Developing and implementing clinical guidelines: lessons from the NICE Schizophrenia Guideline

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SUMMARY. This paper describes the development of the clinical practice guideline on schizophrenia from the National Institute for Clinical Excellence (NICE) and outlines its main recommendations. It reviews the evidence on effective implementation of guidelines generally and examines issues specific to the schizophrenia guideline. It describes NICE's approach to supporting implementation alongside that developed by the National Collaborating Centre for Mental Health (NCCMH) and looks at local implementation examples for schizophrenia.

The paper highlights key considerations for the forthcoming revision of the NICE schizophrenia guideline. It makes recommendations concerning the scope of the guideline and the quality and type of data available to the guideline developers: the lack of data on outcomes such as quality of life and social functioning, the challenges presented by unpublished papers and areas where evidence is limited. Since publication of the schizophrenia guideline, the NICE development process has undergone significant methodological improvements. The grading of evidence has been refined and more recently NICE proposed that grading of recommendations be dropped. Consensus methods are increasingly and more effectively used to deal with areas where the evidence-base is limited. NICE and the NCCMH have developed a more implementation-ready range of guideline products.

The initial NICE guideline on schizophrenia was positively received nationally and internationally. This paper highlights challenges that will be involved in updating the guideline and ways to refine the methodology of development. Ultimately the impact of the guideline will be measured not in its methodological rigor but in how its successful implementation improves patient care.

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INTRODUCTION

The National Institute for Clinical Excellence[1] (NICE) was established in 1999 to develop guidance for the National Health Service in England and Wales. It produces guidance in three areas: clinical practice; health technologies; public health and constitutes the largest single programme of clinical guidance in the world. In December 2002 it launched its first clinical guideline, on the treatment and management of schizophrenia (NICE, 2002a). This guideline was produced by the National Collaborating Centre for Mental Health (NCCMH), one of seven collaborating centres established by NICE to develop guidelines, and partnership between the Royal College of Psychiatrists and the British Psychological Society. This paper briefly reviews the development of the guideline, considers the challenges of implementing the guideline and the lessons learnt from the original guideline's development.

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[1] Since April 2004 NICE has merged with the Health Development Agency and is called the National Institute for Health and Clinical Excellence but the acronym remains the same.

THE NICE SCHIZOPHRENIA GUIDELINE

The guideline offers best practice advice for the care of adults (aged between 18 and 60 years) with schizophrenia. It covers the initiation of treatment, the acute phase of treatment (often referred to as stabilisation) and the recovery (or maintenance) phase and provides guidance, in the form of clinical practice recommendations, on psychological, pharmacological and service level interventions.

The development of the guideline followed established NICE procedures. A multidisciplinary guideline development group (GDG) including psychiatrists, psychologists, nurses, patients and carers, along with NCCMH technical staff was established to develop the guideline. The method used by the GDG (based on the best available evidence) was derived from methods outlined by NICE (NICE, 2002b) and is fully described in National Collaborating Centre for Mental Health. (2003). There are five steps in the process and these are:

1. Define the clinical questions focused on key areas of clinical uncertainty.
2. Develop and implement appropriate search strategies.
3. Design protocols for the evaluation of the evidence identified.
4. Synthesise and (meta-) analyse the evidence, guided by the clinical questions.
5. Generate summaries of the evidence and develop the recommendations for clinical practice.

In line with conventions at the time, but adapted specifically for the guideline, recommendations were graded according to the level of evidence supporting them (Table I).

Table I. – *Grading of recommendations.*

A	At least one randomised controlled trial (RCT) as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia and Ib) without extrapolation
B	Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels IIa, IIb, III); or extrapolated from level I evidence
C	Expert committee reports or opinions and/or clinical experiences of respected authorities. This grading indicates that directly applicable clinical studies of good quality are absent (evidence level IV), or with extrapolation from higher levels of evidence
NICE 2002	Recommendation drawn fron the NICE technology appraisal of the use of the newer (atypical) antipsychotic drugs for schizophrenia
Good practice	Recommended good practice based on the clinical experience of the GDG and arrived at through consensus.

