



NICE Guidance for Psychosis in Young People

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Managing Adolescent first episode Psychosis: a feasibility Study

1



Outline

- Background
 - Developmental perspective
 - NICE CG 155
- Psychosis in Children and Young People
 - Psychological interventions
 - Antipsychotics
- Clinical Equipoise
- CG 155 Research Recommendations
- Summary & Questions

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2

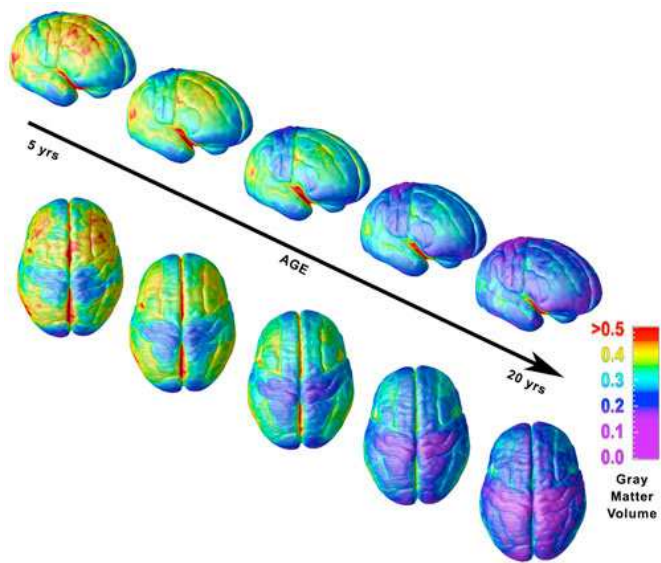
Children are not Just Little Adults



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3

Developmental Brain Changes



4

NHS
National Institute for
Health and Clinical Excellence

**Psychosis and schizophrenia
in children and young people**

Recognition and management

Issued: January 2013

NICE clinical guideline 155
guidance.nice.org.uk/cg155

NHS Evidence has accredited the process used by the Centre for Clinical Practice at NICE to produce guidelines. Accreditation is valid for 5 years from September 2009 and applies to guidelines produced since April 2007 using the processes described in NICE's 'The guidelines manual' (2007, updated 2009). More information on accreditation can be viewed at www.evidence.nhs.uk

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5

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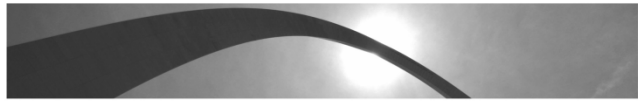
NICE clinical guideline 155
guidance.nice.org.uk/cg155

**'Are there grounds for believing that treatment in
children and young people should be any
different from adults?'**

NHS Evidence has accredited the process used by the Centre for Clinical Practice at NICE to produce guidelines. Accreditation is valid for 5 years from September 2009 and applies to guidelines produced since April 2007 using the processes described in NICE's 'The guidelines manual' (2007, updated 2009). More information on accreditation can be viewed at www.evidence.nhs.uk

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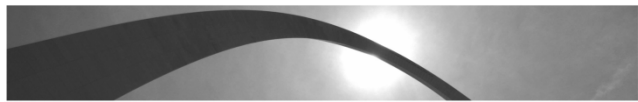
6



NICE Guideline (CG155): Recommendations

- For transient or attenuated psychotic symptoms:
 - **do not** offer antipsychotic medication
 - consider CBT with/or without family intervention
 - Treat presenting problems: anxiety, depression, substance misuse
- For psychosis:
 - Offer antipsychotic in conjunction with psychological interventions (family intervention and individual CBT)
 - When prescribing antipsychotics:
 - use knowledge of side-effects to inform a collaborative drug choice
 - follow baseline investigation and monitoring schedule

7



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8



What's the evidence-base?

