BJPsych The British Journal of Psychiatry (2015)
206, 357–359. doi: 10.1192/bjp.bp.114.155945

Editorial

NICE CG178 *Psychosis and Schizophrenia in Adults: Treatment and Management* – an evidence-based guideline?

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Summary
National Institute for Health and Care Excellence (NICE) clinical guideline (CG)178 was published in 2014. NICE guidelines occupy an important international position. We argue that CG178 overemphasises the use of cognitive–behavioural therapy for schizophrenia and those 'at risk' of psychosis, with recommendations that do not always reflect the evidence base. The CG178 recommendations on medications are limited.

Declaration of interest
M.T. chaired the SIGN 131 guideline, and has accepted fees and/or hospitality from Endo, Janssen, Lundbeck and Roche in the past 3 years.

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The National Institute for Health and Care Excellence (NICE) is renowned for producing impartial and evidence-based clinical guidelines, with a rigorous development process leading to consistent, reliable and cost-effective recommendations. NICE recommendations can have far-reaching implications at regional, national and even international levels. Despite this, NICE has been associated with controversy; for example, in its restriction of the use of acetylcholinesterase inhibitors in patients with Alzheimer's dementia of moderate severity.[1] In this paper we summarise and critique NICE clinical guideline (CG)178: *Psychosis and Schizophrenia in Adults: Treatment and Management*.[2]

Psychosis and schizophrenia?

NICE CG178 replaces the previous 2009 title 'Schizophrenia'[3] with 'Psychosis and Schizophrenia'.[2] In the guideline introduction, CG178 defines 'psychosis' as a group of psychotic disorders that include schizoaffective disorder, schizophreniform disorder and delusional disorder but does not explain the rationale for this title shift. Although in common parlance, the term 'psychosis' is not found within either DSM or ICD diagnostic manuals, and some services include bipolar I disorder as psychosis. Potential ambiguities can lead to confusion.

Psychosocial *v.* pharmacological interventions

CG178 emphasises psychosocial interventions. Only 24% of the recommendations are reserved for medication and most of these are coupled with offering cognitive–behavioural therapy (CBT) and/or family intervention to all patients. A contemporaneous evidence-based schizophrenia guideline: Scottish Intercollegiate Guideline Network (SIGN) 131, has 60% of its recommendations devoted to pharmacological interventions alone.[4] The bias of CG178 towards psychosocial interventions appears mostly based on the premise that antipsychotics are harmful. It is vital to keep in mind that medication-related adverse effects come to light after extensive research and clinical experience over a long duration. Therefore absence of evidence for adverse effects of psychosocial interventions should not be taken as evidence of absence, because of less rigorous testing. Possible adverse effects of CBT include stigma and deterioration of mental state because of overstimulation. CBT is also costly, hard to quality assure, time consuming and not always readily available. Importantly the effectiveness of CBT depends largely on the skill of the therapist, and its fidelity can be difficult to evaluate.

On the other hand medications are easy to administer and there is little doubt that the advent of antipsychotics in 1952 has had a positive impact on the lives of people with schizophrenia. For example, a large population-based study found that people with schizophrenia on maintenance antipsychotic medications have a longer lifespan compared with individuals where no antipsychotic was used.[5]

CBT as a panacea?

There has been increasing interest in CBT as an adjunct to antipsychotic medication in the treatment of schizophrenia. CG178 draws its recommendations on CBT from 31 randomised controlled trials (RCTs, $n = 3052$) of CBT *v.* any type of control. Based on this and another review of CBT for (only) an 'at risk group for psychosis',[6] CG178 makes strong recommendations on CBT for all people with schizophrenia or psychosis at all stages of the illness, including those at risk of psychosis – stating 'offer CBT'. A recent larger meta-analysis concluded that CBT has a small therapeutic effect on schizophrenia symptoms and that even this small effect is reduced further when sources of bias, particularly masking, are controlled for.[7] NICE has not updated its clinical evidence in this area from the 2009 guidance[3] but has changed the recommendations in 2014,[2] with psychological interventions and antipsychotic medication now being presented in parallel.