Based on a scheme from: NHS Executive. *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS.* London: 1996.

Where it was not possible to identify (or more usually undertake) a high-quality systematic review (i.e. one based on RCTs) or where the GDG were of the opinion (on the basis of searches undertaken) that there were unlikely to be RCTs that directly addressed the clinical question, an informal consensus process, based on narrative reviews developed by GDG members, was adopted. (Research recommendations were also developed to address significant gaps in the evidence).

NICE has a strong commitment to rigour and transparency in its methods. In line with this the guideline went through two rounds of formal consultation with registered stakeholders (including patient organisations, professional organisations, health care providers and the pharmaceutical industry) before a final draft was agreed. Three versions of the guideline were developed, the full guideline (National Collaborating Centre for Mental Health, 2003) (containing details of the method and evidence reviewed), the NICE guideline (NICE, 2002a) (a summary of the recommendations) and the Information for the Public (NICE, 2002c) (a version of the NICE guideline written for patients, carers and the public). A training website and CD-ROM were also developed (www.rcpsych.ac.uk/cru/sts/index.htm) to support clinicians in the use of the guideline.

Key messages from the guideline

The schizophrenia guideline contained 69 recommendations and 40 Good Practice Points (GPPs) and incorporated the recommendations from the NICE Technology Appraisal on Atypical Antipsychotics (NICE, 2002d). Of the recommendations 14 were concerned with psychological interventions, 44 with pharmacological interventions and 11 with service level interventions. Whilst the recommendations, including those taken from the Technology Appraisal, focused on interventions which in principle (and usually in practice) were based on empirical evidence GPPs usually referred to aspects of care that it was unlikely would ever be subjected to formal evaluation. For example, GPPs included advice on referral procedures, clinician-patient relationships and consent procedures. In the schizophrenia guideline a number of GPPs did, however, relate to some issues (for example, depot medication) which were open to empirical testing. In subsequent guidelines, this changed and such items became formal recommendations.

The guideline presented an optimistic approach to treatment with a strong focus on joint patient-clinician decision making, the use of advance directives and the provision of appropriate information to patients and carers. Pharmacological recommendations focused on the pro-

motion of atypical antipsychotics as first line treatments and the use of low to moderate doses and the avoidance of combined antipsychotics. In psychological treatments recommendations were made for both cognitive behavioural and family interventions, particularly for patients with persisting symptoms. The guideline also made recommendations on the role of family doctors in monitoring the physical health of people with schizophrenia. Recommendations were also made for specialist services including Assertive Outreach Teams, Crisis Resolution and Home Treatment, Services for First Episode Psychosis and Supported Employment Programmes.

Response to the guideline

The guideline was launched in December 2002 and the initial response to the guideline was positive from professionals and patients alike. There was wide coverage of the launch by professional and popular press; the *British Medical Journal* (Mayor, 2002; Hargreaves, 2003) welcomed the guideline's holistic and social approach and the recommendations regarding patient involvement. A leading UK patient organisation, Rethink, said of the guideline, in a national newspaper (*The Guardian*), "This is the first big step on a long road to providing first class mental health treatment for all".

Formal reviews have also been positive. The World Health Organization and the World Psychiatric Association carried out an evaluation of 24 national schizophrenia guidelines (Gaebel *et al.*, 2005). The NICE guideline came top by a considerable margin on all but one of the chosen domains and was clearly rated best overall. A review by Aymerich *et al.* (2004) came to similar conclusions. Further international recognition has come from Italy where a translation of the full guideline (Carra *et al.*, 2004) has been undertaken and is being followed up by a programme of audit and implementation.

However, rigorous methods alone do not mean that a guideline will be implemented and despite the positive reviews there is much that could be done to improve on the current guideline. The rest of this paper addresses these two issues, drawing on the NCCMH experience of both implementation and further methodological work on a number of guidelines.

