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Use of Comparative Effectiveness Research in Drug Coverage and Pricing Decisions: A Six-Country Comparison

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Abstract: Comparative effectiveness research (CER) has assumed an increasing role in drug coverage and, in some cases, pricing decisions in Europe, as decision-makers seek to obtain better value for money. This issue brief comparatively examines the use of CER across six countries—Denmark, England, France, Germany, the Netherlands, and Sweden. With CER gaining traction in the United States, these international experiences offer insights and potential lessons. Investing in CER can help address the current gap in publicly available, credible, up-to-date, and scientifically based comparative information on the effectiveness of drugs and other health interventions. This information can be used to base coverage and pricing decisions on evidence of value, thereby facilitating access to and public and private investment in the most beneficial new drugs and technologies. In turn, use of CER creates incentives for more efficient, high-quality health care and encourages development of innovative products that offer measurable value to patients.

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INTRODUCTION

Comparative effectiveness research (CER) has been widely supported by the Obama administration, as well as clinicians, insurers, patient groups, and other policymakers as a mechanism to improve health outcomes, quality of care, and consumer choice by providing comparative information on available health interventions.[1] It is also considered a way to help focus purchasing and pricing decisions to slow increases in health care spending and improve value. In the United States, spending on pharmaceutical drugs has increased significantly over the last 10 years, accounting for almost 13 percent of health care costs, and annual growth in per capita pharmaceutical expenditure has outpaced other industrialized nations, including the United Kingdom, Germany, and France.[2]

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Last year, the American Recovery and Reinvestment Act (ARRA) allocated $1.1 billion to advance CER in the U.S. In addition, the Patient Protection and Affordable Care Act establishes a new, nonprofit body, the Patient-Centered Outcomes Research Institute. While these pieces of legislation provide support and guidance for how CER will develop in the U.S., questions remain about how it will be implemented and used in practice and its potential impact on policy.

Over the last 20 to 30 years, many European countries have established CER systems to inform pricing and coverage decisions in health insurance and to aid in the development of clinical practice guidelines.[3] These countries use CER to systematically determine the relative value provided by new technologies and to give providers and patients information for making treatment choices.[4] This, in turn, serves to encourage the efficient and effective use of health technologies and to support innovation by identifying and rewarding high-value products. Although CER has been mainly applied to drugs, it is increasingly being used to evaluate medical devices, treatment procedures, and public health interventions.

In developing and supporting their respective CER systems, European countries have faced many of the issues currently challenging the U.S. Specific issues that hold relevance for the U.S. include the governance of CER and, in particular, the scope and authority of a CER entity and its relationship to government, stakeholder involvement, how CER is conducted and used in coverage and pricing decisions, and, how such recommendations are disseminated to local decision-makers, providers, and patients.

This issue brief focuses on the use of CER in decisions about drug coverage and pricing in six European countries (Denmark, England, France, Germany, the Netherlands, and Sweden), exploring the aforementioned issues. Although there are considerable differences between Europe and the U.S., namely around the organization and funding of health care, examining Europe's experiences may serve to inform developments in the U.S.

CER FUNCTIONS AND GOVERNANCE

Decisions must be made in all third-party payment systems regarding what drugs to cover and how much to pay. When such decisions are based on CER, it typically involves two stages: an *assessment* of a drug's benefits, relative benefits, and costs, followed by an *appraisal* (i.e., interpretation and consideration) of the evidence to inform coverage and, sometimes, pricing decisions. These two stages may or may not be carried out by the same agency (Table 1). In the European countries examined in this brief, the CER bodies assume different roles, in terms of decision-making authority and relationship to government (i.e., whether they are integrated with government or are at an arms-length distance). Some bodies act in a regulatory capacity, making decisions about coverage or pricing. Others take an advisory role, making coverage or pricing recommendations to government, often the Ministry of Health, which then renders coverage or pricing determinations. In countries with advisory bodies (France, Germany, the Netherlands), the Ministry of Health oversees the assessment process or sets priorities for assessment to some degree.[5] The bodies can also be categorized as those that "produce" CER (England, Germany, Sweden)—that is, they conduct evidence synthesis, economic modeling, and other studies—and those that mainly "use" existing CER, typically submitted from manufacturers, to make coverage recommendations or decisions (Denmark, France, the Netherlands).

