

PART FIVE

Research, evidence and recommendations

Involving participants in the design and conduct of trials: the ProtecT study

Jenny Donovan

Introduction

Randomised trials are the design of choice for evaluating the effectiveness of interventions, but many trials recruit slowly or include only a small proportion of eligible participants, potentially threatening validity and wasting resources. Rates of recruitment to trials are difficult to ascertain, but have been reported to be as low as 5–10% of eligible patients for cancer trials. Systematic reviews of the literature have identified a number of barriers to participation for clinicians and patients, but indicated that few evaluative studies have been undertaken to understand or improve trial recruitment.

There can be few issues in healthcare as controversial as population screening for prostate cancer. Debate is conducted in the scientific arena, but the controversy is fuelled by considerable polemic and media pressure. This has led to marked differences in policy between the US (where intensive screening has been introduced in some states) and the UK (where it has not). A number of systematic reviews of the literature have detailed the lack of clear evidence for a benefit from population screening and the possibilities of harm. A key issue is that current screening tests will identify prostate tumours in large numbers of men but it is not yet possible to distinguish between those that will behave aggressively and threaten life and those that will remain innocuous. There are no randomised controlled trials to provide robust evidence about which treatment to recommend, and observational data suggest similar outcomes in relation to mortality for the major treatment options (surgery, radiotherapy and monitoring). Each of these treatments can, however, result in damaging side effects, including impotence and incontinence for the radical interventions, and anxiety and the risk of progression for monitoring.

The aim of the ProtecT (prostate testing for cancer and treatment) feasibility study was to establish whether it was possible to recruit patients to a randomised controlled trial of surgery, radiotherapy and active monitoring for localised prostate cancer. Nested within the study was a randomised trial

comparing the effectiveness and cost-effectiveness of urologists and nurses in recruiting patients, and the option of recruitment to all three arms (surgery, radiotherapy and monitoring) or the two radical treatments. Detailed qualitative research was also carried out as part of the trial involving in-depth interviews with trial participants and recruitment staff, and tape-recording of the recruitment appointments. Effectively, we embedded the feasibility phase of this controversial trial within qualitative research, allowing us to investigate recruitment issues from the perspectives of trial participants and recruitment staff, as well as to examine the feasibility of the trial.

Methods

Men aged 50–69 years from primary care centres in three cities were invited to attend a 30-minute prostate check clinic appointment in which they were informed about the study and asked to consent to a prostate-specific antigen (PSA) test. Men with a raised PSA were invited for biopsy and further diagnostic tests. Men with confirmed localised prostate cancer were invited to participate in the randomised trial of recruitment, where they were randomised to a nurse or urologist for an ‘information’ appointment to discuss recruitment to the treatment trial. In the information appointment, the need for the trial was explained in detail, along with the advantages and disadvantages of each treatment, and the recruiter attempted to randomise the patient to the treatment trial or reach a patient-led preference for treatment. In-depth interviews with trial participants explored interpretation of study information. Audio tape-recordings of recruitment appointments enabled scrutiny of content and presentation of study information by recruiters and interpretation by participants.

Results

Between 1999 and 2001, 8505 men from 18 primary care centres attended prostate check clinics, and 12% had raised PSA levels. In total, 224 cases of prostate cancer were found (165 clinically localised). One hundred and fifty (90% of eligible cases) consented to randomisation between a nurse and urologist. Urologists achieved a higher rate of recruitment to the treatment trial (71% compared with 67% for nurses), but this was not statistically significant (chi-square test 0.60), and a cost-minimisation analysis showed that the urologist arm was more expensive because greater salary costs outweighed their tendency for shorter appointments. The three-arm trial was the most popular option, with 84% opting for this, rather than the two-arm trial ($P < 0.001$).

Initial qualitative findings showed that recruiters had difficulty discussing uncertainty and equipoise and unknowingly used terminology that was misinterpreted by participants. Findings from this qualitative research were implemented: the order of presenting treatments was reversed to ensure equivalence;

misinterpreted terms were identified and avoided; the non-radical arm was redefined and specified; and randomisation and clinical equipoise were presented accurately and acceptably. Scrutiny of later appointments examined the impact of changes to content and presentation of information. Consent to randomisation increased from 40% to 70%.

Conclusion

The full-scale three-arm ProtecT randomised trial of treatments, funded by the NHS Research and Development (R&D) HTA Programme, is now underway in nine centres in the UK. The randomisation rate has fluctuated a little over time and by centre, but overall remains in excess of 70%. The use of qualitative research methods has allowed the views of participants and recruitment staff in the ProtecT study to be elicited, understood and incorporated into the design and conduct of the trial. Changes to study information and presentation determined by the qualitative research have resulted in high levels of randomisation acceptable to patients and clinicians. It may be that embedding randomised trials within qualitative studies may enable the most difficult evaluative questions to be tackled, and could have substantial impact on recruitment to apparently routine and uncontroversial trials.

How the pharmaceutical industry gets patients involved in clinical trials

Carol Aliyar

The primary challenge facing most pharmaceutical companies is to reduce the time it takes to develop new and effective medicines. As an industry we have spent enormous sums re-engineering and streamlining the clinical trial process in an attempt to reduce timelines and bring products to market faster. However, current thinking pinpoints patient recruitment and retention as the most significant challenges facing clinical research in the UK. The failure to recruit enough patients on time accounts for 85–95% of all days lost during clinical trials.¹ Is it any wonder therefore that the industry is determined to address this core issue: patient recruitment.

Before we can begin to examine solutions in detail we have to understand the reasons that lead to poor patient recruitment into trials. There are many, the most common are discussed below.

Complex protocol design

The regulations governing the conduct of clinical trials are many and currently evolving. This is not only to ensure that the results are accurate and reliable, but also to protect the rights of patients taking part. Once the purpose of a trial has been decided, a detailed protocol is drafted. The protocol describes in detail how the trial will be conducted. It will describe:

- entry criteria
- the type of patients to be recruited, to include the nature of the disease under research, age, sex and medical history, etc.
- how many patients will be expected take part and for how long will they be in the trial
- the number and detail of study assessments, e.g. blood tests, ECGs, to be performed.

Protocols are designed to meet the development plan for the compound while complying with regulatory and scientific requirements. They must satisfy the concerns of scientific committees who are somewhat removed from the practicalities of recruiting patients. As a result is it any surprise that when investigators, and more importantly patients, are presented with the prospect of a trial, they do not necessarily like what they find?

One company analysing data from eight studies across various indications found that the most common reason for an eligible patient to refuse to participate in a trial was the time constraint inherent in the protocol.

One approach to improve patient participation in clinical trials is therefore to simplify the protocol. It has been suggested that for such an approach to be successful it would require a change in the way industry develops protocols and may benefit from the involvement of patients at much earlier stages in the development process. How could this be achieved?

One way is to establish a patient advisory group.² This group could contribute invaluable, pragmatic input to:

- the design and conduct of the trial
- development of patient-centred outcomes
- provide insight on how to make some trials work
- simplify the patient information sheet
- review the materials to be used to support patient recruitment.

For such an approach to be successful the advisory group would have to be totally independent of the sponsor. The advisory group members would be volunteers, who would not be able to participate in the research programme themselves. Otherwise this may be viewed as yet another ploy to gain access to patient groups interested in participating in trials.

Poor site selection

In order to conduct trials we require the support of either GPs or hospital physicians to perform the research. In the past their selection has often been less than systematic, if not serendipitous. The reason these individuals got involved was either a genuine scientific interest in the research area or the opportunity to generate revenue to fund their own local academic research. However, this type of random selection resulted in 30% of investigator sites failing to recruit a single patient. This was unacceptable, and therefore a more analytical approach to selecting sites was required to support a more predictable approach to recruitment of patients into trials. As an industry we often overlook a clinician's interpersonal skills, intuition and experience which they can deploy as investigators to select participants into trials. Investigators' relationships with their patients are paramount and often directly impact a patient's willingness to contribute to research. An investigator must also be able to determine if this patient will be

compliant. Do they really understand the trial? What is the patient's motive for participating in the trial? What could be the impact on their home life?

Box A What makes a good site?

