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Clinical Guidelines: A NICE Way to Introduce Cost-Effectiveness Considerations?

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ABSTRACT

The National Institute for Health and Care Excellence (NICE) in the United Kingdom initiated its clinical guidelines program in 2001 and more than 200 guidelines have been produced to date. As with most of NICE's other programs, the clinical guidelines program also must take into account the relative costs and benefits of interventions when deciding whether to recommend them. The three main advantages of the program are that 1) it represents an important collaboration with the medical profession, thereby increasing the likelihood of recommendations being adopted; 2) the guidelines provide an opportunity to review all aspects of the clinical pathway, rather than focusing on only the adoption of a new technology; and 3) the guidelines offer the potential to discuss disinvestment as well as new investment. All the guidelines contain a systematic review of the relevant economic evaluation literature, and the 12 guidelines published from January 1 to August 31, 2015, contain 28 de novo economic analyses. The main challenges encountered in the guidelines program are that 1) there is an inevitable tension in advising on the quality of care that individual patients could expect while recognizing the broader public health objectives of equity, fairness, and efficiency; 2) the impact of economics is sometimes lessened because of the lack of time to conduct de novo analyses; and 3) unlike NICE's technology appraisal program, the adoption of recommendations is not mandatory for the UK National Health Service.

Keywords: clinical practice guidelines, cost, cost-effectiveness analysis, oncology, value frameworks.

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Background to the Clinical Guidelines Program of the National Institute for Health and Care Excellence

The clinical guidelines program is one of several programs operated by the National Institute for Health and Care Excellence (NICE) in the United Kingdom. Others include programs on technology appraisal, public health, social care, diagnostics, medical technology (devices), and interventional procedures. One of the distinctive features of the clinical guidelines program is that it focuses on improving the present standard of care, whereas most of the other programs focus on assessing new technologies entering the National Health Service (NHS) in the United Kingdom.

NICE has a strong commitment to cost-effectiveness. Its procedures state that "[t]hose developing *clinical guidelines*, *technology appraisals or public health guidance must* take into account the relative costs and benefits of interventions (their 'cost effectiveness') when deciding whether or not to recommend them" [1]. But "[d]ecisions about whether to recommend interventions should *not be based on evidence of their relative costs and benefits alone*. NICE must consider other factors when developing its guidance, including the need to distribute health resources in the fairest way within society as a whole" (principle 3).

The clinical guidelines program was initiated in 2001 and since then more than 200 guidelines have been published. Typically, they give broad guidance covering all, or specific, aspects of the diagnosis and management of a particular condition. They also incorporate any relevant technology appraisals or interventional procedure guidance that NICE has already produced for the condition concerned. Unlike NICE's technology appraisals, the clinical guidelines are not mandatory for the NHS, but often they form the basis of the development of standards to evaluate clinical practice.

A key feature of the clinical guidelines program is that NICE shares the "ownership" of the program with the various "royal colleges" of medicine, which are the central clinical associations in the United Kingdom. Historically, the national collaborating centers producing the guidelines have been located in the various royal colleges, although the guidelines are produced according to a template devised by NICE. The topics for guidelines are selected on the basis of the need to develop quality standards and assigned to the various collaborating centers. A scoping exercise is then undertaken, in consultation with interested parties, including professional societies, the NHS, the Department (ministry) of Health, and, if relevant, technology manufacturers. Then a guideline development group (GDG) is appointed, comprising

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relevant clinical experts and patient/carer representatives. The GDG is provided with technical support, including expertise in systematic reviews and health economics. A critical feature of the process is to identify a number of "key clinical questions," which form the basis for the systematic reviews of existing evidence on effectiveness and cost-effectiveness, plus any de novo economic analysis in situations in which relevant cost-effectiveness evidence is absent or inadequate. Typically, the GDG meets 12 times over a period of up to 2 years. At each meeting, the GDG reviews and discusses the clinical and economic evidence pertaining to one to three key clinical questions.

