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CAN ECONOMIC EVALUATION GUIDELINES IMPROVE EFFICIENCY IN RESOURCE ALLOCATION?

The Cases of Portugal, the Netherlands, Finland, and the United Kingdom

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Abstract

The use of economic evaluation in decision making appears to have increased over the past few years and economic evaluation is looked upon as another measure to help contain costs and improve efficiency in an evidence-based decision-making environment. Following the examples of Australia and the Canadian Province of Ontario, four European Union (EU) countries (Finland, the Netherlands, Portugal, and the United Kingdom) have recently introduced economic evaluation guidelines. In addition to the Australian and Canadian guidelines, which constitute a hurdle to reimbursement, the paradigm that seems to be evolving in the four EU countries follows a similar route. Finland and the Netherlands seem to be moving toward the notion of a fourth hurdle to reimbursement, whereas the National Institute for Clinical Excellence in England and Wales was in principle meant to influence practice, although in reality this essentially acts as a hurdle to reimbursement, requiring a different data set to that used by regulatory authorities. Whereas the Portuguese guidelines were developed to assist in preparing economic submissions to support reimbursement decisions, they are unclear about when such evidence will be required and also discuss the dissemination of economic evidence to broader audiences. The introduction of these guidelines poses a number of challenges to policy makers, the implications of which are analyzed in the paper: a) to ensure that economic evaluations are carried out scientifically without industrial or political bias; b) to define an acceptable methodology that would increase their credibility; and c) to address certain practical issues ranging from deciding how to use economic evaluations in policy making to setting up new institutions or improving the coordination and dissemination of evidence. The variation in the use of economic evaluation guidelines in the four EU countries highlights the differences in national pharmaceutical policies and is in line with policy makers' continuous attempts to contain costs. While the paper critically discusses the guidelines, it also points out that a series of methodologic issues need to be addressed if economic criteria are to be introduced in policy making with the aim to improve resource allocation. The paper concludes that economic evaluation as a discipline is beginning to impact on policy, whereas the consistent use of economic evaluation results is, in principle, being adopted by policy makers but needs to go a step further to reach practitioners.

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Faced with rising healthcare costs, many governments are seeking cost-containment policy options. One of the drivers of healthcare expenditure has been the rapid rate of pharmaceutical advance and the prices charged for new medicines (27). One policy option that has frequently been discussed in this context has been the use of economic evaluation of pharmaceuticals and its likely use in pricing and reimbursement decisions (10). An increasing number of countries have encouraged economic evaluation of new medicines to ensure that only medicines proven to be both clinically and cost-effective are reimbursed or made available on formularies. This approach is often referred to as a "fourth hurdle" and is seen as being an additional barrier to market to complement safety, efficacy, and quality. Using economic evaluation can vary from being formally involved in the reimbursement of medicines to being purely voluntary. Australia (3) and the Canadian Province of Ontario (2;36) introduced economic evaluation guidelines in the past for admission of new pharmaceutical products into reimbursement. Although pharmaceuticals have been subject to economic evaluation in the past, this has been largely unsystematic, with no firm policy objective. Evidence to date suggests that even when economic evaluations have been provided, payers and providers do not always use them in making treatment decisions (8;14). A number of barriers to the use of economic evaluation have been suggested and appear to be international (4), including mistrust, particularly from clinicians, and lack of understanding of the results of economic appraisals as well as a series of methodologic issues in their conduct, some of which have been resolved through consensus methods (12;13) while others persist (29;38). An additional issue arises from whether the results of economic evaluations are portable across countries (11). To address these problems, some countries have produced guidelines on how to conduct economic evaluations and how these should be best used. Indeed, the scope for extending the use of economics to assess the cost-effectiveness of new medicines has increased (10). Several countries have attempted to overcome the problems around the interpretability and applicability of evidence by demanding a more systematic approach to the economic evaluation of new medicines. This change in attitude to the use of economic evaluation is reflected in the proliferation of economic guidelines specifying how economic evidence should be presented to inform reimbursement or formulary decisions. Interest in such guidelines is spreading rapidly throughout Europe (7).