- A highly motivated investigator
- Past experience in conducting research trials
- High interest in the therapy area under research
- Appropriate resources that can be dedicated to research
- An investigator who is trained and implementing good clinical research practice
- One who is familiar with the local research environment (ethics committees, PCT, and research and development committees)
- Good knowledge of their patients
- A flexible approach to patient visit schedules

Patient pool

The next common reason affecting recruitment is the availability of willing research participants. The percentage of patients who participate in clinical trials varies from one disease area to another but the figure widely quoted is 5%. Therefore a novel and somewhat radical approach aimed at improving public awareness and understanding of clinical research is needed to expand the patient pool. Sources of patient information about trials are improving as we observe posters, radio, television and Internet advertising. Such advertisement is subject to ethical review and approval; however, this approval is now much more commonplace as committees appreciate the importance of improving patient awareness.

The assumptions we have made as to why patients take part in research are many, but some of the common ones are:

- volunteers are altruistic
- research gives the opportunity to improve their condition by taking a new drug that is not yet available
- a trial gives access to particular procedures they cannot obtain from their own GP
- it is an opportunity for a free health screen.

The above may make taking part in research attractive to some. However, it is without question that a lot remains to be done to learn about why our key stakeholders participate in research.

The starting point must be to gain a greater understanding of patient views and attitudes to clinical trials. Over two years ago, eight sponsors from both the NHS and industry who were concerned about the decline in UK patient recruitment into clinical trials came together and developed a study to look specifically at patients' attitudes and beliefs to participating in clinical trials.³ The soon-to-be reported trial, known as Patients' Attitudes to Clinical Trials (PACT), chose to look at the following:

- measuring the support of patients for clinical trials and their perceptions of the benefits
- determining the willingness of selected patient groups to participate, and examining why
- examining the opinion of patients with some knowledge and experience of clinical trials
- developing a standard questionnaire for future use.

The results of this research are eagerly awaited as they will begin to give an insight to the areas for action with our key stakeholders.

Summary

In summary we should remember that the patient of today is more educated and consumer oriented than ever before. If patient recruitment is no longer to be the weakest link in the chain of research it is vital that all the issues above are addressed. Industry must therefore be proactive in working with patients to help them take responsibility for their own health and healthcare. Only by treating patients as stakeholders can we truly expect them to engage and participate in future trials. The patient must be considered as one of the priorities because without the data from the patient there can be no new submission and consequently no new drugs.

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Consumer involvement in trial design and management

Mark Pitman

The Medical Research Council (MRC) is the largest public sector organisation in the UK for directly funding research relating to human health. For more than 60 years it has led the world in developing the methodology for randomised controlled trials, which are still considered the optimum methodology for assessing the effects of particular interventions on defined outcome measures. The MRC continues to play an active role in this area by: providing funding for clinical trials (mainly studies of clinical effectiveness); developing standards for the conduct of studies; and, through grants to universities and MRC research centres, supporting work on trials methodology.¹

In 2001 the MRC was approached by the CMO for England and asked if it would assist with the establishment of a clinical trial framework to assess the efficacy of potential therapies for the treatment of human prion diseases.

Human prion disease refers to a group of brain illnesses that are believed to result when a normal human protein, the prion protein, adopts an abnormal structure. This change in form is associated with damage to the brain. The most common example is sporadic Cruetzfeldt-Jakob disease (sCJD) that occurs in approximately one person in 1 000 000 in the population. Other forms exist, the most notable being variant CJD (vCJD, 'human mad cow disease'). Although these diseases have different pathogenesis and time courses they are all characterised by rapid neurodegeneration from the point at which clinical symptoms are expressed. There is currently no treatment and death results within months of clinical diagnosis. Thankfully numbers are relatively small compared with some major UK killers such as strokes and cardiovascular disease (50–60 sCJD cases per year in the UK and currently approximately 17 vCJD cases).² Nevertheless, these diseases are characterised by long incubation periods and in the case of vCJD it remains uncertain how many members of the population may be 'carriers' and could succumb to disease at a later date.

Designing a trial for this group of diseases holds many challenges including: the fact that the rapid degenerative nature of these diseases means that there is only a small window of opportunity to collect clinical research data; the poor health of patients limits their ability to get to specialist centres for assessments; while regular monitoring would be beneficial to the research this has to be

balanced with the ability of patients to participate; the relatively small number of cases reduces the potential statistical power of any study; the desperate need of relatives may mean that traditional randomisation (treatment versus placebo) may be unpopular because if there is a chance of receiving any treatment relatives are likely to want their loved one to have it; and it is not anticipated that the first therapy is going to be the 'penicillin' for CJD, thus any study is likely to be looking for small beneficial changes in the patient's condition.

For any study in this field to be successful it was acknowledged that it would be necessary to enrol as many of the CJD cases in the UK as possible. It was clear that this could only happen with the full support of the families of CJD cases along with their support networks. The MRC therefore decided to take the unprecedented step of formally involving 'consumers' in the designing and management of the study. The first stage was a workshop to aid understanding of trials and to discuss the design of the study specifically for CJD. It included exercises outlining the pathway to developing a trial and how to make a trial robust. It was attended by families, individuals at risk, carers, patient support group representatives, clinicians and scientists. Members of The MRC Clinical Trials Unit and the MRC Prion Unit produced a draft trial protocol that provided a framework for discussion.

The day highlighted that there was strong support for a trial: one that supported good research and that was sensitive to the needs of very sick patients. The day may be best summarised by the following quotations from attendees:

'A rare occasion – where consumers/families really feel that they have been listened to.'

'Everyone at high level is really thinking about the issues.'

A report summarising the activities and views expressed on the day has been published.³ These views have been taken into consideration and as a result the draft trial protocol has been significantly modified.

In addition, in an effort to maintain consumer input into the trial, the MRC has invited both the patient support groups (The Human BSE (bovine spongiform encephalopathy) Foundation and The CJD Support Network) to have representation on the trial steering committee (TSC). The MRC has also taken the unprecedented step of inviting a consumer to act as a co-chair to the TSC. In all there are four consumer representatives on the committee.

A TSC is established for every MRC trial to monitor and supervise the progress of the trial towards its interim and overall objectives. With an independent chair and a predominance of independence, membership usually includes the trial co-ordinators, trialists, experts in the field, a lay/consumer representative, a statistician and observers.

Conclusions

Testing the efficacy of potential treatments in new disease areas can provide many complex challenges. Scientists and clinicians have frequently dismissed the involvement of consumers in the development of science because they believe the issues are too technical for them to understand. It has been demonstrated in the first proposed trial for CJD that both the patient and the investigator can benefit from consultation on the design of the trial and share a sense of ownership.

Many trials fail due to poor recruitment; we believe that the involvement of consumers in both the design and management of the first CJD trial make a significant contribution to its success.

Acknowledgements

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- 3 MRC CJD Consumer workshop on clinical trials for CJD – report: www.mrc.ac.uk/pdf-cjd_workshop.pdf

Mix and match? Conjectures on heterogeneous trial populations

H Martyn Evans

Clinical data on the safety and value of a new drug are normally obtained by experimenting on a group of carefully screened patients, who should be as homogeneous a group as it is possible to get, with the intention of eliminating systematic biases and uncontrolled variables. These data are used to define new clinical treatments, which are then administered to the relevant general patient population.

But individual patients commonly vary from the trial population patients, to the extent that they themselves would have been excluded from the trial. It is orthodox that, other things being equal, the clinician may prescribe the new treatment to them if they are not *so* different from the trial population as to make the treatment obviously irrelevant.¹ The doctor decides whether, and how far, it will be safe and useful to prescribe to particular patients; this decision is made on the basis of clinical experience and judgement. Such judgements must concern *either* how closely the patient resembles a presumptively typical trial patient *or* how closely the patient resembles other patients within the clinician's experience whose response to this kind of treatment is known. But this entails that before actually treating a given patient, the relationship between his/her response to the treatment and the response(s) of the trial population cannot be known: every treatment episode is an experiment in which the sample size $n = 1$.

Could we do things any differently?