- These recommendations were predominantly drawn from RCTs conducted in **older adult populations**.
- The much **larger dataset in adults** includes high quality evidence supporting the use of **oral antipsychotics** to improve symptoms and improve relapse rates; **family intervention** to reduce relapse rates; and **CBT** to decrease rehospitalisation and duration of rehospitalisation as well as symptoms.
- The **evidence presented in CG155 for children and young people was generally of low quality and effects were equivocal**
- The adult evidence was deemed strong enough to maintain the use of a combination of oral antipsychotics, family intervention and CBT as the central treatments in most settings for the first episode and subsequent acute episodes.

9



CG 155: Psychological interventions

- There were **no RCTs of CBT** in children and young people aged ≤ 18 years with psychosis or schizophrenia.
- **Six RCTs** (N = 460) conducted in children and young people ≤ 25 years were reviewed. In this age group, **CBT was no more effective than control interventions (i.e. TAU typically including medication)** at improving psychotic symptoms, depression, quality of life, social functioning or suicide.
- However, evidence from the significantly larger **adult** dataset suggested that **CBT is effective at reducing rehospitalisation rates**.

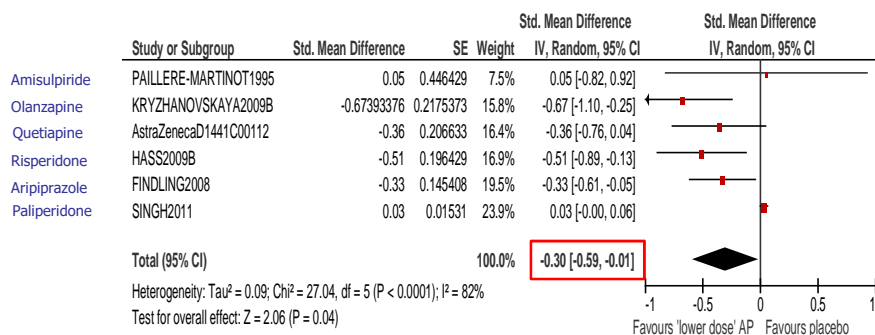
10

CG 155: Antipsychotics

- **Seven RCTs** (N = 1067) providing clinical evidence young people aged ≤18 years for antipsychotic medication compared with placebo in the treatment of the acute episode
- **Quality of evidence low or very low** due to very small sample sizes, a high risk of publication bias and low internal validity of included trials

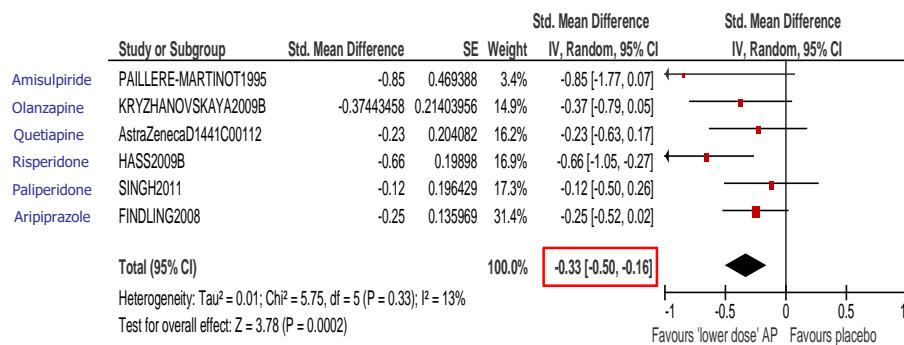
11

Differential Effect: Positive Symptoms



12

Differential Effect: Negative Symptoms



13

JAMA[®]

Online article and related content current as of March 25, 2010.