This paper critically discusses four sets of guidelines that emerged in 1998–99. The Finnish guidelines (32) appear to be a mandatory hurdle to reimbursement demanding economic submissions to support reimbursement decisions. The Dutch guidelines (44) seem to be close to a mandatory hurdle to reimbursement, although it appears that at present an economic submission is only required for products falling outside the reference pricing scheme or making a claim for improved effectiveness (and hence, a higher price). In England and Wales, the National Institute for Clinical Excellence (NICE) guidelines (35) demand an economic submission when requested by the government to support the recommendation of products that are likely to have a significant fiscal impact on the National Health Service (NHS). NICE currently applies only to England and Wales, although Scotland and Northern Ireland are thought to be considering their own similar initiatives. Finally, the Portuguese guidelines (20) permit the government to demand an economic evaluation of a product to support its reimbursement decision but also discuss the relevance of such information to other decision makers. The differences in the content and application of the four guidelines are of special interest when one considers that all four countries have a strong social solidarity

principle (37). At the same time, the four countries chosen differ quite considerably in their stance toward the pharmaceutical industry and in pharmaceutical activities on their territory (23), which implies the existence of industrial policy in addition to health policy considerations. The key questions are whether economic evaluation is being used to aid reimbursement decisions, and whether economics affect clinical practice and lead to improvements in resource allocation in light of technological innovation in the pharmaceutical sector.

CAN ECONOMIC EVALUATION GUIDELINES AID PHARMACEUTICAL POLICY?

While there is evidence suggesting that economic evaluation has not had an impact at prescriber level, it has received political support at a governmental/payer level. Some payers follow the Australian model and demand economic analysis to support reimbursement, whereas other guidelines, such as the U.S. Panel on Cost-Effectiveness, are merely produced as a gold standard for ongoing research. The Dutch, Finnish, Portuguese, and United Kingdom governments have shown a commitment to use economic evaluation, but its acceptance within the political and medical communities is a gradual process. Indeed, the implementation of economic evaluation guidelines faces a series of challenges.

The first challenge is to ensure that economic evaluations are carried out scientifically without industrial or political bias by improving their transparency and accountability (16;31;39). Economic evaluation is often biased in favor of those supporting the research. Although this criticism is most often leveled at the pharmaceutical industry (41), healthcare purchasers may use economic evaluation to reinforce existing beliefs and support pre-determined decisions (26). While greater transparency is needed to ensure accuracy and legitimacy of the results, those with the task of appraising economic evaluation should be sufficiently skilled to detect any bias and should also be aware that most submissions will have some position of advocacy that they wish to support.

A second challenge is that purchasers usually make planning decisions on a population level, while prescribers think on a patient level (45). This may lead to a conflict of interest because, traditionally, providers have been concerned with clinical effectiveness in each patient and purchasers have been concerned with the impact of new therapies on total cost (15). With more stringent government guidance on how economic evaluations are to be completed, this could improve transparency and increase their legitimacy and relevance to stakeholders.

A third challenge is to ensure that economic evaluation is undertaken from a societal perspective to allow for a full assessment of the costs and benefits. Most guidelines to date have stated that a societal perspective is preferable, implying that all relevant costs and benefits are included in economic evaluations. This would include costs beyond those falling on the health service, such as productivity losses brought about by a disease. However, when investing in treatments many health services diverge from a societal to a payer perspective, whereby only those costs falling on the health service are considered. By investing in interventions that may improve workplace productivity, the health service might reduce sick pay and increase taxation revenues for the Treasury, thus improving total societal welfare, although it might not actually be able to realize any savings accruing to society from the intervention. While such an intervention might benefit society as a whole, for the health service it simply increases costs in a constrained budget. Indeed, in many health services, savings accrued in secondary care settings due to primary care interventions cannot even be transferred. Furthermore, a societal approach inherently assumes that a societal objective is welfare maximization. In reality, however, decision makers may deviate from this utilitarian perspective for very rational and transparent reasons. One key reason is equity. Efficiency is often traded off in health services to achieve more equitable allocation of resources. This

is clearly reflected in the Health Action Zones (6) developed in the United Kingdom, where the government has increased the allocation of resources to less privileged areas, which may not be the most efficient resource allocation decision but is a means of reducing some of the inequities in health. Such a trade-off creates problems for the economic researcher by introducing subjectivity into the decision-making process and may undermine evaluations undertaken from a societal perspective.