Imagine instead that trial data are obtained by experimenting on a group of patients who are as varied a group as one is likely to encounter in the relevant general patient population (those suffering from the condition at issue). Individual patients *ex hypothesi* now fully match the relevant trial population: they suffer from that condition (above, say, a threshold that distinguishes the condition from normal health). Imagine now simply that the doctor decides whether to prescribe the treatment on the basis of whether or not the patients in the trial were sufficiently helped by it, in the process making a judgement about how likely it was that patients *just like this one*

were represented in the trial population. The treatment is still, of course, administered in an experiment in which the sample size, as before, is $n = 1$.

However, this sample size can be increased, and its predictive value strengthened, if we imagine the doctor accessing very detailed information about the relevant personal characteristics of individual trial subjects and their treatment responses. This could readily yield what is effectively a loosely controlled experiment where $n = 2$ – i.e. the index patient plus their nearest ‘representative’ in the trial. The size of n rises if there are further relevantly similar patients. For patients ineligible for the conventional trial, there is a substantial chance that someone very like them does appear in the alternative trial I am proposing; remember that in a conventional trial there was no chance, for they would have failed the exclusion criteria.

Of course there are powerful reasons to specify a homogeneous trial population. For instance it protects the entry and exit points of the trial, with specific levels of disease standardised upon entry, enabling us to specify (and, hopefully, to attribute to the experimental treatment) the difference that has occurred during the trial period. But notice that this can be achieved with a heterogeneous trial population as well, if we focus closely on each individual’s clinical progress (derived from their individual entry and exit points) and try to express this in numerical terms that would allow comparability with the results from other patients. (Although difficult, conceptually, this is child’s play in the context of what is attempted in the derivation of QALYs.) Of course some other features of homogenous trial populations could not be mimicked in a heterogeneous population, specifically the ability to control for extraneous variables and to eliminate sources of systematic bias. The data from a heterogeneous patient population would be so contaminated as to be scarcely usable in the orthodox view.

The outrageous question I wish to ask is: Does this matter? Well, yes: but my sceptical suggestion is that it may matter less than we think.

First, all data become contaminated in practice. The purity of data from conventional homogeneous trial populations is itself compromised when we prescribe the trialled treatment to any patients who would have been ineligible for the trial (e.g. if their levels of disease are significantly different from that demanded by the trial then the validity and applicability of the trial’s entry point are compromised).

Second, clinical practice is mysterious. Since all clinical interactions are inherently individual, they themselves logically cannot be made the subject of population-level evidence gathering of the type constituted within clinical trials. It is hard to see how an evidence-based medicine (EBM)-type study of what happens at the individual level could be coherent. If clinical practice works, EBM itself cannot show that it does.

So, third, it follows that the strict chain of actions, involving clinical appeal to data derived at a population level, ends either in inaction or in something undemonstrable within EBM (personal communication, Professor APS Hungin). It may end in inaction because, since no treatment is logically capable of crossing

the gap between a carefully screened population and an unsanitised collection of varying individuals, one concludes that one must stay one's hand. Orthodox population-level data tell us about the probabilities of a treatment response attaching to different subgroups in the trial population (the groups are defined in relation to their response). The trouble is that we don't know which is the relevant subgroup – the 'reference class' – for any subsequent patient until after treating them. Or alternatively the chain of actions ends in something undemonstrable from the EBM standpoint: actions which necessarily stray beyond what would be sanctioned by the strict application of population-level data constitute a leap of faith, sanctioned psychologically rather than logically.

Finally, the difference between the experimental setting of a controlled trial and the naturalistic setting of clinical practice is qualitative, not quantitative. The coherence of generalised evidence from a conventional population-level study is discarded when we apply such results to the individual patient. Unlike the objects of physics or chemistry, medicine's objects – people – cannot ultimately be abstracted from their naturalistic context, in which their behaviour and responses are necessarily individualised.

We can know a great deal about the probabilities concerning what happens to specified proportions of them in closely defined, non-naturalistic circumstances. But the question is whether this is of any help now in treating the Mrs Jones in front of us. To find *this* out, we have to treat her, wait, and see. My suggestion is that this significantly constrains the advantages of using a homogeneous trial population, leaving the heterogeneous trial population looking unexpectedly attractive.

Reference

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The Interventional Procedures Programme

Bruce Campbell and Tom Dent

The Interventional Procedures Programme has come of age this year, publishing the first national guidance of its kind in brief, pragmatic format. Each guidance document comprises general recommendations, followed by background information about the procedure, and then specific sections on efficacy and safety, which include published data and the opinions of specialist advisors. Some guidance concludes with miscellaneous comments of the Advisory Committee, such as uncertainty about long-term outcomes. Any recommendations about training or submission of data to registries are specific, and are made with reference to the relevant professional organisations.

The initial task of the Interventional Procedures Advisory Committee (IPAC) was to consider the list of procedures which SERNIP (the Safety and Efficacy Register for New Interventional Procedures – now no longer in existence) had classified other than as safe and efficacious – some no longer very ‘new’. These have been discussed and the programme has settled into its longer-term mode of receiving notification of new procedures through its website. About six of these notifications come each month from a variety of sources, including doctors, professional organisations, industry and the public.

There will always be some uncertainty about exactly what constitutes a new procedure: how much does an existing procedure need to be modified to be ‘new’? However, there should be no doubt that the programme is committed to reviewing the safety and efficacy of *procedures* and not of devices. As a rule, any fully trained clinician planning to undertake a procedure for the first time should consult the NICE website to check on its status.

When a new procedure is notified to NICE, the interventional procedures team makes initial enquiries to see whether it merits consideration by the committee. Thereafter, two things happen. First the team prepares an ‘overview’, which includes background information and the results of a literature search. The amount and quality of published information varies greatly and is sometimes very sparse. When more exists, the most valid studies are selected for presentation to IPAC. The importance of producing timely guidance militates against a full systematic review of every procedure, and the aim is to present the most significant data which will guide a decision about safety and

efficacy. If ever important published data are missed in the overview, then the public consultation period offers a valuable opportunity for interested parties to point this out: notification of unincluded yet potentially important data is always welcomed and followed up.

The second action after notification of a procedure is to identify and consult specialist advisors. This is done through professional organisations whose medical members may undertake the procedure; there may be more than one of these. The aspiration is to secure advice from nationally recognised specialists who are carrying out the procedure, and also from knowledgeable specialists who are not. They will not always include those individuals conducting the largest numbers of a procedure, unless such people are nominated by their national body. This approach aims to select advisors who are held in high regard by their colleagues; they will not necessarily be enthusiasts, with the bias which can accompany such enthusiasm. The specialist advisors are asked a series of questions about the current and likely future use of the procedure, its efficacy and possible concerns about safety.

IPAC considers the overview and advisors' opinions. Their draft guidance may then recommend that the evidence on safety and efficacy seems adequate; or that uncertainty exists; or occasionally a procedure may be deemed unsafe or inefficacious. If the evidence is not considered adequate, this does not mean that the procedure should not be used, but that it should be used judiciously, and that publication of more data will be valuable. Specifically, and most importantly, clinicians wishing to use the procedure should ensure that patients offered it understand the uncertainty. NICE produces information for patients about each procedure, to supplement the clinician's own explanation. NICE has also agreed with the Department of Health a form of words which may be used to support written consent in such cases.

Clinicians wishing to undertake a procedure with uncertain safety and efficacy are required by the guidance to audit outcomes thoroughly. Before they embark on the procedure, however, they should inform the clinical governance lead of their trust. The response of trusts to such approaches is important to the maintenance of innovation in the NHS. There is no intention that NICE guidance should be used as a reason to prevent properly trained and equipped clinicians from embarking on new procedures, provided they meet the conditions that the guidance specifies. Indeed, if they intend to collect their outcome data for publication or submission to a registry then there is advantage in their efforts, because this will reduce uncertainty about the procedure's safety and efficacy. The guidance will sometimes specify a registry for national data submission and it may highlight particular uncertainties which audit or research should address (for example quality of life measures or long-term outcomes).