CBT for 'at-risk' mental state

CG178 reserves one whole new chapter (Chapter 5) for the 'at risk of psychosis' population. CG178 states that it used data from an earlier guideline entitled *Psychosis and Schizophrenia in Children and Young People*[8] regarding the recognition of at-risk mental

https://doi.org/10.1192/bjp.bp.114.155945 Published online by Cambridge University Press

states, and for the pharmacological, psychosocial and dietary interventions for people at risk of developing psychosis and schizophrenia. The CG178 recommendations for the at-risk group are based solely on an updated systematic review of these studies.[6] Based on this, it gives high-strength recommendations to 'offer' CBT to this group of people as follows:

'5.8.3.1 – if a person is considered to be at increased risk of developing psychosis (as described in recommendation 5.8.1.1):

Offer individual CBT with or without family intervention (delivered as described in recommendations 9.4.10.3) and . . . '[2]

However, the earlier guideline for adolescents (NICE CG155)[8] gives more cautious recommendations that better reflect the evidence:

'5.9.3.1 – When transient or attenuated psychotic symptoms or other mental state changes associated with distress, impairment or help-seeking behaviour are not sufficient for a diagnosis of psychosis or schizophrenia:

consider individual cognitive behavioural therapy (CBT) (delivered as set out in recommendation 6.5.13.3) with or without family intervention (delivered as set out in recommendation 6.6.9.3) and . . . '[8]

Here the recommendation for CBT is low strength, using the word 'consider', and it is clear that CBT is targeted at symptoms of people who are help-seeking. This is in keeping with the available evidence. Nevertheless, using the same data, CG178 makes strong recommendations to offer CBT.

The updated systematic review[6] has five RCTs ($n = 672$) comparing CBT with supportive counselling and provided evidence that CBT may confer a modest benefit in preventing transition to psychosis at 12 months' follow-up in patients at high risk. The authors of the study acknowledge that all participants were seeking help and that the definition of 'at risk group' and 'transition to psychosis' were not consistent between the studies. In fact, only one study used the development of subthreshold psychosis or ultra-high risk mental state (which was the entry criteria for most of the studies) as part of their primary outcome. Despite these limitations, CG178 assumes that a discrete state of high risk for psychosis exists, an assumption that has increasingly been challenged.[9] Extensive work considering whether to add 'psychosis risk syndrome' has been undertaken in recent diagnostic classifications, but this did not happen and the construct is still far from valid or reliable.[10]

CBT is a specific psychotherapy based on a cognitive and behavioural model for specific disorders. CG178 does not provide a cognitive–behavioural model for the 'at risk' group. It is unlikely that one can come up with such a model for such a heterogeneous and poorly defined group. This raises serious concerns regarding the fidelity of CBT for the 'at risk group', and the reference review did not demonstrate how the fidelity of CBT was ensured in the trials. The studies also recruited people who were help-seeking, so the findings cannot be generalised to the whole at-risk population. Although NICE CG155 recommendations reflect this, NICE CG178 does not.[2,8] Furthermore, a recent, better conducted multicentre single-blind RCT[11] concluded that cognitive therapy plus monitoring did not significantly reduce transition to psychosis or symptoms-related distress but did reduce the severity of psychotic symptoms in young people at high risk. Finally, the recommendation to use family therapy for the at-risk group is based on extrapolating the evidence for its effectiveness in reducing relapse rate in established schizophrenia. It is not clear how the extrapolation is justified for family therapy but not for other interventions.