A societal perspective thus allows for a more holistic appraisal of the value of an intervention; nevertheless, the relevance of the results may be limited to the health service decision maker with constrained finances. Under these circumstances, researchers need to carefully consider whether to adhere to economic evaluation principles or move to a stance more relevant to decision making.

The fourth challenge is the use of an acceptable methodology. The U.K. Department of Health has confirmed that many economic evaluations are difficult to understand because they are poorly written and their economic methodology is questionable (42). While there is no standardized measure for effectiveness, more can be done to ensure uniformity and improve clarity. The provision of a standardized reporting format in guidelines may overcome some of these problems and provide a familiar structure to decision makers.

Concern regarding economic evaluations is often targeted at the use of quality-adjusted life-years (QALYs). The attraction of QALYs to decision makers is obvious since they allow interventions in all disease areas to be directly comparable, despite the well-documented concerns over their use (9;17) and the use of a utility tariff derived from societal values in their construction (19;21). The state of Oregon attempted to use QALYs to allocate resources based on their effectiveness, but this approach was ultimately rejected due to perceived discrimination against disabled and elderly people (18). There is also concern regarding the comparability of cost utility studies using QALYs because the several different methods available to derive them have been shown to provide different valuations (1). The less-educated decision maker may thus assume they are comparing like with like whereas in reality there may be different principles underlying the study. The use of QALYs in practice remains rare, and evidence on their use remains controversial (25;34;40). However, all four guidelines agree that QALYs should be the preferred outcome measure when cost-utility analysis (CUA) is used.

COMPARISON OF THE PORTUGUESE, DUTCH, FINNISH, AND NICE GUIDELINES

In comparing the draft guidelines of Finland, the Netherlands, Portugal, and NICE, we first establish how they fit into these countries' social solidarity system. Second, we show how the guidelines impact the transparency of economic evaluation results. Finally, we ascertain the methodologic standards of economic evaluation required by the guidelines.

Economic Evaluation and Policy Making

All four countries have strong principles of social solidarity underlying their healthcare systems and extensive public funding; therefore, it is unsurprising that each has generally come to the conclusion that a broad societal perspective is the most appropriate approach in the application of economic evaluation guidelines. The preference for a societal approach is also balanced with a desire to make the results of economic evaluations directly applicable to their target audience. Whereas the Dutch guidelines state that a "comprehensive societal approach" should be adopted, NICE asks for disaggregated reporting of the impact on the NHS and particular patient subgroups. The Finnish guidelines request a societal perspective, whereas the Portuguese request both a societal approach and a third-party payer approach, reflecting the potential for uses broader than reimbursement. Nevertheless, all four sets of

guidelines express a desire for direct healthcare costs to be included but have reservations about the inclusion of indirect costs. The inclusion of indirect costs must be fully justified in all four countries, since indirect costs may not have a direct impact on the health budget.

The dissemination of the results is not discussed to any depth in the Finnish or Dutch guidelines, probably because these have a very specific audience (the reimbursement authority). However, the NICE and Portuguese guidelines provide much more discussion about the practical implementation of the results. NICE will be disseminating guidance based on the submitted evidence to which prescribers will be expected to adhere. The dissemination of these guidelines may use information technology in the form of PRODIGY (5), a decision support software system that assists general practitioners in prescribing decisions. The Portuguese guidelines specifically state different methods of dissemination as appropriate for different audiences. The NICE and Dutch guidelines are also very specific about the timing of the evaluation. Ensuring the evidence is available at the appropriate time for decision makers will also increase the use of economic evaluation. While the Dutch request that the submission be available to inform decisions on reimbursement at the time of launch, NICE provides a very structured framework on the process for submitting economic evidence and ensuring that it is available to inform purchasing decisions at the time of launch of new products. As such, NICE will be informing manufacturers several months before their expected launch date whether a submission will be required. The first NICE appraisal (33) of Relenza (zanamavir) for influenza treatment represents a paradigm shift for drug development by highlighting the imbalance between the evidence needs of the regulatory authorities permitting the marketing of a therapy and those of NICE. Since the first NICE recommendation appears to revolve around a lack of clinical effectiveness data, then manufacturers of new medicines must begin to undertake not only safety and efficacy trials at phase III but also more pragmatic studies reflecting real-world practice before submission to NICE or a similar agency. How these data needs can be met other than through complex modeling needs to be determined. This also creates confusion for prescribers who are advised not to prescribe a product that has been declared safe and efficacious by regulatory authorities and is available to them. However, if general practitioners do adhere to the NICE guidance, then it has created a barrier to market without using the evidence in either a reimbursement or approval decision.