Whatever form IPAC's preliminary recommendations take, they are subject to public consultation via NICE's website for a month. All those who have expressed an interest in the procedure, specialist groups, patient groups (identified by NICE's Patient Involvement Unit) and interested device manufacturers

are alerted to the consultation period. All consultation responses are considered by IPAC. Any factual errors or important missing evidence mentioned by consultees are pursued. We particularly welcome focused consultation responses which suggest changes and which are accompanied by supporting evidence or reasoning. Consultees also need to understand that the guidance must be brief to be useful.

The guidance is amended in the light of consultation responses and is then considered by the NICE Guidance Executive before being published in English and Welsh, accompanied by information for the public. Hard copies are circulated to all relevant specialists and to trusts, and the guidance is available on the NICE website.

Most interventional procedures guidance is not scheduled for review, but if there is uncertainty and if potentially important publications are expected then a review date may be set. Alternatively, there is always the opportunity for interested parties to refer a procedure back to the programme if they believe that new information makes that appropriate. The programme's outputs are intended to be timely and responsive to clinicians, patients and others affected by the use of procedures.

To succeed, the Interventional Procedures Programme must balance the acquisition and analysis of adequate information against the publication of guidance without undue delay. This depends on close collaboration with all those involved in the use of procedures, who set its agenda and who take the time to offer helpful comment and opinion.

What is the role of research and evidence in policy making?

Martin Eccles

Introduction

NICE has a series of programmes, including technology appraisals and clinical guidelines, which deal daily with the realities of incorporating evidence into policy.¹ If we regard NICE as only one specific example, are there common issues that will confront researchers and policy makers as they attempt to interact in an effort to integrate evidence into policy making? In this article I use the term policy maker in a general way, denoting anyone who is responsible for making allocation decisions about the provision of healthcare; they may do this at any point within the healthcare system from a local to a national level.

The concept that published research should influence policy is, on the one hand, a self-evidently desirable aim and on the other an invitation to step into a world of politics and misunderstandings. Misunderstanding is exemplified by the suggestion of Caplan *et al* that policy makers and researchers inhabit two different (and separate) worlds in one of which researchers see themselves as rational, objective and open to new ideas while seeing policy makers as action and interest-oriented and indifferent to evidence and new ideas.² In the other world policy makers see themselves as responsible, action oriented and pragmatic, and researchers as naïve, jargon ridden and irresponsible in relationship to practical realities.² That this is political territory is illustrated by Fox and Oxman who suggest that there are three different sets of politics at play – the politics of research, the politics of health policy and the politics of collaboration between researchers and policy makers.³

While there is a published literature suggesting how to integrate research findings into policy, this is largely opinion-based with little empirical data describing the effectiveness of strategies to achieve this. In this article I have drawn on three pieces of empirical research to illustrate some of the generalities that need to be considered when contemplating the relationship between evidence and policy making. This is not a systematic review of the literature and thus will inevitably be partial and incomplete; however, I hope that it is informative and will act as a signpost into this area for readers.

Accountability and evidence

Researcher's accountability is to their research community (including research funders) and to those policy makers they would aspire to have use their results. They are accountable for the validity of their methods and the truth of their studies.

For policy makers the position is different. Their accountability is to the public and is for the decisions that they take. However, in taking their decisions they will take into account a range of factors of which scientific research is only one. They will also take account of other factors such as financial implications, public opinion, political climate, the actions of interest groups and the views of opinion leaders. Sometimes they will take more account of these other factors than they will of research evidence. What do we know of the factors that influence them in taking their decisions?

Barriers and facilitators to the use of evidence in policy making

Innvaer and colleagues systematically reviewed the literature on health policy makers' perceptions of factors promoting or inhibiting their use of evidence.⁴ From 24 studies reporting a total of 2041 interviews they identified commonly reported facilitators and barriers. The three most commonly reported facilitators were personal contact (13/24 studies), timely relevance (13/24) and the inclusion of summaries with recommendations (11/24), while the four most commonly reported barriers were absence of personal contact (11/24), lack of timeliness or relevance of research (9/24), mutual mistrust (8/24), and power and budget struggles (7/24).

Others have approached these issues in a different way. *Informing Judgment: case studies of health policy and research in six countries* is a description of six case studies of the inter-relationship between policy and research evidence.³ The case studies demonstrate the importance of context yet also draw generalisable lessons across the differing countries, with their range of histories, cultures and decisions. In their introduction to the report, Fox and Oxman suggest there are a number of generalisations that can be made from the case studies (*see* Box A) over and above the single statement that 'The proper purpose of collaboration between researchers and policy makers is to use evidence from research to inform judgments for which policy makers are accountable.'

In a further case report, Scheel *et al.* described a study where a further dimension of the relationship between researchers, evidence and policy makers was illustrated – the non-use of research findings.⁵ The authors describe a collaboration between researchers and policy makers designing and running a randomised controlled trial to evaluate two strategies to implement a return to work policy (Active Sick Leave – ASL). However, the collaboration appeared to

Box A Generalisations on the relationship between researchers, evidence and policy makers (Adapted from Fox and Oxman, 2001)³

- Because both research and policy making are complex activities and very different from each other, mutual understanding requires conscious effort. To inform policy making more effectively, researchers need better systematic understanding of political culture.
- Policy makers can help achieve mutual understanding by respecting researchers' knowledge, competence and needs.
- Policy makers and researchers must learn to accommodate differences in the time frames within which they operate.
- Collaboration builds on good experiences for both researchers and policy makers. To achieve good experiences, a policy maker said, the 'rules of engagement must include appropriate expectations and appropriate definitions of success'.
- Effective collaboration between researchers and policy makers is likely to be enhanced if both groups continue to work together after the policy-making process to evaluate the results of implementing the policy.
- Trust between individuals is built up over years. The process of making health policy should create and maintain opportunities for long-term collaboration between policy makers and researchers when this is possible.

fracture when the policy makers did not wait for the final results of the trial. During the course of the trial it became apparent that there was an external policy move to use ASL more generally, in the expectation that it would reduce time off work by 20%. The strategy to be used in this policy was one that the trial had already demonstrated did not increase the uptake of ASL. In addition, when the final results of the trial became available, showing no effect of either strategy to implement ASL on time off work, disability or quality of life, they were ignored by most of the policy makers involved.

This example of non-use raises the question of what is expected from the 'use' of research findings. In their review of health policy makers' perceptions of factors promoting or inhibiting their use of evidence, Innvaer and colleagues describe three types of use – direct, selective and enlightening.⁴ These three can be regarded as points on a continuum from a piece of research fully and totally answering a policy need, through to a piece of research stimulation thinking or insight around a policy decision but having no direct impact. The ASL example, at most an example of enlightening, more realistically suggests the need for a fourth category of explicit non-use of research findings as it seems to represent a circumstance where factors other than research evidence outweigh any impact of the research evidence so much that it is not used.

Some realities

Having identified the importance of mutual understanding, effective communication and mutual trust it is then appropriate to consider something of the realities of researchers and policy makers trying to interact. Lomas described a number of challenges, for both researchers and policy makers, identified by Canada's Health Services Research Foundation bringing together a group of researchers and policy makers and asking them to describe the realities of trying to interact with each other.⁶ The group identified the differing time lines of the two constituencies and added a lack of available time for both groups. They also identified that, in most systems, there are multiple researchers and multiple policy makers with no clear points of contact between, or entry points into, their respective worlds. From outside there is often no way of knowing who within a system is influential and who is not; added to this is the fact that neither population is stable, both being prey to personnel changes and restructuring. Finally, they suggested that there is only limited mutual understanding of technical issues; researchers don't understand the technical aspects of policy making and policy makers don't understand the technicalities of research method.

Conclusions

It is tempting to suggest that the solution is to address the generalisations that Fox and Oxman describe.³ However, Lomas's realities reflect the *real politic* of researchers and policy makers interacting and emphasise the view of all the authors cited in this article – there are no simple solutions.⁶ As Fox and Oxman suggest, 'both policy makers and researchers must continue struggling to help ensure that judgements about health policies are well informed by research evidence. The alternative is to acquiesce to poorly informed health policies'.³

Acknowledgements

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What is the role of research and evidence in cancer policy?