Sometimes, external organizations are involved in assessments. In England, the National Institute for Health and Clinical Excellence (NICE), for example, coordinates independent reviews conducted by academic research centers.[6] The use of independent reviews may lend greater transparency to the CER process and help to prevent or resolve potential disputes because the organization conducting the assessment is not affiliated with the decision process, thereby minimizing perceived conflicts of interest.[7] However, the use of external organizations for assessments can also generate questions about responsibility and accountability.

Table 1. Key Drug Review and Decision-Making Bodies in Select Countries, 2009

	Assessment Process				Appraisal Process
Country	Review Body	Function	Role	Relationship to Government	Coverage and Pricing[a]
Denmark	Reimbursement Committee of the Danish Medicines Agency (DKMA)	Coverage	Regulatory	Integrated	DKMA
England	National Institute of Health and Clinical Excellence (NICE)	Coverage	Regulatory	Arms-length	NICE
France	Evaluation Committee for Medical Products of the National Health Authority (HAS)	Coverage	Advisory	Integrated	Ministry of Health and Sport (coverage)
	Economic Committee for Health Products (CEPS)	Pricing	Regulatory		CEPS (pricing)
Germany	Institute for Quality and Efficiency in Health Care (IQWiG)	Coverage	Advisory	Arms-length	Federal Joint Commission and Ministry of Health
Netherlands	Health Care Insurance Board, Committee for Pharmaceutical Aid (CHF)	Coverage and Pricing	Advisory	Integrated	Ministry of Health, Welfare, and Sport (coverage and pricing)
Sweden	Dental and Pharmaceutical Benefits Board (TLV)	Coverage and Pricing	Regulatory	Arms-length	TLV (coverage and pricing)

Note: All countries (except France) also have dedicated national agencies that primarily coordinate and disseminate assessment reports on drugs and other health technologies and interventions. However, they are not involved in making drug coverage decisions. For further information on these agencies, see M. Velasco Garrido, F. B. Kristensen, and C. P. Nielsen et al., *Health Technology Assessment and Health Policy-Making in Europe: Current Status, Challenges and Potential* (Copenhagen: World Health Organization, 2008).
[a] Denmark, England, and Germany operate a free pricing system, with prices generally set by industry. However, manufacturers must notify the DKMA, Department of Health, and the Federal Association of Sickness Funds in Denmark, England, and Germany, respectively, with prices.
Source: C. Sorenson, M. Drummond, and P. Kanavos, *Ensuring Value for Money in Health Care: The Role of Health Technology Assessment in the European Union* (Copenhagen: World Health Organization, 2008).

STAKEHOLDER INVOLVEMENT

The guidance and decisions resulting from CER can have a significant impact on treatment availability, as well as clinical practice. Consequently, in addition to policymakers, a range of stakeholders—physicians, pharmacists, health economists, insurance and industry representatives, and patients—are interested in the process and want their views to be considered.

An Organization for Economic Cooperation and Development study found that patients and consumer groups were the least likely stakeholders to be involved in the assessment process.[8] Increasingly, however, academics and review bodies in England, Germany, and Sweden have recognized the importance of involving patients and consumers to provide useful insight into a drug's "real-world" value.[9] For example, NICE in England has established a Citizens Council to gather public perspectives on key social and ethical issues, such as whether age and disease severity should be taken into account when NICE makes decisions about treatment availability and use. Despite growing acknowledgement that involvement of patients and consumers may improve CER processes, few systems have formal mechanisms in place to facilitate such participation.