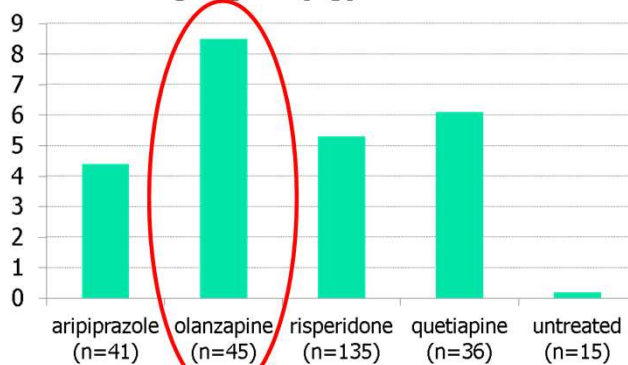
Cardiometabolic Risk of Second-Generation Antipsychotic Medications During First-Time Use in Children and Adolescents

Christoph U. Correll; Peter Manu; Vladimir Olshanskiy; et al.

JAMA. 2009;302(16):1765-1773 (doi:10.1001/jama.2009.1549)

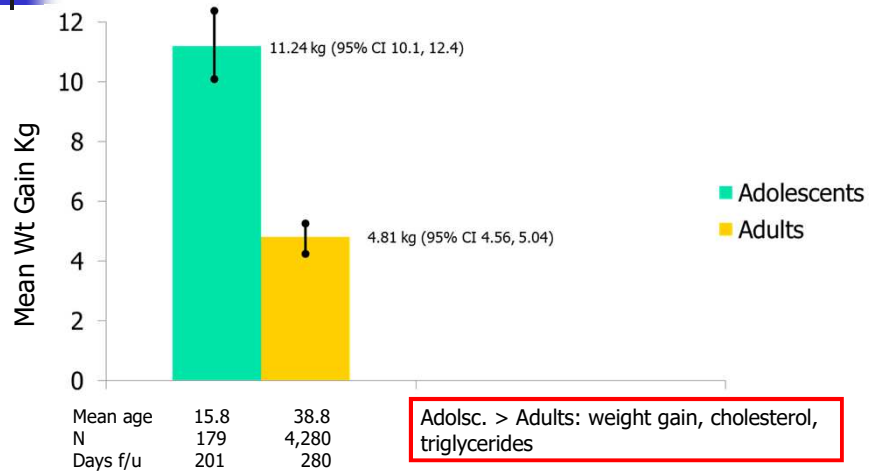
<http://jama.ama-assn.org/cgi/content/full/302/16/1765>

Weight gain (kg) 0-12 weeks



14

Weight Gain with Olanzapine: Adolescents vs. Adults



Kryzhanovskaya et al. (2012) J Child Adolescent Psychopharm. 22: 157-165

15

Reducing the future burden of ill-health from diabetes and cardiovascular disease



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16

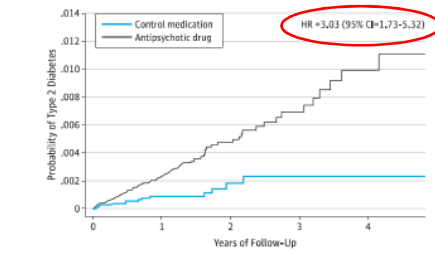
Original Investigation

Antipsychotics and the Risk of Type 2 Diabetes Mellitus in Children and Youth

William V. Bobo, MD, MPH; William O. Cooper, MD, MPH; C. Michael Stein, MB, ChB; Mark Olfson, MD, MPH; David Graham, MD, MPH; James Daugherty, MS; D. Catherine Fuchs, MD; Wayne A. Ray, PhD

JAMA Psychiatry. 2013;70(10):1067-1075. doi:10.1001/jamapsychiatry.2013.2053
Published online August 21, 2013.