Robert Haward

Introduction

This article uses cancer care to illustrate the influence of evidence on policy development. The first comprehensive cancer policy in the UK was developed by the Chief Medical Officers (CMOs) of England and Wales and known as Calman–Hine, published in 1995.¹ This was the first time a major disease had been covered by a single policy, and paved the way for the national strategic frameworks for other disease groups such as coronary heart disease.

The development of the policy followed mounting disquiet about the adequacy and performance of UK health services for cancer patients. There was striking consistency in the issues coming forward from patient groups, cancer professionals and in media coverage. These were reinforced in published studies.^{2–5} The main concern was the variability in management experienced by patients. This was exacerbated by the ‘lottery’ of referral, whether patients had early access to cancer specialists (surgeons and oncologists) or only to generalists. Experience suggested this process operated erratically, yet influenced the subsequent management and outcomes for many people.

Cancer policy: the Calman–Hine initiative

The two CMOs secured a political mandate to develop cancer policy, a field in which both had considerable personal knowledge. The mechanism they used to develop their policy was unusual in that they established a small expert advisory group to prepare the policy document and gave them an unusually ‘free hand’ in so doing. This group elected to meet experts and consider research evidence on several important themes, namely:

- international comparisons:
 - of outcomes
 - of inputs to cancer care (manpower, facilities and resources)
- the performance of cancer services in the UK

- alternative models for delivering cancer services
- the importance of specialisation and caseload.

The evidence was not presented in the policy document itself, but Selby and colleagues published a summary on behalf of the group.⁵ The evidence base for moving from a generic to a specialist multidisciplinary model was particularly crucial and some UK studies were particularly influential, notably the ones by Gillis, Junor and Sainsbury.^{6–8} Although the policy was subject to consultation, its content and format were largely unchallenged. The policy received a broadly supportive reception from patient and professional audiences.

Calman–Hine has been hugely influential as a framework of principles, structures and processes for good cancer care. It did not cover specific issues for each type of cancer, such as personnel, facilities, clinical organisation, and the effectiveness of diagnostic and treatment modalities.

Service guidance: the ‘Improving Outcomes’ project

Immediately following the publication of Calman–Hine the Department of Health established a programme to produce guidance for each site of cancer. Service guidance was aimed at those responsible for commissioning or managing the delivery of cancer services, including cancer networks. It specified the clinical structures and processes necessary for each site of cancer (or group of sites, e.g. gynaecological malignancies) if good outcomes were to be achieved. Published policy has so far covered breast, colorectal and lung cancers together with gynaecological, upper gastrointestinal, urological and haematological malignancies; these represent about 80% of cancers in the UK (based on incidence, excluding non-melanoma skin cancer). Further titles are planned.

The development methodology was derived from an intensive exercise at the outset, and has remained largely unchanged. It utilises evidence of all kinds, including clinical effectiveness but falls short of the level of clinical detail appropriate for practice guidelines. The published format evolved during work on the first topic (breast cancer). The methodology and role of the project has been described by Haward.^{9,10} Each manual is accompanied by a comprehensive tabulated summary of the evidence prepared by the Centre for Reviews and Dissemination at York University which co-ordinates the evidence reviews.

Service guidance: using evidence

A wide range of evidence is used to formulate service guidance. Health service information, audit data, cancer registry and epidemiological studies are used to examine variations in the performance and outcome of current services, and to make comparisons with other health systems. This gives important indications

about the need for change, although expert advice is often required to interpret such material.

The strongest evidence is derived from systematic reviews where these are available, more usually individual trials and observational studies need to be assessed. Many important questions about services have never been tested in well-designed studies, and expert opinion may be the only guide in formulating some recommendations. Service guidance cannot ignore crucial issues in the care pathway, such as referral criteria, follow-up arrangements, or palliative support, merely because no high-quality peer-reviewed papers exist. The key to deploying such varied evidence is transparency and clarity to ensure that users can examine the evidence base supporting particular recommendations.

Service guidance: factors influencing service organisation

Figure A illustrates the concept that the optimum arrangement of services is influenced by several components which may overlap. For example volume and specialisation go together, making it difficult to establish the relationships between individual factors and outcomes. This literature has grown in recent years with several systematic reviews.^{11–15}

In a forceful editorial Hillner described the cumulative weight of this evidence; 123 of 128 published studies showed a volume–quality relationship.¹² In oncology he identified consistent and often striking examples of better outcomes with higher volume. Hillner argued that this evidence should be

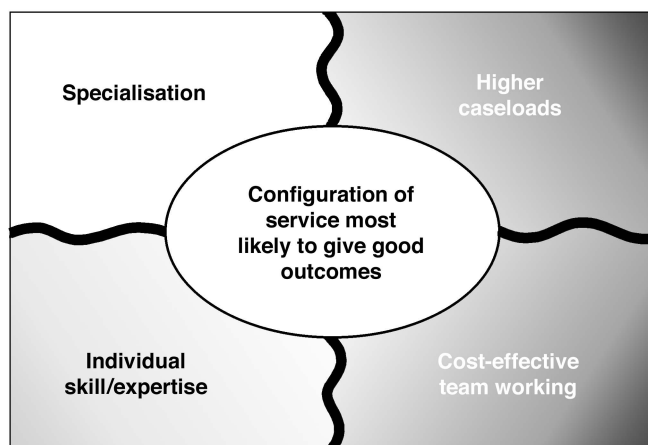


Figure A Schematic representation of factors influencing service configuration.

considered more seriously as a driver for change in cancer care, concluding that 'if these decisions did not involve livelihood, prestige, and power, we would have demanded action long ago'.¹²

This evidence has been taken seriously in the preparation of cancer service guidance, despite the difficulties in interpretation of the evidence. There are possibilities for bias, including case-mix adjustment, publication bias and the statistical limitations of examining single dimensions of multifaceted issues. The guidance developers have made recommendations for those cancers for which there is sound evidence of benefit, setting appropriate thresholds for the UK context.

Conclusions

In the last decade cancer policy making has been innovative and productive. Throughout this process evidence has been utilised more extensively and systematically than ever before, although limited by weaknesses and gaps in available evidence.

These policies are changing the delivery of cancer services, with improved clinical decisions and patient management. These changes will lead to better outcomes. Key changes include:

- more resources: particularly manpower and facilities, with well-defined structures, service inter-relationships and clinical processes
- multidisciplinary teams: site specialists making clinical decisions together about managing their patients
- reduced fragmentation of care: all patients are referred to identified site specialists working in multidisciplinary teams, each with a clear remit and sufficient caseload
- reconfiguration: high morbidity and mortality procedures are managed in hospitals with extensive experience and expertise.

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The role of evidence in improving market access

Julia Earnshaw

Introduction

Since the 1960s and the introduction of regulation on the use of medicines, prescribing has become increasingly evidence based. As well as the assessment of efficacy, safety and quality prior to gaining a product licence, any commercial claims made by manufacturers concerning the benefits of medicines have been regulated by the Association of The British Pharmaceutical Industry (ABPI) Code of Practice.¹ Despite this evidence-based approach, individual prescribing decisions were still influenced by factors such as personal experience, values and beliefs, and influence from others. As a result considerable variation in prescribing remained and a number of initiatives have been introduced to address this. These included the widespread establishment of local drug and therapeutics committees, the promotion of practice formularies and clinical guidelines and employment of local prescribing advisors. Many of these initiatives drew on evidence to inform their recommendations; however, variable decision making continued, leading to 'postcode prescribing'. In 1998 the publication of *A First Class Service* proposed the initiation of the NICE to make evidence-based recommendations on the appropriate use of medicines at a national level.² These local and national initiatives effectively formed an additional 'fourth hurdle' before medicines could be used in the NHS. The term 'market access' has been coined to reflect the need by manufacturers to overcome this hurdle.

How does evidence inform market access decisions?

The emergence of new decision makers on the use of medicines has resulted in the need for additional evidence. In addition to the traditional information on efficacy, quality and safety, the manufacturers increasingly have to provide additional evidence, including clinical and cost-effectiveness. To meet these needs GlaxoSmithKline provide a range of information at different stages of the medicines life cycle.