Once completed, the guideline is circulated for extensive consultation and is then revised before the sign-off by NICE. Several documents are produced, the main one being a summary of the recommendations, the "NICE guidelines." In addition, interested individuals can also obtain the "Full guidelines," or, in the newer guidelines, a range of documents that give details of the evidence and analyses used to support the recommendations. There is also a nontechnical version, called "Information for the public," which can be helpful for patients and their families. NICE also supports the implementation of the guideline with a number of tools and resources for the NHS, the most important ones being a "baseline assessment tool" and a "costing statement," which helps health authorities estimate the likely financial impact of adopting the recommendations in the guideline. The present list of published guidelines, plus those in development, can be accessed via the NICE Web site (http://www.nice.org.uk). The earlier guidelines are called "clinical guidelines," and the more recent ones are called "NICE guidelines" [2].

Advantages of the Clinical Guidelines Program

The NICE clinical guidelines are probably not as widely known as its technology appraisals, which sometimes attract attention because they imply rationing or restrictions on the availability of new treatments and procedures. The guidelines, however, do have a number of important advantages. First, because the operation of the program is shared with the medical profession, it represents an important collaboration aimed at improving the standard of care in the NHS. Thereby, it is more likely that clinical opinion leaders will be willing and able to help in encouraging the adoption of recommendations. Second, the guidelines provide an opportunity to review all aspects of the care pathway, rather than focusing on only the adoption of a new technology. Third, the guidelines offer the potential to discuss disinvestment (in practices and procedures) as well as new investment.

A common criticism made of technology assessment by health care decision makers is that it often only offers advice on how to spend resources on new technologies and rarely discusses how those resources can be found, especially in situations (like the one faced by the NHS in the United Kingdom) of having a fixed budget. During the production of a guideline, the GDG often discusses practices or procedures that may be discontinued because they are of limited use, or can be streamlined because they are at present being applied in an inefficient manner. Some of these suggestions are included in the "Do not dos" list published on the NICE Web site [3].

Contributions of Economic Analyses

As mentioned previously, the role of the health economist supporting the GDG is to undertake systematic reviews of the economic evaluation literature relevant to each of the key clinical questions and, if necessary, conduct a de novo economic analysis. Table 1 details the economic analyses conducted for the guidelines published from January 1 to August 31, 2015. The expectation is that normally one to two new economic analyses will be required per guideline. It can be seen that de novo analyses were conducted to help answer at least one of the key clinical questions for all but one of the guidelines over the period considered here. Some of the analyses were merely costing studies, or adaptations of existing economic analyses, but most of them used a decision-analytic model and are comparable with the analyses carried out in the context of NICE's technology appraisals.

The economic analyses can support the guidelines in a number of ways. In the case of lipid modification (CG181), an economic analysis was conducted to support the recommendation that a high-intensity statin (e.g., atorvastatin 20 mg daily) should be offered for the primary prevention of cardiovascular disease in people who have a 10% or higher 10-year risk of developing the disease. It was thought that this recommendation might be controversial, given the high number of individuals who would be brought into therapy and the likely budget impact. Extensive cost-effectiveness modeling provided a robust defense of the recommendation on economic grounds.

In the case of bladder cancer (NG2), NICE was aware that this is one of the most expensive cancers to manage, and so economic considerations were potentially important. In this case, two economic analyses were carried out. The first analysis compared a single instillation of chemotherapy immediately after transurethral resection of bladder cancer tumors versus no chemotherapy. The study found that chemotherapy was highly cost-effective in all risk groups. The second analysis assessed the cost-effectiveness of reduced follow-up and/or using newer tests and procedures compared with present practice. It was found that reducing cystoscopic follow-up was cost-effective in low- and intermediate-risk patients.

Therefore, taken together, these economic analyses addressed both the potential for investment in therapy as well as the potential disinvestment. From time to time NICE has produced lists of items of its guidance that have the potential for cost reductions [4]. Table 2 provides some examples of the possibilities for cost reductions relating to clinical guidelines. This list is based on costing work undertaken at the time the guidance is published and covers all clinical guidelines from January 2005. (Some of the earlier guidelines on the list have since been updated and are no longer applicable.) All guidance that was considered to deliver a net saving has been identified. There may be elements of other guidelines that will deliver savings, but in some circumstances fully implementing the guidance requires investment. These figures are only estimates and are not to be taken as NICE's view of desirable, maximum, or minimum figures, but they are useful in providing a sense of the scale of savings achievable. Also, these "savings" are *potential* savings only. In many cases actions will be required to realize them. NICE encourages users of the costing templates to modify the assumptions used in the templates to more accurately reflect local circumstances.