Supporting Guideline Implementation

At its inception NICE was given responsibility only for the development and dissemination of clinical guidance, implementation was a matter for the wider healthcare system. More recently, this has changed and NICE has established an implementation directorate to support the NHS directly in the implementation of clinical guidance. However, when the schizophrenia guideline was launched in 2002, responsibility for its implementation lay solely with NHS organisations. Not surprisingly, this implementation has been patchy. What follows is a brief review of implementation work on clinical guidelines, the more recent responses of NICE and the Department of Health and an example of a local implementation programme.

The Evidence for Effective Implementation

To be effective, any implementation plan should be evidence based and, if it is to be sustained, cost-effective. It follows that both the NCCMH and NICE have, given their position in developing evidence based practice, a particular responsibility to pay heed to the evidence base for implementation. Fortunately, an evidence base in support of guideline implementation exists, although its capacity to inform and direct any specific implementation plan is limited. Perhaps the most important message to emerge from the guideline implementation literature so far is that the majority of interventions to support implementation have only small to moderate effects. These effects, in terms of improved practices, have been estimated to fall broadly within the range of 6% to 14% (Grimshaw *et al.*, 2004) although a number of projects have reported higher rates of implementation, between 30-60% (Grol & Jones, 2000). Educational outreach (often referred to as academic detailing), reminders and multi-faceted approaches (Von Korff & Goldberg, 2001) are some of the more successful interventions, with audit and feedback and the use of opinion leaders usually less successful (Grimshaw *et al.*, 2004). One less encouraging aspect of implementation research is that the overall improvement is often much the same for poor performers as good performers, with the result that programmes may do little to reduce variation in practice. Most interventions focus on changing health professional behaviour, but as yet the absence of a clear typology which describes health professional behaviour has, it has been argued, (Michie *et al.*, 2005), significantly held back the development of effective strategies to support implementation. Michie and colleagues (Michie & Johnstone, 2004; Michie & Lester, 2005) have also argued, and presented some pilot work in support of the fact, that the manner in which guidelines are written can have a significant impact on their uptake both by professionals and patients.

In an evaluation of the implementation of NICE technology appraisals, Sheldon *et al.* (2004) reported on the uptake of NICE guidance on health technologies (primary pharmaceuticals and some surgical procedures). They described

variable uptake, with the guidance often being followed for pharmaceuticals (in particular drugs for cancer and obesity) but with a lower uptake for a range of surgical procedures. Factors associated with successful implementation included: strong professional support; a stable and convincing evidence base; no increased or unmet costs; good systems for tracking implementation; lack of professional isolation; and clear guidance which reflects the clinical context.

A report by the UK National Cancer Director, in June 2004 (Department of Health, 2004a), highlighted the significant regional variation across England in the uptake of cancer drugs recommended by NICE. The main reasons it cited for this were: issues of capacity; individual clinician decision making; the presence of clinical trials and the presence or lack of effective forward planning for upcoming guidance. Alongside this report, the Department of Health sent a letter to the NHS (Department of Health, 2004b), outlining a programme of action to support the NHS in implementation of NICE guidance, including the proposal that all trusts should have a NICE «champion», dedicated to the implementation of NICE guidance. How far this particular recommendation has been taken up is yet to be seen, as there were no additional resources devoted to this. The most significant national initiative by the Department of Health has been to include the implementation of NICE guidance as a key element of the national standards developed for all healthcare organisations. Compliance with these standards is monitored as part of NHS organisations' annual performance reviews by the Healthcare Commission (Department of Health, 2004c).

In April 2004 NICE established a programme to support implementation (www.nice.org.uk/implementation), the content of which was defined through a series of workshops held with the NHS. This programme focuses on six key themes:

- Active engagement with the NHS
- Intelligent dissemination
- Implementation tools
- Education
- Evaluation
- Spreading good practice

All of these areas are progressing, and an early focus has been on the implementation tools. For each clinical guideline developed, NICE now produce a costing tool for local use, a slide set for supporting dissemination of key messages within trusts and specific implementation advice for trust implementation leads. NICE have also recently released "How to put NICE guidance into practice" a step by step guide to implementation (NICE, 2005a).