During development, information is provided on a six-monthly basis to those in the NHS responsible for planning budgets at a local and national level. A document provides background information on products in development with more detailed information on compounds likely to have budgetary impact in the next three years. More detailed information is provided in Advanced Planning Information/Formulary Packs in the six months prior to launch to inform local decision making and planning.

How is evidence used in decision making by NICE?

Evidence also plays a key role in defining topics that will be selected for review by NICE. Information provided to the Horizon Scanning Centre identifies potential subjects for NICE appraisal. Specific feedback on consultation documents ensures that the evidence available to inform the topic selection process is accurate and up to date.

Once a topic has been selected for review by NICE it enters the appraisal process. The recent draft *Guide to the Methods of Technology Appraisal* stated 'consideration of an inclusive and high-quality evidence base is fundamental to the appraisal process'.³ The evidence base includes an independent assessment from one of the HTA groups, and submissions from manufacturers and sponsors, patient and carer groups, healthcare professionals and clinical specialists/patient experts. In a typical submission to NICE, GlaxoSmithKline would provide:

- details and results of all relevant (within licence) clinical trials for which we are the sponsor or that are known to us
- listings of other clinical trials that are not relevant, e.g. outside scope
- if appropriate, a systematic review and meta-analysis of studies
- other research evidence where relevant to the scope, e.g. cohort/observational studies/epidemiology/burden of illness
- cost-effectiveness evidence including an electronic copy of any model used
- NHS budget impact information.

However, there is a recognition that despite this evidence-based approach it is unlikely that perfect information will exist. This is particularly the case for new medicines where the regulatory clinical trials may well provide imperfect evidence due to factors such as choice of comparator, length of follow up, use of intermediate endpoints and lack of generalisability. Hence decisions will still be taken under conditions of uncertainty. The need for other factors to be taken into account is also recognised in the draft *Guide to the Methods of Technology Appraisal*.³ This document flags the difference between the two stages in the NICE process, those of assessment and appraisal. Appraisal is defined as:

‘A consideration of the outputs of the assessment process within the context of additional information ... The appraisal committee translates the evidence available in the assessment report and elsewhere into an appraisal decision, applying judgements on the importance of a range of factors that may vary from appraisal to appraisal.’

The impact of these judgements is clear when the range of cost-effectiveness values in medicines approved by NICE is considered (*see* Figure A).⁴

To what extent do NICE decisions inform local decision making and improve market access?

It is now mandatory for local decision makers to fund medicines that have received a recommendation by NICE. In theory therefore, except for demographic variation, one would expect similar use of NICE-recommended medicines. In reality there remains significant variability – for example recent data suggests that the uptake of trastuzurnab (Herceptin) remains variable, with many patients not receiving this treatment despite a positive NICE recommendation.⁵ So why is this?

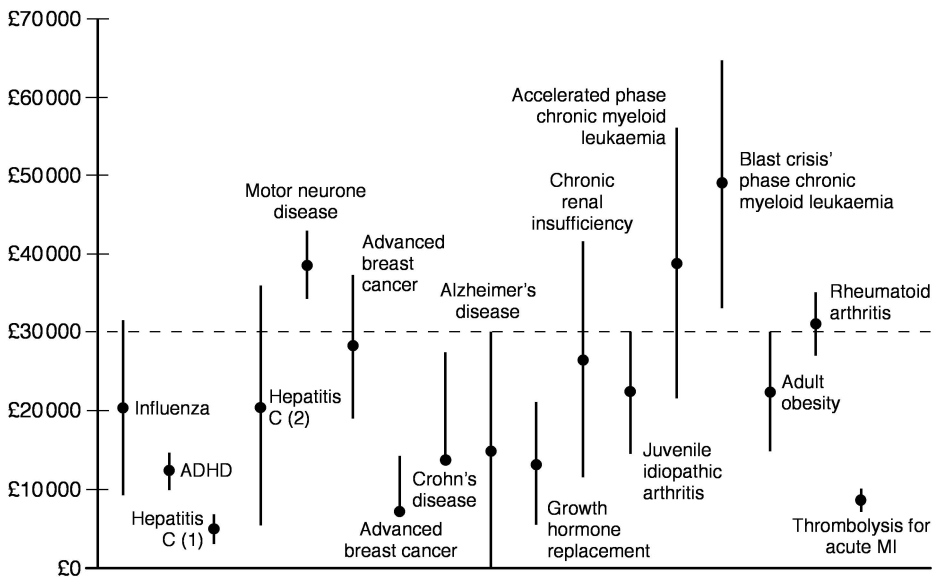


Figure A Range of cost/quality adjusted life years values in technologies approved by NICE. ADHD: attention deficit hyperactivity disorder; MI: myocardial infarction.

The Management of Medicines (MANMED) survey in 2001 assessed primary care organisations' (PCOs') and hospital trusts' approach to medicines management.⁶ Specifically they asked what action had been taken in response to the NICE guidance on proton pump inhibitors and rosiglitazone. The level of response ranged from no action to nine types of action. The same project also reviewed the literature on the success of alternative approaches to medicines management and found that although a wide range of approaches is possible, there is little evidence of what is most effective. Subsequently GlaxoSmithKline has undertaken market research with 50 prescribing advisors across the UK; 64% agreed that their PCO prioritised implementation of some areas of NICE guidance over others. A range of factors impacted on which guidance was most likely to be prioritised, including whether the guidance was linked to a national target, whether it was an issue locally and whether it supported current clinical practice. Clearly therefore values and judgements made at a local level will impact on the implementation of NICE guidance. As a result, despite the introduction of NICE, market access barriers will still exist at a local level affecting the use of specific medicines.

Conclusions

A range of mechanisms has been introduced that provide additional hurdles beyond the regulatory process and restrict the uptake of medicines within the NHS. Despite the evidence-based nature of these hurdles, value judgements and other factors continue to influence decisions and their implementation. Therefore although evidence is clearly critical to achieving market access, it is unlikely that this will be the only factor in the uptake of new medicines.

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The role of health economics in making recommendations to the NHS

Martin Buxton

Introduction

In an independent review by WHO, the appraisal function of NICE was hailed as an important model for technology appraisals internationally.¹ The commitment to rigorous methodology was applauded. It is clear to all that the analysis of cost-effectiveness (CEA) is central to this methodology, and revised guidance on the Institute's preferences for the presentation of CEA is shortly to be issued.² However, there is a continuing debate as to whether NICE guidance is always implemented as fully or as quickly as it might be, despite the obligation on the NHS to do so.^{3,4} The impression is that implementation is patchy.

This may be a manifestation of resistance to more central control over local spending priorities. However, it may also reflect a disconnection between the analyses that underlie NICE's consideration of cost-effectiveness and the short-term managerial and political reality of the NHS. The WHO review team suggested that NICE needs to address more fully the local budgetary implications of adopting technologies that have been appraised on the basis of their acceptable cost-effectiveness ratio.¹

The problems behind the rationality of cost-effectiveness analyses

CEAs for NICE are very appropriately required to take account of all NHS and personal social service costs. For example, analysis may suggest that the additional costs of the GP prescribing of a new drug would lead to a subsequent reduction in the patients' use of specialist tertiary services. These might have earmarked funding from the National Specialist Commissioning Advisory Group. In such a case, the reasonable net cost to the NHS on which NICE focuses, might hide widespread increases in primary care prescribing budgets

counterbalanced by savings focused in a quite different NHS budget. What is more, the costs and savings are rarely contemporaneous. Typically in health, we invest up front to achieve future health benefits and so the cost savings (that future improved health may bring) may occur a long way ahead. Many of the interventions that NICE has recommended may have benefits (and associated cost savings) that are not fully realised for 20 years or more.

CEA handles this in part by allowing for the fact that society has preferences for benefits sooner rather than later and the costs later rather than sooner. But the strength of this preference, which is exhibited in the chosen discount rate(s), is set by HM Treasury. They now judge that the appropriate rate of discount is 3.5% per annum for costs and benefits.⁵

The assumption is that society can achieve costless transfers between budgets and at the discount rate in question, between time periods. That is not the managerial reality in the NHS. Budgets are not easily adjusted. Nor are managers generally able to transfer funds intertemporally. I suspect that the PCT finance officer who argues that his current serious overspending will be easily met from a reduction in someone else's budgets 20 years hence would be forfeiting his performance-related pay!