In all of the six countries, manufacturers are generally involved prior to the assessment process, when they submit a dossier of evidence to the review body.[10] They do not normally participate in the actual assessment or appraisal process. Some commentators and analysts have argued for earlier and greater industry involvement.[11] For example, early involvement of manufacturers can help identify and resolve data gaps or problems at the beginning of assessments, thus improving the quality and efficiency of the review. However, while involving industry may be beneficial, it can give rise to concerns about reduced objectivity of assessments.

Although stakeholder involvement may increase the resources and time required to complete assessments, it can enhance the relevance of and trust in the CER process. In particular, increased engagement by

stakeholders can improve the quality of assessments, lower the number of appeals, and lead to better acceptance and use of recommendations.[12]

CONDUCTING ASSESSMENTS

Assessments involve many of the same principles and processes across the six countries, but they differ in some key areas, such as selecting which drugs to review, the type and quality of evidence required, and methodological approaches (Table 2). Many countries publish guidelines outlining their evidence and methodological requirements, but the guidelines often vary in detail and transparency.[13]

It typically takes three months to two years to review drugs for coverage, raising concerns about delays in patients' access to new drugs. To address this concern and facilitate speed to market, France, Germany, and the Netherlands have introduced expedited review processes for highly innovative drugs or for those treating life-threatening illnesses. Similarly, England has led efforts to shorten reviews by introducing fast-track processes such as single technology appraisals that place more emphasis on manufacturer data and less on extensive external systematic review and consultation. These various initiatives have allowed some drugs to be available a few months after launch.

DECISION-MAKING AND IMPLEMENTATION

Applying CER to Drug Coverage Decisions

The decision to cover a drug is based on appraisal of the evidence. Review bodies employ a variety of criteria to inform coverage decisions (Table 3). In all these countries, a drug's relative therapeutic benefit is the most important criterion in determining coverage status, followed by cost-effectiveness, which is measured using cost per quality-adjusted life year (QALY) ratios.[14] Cost-effectiveness is particularly important for drugs that have new indications, are expensive, are expected to be widely used, or whose benefits differ by indication or patient subgroup.[15] England, Germany, the Netherlands, and Sweden explicitly use cost-effectiveness in coverage decision-making, whereas its role in the review process is not always clear in Denmark and France.

Some countries use a cost-effectiveness or price threshold to establish whether a drug provides sufficient value and to determine coverage status and, in some cases, reimbursement levels. A threshold generally represents the amount of money a society is willing to pay for an additional unit of health outcome (i.e., an additional QALY). Such "decision rules" are often implicit and case-dependent. The value of the annual cost threshold varies by country: it is generally set at £20,000–£30,000 ($30,000–$45,000) in England, €20,000 ($30,000) in the Netherlands, and 500,000SEK ($62,000) in Sweden.[16] Following recent changes to IQWiG's authority to consider costs in its assessments, Germany uses prior funding decisions for similar products to determine the maximum ceiling reimbursement level for a drug, as opposed to a cost per QALY threshold. In several of these countries, CER bodies are striving to ensure that the threshold effectively captures product value. For example, the Netherlands and Sweden are considering adopting a revised approach that adjusts the threshold according to need or equity considerations, especially for drugs that are potentially expensive or address unmet medical needs (e.g., cancer drugs and therapies treating rare conditions). England recently agreed to extend its threshold for drugs aimed at end-of-life care under some circumstances to facilitate cancer drug access in the NHS.