The NCCMH has also been working to support implementation. For example, working with NICE to support the use of clinical guidelines in both undergraduate and postgraduate training; developing implementation materials (the schizophrenia CD-ROM and a primary care learning pack focused on depression and anxiety) and linking with other national and local organisations (for example, the National Institute for Mental Health in England's (NIMHE) regionally based Development Centres) to support initiatives in education, training and evaluation.

Effective Local Implementation

Although national organizations can support implementation, guidelines will only be used in practice if they are locally owned and implemented. This means that structures and processes for implementation have to be established locally. An example of local implementation in support of NICE guidance is a project in North London. The particular sector of North London where the project is based contains three specialist Mental Health Trusts, five Primary Care Trusts and one Strategic Health Authority (with responsibility for overall performance management). Coordination of implementation across the sector is therefore a challenge, but it was clear to the project leads that a joint working approach was essential given that so many mental disorders present in both primary and secondary care and their management is often shared between the two.

The project has a steering group, with membership from the relevant trusts with board level support, and includes senior clinical and managerial staff, patient members as well as clinical governance and finance staff. The key roles of this group are: to oversee implementation and set strategic direction; to establish the most effective processes for implementation; and to establish a project group for each guideline. The project takes a whole systems approach and integrates its activities as far as possible with existing clinical and managerial structures.

The project groups established by the steering group each have a senior clinical lead, membership from primary and secondary care services and patients and administrative support. The key roles for the group are to:

- Identify key local priorities for implementation
- Assess the current performance against these priorities
- Identify the implementation challenges (including resources, service changes and training needs)
- Develop a phased implementation plan
- Make recommendations to local management groups
- Monitor implementation

Some idea of the processes involved can be obtained from the example given below from the schizophrenia implementation group. The local priorities that the group identified for implementation were:

- Appropriate use of atypical antipsychotics
- Access to CBT and family interventions
- Patient involvement in decision making
- Physical health checks in primary care
- Appropriate use of rapid tranquillisation

To date progress has been made in addressing all areas, where possible integrating the project groups' work with that of existing programmes (for example, the audit of atypical antipsychotics by the pharmacy department). In some cases there is joint work with other guideline implementation groups for example, working with the NICE Management of the Violence Guideline group on rapid tranquillisation. One area, psychological therapies, is described in more detail, in part because the problems presented have implications beyond any one guideline.

In the UK healthcare system the demand for psychological therapies far outstrips supply and presents a challenge to the implementation of all NICE mental health guidelines (seven out of nine guidelines so far produced have recommended psychological interventions as first line treatments). In addition to a shortage of trained therapists, the systems both for training therapists and ensuring their competence are also underdeveloped. The response in the North London sector has been to: audit needs for such therapies carefully (and manage demand accordingly - interestingly it is not as great as anticipated); train existing staff to competence using adherence measures originally developed for clinical trials (Startup *et al.*, 2002); maintain competence with effective supervision; train staff in their teams thereby overcoming the problems often associated with external training (Gournay, 2005); and redesign team structures to support implementation (e.g. build responsibilities for the provision of treatment into specific team members' job descriptions).

Another approach to promoting local guideline implementation is that of the Italian Society of Psychiatric Epidemiology, where following a translation of the NICE schizophrenia guideline (Carra *et al.*, 2004), the society has completed a major task in developing audit criteria for the whole guideline. These audit criteria then form the basis for locally driven implementation programmes. This approach has some similarities with the quality improvement programme, "Better Services for People who Self-harm", developed in the UK in support of the implementation programme for the NICE Self-Harm guideline (NICE, 2004; www.rcpsych.ac.uk/cru/auditselfharm.htm).

Revising the NICE schizophrenia guideline

Since the publication of the schizophrenia guideline in 2002 the NCCMH has gained considerable experience of developing other guidelines and in doing so, has identified refinements to the guideline development method which are described below.