Challenges and Issues for Further Discussion

Despite the attractions of introducing cost-effectiveness considerations into NICE clinical guidelines, many challenges remain. First, some economists have argued that, compared with NICE's technology appraisal program, the influence of economics has been lower because of the joint ownership of the program with royal colleges. For example, Wailoo et al. [5] argued that NICE clinical guidelines should be subjected to independent appraisal like the technologies considered in NICE's technology assessment program because the cost-effectiveness of some clinical procedures might not be sufficiently scrutinized. Littlejohns et al. [6] acknowledged this concern and pointed to the inevitable tension

Table 1 – Examples of de novo economic analyses in NICE clinical guidelines (January 1–August 31, 2015).

Guideline	Topics studied
Gastroesophageal reflux disease: children and young people (NG1)	Changes to feeding in infants
	Antacids/alginates
	Medical management approaches
	Fundoplication surgery
	Enteral tube feeding
Bladder cancer (NG2)	Single instillation of chemotherapy immediately after transurethral resection of bladder cancer tumors vs. no chemotherapy
	Reduced follow-up and/or using newer tests and procedures vs. present practice
Diabetes in pregnancy (NG3)	Self-management programs in women with diabetes planning a pregnancy
	Screening, diagnosis, and treatment for gestational diabetes
	Screening for congenital cardiac malformations
Medicines optimization (NG5)	Medicine review cost analysis
Challenging behavior and learning difficulties (NG11)	Parent training for the management of behavior that challenges
	Psychosocial, pharmacological, and combined interventions for the management of sleep problems
	Antipsychotics for the management of behavior that challenges
Violence and aggression (NG10)	None
Anemia management in people with chronic kidney disease (NG8)	Diagnostic tests for predicting response to iron therapy
Bronchiolitis in children (NG9)	Bronchodilators, corticosteroids, and in combination
	Costs of CPAP and high-flow oxygen
	Costs of giving intravenous fluids or nasogastric hydration
	Hypertonic saline vs. normal saline
Suspected cancer: recognition and referral (NG12)	Tests to diagnose colorectal cancer for patients aged 40 y and older with a change in bowel habit
Melanoma: assessment and management (NG14)	Sentinel node biopsy alongside wide excision vs. wide excision only (stage IA to stage IIC)
	Alternative follow-up strategies in high-risk cutaneous melanoma
Diabetes (type 1 and type 2 in children and young people) (NG18)	Multiple daily injections vs. mixed insulin injections
	Different frequencies of capillary blood glucose monitoring
	Blood ketone monitoring vs. urine ketone monitoring
Type 1 diabetes in adults (NG17)	Long-acting insulins and once- vs. twice-daily insulin
	HbA_{1c} threshold to reduce the risk of complications
	Continuous glucose monitoring vs. standard monitoring of blood glucose

CPAP, continuous positive airway pressure; HbA_{1c}, glycated hemoglobin.

between advising on the quality of care that individual patients could expect while recognizing the broader public health objectives of equity, fairness, and efficiency. They argued that economists should be more involved in the guidelines development process.

Second, the potential impact of economics can be lessened because of the lack of time available to undertake de novo analyses. On occasions, the precise topics for the economic analyses have been identified rather late in the guidelines development process. If, as is often the case, the existing economics literature does not provide enough to answer the question being proposed, then the necessary de novo analysis can be a little rushed. Third, because the implementation of the recommendations from clinical guidelines is not mandatory for the NHS, it is possible that they may not be fully implemented. NICE does encourage implementation through the development of quality standards on the basis of the recommendations, although ultimately implementation can be achieved only by winning over hearts and minds. To the extent that some recommendations are not implemented, this is likely to dilute the impact of guidelines on improving efficiency.