Furthermore, these CEA studies typically take no account of transition costs, but reflect the situation in a new steady state.

So the assumptions within CEA do not accord with the managerial reality, or necessarily with the political priorities manifest in other pressures on the health service.

Possible solutions

So what can be done? Some might suggest that NICE could place less attention on CEA and more on budget impact in making its decisions. That would be a retrograde step. However, a simple and positive step would be to provide a much more detailed and disaggregated budget impact statement. This should not be difficult to achieve if the underlying cost-effectiveness studies are well constructed. Suitably presented, this would enable all parties at a local level to see and understand the balance of costs between different parts of the NHS and how it changes over time.

Disaggregated costs from each set of guidance could then be netted up to see what is implied for aggregate shifts in budgets over time. It may be that, by fortunate chance, the net effects balance out, or the shift in pressure on particular budgets is marginal. If so, the detailed evidence to show that will prove to be a reassurance. If they do not balance out, then budget allocations for the following years could be adjusted to reflect any significant imbalances.

Moreover, if at some point there were to be earmarking of funds for NICE advances, then this annual totting up of where costs are falling would help ensure that the funds were appropriately allocated at the 'micro-level'.

Discussion and conclusion

The current and proposed methodological guidance does not reflect a pure welfare-economics perspective. If, as many economists would argue it should, NICE were concerned about, and gave equal weight to, costs and cost savings, including those falling on parties other than the NHS and personal social services, the problem would be very much greater. Even within the NHS, costs may fall disproportionately on certain budgets. The recent focus on new cancer drugs may itself have meant that certain budgets were disproportionately stretched. Where problems are foreseen at a micro-level, there should be clearer and more specific expectations from NICE as to how soon, and how fast, a technology should be introduced, so facilitating local micro-planning.

NICE should not back away from the rational process of basing its decisions about the introduction of new (or occasionally the withdrawal of existing) technologies on the balance between the health benefits they provide and the net costs they impose to the health system as a whole. But all parties must recognise that this rational economic logic does not necessarily fit easily into a health service that is highly constrained in the way it can, in the short term, reallocate resources between budgets and over time.

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NICE challenges

Alan Maynard

Having been involved in the creation of NICE in 1997, I regard it as an essential NHS agency and I hope it and complementary agencies can cope better with the challenges discussed below.¹

Incremental drift in technology adoption in the NHS

The producers of new technologies continue to market unproven technologies (in terms of cost-effectiveness) directly to clinicians and other potential users. This marketing leads to the adoption of unproven interventions and technological 'creep'. This needs to be dealt with by legislation and inspected by the Commission of Healthcare Audit and Inspection, and the Foundation Hospital Regulator. Clinical experimentation with unproven technologies can not only damage patient health but also creates expenditure inflation.

Being explicit about rationing

Despite assertions to the contrary, NICE is the agent of NHS rationing.² Rationing is ubiquitous and involves depriving (or not offering) patients of care from which they would benefit, and which they would like to have.

The dominance of cost-effectiveness over clinical effectiveness

What is clinically effective may not be cost-effective (e.g. beta interferon for the treatment of multiple sclerosis). What is cost-effective is always clinically effective. To prioritise or ration competing therapies, it is necessary to rank them in terms of their relative cost-effectiveness. This has been the focus of many NICE appraisals, although not all of them offer explicit cost per QALY estimates as yet.

The dominance of equalising quality adjusted life years expectancy over efficiency

Beware of narrow-minded economists ‘paddling’ the efficiency (cost-effectiveness) canoe! The NHS was created to mitigate inequalities in health. These have increased over recent decades and can be mitigated by devising equity weights for QALYs that reflect society’s desire to pursue greater equality in QALY expectancy. Such weights may reflect rich/poor, young/old and other equity considerations, e.g. Williams’ ‘fair innings’ arguments.³ To ignore the equity issue is to ignore the purpose of the NHS.

Processes for selecting technologies for approval

Although efforts have been made to broaden the ‘church’ from which appraisal suggestions are derived, there continues to be over-emphasis on new technologies and relatively little attention paid to old technologies that may be redundant. If the latter were appraised, resources would be freed to mitigate the inflationary pressure NICE imposes on the NHS.

Eliciting the preferences of a wider group of NHS managers might be helpful. Their increasing exposure to review in the ‘star wars’, CHI/CHAI reviews and by the Foundation Trust Regulator will make them increasingly determined to identify resource saving by identifying and eradicating useless technologies.

Constraining NICE-induced inflation

De facto the NICE ‘fourth hurdle’ is set, give or take £5000, at around £25 000 per QALY. This has led to NICE approval of some marginal therapies, especially in the cancer area. There are intense funding pressures in the NHS. These are exacerbated by the inflationary new contracts for GPs and consultants, the New Deal, the European Union (EU) Working Time Directive, increased National Insurance contributions and other changes that add to expenditure with little benefit in terms of service activity or quality.

The NICE hurdle is essentially arbitrary but too generous for its appraisals to be funded in the NHS. Its inflationary impact is intolerable. This problem can be addressed by:

- acquiring the preferences of NHS chief executives and using them to determine the hurdle. This would probably reduce the cut-off to £12 000–15 000 per QALY, with many more technologies failing to win NICE approval

- giving NICE a notional budget (e.g. £500 million a year) and requiring it to stay within budget
- giving NICE a real budget of £500 million per year and requiring it to stay in budget by funding implementation of all its proposals.

The third option is superior in that it would require NICE to determine the value of the QALY at the margin and also incentivise it to balance cost-adding and cost-reducing appraisals. The politics of these options would be complex and difficult. The alternative will lead to variations in the take-up of NICE advice and exacerbation of 'postcode' prescribing.

Overview

NICE is an essential NHS rationing agent. Its development requires that it and the government meet these six challenges. If this does not happen, the resultant organisation will be unable to meet its obligations, i.e. resources will be used inefficiently and the NHS will fail to reduce inequalities in quality adjusted life expectancy.

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Priority setting and healthcare commissioning: is there a case for a UK network?

Angela Bate, Cam Donaldson and Tony Hope

Priority setting and healthcare commissioning

Hidden among recent attention given to the development of foundation hospitals has been government recognition of the need to strengthen the role of commissioning, backing up an earlier commitment to give PCTs responsibility for this task.¹

'Effective commissioning' is essentially about making decisions concerning the types and levels of care to be funded within a given budget in order to meet the health objectives of specific geographic populations. This is inextricably related to the task of prioritising between competing claims on these scarce resources, which has been part of the UK NHS for decades, and is now globally recognised; note the recent establishment of the International Society for Health Care Priorities.

Current debates focus on the question of how best to determine priorities.²⁻⁴ Evidence-based approaches have been exemplified through the creation of national bodies, such as NICE, its role being to produce national guidance on individual technologies ('appraisals') and the management of specific conditions ('clinical guidelines').⁵ But the question remains as to what local decision makers do with such information in their own contexts of managing scarcity. What, for example, are the local frameworks within which the products of such important national bodies are to be applied?

The role of NICE

How does NICE perform in terms of aiding priority setting? This topic has been widely discussed, with authors rising to the challenge of constructing snappy titles to include a pun on the word 'NICE'!⁶⁻¹⁰ Some of the main criticisms have been:

- NICE takes too ‘mechanistic’ an approach to evaluation, focusing on health outcomes in terms of QALYs and paying too little attention to other factors that should affect priorities. The NICE approach gives the impression that priority should be given to technology-related healthcare interventions, like pharmaceuticals and devices, which more obviously lend themselves to the methods that NICE adopts.
- In practice, choice must be made between alternatives, whereas NICE conducts ‘one-off’ evaluations. Acceptance of a technology which produces additional benefits, but at additional cost, is, at best, of partial use to decision makers working under resource constraints, choosing between alternative healthcare programmes. Indeed, it has been predicted that ‘saying yes’ results in either continued expansion in expenditures, or commissioners ‘slavishly funding marginally cost-effective drugs approved by NICE and diverting funds away from more cost-effective existing services that lack politically powerful advocates’.⁶
- Although NICE was set up, in part, to avoid postcode prescribing, the services from which funds are diverted will vary locally so that the issue of ‘equity across the country’ remains.