Table 2. Comparative Drug Review Methods Used in Select Countries, 2008

	Denmark	England	France	Germany	Netherlands	Sweden
Selection criteria for drugs to review	Every new drug[a]	Drugs referred by Department of Health, which are then prioritized based on a variety of criteria, such as health impact, disease burden, and clinical/policy relevance	Every new drug[a]	Drugs referred by the Federal Joint Commission, which are considered to have potential health/cost impact, or where available evidence is inconclusive or controversial. Typically, these are drugs that cannot be easily classified under the reference pricing system.	Drugs that cannot be classified under reference pricing system	Every new drug[a]
Evidence requirements	RCT data preferred; health economic information recommended, but not required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include manufacturer data	RCT data preferred; health economic information recommended, but not required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include industry data	RCT data preferred; health economic information required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include manufacturer data
Preferred or required approach (for health economic component)	N/A	CEA[b] CUA	CEA CUA CMA	Efficiency frontier analysis	CEA CUA	CEA CMA
Choice of comparator	N/A	Current best alternative or routine treatment	Three comparators required from same therapeutic group: most frequently used cheapest most recently added to the positive list	Most effective treatment, most widely used, or routine treatment	Routine treatment	Three comparators required from same therapeutic group: routine treatment nonmedical intervention no treatment
Principal outcome measures	N/A	Mortality Morbidity Quality of life	Mortality Morbidity Quality of life	Mortality Morbidity Quality of life	Mortality Morbidity Quality of life	Mortality Morbidity Quality of life Willingness to pay

	Denmark	England	France	Germany	Netherlands	Sweden
Costs	N/A	Direct costs Indirect costs, depending upon the assessment	Varies If indirect costs are included, must be reported separately	Direct costs Indirect costs	Direct costs If indirect costs are included, must be reported separately	Direct costs Indirect costs
Modeling	Yes	Yes	Yes	Yes	Yes	Yes
Sensitivity analysis	Yes	Yes	Yes	Yes	Yes	Yes
Subgroup analyses required or considered[c]	Yes	Yes	Yes	Yes	Yes	Yes
Equity issues considered[d]	No	Yes	No	No	No	Yes, but not clear how accounted for

[a] This entails reviewing every new drug dossier submitted by manufacturers to support a coverage decision. Thus, in principal, manufacturers ultimately decide which drugs are reviewed.
[b] CEA = cost-effectiveness analysis; CMA = cost-minimization analysis; CUA = cost-utility analysis. CEA is the most widely used assessment approach, of which CUA is type of CEA. CUA uses quality-adjusted life years (QALYs) as the principal measure of health benefit in economic evaluation, which allows comparison of the value of money of different drugs across different therapeutic areas. Efficiency frontier analysis, alternatively, focuses on ascertaining the relative costs and benefits of different drugs within a given therapeutic area. For discussion on the methodological merits and demerits of CUA and efficiency frontier analysis, see A. Oliver and C. Sorenson, "The Limitations and Challenges to the Economic Evaluation of Health Technologies," in *The Economics of New Health Technologies: Incentives, Organization, and Financing*. ed. Joan Costa-Font, Christophe Courbage, and Alistair McGuire (Oxford: Oxford University Press, 2009), and M. Drummond and R. Rutten, *New Guidelines for Economic Evaluation In Germany and the United Kingdom. Are We Any Closer to Developing International Standards?* (London: Office of Health Economics, Nov. 2008), available at: www.ohe.org/page/publications/publication.cfm?catid=35&itemid=624&archive=0.
[c] Subgroup analysis is used to explore how cost-effectiveness varies by characteristics of different patients or patient groups eligible for treatment.
[d] Includes whether the costs and benefits of available care are equally and fairly distributed among those using a given service. Typically, in CEA, this would translate to each additional QALY considered of equal importance for each person, regardless of age, gender, and individual ability or resources to seek care. Currently, however, CER mainly focuses on efficiency to maximize population health within available budgets. Even when equity is considered, judgments are usually made implicitly and on a case-by-case basis.
Source: C. Sorenson, M. Drummond and P. Kanavos, *Ensuring Value for Money in Health Care: The Role of Health Technology Assessment in the European Union* (Copenhagen: World Health Organization, 2008).

As outlined in Table 3, other criteria, such as disease burden, may be used to assess the value of a drug. Many stakeholders contend that more consideration should be given to such factors in coverage decisions and that greater transparency and explicitness is needed regarding how they factor into the decision process. That is, when are such factors considered and what weight are they given. This is particularly true of more qualitative factors, such as equity.