- US Medicaid cohort age 6-24
- >28,000 initiated with APs
- >14,000 matched-controls
- Type 2 diabetes HR 3.03
- **Age 6-16; HR 3.13**
- Risk associated with atypicals and cumulative dose



17

Supplementary information on baseline investigations and monitoring

Table 1 Baseline investigations and monitoring for children and young people who are prescribed antipsychotic medication (read in conjunction with the BNF, BNFC and SPC)

	Baseline investigations before starting antipsychotic medication	Monitor weekly for the first 6 weeks	Monitor at 12 weeks	Monitor every 6 months thereafter	Monitor regularly throughout treatment, and especially during titration
Weight ¹ (plotted on a growth chart)	Yes	Yes	Yes	Yes	
Height ¹ (plotted on a growth chart)	Yes			Yes	
Waist and hip circumference (plotted on a percentile chart)	Yes			Yes	
Pulse	Yes		Yes	Yes	
Blood pressure (plotted on a percentile chart)	Yes		Yes	Yes	
Fasting blood glucose	Yes		Yes	Yes	
HbA _{1c} (glycosylated haemoglobin)	Yes		Yes	Yes	
Blood lipid profile	Yes		Yes	Yes	
Prolactin level	Yes		Yes	Yes	
Movement disorders (extrapyramidal symptoms, akathisia, dystonia and tardive dyskinesia)	Yes				Yes ²

NICE (2013) CG 155

18



NICE CG 155 (Update 2016)

- 1.3.15 When choosing between **olanzapine** and other 'second generation' antipsychotic medications, discuss with the young person and their parents or carers the increased likelihood of greater weight gain with **olanzapine**.
- Inform them that this effect is likely to happen soon after starting treatment. [new 2016]



Antipsychotics - Summary

- Small, significant differences were found favouring 'lower dose' antipsychotics over placebo for total symptoms (SMD = -0.32), negative symptoms (SMD = -0.33) and for positive symptoms (SMD = -0.30).
- no evidence for differences in efficacy between antipsychotics
- Antipsychotics differ in adverse effect profiles
- Weight gain and metabolic effects greatest with olanzapine



CG 155 GDG Conclusions:

- **Pharmacological interventions**
 - Efficacy similar in children and young people to adults, but evidence is of lower quality, and side effects may be worse in children and young people
- **Psychological interventions**
 - No direct evidence of efficacy psychological interventions in children and young people, but **indirect** evidence of benefit in adults
 - some limited **indirect** evidence from young adults that psychological interventions may be effective in the absence of antipsychotic medication.

21



CG 155 GDG Conclusions:

- **Psychological interventions alone?**
 - the GDG took the view that if the child or young person and their parents or carers wished to try a psychological intervention without antipsychotic medication in the first instance, this could be trialled over the course of a month.
 - The GDG emphasised that there is **little evidence** that psychological interventions are effective without medication
 - GDG emphasised the particular importance of **family involvement and interventions** in this young age group, owing to their greater dependency and continuing development.

22

CG155: Research Recommendation

- What is the clinical and cost effectiveness of:
 - psychological treatment alone
vs.
 - antipsychotic medication alone
vs.
 - psychological treatment and antipsychotic medication combined
- for young people with first episode psychosis?

23

Pyle et al. *Trials* (2019) 20:395
<https://doi.org/10.1186/s13063-019-3506-1>

Trials

STUDY PROTOCOL

Open Access

Study protocol for a randomised controlled trial of CBT vs antipsychotics vs both in 14–18-year-olds: Managing Adolescent first episode Psychosis: a feasibility study (MAPS)



Melissa Pyle^{1,2}, Matthew R. Broome^{3,4,5,6*}, Emmeline Joyce¹, Graeme MacLennan⁷, John Norrie⁸, Daniel Freeman^{4,6}, David Fowler⁹, Peter M. Haddad^{1,10}, David Shiers^{1,2}, Chris Hollis¹¹, Jo Smith¹², Ashley Liew^{3,13,14}, Rory E. Byrne^{1,2}, Paul French^{1,15}, Sarah Peters², Jemma Hudson⁷, Linda Davies¹⁶, Richard Emsley¹⁷, Allison Yung^{1,2,18}, Max Birchwood¹⁹, Eleanor Longden^{1,3} and Anthony P. Morrison^{1,2}

24