Attempts to Improve Transparency

Transparency refers not only to the funding and independence of a study but also to its presentation. The Dutch guidelines took the strictest approach and declared that all submissions of economic data must be conducted by independent agencies (i.e., not pharmaceutical companies). NICE and the Portuguese guidelines state that sponsorship of studies should be clearly stated and the independence of the author should also be acknowledged. The Finnish guidelines do not appear to have any disclosure policies. While disclosure is a positive step in improving the transparency of economic evaluation, it does little to strengthen the research findings, since authors' independence does not guarantee robustness. All four guidelines recommend a standard reporting format, expecting that decision makers with limited understanding of economic evaluation should be able to extract relevant information easily. Furthermore, all four report resource use and costs independent of one another, allowing decision makers to more easily assess the impact of a new medicine.

Methodologic Issues

A comparison of the key methodologic features of the four guidelines is shown in Table 1. The four countries' guidance on methodologic standards and design has broad similarities but fine differences. While they all accept CUA, there are differences with regard to the use

Table 1. Highlights from the Guidelines of Finland, Portugal, the Netherlands, and the UK (NICE)[a]

Key feature	Finland	Portugal	The Netherlands	NICE
Main policy objective	Reimbursement	Reimbursement	Reimbursement	Practice guidelines (to be used in reimbursement policy by default)
Perspective	Societal	Societal (1)	Societal (2)	Societal/payer[b] (2)
Standard reporting format included	No	Yes (14)	Yes (18)	Yes (3)
Disclosure of funding/ authors' interests	No	Yes (15)	Yes (4)	Yes (7)
Target audience	Researchers conducting economic evaluation and Pharmaceutical Pricing Board	General set of references for researchers undertaking economic evaluation, and policy makers	Minister for Health, Welfare & Sport; patients, prescribers, suppliers, insurers, and researchers	NICE appraisal group
Time frame	Required at time of submission for marketing authorization	—	Economic evaluation must be presented when the drug is being considered in the basic package of care (3)	7-11 months for the appraisal group to develop practice guidelines once they have received the evaluations
Preferred analytical technique	Any one of CMA, CEA, CUA, CBA	Any one of CMA, CEA, CUA, CBA (7)	CEA (5)[c]	CUA (Annex C, 8)
Preference for effectiveness over efficacy	Yes (8)	Yes (2)	Yes (10)	Yes (by default)
Choice of comparator	Most commonly used therapy, best or minimum practice (6)	Least expensive and most effective (3)	Standard treatment that has proven effective (7)	No preference but choice must be specified (Annex C, 9;11)

Costs to be included	All direct health costs and comparable social costs; indirect costs may be presented separately (7)	Direct healthcare costs, costs from social services and other related sectors, costs borne by the patient. The inclusion of productivity losses, measured using the human capital method, should be justified (8)	Direct medical and nonmedical costs. Future healthcare costs for unrelated diseases in any additional life should be excluded. Productivity losses calculated using the friction cost method should be presented separately (13)	Net health service costs, any associated government funded personal and social services costs and savings. Costs avoided as a result of treatment and costs arising in different years should also be reported. Overhead and capital costs should be factored in (19)
Source of costs	Not stated	Mentions standard costs, which refer to prices of treatments (9)	Published standard costs planned for 1999 (15)	Not stated
Time horizon stated	Yes (10)	Yes (6)	Yes (9)	Yes (10)
Preferred outcome measure	Preference for QALYs in a CUA	Preference for QALYs in a CUA (10)	Preference for QALYs in a CUA (12)	Not stated, although states health improvement should in standard measures for combining be expressed life and years quality of life (QALYs) (Annex C, 13)

Source: Authors' compilations from the guidelines of Finland, Portugal, the Netherlands, and NICE in England and Wales.