In all countries, it is rare for an approved drug to not be accepted for any level of coverage following review, but many are reimbursed with conditions (e.g., for use only in certain indications and patient groups) or are subject to a reference pricing system (in Denmark, Germany, and the Netherlands).[17,18] This is particularly true regarding "me-too" drugs—products that do not offer additional benefit compared with similar drugs already available. In general, countries are becoming increasingly selective in coverage determinations, especially for expensive products, where demonstrating added therapeutic benefit or a certain level of innovativeness is increasingly required for reimbursement.

In some cases, decision-makers are also making coverage conditional on post-market demonstration of a drug's costs and benefits. England, France, the Netherlands, and Sweden have introduced risk-sharing agreements and coverage with evidence development (CED) schemes with manufacturers. Risk-sharing agreements allow coverage based on meeting certain, specified conditions, such as cost, volume, market share, and cost-effectiveness targets.[19] If the conditions are not met, then coverage may be withdrawn or the drug's price reduced.[20] For example, after NICE controversially recommended against the use of various products for multiple sclerosis, the government established a risk-sharing scheme with manufacturers to supply these treatments on the NHS. Under the scheme, patients were monitored annually

and the amount paid for the drugs was adjusted on a sliding scale if patient outcomes differed from an agreed cost per QALY of no more than £36,000 ($59,000). The implementation of the scheme, however, has faced multiple challenges, including slow organization and uptake. The CED approach applies a similar strategy. Coverage is conditional, based on the collection of post-market evidence and reevaluation. These types of approaches are particularly suitable for severe conditions or areas of high unmet need, high-cost drugs, and situations where there is strong political or patient lobbying for access. Their overarching aim is to facilitate patient access to potentially important new treatments, while duly ensuring that public funding decisions are sufficiently based on evidence of value for money.

While the drug assessment and appraisal process typically occurs prior to market launch, some countries (France, the Netherlands, Sweden) also undertake systematic reevaluations after drugs have been used in practice to identify products that do not demonstrate good value or those that have become obsolete. This approach allows a greater range of drugs to be assessed for value, especially considering that in many countries not every new drug is reviewed. Evidence from post-market reviews can be used to modify pricing and coverage status, where appropriate, or to determine areas for disinvestment (i.e., removal from list of publicly covered drugs). Denmark has recently announced a five-year review of the pricing and coverage status of existing drugs, and Sweden has been evaluating all drugs approved prior to 2002.[21] England has also called for greater NICE involvement in supporting disinvestment.[22] Reevaluation features centrally in risk-sharing agreements and CED, which normally require pre- and post-market review.

The effective use of CER in drug coverage decision-making depends on several factors, including:[23]

- the compatibility of the evidence and recommendations generated by the assessment and the information needs of decision-makers.
- the time taken to complete assessment.
- the transparency of the assessment process, and
- the level of knowledge or understanding of the assessment process (particularly technical aspects) among decision-makers.

Table 3. Key Criteria Used by Countries to Make Drug Coverage Decisions, 2008

Decision criteria	Denmark	England	France	Germany	Netherlands	Sweden
Therapeutic benefit	✓	✓	✓	✓	✓	✓
Cost-effectiveness	*	✓	*	✓	✓	✓
Necessity (disease burden, severity)				✓		✓
Availability of treatment alternatives		✓		✓	✓	✓
Public health impact			✓			
Equity		✓				✓
Innovative characteristics (e.g., ease of use)		✓	✓		✓	
Budget impact		✓	✓		✓	
Ethical/legal considerations		✓			✓	
Feasibility of assessment		✓				

* Unclear if and when cost-effectiveness is considered.
Source: C. Sorenson, M. Drummond, P. Kanavos. *Ensuring Value for Money in Health Care: The Role of Health Technology Assessment in the European Union* (Copenhagen: World Health Organization, 2008).