Over time, the acceptability, prominence, and quality of economic analyses in guidelines have increased, as evidenced by the list of economic analyses given in Table 1. In addition, the number of key clinical questions examined in each guideline has been reduced, from more than 20 to around 10 to 15. This has been partly achieved because the topics in the more recent guidelines have been narrower in scope, seldom covering the full clinical pathway of a given disease, as was the case in many of the earlier guidelines. Also, the key clinical questions are being identified earlier in the guideline development process, thereby giving the economist more time to conduct analyses if these are needed. Finally, NICE has invested in the production of resources and tools to facilitate the implementation of guidelines, but it is difficult to obtain accurate evidence on the extent of implementation.

Conclusions

The NICE clinical guidelines program complements the institute's other programs of work, which mainly address new health technologies. Clinical guidelines offer the possibility of prioritizing topics for clinical and economic assessment on the basis of considering the whole clinical pathway. Opportunities for disinvestment can be considered alongside possibilities for additional investment. The guidelines development program, however, needs to be adequately resourced, including the provision of health economists' time to undertake the necessary literature reviews and de novo analyses that are usually required. Although issues in the development and use of clinical guidelines are likely to vary by jurisdiction, NICE's experience indicates that it is both feasible and useful to incorporate economic considerations.

Table 2 – Examples of potential cost reductions resulting from NICE clinical guidelines [7].

Guidance number	Short title	Why does this guidance save money?	Estimated saving per 100,000 (£)
CG34	Hypertension (partial update of CG18)	The recommendations update previous guidance on prescribing drugs for hypertension. Following the revised recommendations will cost more in drugs, but this is far outweighed by the predicted number of cardiovascular events (heart attacks and strokes) that will be avoided if hypertension is better controlled.	−446,627
CG30	Long-acting reversible contraception	The recommendations relate to offering women seeking contraception an informed choice and access to long-acting reversible methods. These methods are more reliable than the oral contraceptive pill, wherein user-error often results in unplanned pregnancy. The additional cost of providing these methods is more than offset by the costs of unplanned pregnancies (reduced terminations or reduced births).	−214,681
CG127	Hypertension (update)	Following an initial investment in home blood pressure equipment monitoring, in future years, as more people benefit from more accurate diagnoses using ambulatory blood pressure monitoring, a cumulative effect of people not being on antihypertensive drugs starts to be seen. Savings from reduced treatment costs (because of not providing treatment for people who are not truly hypertensive) will start to outweigh the additional costs of diagnoses from year 3.	−20,464
CG108	Chronic heart failure (partial update)	Implementing the recommendations is anticipated to result in increased costs for diagnosing and monitoring patients with congestive heart failure at an earlier stage, and increased costs for rehabilitation. This is, however, more than offset by anticipated reductions in acute admissions in this patient group that has frequent readmissions.	−19,000
CG115	Alcohol-use-disorders: prevention	The guideline is one of three pieces of NICE guidance addressing alcohol-related problems and should be read in conjunction with PH24 (alcohol use disorders—prevention) and CG100 (alcohol use disorders—physical complications). It is anticipated that implementing this guidance will lead to additional costs because of the increase in the proportion of people with mild alcohol dependence receiving psychological interventions and increase in the number of people with moderate and severe dependence receiving medication to prevent relapse following successful withdrawal. These costs are likely to be offset by a reduction in the number of people who are dependent on alcohol, a reduction in the number of people who relapse following successful withdrawal, and by savings due to people being offered an intensive community program rather than residential rehabilitation.	−18,600
CG107	Hypertensive disorders during pregnancy	Increased costs for greater use of aspirin and monitoring of proteinuria are considered to be more than offset by reductions in adverse outcomes with increased costs for treating pre-eclampsia, preterm deliveries, and babies needing special care.	−15,300
NG2	Bladder cancer: diagnosis and management	Savings could arise from a reduction in the number of people with low-risk non–muscle-invasive bladder cancer receiving follow-up cytoscopies in secondary care after 12 mo. There could be increased drug costs of giving people suspected of low- or intermediate-risk non–muscle-invasive bladder cancer a single dose of intravesical mitomycin C given at the same time of a TURBT procedure.	−11,500
CG81	Breast cancer (advanced)	One of the recommendations in this guidance recommended a change to present practice relating to	−9,690