[a] All guidelines are in draft form and are subject to change. The reference number of the relevant guidelines is in parentheses.

[b] The NICE guidelines seem to favor the costs accruing to the NHS more than patient costs, unlike the Portuguese and Dutch guidelines, which account for patient and family costs.

[c] A cost-utility study is often suggested to accompany a cost-effectiveness study.

[d] Justification is needed when there is a departure from the preferred analytical technique.

[e] Portugal: the preferred technique depends on the context, but cost utility is preferred to cost benefit.

[f] While the need for discounting was mentioned, an actual rate was not supplied in the NICE guidelines.

of other techniques. In the Netherlands, cost-effectiveness analysis (CEA) is recommended, but when an intervention is likely to have a significant impact on quality of life, CUA is used and outcomes are presented in QALYs. Cost-benefit analysis (CBA) is not an option because the methodology on willingness to pay is still under development. Portugal accepts cost minimization (CMA), CEA, CUA, or CBA, although CUA is presumed preferable to CBA. If CEA is undertaken, it is recommended that CUA accompanies it on the grounds of increased comparability. In all circumstances the chosen method must be justified. NICE prefers CUA, and all departures from it must be justified. This differs from the Netherlands, Finland, and Portugal, which recommend using a number of analytical techniques. The NICE Appraisal Group will use the outcomes of this technique to make decisions about the comparative costs and benefits of different treatments, therefore comparability is of utmost interest. The Finnish guidelines recognize CMA, CEA, CUA, and CBA and stipulate that the most suitable approach for each study should be adopted and justified. This would depend primarily on the impact on patient health of the therapies being evaluated.

All four guidelines purport to be interested in effectiveness and state that, where only efficacy data are available from trials, then modeling is an acceptable approach to estimating effectiveness.

Most economic evaluations tend to be incremental analyses comparing a new therapy against existing treatments. The four guidelines include a section on the choice of comparator therapy. In the Netherlands, the *standard treatment*, which has proven effectiveness, should be used as the comparator. In circumstances where effectiveness has not been proven, then the *usual treatment*, which is the most widely used treatment, should be used. The choice of comparator may also be determined by using the Pharmacotherapeutic Kompas, which lists substitutable therapies. In Portugal, three possible comparators can be used. Preference is given to the most effective procedure that has the least costs when more than one exists. If the cost-effectiveness is not known, then the most clinically effective should be used. When clinical and cost-effective profiles are uncertain, then current practice is recommended. Finland uses a similar approach, suggesting that a new product should be compared with the procedure or medicine that it will replace. If this is not the most commonly used therapy, then it should be included as an alternative. Best or minimum practices are also suggested as comparators. The U.K. guidelines do not specify the comparator, but choices must be justified.

Under all four guidelines, resources and costs must be presented in disaggregated format and their relevance to the health service must be justified. Currently, there are two major methods available for the inclusion of productivity cost: the friction cost method and the human capital approach. The Netherlands requests use of the friction cost method, the Portuguese state that the human capital approach should be adopted, and the Finnish and NICE guidelines do not state a preference. There is very little discussion in the four guidelines about the preferred source of cost data. Without unit costs there exists the potential for a great deal of variance in the cost data used in economic evaluations. This could be overcome by making standard unit costs available to researchers to eliminate one source of bias.

All guidelines agree that QALYs should be the preferred outcome measure when CUA is used. However, the degree of prescription around the outcome measure varies. The Finnish are not specific about the preferred measure, whereas the NICE and Dutch guidelines place great emphasis on QALYs. The Portuguese provide a thorough discussion of the outcomes, including life-years gained, QALYs, and disease-specific measures of quality of life. All are permitted if they are justified. Finally, all four guidelines recommend discounting of costs and benefits, taking into account the value of money invested or health gained over time to enable present value comparisons. If the rates applied to costs and benefits are different, then a sensitivity analysis is required. This would enable more accurate information about the reliability of the results and major sources of uncertainty, assumptions, and limitations to

be addressed. Under all guidelines, confidence intervals should be used as the parameters of variance for inputs derived from samples. Where input variables have been used that were not derived from samples, then the degree of variance used in the sensitivity analysis should be justified. Only the Dutch guidelines may require multivariate analysis, whereby several assumptions are varied simultaneously.