Role of CER in Drug Pricing and Cost-Sharing

CER evidence is also employed to support pricing decisions, although its use differs across countries. Such evidence more directly influences pricing decisions in France, Sweden, and, potentially in the future, England. France considers a drug's comparative therapeutic advantage over existing alternatives within the same indication in price negotiations with manufacturers. The greater the level of therapeutic improvement, the higher the potential price relative to similar products. Drugs offering no added value over existing comparator products must be priced lower to be reimbursed. Sweden uses value-based pricing (VBP), adopted in 2002, an approach whereby coverage and pricing decisions are made concurrently based on an assessment of health needs and cost-effectiveness. For example, if the drug price requested by a manufacturer is unusually expensive in relation to the benefits or value provided, the drug may either not be covered or its price might be reduced. Moreover, pricing may be varied by patient subgroup since those with certain diseases may benefit more than others. This approach has been heralded as a mechanism to obtain greater value from existing pharmaceutical budgets and create a stronger link between coverage and pricing decisions.[24] A pilot VBP scheme has also been recently implemented in England. In other countries, particularly those with reference pricing systems, CER evidence can indirectly influence pricing decisions to the extent that it aids in forming a judgment about whether or not a drug offers additional therapeutic value relative to other, similar products (i.e., reference groups). If so, the drug may be granted a higher price or coverage level than the reference amount.[25] In this sense, CER essentially serves as a tool for price justification.

Although limited evaluation exists on the effectiveness of using a value-based approach to drug pricing, there is some evidence to suggest that higher margins are gained by drugs that demonstrate significant advances in therapy.[26] Moreover, a value-based pricing approach may furnish important market signals to industry as to what type and level of innovation is most useful and will be rewarded.[27]

CER evidence also influences levels of cost-sharing in some countries. In France, a drug's demonstrated level of therapeutic benefit, coupled with the severity of the disease treated, corresponds to different levels of copayment borne by the patient.[28] For example, cost-sharing arrangements range from 35 percent, 65 percent, and 100 percent, based on "major" or "important," "moderate," and "weak or "insufficient" benefit, respectively. Drugs deemed as irreplaceable and particularly expensive (e.g., HIV drugs) are covered in full. This tiered payment system aims to motivate patients (and their physicians) to choose high-value drugs. In reference pricing systems, such as in Germany, patients are often required to pay any price above the maximum reimbursement price (i.e., in the case of premium-priced drugs). This approach assumes that some patients will be willing to pay for the additional benefits provided by higher-priced (i.e., generally newer) drugs. Consumers then, in turn, send signals regarding the value they place on certain benefits. In practice, however, it is unclear that patients have the necessary information and ability to ascertain the relative benefits across products in a meaningful way. It is therefore important for CER information to be made widely available and effectively communicated to patients and the public. For low-income patients, who may not have access to higher-priced products, there is generally a low level of cost-sharing. In certain cases, low-income patients and other groups (e.g., children, people with chronic conditions) are regularly exempt from out-of-pocket payments. In Denmark and France, complementary private health insurance may also cover some or all of the out-of-pocket costs.

Disseminating and Implementing Drug Coverage Decisions

In several of the countries, coverage decisions apply nationally, but regional or local authorities have some discretion in implementing national decisions in Denmark, England, and Sweden. In Sweden, for example, local coverage decisions are often more restrictive than national recommendations, in part due to budget constraints.[29] Regional differences in coverage in Denmark and England have also resulted in geographical variation in

access to some drugs. Such variations can be attributed to a lack of sufficient funding to implement the national coverage decisions, inadequate or delayed local uptake of guidance, poor financial planning by local authorities, insufficient health economics expertise among local formulary committees, and divergent local health needs.