A primary concern in guideline development is with the initial scope which determines the subsequent shape and work-plan of the guideline. Criticism of the schizophrenia scope came from two perspectives. Clinicians felt that important issues concerning diagnosis, (e.g. dual diagnosis) and certain clinical groups (e.g. children and adolescents or learning difficulties) had not been included. Patient organisations were concerned that the guideline failed to cover important aspects of social care (e.g. housing) despite the fact that these are outside the remit of NICE which is concerned only with healthcare, albeit an appropriately, broadly defined version of healthcare. However, even with this "limited" scope the guideline development group had difficulties, largely due to the pressure of time, which meant that two issues were not dealt with. The first concerned the treatment of depression in schizophrenia and the second pharmacological augmentation strategies (e.g. the use of combination antipsychotics for treatment resistant schizophrenia). The revision of the guideline (scheduled for 2006/7) should enable these issues to be considered but determining the right scope will always remain somewhat of a "political" issue. The experience of the subsequent five guidelines undertaken by the NCCMH points to the fact that the more circumscribed the scope the more effective can be the review of the evidence. Broad scopes covering complex disorders, such as schizophrenia, may be necessary as an initial step to engage healthcare managers, professionals and patients but in the long-term the consequences of these broad scopes (e.g. long development times and significant implementation challenges) may be detrimental.

The second major methodological problem that arose was with the type and quality of the data available. This primarily centres on outcome data which for a disorder like schizophrenia is often focused too narrowly on symptoms to the exclusion of other outcomes such as quality of life and social functioning. Also little data is available on longer-term outcomes. Both limit the applicability of the evidence base to routine care. In addition, there was very limited hazard/harm data available, for example, during the development of the guideline there was considerable concern about the use of atypical antipsychotics and the onset of diabetes and weight gain. Although there have been some improvements in this data set since that time the gen-

eral limited availability of hazard/harm data remains a real problem for guideline development. The consequences of this can be very serious, see for example the work of Craig Whittington *et al.* (2004) on the risk/benefit ratio of antidepressants in children and adolescents. In other areas there is also an almost complete absence of relevant research. For example, we know little about the specific benefits of pharmacological interventions for older people or younger people with schizophrenia. There is also a paucity of UK/European based data for a wide range of service interventions (for example, Assertive Outreach or Crisis Interventions Teams). Although some progress has been made in these areas, for example on UK based service interventions (Johnson *et al.*, 2005; Killaspy *et al.*, in press) and European studies of younger people with schizophrenia (Petersen *et al.*, 2005) the dataset remains limited.

The schizophrenia guideline was the first guideline produced by NICE and as such was something of a test bed for both NICE and the NCCMH of their guideline development methods. Inevitably, this prolonged the development time but there has been an increasing emphasis on more efficient methods of guideline production reflecting a concern within the UK healthcare system about the timely assessment of healthcare interventions. Developments have included refinements of the search systems and a move away from reliance on existing systematic reviews. Although existing reviews appear to offer a more efficient way of assessing the evidence they often failed to directly address the group's clinical question. As a consequence the time spent refining and revising existing reviews often proved more time-consuming and less satisfactory than developing de novo reviews. The problem of the absence of harm/hazard data has already been identified above but even where data exists it is often not easily accessible. Most obviously this problem exists with unpublished pharmacological trials (c.f. Whittington *et al.*, 2004). This data, however, is not always best obtained from controlled trials and other significant sources of this data exist. For example, better links with national and European drug regulators or access to such systems in the UK as the General Practice Research Database (a large primary care database) (Lawson *et al.*, 1998) may improve access to harm data.

Another problem, specific to NICE, concerned the integration of the Technology Appraisal (NICE, 2002d) on atypical antipsychotics into the schizophrenia guideline. This made a high-quality cost effectiveness evaluation of the atypicals available to the guideline. However, this work was not completed by the guideline development group, and inevitably differences concerning ownership and style of recommendations presented considerable problems of integration. Subsequent to the schizophrenia guideline, experience on other guidelines has led to more effective joint working and, as will be the case with the updated schizophrenia guideline, many technology appraisals are updated through their integration into an appropriate clinical guideline. The Technology Appraisal also brought a strong emphasis on cost effectiveness to the guideline which has led to an increasing focus on cost effectiveness in clinical guidelines.