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Table 2 – *continued*

Guidance number	Short title	Why does this guidance save money?	Estimated saving per 100,000 (£)
		patients receiving trastuzumab for advanced breast cancer. It is recommended that treatment is discontinued if the disease progresses outside the central nervous system. It was considered that 50% of women taking trastuzumab and in whom the disease progresses outside the central nervous system presently continue to take trastuzumab. In addition to quantified savings relating to trastuzumab, we anticipate a reduction in hospital admissions as a result of improved treatment of patients with bone metastases. Bone metastases account for over a third of all nights in hospital in advanced breast cancer care.	
CG75	Metastatic spinal cord compression	Implementing the guidelines is anticipated to increase surgery for the prevention and treatment of metastatic spinal cord compression at a cost of £14 million. This is more than offset by the reduced care costs for the increased periods that patients keep the ability to remain mobile. The cost difference per patient per day between those who are able to walk and those who are immobile is £180, a part of which is social care costs. On the basis of those patients expected to be discharged home and cared for in the community, a national saving of £17.5 million was estimated.	−8,974
CG69	Respiratory tract infection in primary care	The use of a no prescribing or a delayed prescribing policy for a number of conditions (detailed in the guideline) is anticipated to lead to a reduction of £3.7 million in antibiotic prescribing nationally. In addition, there may be benefits, which are not possible to quantify, arising from reduced use leading to less antibiotic resistance and reduced adverse events associated with antibiotic use.	−7,299
CG33	Tuberculosis	Most of the savings could arise from changes recommended in the BCG vaccination program for children between the age of 10 and 15 y. In addition, we anticipated reduced costs of treating active infection through better identification leading to reduced transmission.	−7,239
CG40	Urinary incontinence	We anticipated a reduction in the cost of urodynamic investigations that would be carried out before conservative treatment or surgery.	−6,506
CG58	Prostate cancer	A number of recommendations relating to whether to biopsy, when to offer active surveillance, and the use of hormonal treatments are predicted to save money. These savings are offset by increased use of radical external beam radiotherapy.	−5,396
CG54	Urinary tract infection in children	A change in the cost of urine collection is estimated to cost £2.9 million, which is offset by the anticipated reduction of £5.0 million in the number of referrals and imaging procedures.	−4,210
CG80	Breast cancer (early)	The recommendations relating to pretreatment ultrasound evaluation of the axilla are considered to avoid additional surgery if nodal disease is identified before initial surgery.	−2,698
CG99	Constipation in children and young people	The recommendations are anticipated to increase prescribing costs, but lead to fewer outpatient attendances and inpatient admissions.	−2,020
CG64	Prophylaxis for infective endocarditis	It is anticipated that a reduction in prophylactic antibiotic prescribing will lead to reduced expenditure. In addition to the quantified savings in antibiotics, savings from reduced adverse effects of antibiotics such as anaphylaxis and antibiotic resistance will occur.	−1,411
CG60	Surgical management of OME	The recommendations are anticipated to result in a reduction in adenoidectomies and in antibiotic prescribing for OME.	−776

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Table 2 – *continued*

Guidance number	Short title	Why does this guidance save money?	Estimated saving per 100,000 (£)
CG100	Alcohol use disorders—physical complications	Implementing the guidance is anticipated to require investment in alcohol specialist professionals (£5.9 million) and an increase in assessment and surgery for chronic alcohol-related pancreatitis (£1 million). This is, however, more than offset by an anticipated reduction because of symptom-triggered drug treatment for withdrawal (saving £7.1 million).	Assess locally
CG37	Postnatal care	The annual costs have been found to vary from an initial cost of £6.8 million to a potential saving of £1.1 million because of the effect of increasing savings and reducing training costs over time. The savings arise from a reduction in the incidence of childhood disease because of the protective effects of breast-feeding, assuming that following the recommendations will lead to an increase in the number of mothers who breast-feed. (See also public health guidance on maternal and child nutrition [PH11].)	Per average unit experiencing 2,534 births per annum net savings range £5,000–£9,000

BCG, Bacillus Calmette-Guérin; OME, otitis media with effusion; TURBT, transurethral resection of bladder tumor.

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