Information is also included about the time horizon of the evaluation. Effectiveness can be better measured when the evaluation covers the entire treatment period, although this will often need to be estimated using modeling at the time of launch. In the Netherlands and Finland, this has implications for deciding whether to include new interventions in the basic package of care because the evaluation will not include information on medium-to long-term costs, so there has to be greater reliance on efficacy and modeling.

The presentation of results must be reported incrementally as well as in a total cost and benefit analysis. NICE requests that the aggregate cost of a particular therapy is given, which details the total cost to the NHS and the number of patients who will be affected. The Dutch specify that estimates of the impact on the healthcare budget be included in submissions.

All four guidelines discuss the importance of conducting subgroup analysis to identify populations benefiting most from the intervention. In the Netherlands, subgroups of disease subtypes, degree of severity, and the presence or absence of comorbidity must be identified. This provides more relevant information when deciding whether to use or withdraw a treatment from a particular patient group. NICE points out that subgroups for which results are likely to differ significantly should be identified (Annex C, 16), while in Finland it is advised that subgroups should be included where these might provide information of relevance to the pricing negotiations. The Portuguese recognize that any subgroup analysis will not have been powered to detect statistical significance, so these should only be performed where they have been specified *a priori* and sample sizes determined to undertake this analysis.

The relevance of the results and the study participants to each of the four countries' populations is discussed to some degree. Finland and the Netherlands recognize that for economic evaluations carried out alongside trials, Finnish or Dutch data might not be available. In such cases the relevance of the study and its results should be interpreted. NICE does not provide any discussion on this, probably reflecting the strength of pharmaceutical research and development and the extent of international clinical trials conducted in the United Kingdom. In Portugal, data not taken from a national context must be adapted and fully reported to avoid adverse evaluation outcomes. Equity considerations only appear to be included in the NICE guidelines, in that any differences in the impact of therapies on specific groups and their potential to improve existing health inequalities must be highlighted.

STRENGTHENING THE LINKS BETWEEN RESEARCH, POLICY, AND PRACTICE

Evidence to date shows that the results of economic evaluation have been underused in practice, suggesting that the links between research, policy, and practice need to be strengthened. Figure 1 illustrates how an "ideal" evidence-based health service might operate where information and resources are fluid between the research and pharmaceutical sectors, leading to applied results.

By producing guidelines and encouraging the use of economic evaluation, each of the four countries has made progress towards this ideal model, although each has also fallen short of implementing some of the conditions necessary to achieve an efficient exchange of information. NICE has, at least in the short run, opted to use such evidence to produce practice guidelines (Figure 2). A number of inferences emerge from this policy decision. By producing practice guidelines, NICE (supported by other agencies such as the Commission

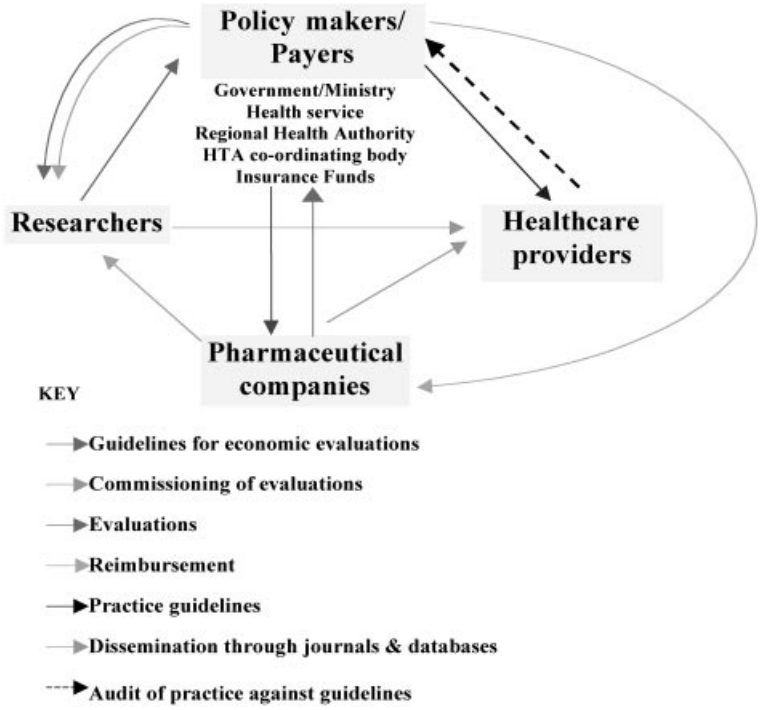

Figure 1. Potential links between research, policy, and practice.