The emphasis on efficiency has also been reflected in the guideline development process itself. There has been a move away from a reliance on large formal guideline development groups as the main means of the evaluation of evidence to them having a more supervisory role focused on identifying key clinical questions, determining methods and agreeing recommendations. The majority of the detailed assessment of evidence is done by group members in smaller "topic" groups. Such an approach makes for a more efficient use of guideline development time and a more satisfactory experience for guideline members. The NCCMH also increasingly uses external peer reviewers and focus groups to examine specific aspects of the guideline whilst in development. For example, a specific focus group on the wording and presentation of recommendations of the Post Traumatic Stress Disorder guideline for primary care was convened as part of the development process for that guideline.

The NCCMH has increasingly used consensus methods to deal with areas of significant clinical uncertainty where the evidence base is very limited. Two recent examples of this are; the development of a consensus conference (drawing on national and international experts from outside the guideline development group) to develop recommendations on the diagnosis and assessment of bipolar disorder in children and adolescents and a consensus conference on the pharmacological management of pregnant women with psychiatric disorders, again drawing on international and national experts from outside the development group.

One of the challenges any guideline development group faces is to accurately reflect and capture in a rigorous, comprehensive and reproducible way the response of the guideline development group to the evidence presented to it. Issues concerning, for example, patient populations in trials, the healthcare setting, and the size of the effect reported, all influence the decisions made about a particular recommendation. Without a systematic approach this is often very difficult to capture. Within the NCCMH, the GRADE system for evaluating evidence has been used in an attempt to address this issue (GRADE Working Group, 2004). More controversial, is the suggestion within NICE (2005b) that the system for grading recommendations de-

scribed in the first section of this paper be dropped. Whilst in widespread use and providing an apparently convenient and comprehensible reference point for the interpretation of recommendations, the system presents many problems. For example, acetyl-cysteine (Prescott *et al.*, 1979), a well-established and effective antidote in the treatment of paracetamol overdose, has never formally been subject to randomised controlled trials and in the NICE self-harm guide (NICE, 2004) warranted only a C level recommendation despite being a well-established, lifesaving intervention. Given that some organisations place a priority on the implementation of A and B level recommendations it is apparent that such a system could lead to the non-adoption of important recommendations. Moving away from grading of recommendations also allows for the development of more complex recommendations which integrate evidence from a number of different sources and by doing so more accurately reflect the process of clinical decision making (where clinicians are often choosing from a range of possibilities rather than a single treatment) thereby potentially supporting implementation.

The final point about further refinements of the process concerns the products which NICE and its associated bodies produce. Since the publication of the first clinical guideline it has been recognised that the full summary of clinical practice recommendations (the NICE guideline, which often stretched to over 50 pages including appendices) was impractical for routine dissemination in the NHS and potentially presented a significant barrier in itself to effective implementation. More recently this has been replaced by the Quick Reference Guide which intends to provide a succinct summary (usually not more than 15 pages) of the recommendations. These have met with some success but it is likely that further targeting for specific professional groups, perhaps with tailored sets of recommendations, will be required. It is also likely that patient focused versions of the guideline will play an increasingly important part in promoting implementation by empowering patients as agents of change. (The NCCMH has begun to do this in conjunction with patient organisations such as the Eating Disorders Association with which a joint leaflet summarising the eating disorders guideline and focusing specifically on patients was produced (www.edauk.com/nice/index.htm))

CONCLUSION

The NICE schizophrenia guideline has received a positive national and international reception since its publication in 2002. However, for any real benefits to be obtained from its publication it needs to be effectively implemented. This paper has described a number of approaches which may support effective implementation and also some further refinements to the development of future versions of the guideline which should lead an improved and more readily implementable product. The NICE guideline's implementation should be subject to careful evaluation; the real test of its value being whether or not it improves patient care. Without this, methodological rigour will count for very little.

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