CBT alone for first-episode psychosis

In recommendation 14.3.4.2, CG178 has taken a bold step of recommending CBT and family therapy alone for people with first-episode psychosis who wish to have it.[2] CG178 acknowledges that psychosocial interventions are more effective in conjunction with antipsychotic medication, but still suggests CBT as the only treatment for 1 month or less. This is controversial in view of the lack of robust supportive evidence and this recommendation is based on one small – only 17 participants left by the end – pilot study that has many limitations.[12] James Coyne, a psychologist, has criticised this study's method, analysis and lack of pre-registration, adding that to 'promote CBT as if it had been shown to be an effective alternative (to antipsychotic medication) would be premature and inaccurate, if not a cruel hoax'.[13]

A related point is that CG178 seems oblivious to the fact that many patients with acute schizophrenia have impaired insight into their illness and health needs[14] and thus may not have capacity to consent to treatment. Failure to offer the most evidence-based treatments promptly could be viewed as breaching the duty of care by the practitioner. Moreover, CG178 seems to have ignored those who refuse psychotherapy and makes no recommendations on offering medication alone anywhere in the guideline.

Recommendations on antipsychotic medications?

The CG178 recommendations on antipsychotic pharmacotherapy[2] are non-specific and vague apart from suggestions regarding baseline and subsequent physical monitoring, perhaps reflecting the absence of a relevant expert on the guideline's committee. The medication recommendations also do not reflect contemporary meta-analytic evidence that there are modest but significant efficacy differences between antipsychotics.[15] Surprisingly, the only specific antipsychotic adverse side-effect mentioned in CG178 is photosensitivity with chlorpromazine. Also the recommendations do not mention accepted dosing differences between first and subsequent episodes of illness, and there is a carelessly worded recommendation (10.11.1.11): 'do not use a loading doses of antipsychotic medication' illustrating that CG178 has overlooked that long-acting injectable paliperidone palmitate requires a loading dose.[16]

By way of contrast, other comparable schizophrenia-related guidelines, such as those from the British Association for Psychopharmacology (BAP)[17] and SIGN 131,[4] offer specific strategies for managing, for example, the adverse effects of antipsychotics, treatment-resistant schizophrenia and negative symptoms.

Other psychosocial interventions

Apart from CBT and family interventions, NICE has reviewed adherence therapy, art therapies, cognitive remediation, counselling and supportive therapy, psychodynamic and psychoanalytic therapies, psychoeducation, social skills training and psychological management of trauma. Although the review on trauma is new for CG178 all other reviews have not been updated from the NICE 2009 guideline.[2,3] CG178 concludes that there is sufficient evidence only for art therapies to be offered to service users with psychosis and schizophrenia (recommendation 9.3.8.1) based on a limited review of six RCTs. These RCTs had small sample sizes ($n = 24$–90); many of the studies either omitted information regarding randomisation and rater masking or reported difficulties in these areas; high attrition rates ($>40\%$) in half the studies and therapist time was often not controlled for. A later better conducted multicentre study gave negative results for effectiveness of art therapy for schizophrenia.[18] So in our opinion art therapy does not have sufficient evidence to be recommended for schizophrenia. There is evidence that cognitive remediation

https://doi.org/10.1192/bjp.bp.114.155945 Published online by Cambridge University Press

therapy may improve cognitive outcomes, albeit with limited evidence as to how this may translate into improved social and functional outcomes.[4] Social skills training has some evidence that it improves personal and social functioning in people with schizophrenia.[4]

Conclusions

In our view CG178 promotes some psychosocial interventions, especially CBT, beyond the evidence. CG178 also make some strong recommendations based on no evidence at all, for instance that the dose of CBT should be at least 16 planned sessions.[2] The CG178 research recommendations are predictable, given comments above. It quotes a moderate-sized open trial from The Netherlands that reported successful discontinuation of medication in 20% of patients, confirming the well-known fact that about 20% of people who have an acute episode of schizophrenia recover completely.

NICE occupies an important academic, clinical and political position – in a sense it has the power to create measures of current and future knowledge through their definition of 'gold-standard' treatment paradigms that have an impact on policy-making and setting of the research agenda. So it is unfortunate that CG178 appears to be open to a critique of bias.

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First received 7 Aug 2014, final revision 9 Dec 2014, accepted 21 Dec 2014

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