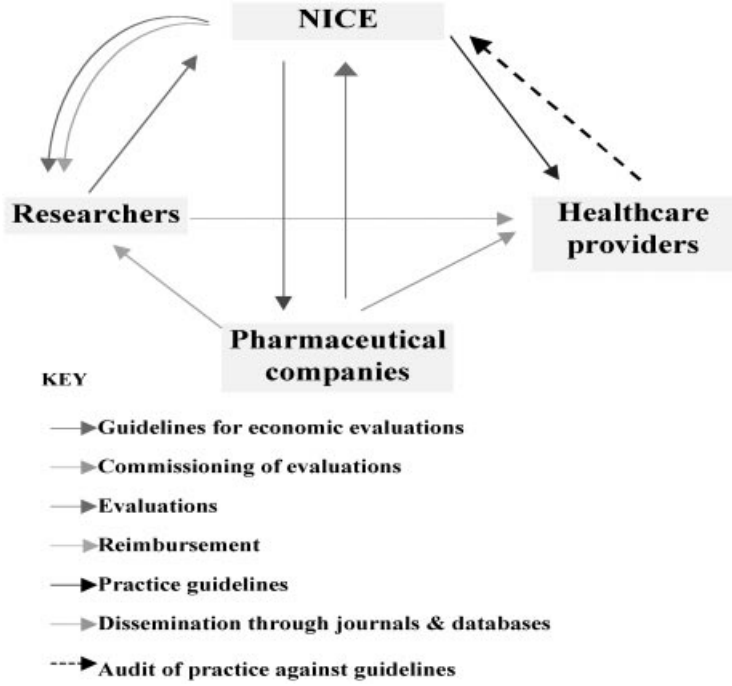

Figure 2. Links between research, policy, and practice—NICE.

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for Health Improvement [CHI]) may contain the clinical freedom of prescribers. Audit to monitor adherence to these guidelines may eliminate inefficiencies in current prescribing and may have an effect equivalent to a fourth hurdle, though this depends on practical implementation. By demanding economic evaluation selectively, the government is also clearly attempting to appease the pharmaceutical industry that contributes to the U.K. balance of payments. This is also reflected in the willingness of NICE to finance research, a consideration not included in the other countries' guidelines. Demanding economic evaluation of new products launched in the United Kingdom would ultimately lead to a more effective prioritization of pharmaceutical research and better rewards for the industry, if it were truly producing novel compounds (30). No prescriber incentives or penalties have been announced yet and, since NICE has no influence over the marketing approval of new medicines, manufacturers are free to market their products regardless of NICE. Enforcing compliance with guidelines may have wider implications for publicly funded systems because the drug may only be made available outside its remit, thus creating a two-tier system based on ability to pay. Two types of reimbursement decisions can be made: a) absolute decisions, which involve whether a health service will pay for the medication; and b) flexible reimbursement decisions, which encourage drug use where it is more cost-effective, although these have been associated with perverse incentives so that a patient might wait until their condition worsens to become eligible (22). The Relenza guidance falls into the former category and denies everyone access to the treatment regardless of their ability to benefit.

The Portuguese, Finnish, and Dutch guidelines emphasise the role for economic evaluation in pharmaceutical reimbursement and inclusion into a positive list. However, patients can pay directly for medicines not included in this list. In such cases, there would be a strong case for manufacturers to claim that they should be free to make evidence available directly to patients, although such advertising remains unlawful under current EU regulations. The Portuguese place a greater emphasis on dissemination, suggesting methods for making evidence available to specific interested parties, including patients and patient associations. While this may strengthen the link between policy and practice by improving accessibility to evidence, all three countries appear to have placed less emphasis than NICE on institutionally linking evidence-based medicine and health policy. None of the three guidelines see a role for government-commissioned research, audit of practice, or the direct dissemination of evidence submitted to them as part of the reimbursement process.