Successful dissemination and implementation of coverage decisions is a key challenge. Review bodies use different strategies to enhance the adoption of drug coverage decisions or recommendations. In England, France, Germany, and the Netherlands, review bodies disseminate information in newsletters, patient information Web sites, published guidance, and official national bulletins and publications to apprise stakeholders of comparative drug information, recent decisions, and policy changes. In England and Sweden, experts and formal field-based teams are used to promote implementation at the local level. Decision-makers in Denmark, England, and Sweden use financial strategies, like providing additional financial support to regional or local authorities to cover the cost of supplying new drugs. Denmark uses decision-support tools, such as the mini-HTA (health technology assessment), to assist local and regional hospital managers in setting priorities and budgeting and planning for the introduction of new drugs and other health technologies. Another strategy used in almost all countries is participation in international networks, such as the European Network for Health Technology Assessment, to facilitate methods development and enhance the transferability and transparency of CER.

Regulatory levers have recently been used in Denmark and England to reduce geographical variation in coverage. In England, for example, it is mandatory for NICE recommendations to be implemented within three months of dissemination. However, compliance with the mandate has been variable, and there is concern that these requirements may steer the NHS toward funding interventions that NICE assesses and away from other, possibly higher priority, investments.[30]

Overall, successful implementation is facilitated when decision-makers are committed to using assessment findings in drug coverage determinations, policy or regulatory measures are available to support and enforce the uptake of decisions by national and local authorities, stakeholders are involved in the assessment process, and, assessments and decisions are transparent. Moreover, it is important to ensure that all relevant stakeholders are informed of decisions and the potential impact on care access and delivery. The various means of CER dissemination used by these countries serves to ensure that providers and patients have access to credible sources of evidence-based comparative drug information. Unlike the U.S. and elsewhere, direct-to-consumer advertising is prohibited across Europe.

CONCLUSIONS AND POLICY IMPLICATIONS FOR THE UNITED STATES

CER has assumed an increasing role in drug coverage and, in some cases, pricing decisions in Europe. Not only does it contribute to evidence-based decision-making, it also assists in identifying the drugs that offer the most value for money. The six countries reviewed here have adopted different approaches to using CER in drug coverage decisions, but all strive to ensure rigorous, relevant, and transparent assessments.

Drug reviews are useful only if the resulting recommendations are used by policymakers, reflected in clinical practice, and support patients' access to high-quality and beneficial health services. Consequently, many countries have introduced innovative approaches to enhance the use and impact of CER in drug reviews and improve the coverage decision-making process. Strategies such as risk-sharing agreements and CED address the inadequacy of data often available at the time of assessments and decrease the time to market for promising new drugs. These approaches are sometimes used in conjunction with post-market review and, in some countries, value-based pricing to ensure greater value, efficient use of resources, and a more robust assessment process. They also help to better align pharmaceutical spending or purchasing decisions with value considerations, and offer signals to industry on where to focus their CER efforts and, more broadly, research and development investments.

International collaboration is another strategy that is gaining traction. While there is general consensus that the appraisal process should be undertaken within

national and local contexts, there are potential efficiencies to be gained from enhanced collaboration around assessments. Increased sharing of information (e.g., methods, data requirements, results) across countries may save costs and reduce duplication. International collaboration may also facilitate evidence development for promising technologies, where existing data are often limited and pooled expertise is increasingly required. Moreover, it can support CER capacity building in countries with limited experience or without formal systems. The feasibility and effectiveness of international collaboration is dependent, however, on addressing potential challenges, such as attaining agreement on review priorities and assessment perspectives (e.g., societal vs. payer), standardizing methods, ensuring that supporting studies or assessments meet the needs and circumstances of different countries, and protecting the confidentiality of commercial data.

Other strategies can improve the timeliness of assessments and ensure the implementation of coverage decisions, especially at the local level. The introduction of expedited or "fast-tracked" review processes has facilitated the speed of assessments, as national decision-makers in Europe increasingly look to new approaches to ensure patient access to important new treatments. A balance must be attained, however, between expediting reviews and ensuring a robust process. Strategies to support effective and timely implementation include the use of additional funding and training in financial planning for local authorities and mandates for compliance. Countries employ a variety of communication media, such as Web sites, disease management guides, and lay publications, to ensure that patients and providers are informed of the outcomes of CER research and have access to up-to-date, evidence-based drug- and disease-specific information.