To address these problems, something additional is required in order to make the link between national and local priorities. The recent House of Commons Health Committee Report on NICE stated that: making NICE guidance mandatory raises challenges for NHS priority setting; practical systems and structures should be put in place to improve capacity to implement guidance, as implicit prioritisation is insufficient; and the government must work towards ‘a comprehensive framework for healthcare prioritisation, underpinned by an explicit set of ethical and rational values to allow the relative costs and benefits of different areas of NHS spending to be comparatively assessed in an informed way’.¹

But what might such a framework look like and how can we ensure it conforms to ethical and economic principles while recognising both the complexities of healthcare, and what is already going on in commissioning organisations in this respect? To us, these are challenging questions which can be addressed only through the creation of a national network to share experiences and develop best practice.

The need to create a UK network

Resource scarcity will never go away and the imperative to examine local needs will always be there. NICE guidance has to be examined in this context. The commissioning task in the ‘New NHS’ involves trading local and national priorities, and centrally driven targets and guidance. Though currently undertaken within PCTs, the ways in which these decisions are made and the consistency in approaches are difficult to establish.

In recent years, much progress has been made, internationally, on developing

frameworks, based on both economics and ethical principles, which recognise scarcity, the complexity of healthcare and, thus, the need for pragmatism to be built into priority-setting processes.¹¹⁻¹⁶ In 'evaluations' of such frameworks, managers typically stated that they allow proposed service developments to be treated equally, according to predefined criteria, and that they provide the opportunity to consider weighing-up, once development monies are spent, the relative priority of currently unfunded developments against potential areas for disinvestment.^{13,14}

In the absence of NICE becoming a national healthcare rationing agency (as suggested elsewhere⁶), how can best practice in priority setting and, thus, commissioning, be developed and disseminated throughout the NHS? Such dissemination is necessary to enhance PCT capacity to effectively, efficiently and equitably receive guidance and implement targets while accounting for local needs. Moreover how can these practices be adopted routinely by commissioners? Are there the necessary information systems and incentives in order for such processes to become fully embedded within management structures and local delivery and development planning processes?

In order to meet such challenges, it is important to bring together both management and research communities in a UK network to ensure that processes are both pragmatic and based on relevant principles of economics and ethics. The result would be two main types of 'living' tools to guide local development planning: one, based on economic principles, providing a step-by-step guide to assessment of the current situation in any given PCT and how to weigh up options for change, the other providing guiding principles against which to evaluate the ethics of any process.

Conclusion

A national network as described above will help PCTs, and other commissioning bodies, to:

- implement guidance and targets while ensuring that other local needs are met and identify some serious clashes between national targets and local needs
- minimise the threat of local development monies being taken up by meeting targets based on national guidance. This can be achieved by justifying why local plans to meet targets based on national guidance might vary
- reconcile ministerial concerns for good quality across the board in the NHS with the need for local discretion on meeting claims on resources.

To do this, it is urgent to recognise first, that priority setting is integral to the delivery of healthcare and, second, that the best way forward is to create a network of expert practitioners and academics to develop and disseminate best practice in priority setting.

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Who has the responsibility for picking up the research agenda?

Chris Counsell

The title for this talk was given in advance by the organisers of the conference and perhaps reflects a perception that the changes in the legal and organisational framework for research in the NHS is leading to a fundamental change in the drivers for research. Whether or not this is true is one question, whether or not there ought to be a change is another. Certainly, NHS organisations have to take the governance of research more seriously than before and not all non-NHS researchers have fully recognised this changed environment. But this does not automatically mean that R&D is any more important to NHS managers or that they are interested in driving research in their organisation.

The NHS, like all healthcare systems, relies heavily on technological advancement and innovation – new techniques, new drugs, new devices, new ways of working. In industries where innovation is important to keep ahead of competitors, R&D is actively built into the business plans. This appears not to be so in the NHS. The following are some possible reasons.

Support costs

Until the reforms of 1991 and the establishment of an R&D Directorate within the Department of Health, research happened in the NHS without any great planning or strategic purpose. The reforms were supposed to change all of that with a National Director of R&D and supporting team in the Department of Health, together with regional offices to put into effect locally the strategy agreed nationally. The subsequent changes in the funding arrangements in the wake of the Culyer report meant that R&D was apparently secure financially and strategically. But arguably, R&D has not noticeably benefited as a result, since outside its compartment, in mainstream NHS management, R&D can safely be ignored. Although R&D spending has not fallen in real terms, it has not increased to match the overall increase in NHS funding in recent years. There was once a target for R&D expenditure to exceed 1.5% of total NHS

expenditure. In fact R&D now accounts for less than 1% of total NHS spending and is continuing to fall. Moreover, apart from minor tinkering at the edges, the allocation of the budget to individual NHS Trusts has been locked at the relative values declared in 1996 regardless of any subsequent changes in the quantity or quality of research activity.

Research costs

Although a substantial amount of research is carried out on NHS patients using NHS facilities, the majority of research is simply done *to* the NHS or for the NHS (in the sense that it is good for it), rather than with the NHS or even by the NHS. The majority of healthcare-related research funding is channelled through the Universities. The Association of Medical Research Charities has noted that less than 2% of the research funds from its members are awarded to NHS organisations. Research Council funding and even DoH research funds are overwhelmingly allocated to Universities. There is little opportunity for NHS organisations to have their direct research costs considered in the funding. Moreover, the research priorities of academic institutions can occasionally be at odds with the clinical needs of the NHS locally, regionally or nationally.

Infrastructure

NHS organisations have limited access to dedicated funds for facilities and infrastructure to support research – such as laboratories, pharmacies, IT, or clinical trials management facilities. Routine clinical facilities are often over-stretched and are not always adequate for specialist research needs. Extending these facilities for research use is likely to be more cost-effective than funding dedicated facilities but this is rarely considered.

Research *and* development?

Like industry, and unlike academia, the NHS is both a producer and an end-user of research. So not only should the NHS know what research it needs, but it should also have the means to implement the results of the research. In practice though, NHS R&D is mainly concerned with the ‘R’ side of R&D. The criteria for judging the quality of R&D are very much research focused – peer-reviewed, original, generalisable, publishable, externally funded. The majority of external funding is only focused on the research end of the spectrum. This gives the impression that ‘R’ is valued while ‘D’ is not. In industry, R&D usually stands for research and development, in the NHS R&D tends to stand for research, the ‘&D’ is silent. Development activity clearly does occur but it is not overtly co-ordinated in the way research is.

In immediate resource terms R&D is of little positive relevance to NHS managers and there is therefore little incentive for them to consider the needs of R&D. Given all of this it seems unlikely that NHS Trusts will pick up the research agenda. Foundation Hospital Trusts could change all of that if, like industry, the management sees thriving R&D activity as essential for driving forward the business. However, a more widely held fear seems to be that the converse is likely to be true and that R&D will be of even less relevance than now.

What has happened in recent years is an increase in regulation of the governance of research through the DoH's Research Governance Framework and the EU Directive on Clinical Trials. These recognise that researchers, employers, funders, sponsors and healthcare providers all have distinct roles and as a consequence have raised the profile of NHS Trusts in this process. Trusts are responsible for the care of the patients that could be compromised by any research that interferes with established clinical practice. While in the past NHS Trusts didn't seem to know what research was being done on its patients, now the Chief Executives are legally accountable for the impact of the research.

Does it matter? A cynic might say that research (and development) continues in the NHS despite everything that has happened in the past 10 years rather than because of it. New drugs, devices and techniques are introduced into the NHS. But research does not appear to be a primary business driver for any healthcare system around the world. If R&D were taken more seriously by mainstream NHS management would that lead to more rapid improvements in the quality of the service provided?

If the NHS is not driving research, who is? It remains predominantly the researchers themselves. Funding priorities may change – the DoH is linking theirs increasingly to the National Service Frameworks – but it relies on the same researchers to carry the programmes forward and sit on the same committees that decide the allocation of research funds.