In Portugal, the guidelines act more as educational guidance rather than as a decision-making tool. Potentially, they may be required for all pharmaceutical companies that request reimbursement subsidy.

The Finnish and Dutch do not discuss the role of practice guidelines or dissemination of evidence to any extent. While there is an opportunity for practice guidelines to be developed and disseminated to doctors, the key objective for the Dutch and the Finnish is to collect more strategic information to be used in reimbursement decisions.

POLICY IMPLICATIONS

The analysis has shown that economic evaluation as a discipline is increasingly been used to determine policy on payment, reimbursement, and clinical use and therefore influences resource allocation. While there are marked similarities in the four guidelines, the differences reflect the needs of national policy makers. Despite these differences, each of the four countries has created the opportunity to limit market access and spending predominantly on new medicines: Finland, the Netherlands, and Portugal through denying reimbursement and NICE through a negative recommendation. The guidelines come in addition to other methodologies all four countries have in place to explicitly or implicitly control pharmaceutical expenditure (24), and could be seen as an additional cost-containment measure

targeting new products. Whether resources should be diverted to reducing the use of older, widely used products whose effectiveness has never been scrutinized has not been debated.

Removing waste, promoting efficiency in resource allocation, improving clinical and cost-effective decision making, and doing away with postcode prescribing are desirable targets, given the inevitability of rationing (28). Economic evaluation should assist in the achievement of the above objectives but faces challenges and problems. Before resources can be used more strategically in practice, economic evaluation needs to become a more significant part of the decision-making process, based on practical implementation (43). The medical profession favors evidence on clinical effectiveness but remains cynical about cost-effectiveness. Here, the split between societal versus individual "good" is prominent. Another challenge to ensuring that practice follows evidence is the development of strategic dissemination methods other than databases, flyers, or academic journals. Using legislation to disseminate the results of economic evaluation is the most explicit method available but is difficult to accomplish because it requires consensus, which is not easily achieved when the discipline is still in development.

Thus, the implementation of a hurdle to reimbursement needs to tackle several issues of a methodologic and practical nature. First, the reliance on efficacy data to make decisions about effectiveness, although problematic, highlights the additional steps manufacturers must take to prove both by satisfying regulators in terms of safety, quality, and efficacy, and reimbursement authorities in terms of effectiveness. Proof of effectiveness would consequently require additional trials in society, costing time and resources. Second, guidelines would need to be updated regularly since evidence may change over time. This demands that those issuing guidelines need to continuously appraise emerging evidence and have the resources to do so. Third, precision is needed if guidelines are to assist in decision making. Vagueness will not increase certainty about the effectiveness of the intervention evaluated but only encourage inefficient prescribing. Fourth, the gap that exists between policy and practice may reflect policy makers' objectives rather than being an oversight and may arise because of the balanced approach taken to health policy whereby other factors, such as equity and industrial policy, are taken into account. Fifth, as the collection of evidence is time-consuming, clear goals from the outset are required. Sixth, while the four countries reviewed indicate that policy makers are clearly willing to use economic evaluation in decision making, a key question is how to use economic evaluation in a way that accepts that the health service is financially constrained, including the inability to move funds easily. Finally, the initial workings of NICE have also highlighted that the evidence needs of these new organizations may be different from those of existing regulatory authorities. This may require modeling or extrapolation, and reimbursement authorities need to ensure that they are capable of appraising and accepting the limitations of such evidence if they are to move toward a position of evidence-based policy making.

Moving from policy to practice, it is true that while economics may be used at policy level, it is rarely used at treatment level. This may need to change in the future, since ignoring economic evidence in individual decisions clearly has a broad impact on the efficiency of health services. There is always an opportunity cost of a treatment, and resources must be directed to treatments providing the most benefit at least cost. Each of the guidelines could be made to have a more significant impact on practice through systematic rather than selective use of economic evaluation, education of practitioners, reinforcing guidance with penalties, or linking the use of economic evaluation with other proxy demand measures, such as physician-fixed budgets.

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