onset schizophrenia. *Journal of Child and Adolescent Psychopharmacology* 23: 110–6
10. Findling RL, McKenna K, Earley WR et al. (2012) Efficacy and safety of quetiapine in adolescents with schizophrenia investigated in a 6-week, double-blind, placebo-controlled trial. *Journal of Child and Adolescent Psychopharmacology* 22: 327–42
11. Calvo A, Moreno M, Ruiz-Sancho A et al. (2014) Intervention for adolescents with early-onset psychosis and their families: a randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry* 53: 688–96
12. Clemmensen L, Vernal DL, Steinhausen HC (2012) A systematic review of the long-term outcome of early onset schizophrenia. *BMC Psychiatry* 12: 150