The experiences with CER described in this brief offer several potential lessons for the U.S., including the following:

- In the U.S., there is a lack of publicly available, accessible, and robust comparative information on the effectiveness of drugs and other health interventions. This gap makes it difficult for clinicians, other decision-makers, and patients to make informed choices on which interventions work best and under what circumstances. To support evidence-based decision-making and to meet public expectations of safety, effectiveness, and value for money, the U.S. needs to invest in CER, as other industrialized countries have done.
- Currently, while there are no blanket prohibitions in the Patient Protection and Affordable Care Act regarding the use of CER by public and private payers, it remains to be seen how such research will be used in the U.S. Based on the experience of Europe, the uptake and impact of CER may be limited if it does not have the authority to formally link research with policy and practice. Establishing a more formal link can improve the transparency of coverage decisions in the public domain and ensure that such policies are based on independent, scientific assessment.
- To have the greatest impact on health system performance, policymakers should consider extending CER beyond drugs to a wide range of health technologies, health services, and delivery systems. Clear and transparent research priorities should be set, with stakeholders given a voice in identifying areas for review.

- While there is uncertainty regarding the governance, structure, and processes of a formal CER enterprise in the U.S., policies and practices in other countries highlight the importance of: ensuring a level of independence from central government and other key stakeholder groups (e.g., industry, insurance bodies), establishing and maintaining clear lines of accountability and transparency, supporting broad stakeholder representation and participation, and employing rigorous and explicit methods for evidence generation and analysis.
- To support robust methods and more effective decision-making, the federal initiative should support research that is both comprehensive, in terms of looking at more complete outcome measures, and relevant to real-world clinical decisions. This will entail building a robust CER data infrastructure by using and linking a variety of data sources, from electronic health records to large observational databases. It will also involve collaboration among key stakeholders (e.g., governmental bodies, academia, private sector, health associations), both nationally and abroad, to facilitate and expedite CER studies.
- Recent innovations to speed up the CER process to facilitate patient access to new drugs, such as risk-sharing agreements and CED, could be considered or strengthened. CED, in fact, was developed originally by the Centers for Medicare and Medicaid Services (CMS) and has been subsequently used in a few coverage decisions. In certain circumstances, relevant decision-makers could collaborate with manufacturers prior to a drug coming onto the market to ensure that the necessary data are collected to support CER studies. NICE has taken this approach on a few occasions.
- CER is only useful to the extent that it is used to improve policy and practice. As such, wide dissemination and use of CER findings is essential. The U.S. could use CER to improve drug access and secure better prices through value-based insurance design, tiered benefits, and cost-sharing based on effectiveness. CER can also be employed to develop practice guidelines or decision tools to help providers better match medical care to the unique needs of individual patients and to foster health research and development toward high-value, high-impact innovation.

There are indeed clear differences between U.S. and European health systems, due in part to divergent political and historical traditions, incomes, and cultural attitudes. However, faced with the challenges of, as well as opportunities for, improving the effectiveness, value, and quality of health services, the United States can gain valuable insights from international experiences with CER.

Notes

[1] Although definitions differ, CER can be broadly defined as the comparison of alternative health care interventions.

[2] Organization for Economic Cooperation and Development, *OECD Health Data 2008: Statistics and Indicators for 30 Countries* (OECD: Paris, 2008).

[3] In their home contexts, these programs are commonly referred to as health technology assessment. As CER is the term generally used in the U.S. context, this term is used in this brief.

[4] M. Drummond, "Making Economic Evaluations More Accessible to Health Care Decision-Makers," *European Journal of Health Economics,* Nov. 2003 4(4):246–47.

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[25] As a result of reference pricing, coverage levels are often set at the price of the cheapest generic drug and most drugs prices converge to the reference price. This creates a floor for price competition, since there are no financial incentives to price below the reference price. However, countries may differ in how they value differences across products, particularly in terms of whether products representing incremental improvements are permitted to obtain a premium price over existing therapeutic alternatives.

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