COMMENTARY

Hurdles to Technology Diffusion: What are Expectations for PET?

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Regulatory and economic hurdles to the introduction and the diffusion of expensive new medical instrumentation have changed substantially over the past decade. The process of diffusion has been slowed by the introduction of new hurdles and by the gradual shift in their relative importance. FDA approval, affirmative coverage decisions, and the setting of appropriate levels of reimbursement greatly influence the diffusion and utilization of major new technologies. Positron emission tomography (PET) is not an exception. This paper examines the mechanics of these hurdles and their impact on the availability of PET.

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ENVIRONMENTAL FACTORS

The decade of the 1980s was marked by implementation of the 1976 Medical Device Amendments and by significant changes in the way health care technologies were reimbursed. As the decade began, payment for technology was based on a retrospective fee-for-service basis. Conventional services that were billed were reimbursed. However, early in the decade, payors began to question the value of the services that they reimbursed. Increasingly, payors began to evaluate the safety and effectiveness of specific technologies when applied for specific clinical indications in order to make explicit determinations about payment. Payors established technology assessment processes of widely varying degrees of rigor to support their coverage decision-making processes. The foci of the earliest assessment activities were expensive new procedures and instrumentation. For instrumentation, this environment added a new hurdle, the coverage decision-making process, to the existing and initial hurdle of FDA approval.

The 1980s also marked the implementation of a prospective payment system on a national level for Medicare. Payment was based upon the fitting of the service or the application of a technology into a specific diagnosis-related grouping. The groupings fixed limits on payment for technologies that were sometimes quite different in their complexity and sophistication. Private payors also became active in gathering and analyzing cost and charge data and then setting specific levels and ranges of reimbursement. Thus, estimation of the availability and level of reimbursement became increasingly significant calculations in decisions about the acquisition and utilization of health care technologies.

FDA APPROVAL PROCESS: DEVICES AND DRUGS

The granting of authority to the FDA over market control of the introduction of devices is a relatively recent event. In 1976, the Medical Device Amendments to the Food, Drug and Cosmetic Act were passed. These amendments charged the FDA with assuring the safety and effectiveness of devices introduced into interstate commerce for use in health care. The statutory definition (*1*) of a device is quite broad and can include anything from a tongue depressor to a linear accelerator. To provide some guidance for the implementation of the 1976 Amendments, Congress established three classes of devices. The class designation determines the extent of regulatory control to be exerted by the FDA in assuring the safety and effectiveness of medical devices.

Class I devices and Class II devices are those for which general controls and performance standards, respectively, are required. The FDA has not yet developed formal performance standards to distinguish devices in these classes. Thus, presently Class I and Class II devices are subject to the same general controls.

A Class III device is defined as a device that may be used in supporting or sustaining human life, may be of substantial importance in preventing impairment of human health, or may present an unreasonable risk of injury (*2*). To assure the safety and effectiveness of Class III devices, the FDA requires that the sponsor (manufacturer) provide reasonable assurance that the device is safe and effective for its intended use before approval for marketing may be given. These requirements differ somewhat from those for drugs. Approval of a drug for marketing must be based upon evidence obtained from controlled clinical

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trials, whereas the evidence necessary to establish the safety and effectiveness of a Class III device is more broadly defined as "valid scientific evidence derived from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, and reports of significant experience with a marketed device" (*3*). In addition, the FDA is authorized to rely on information that is not derived from investigations (*3*). The underlying philosophy of approval of a Class III medical device is that an increase in the severity of the illness to be managed or the risk that attends the application of a device requires an increase in the evidence supporting the safety and effectiveness of the device. This evidence along with supporting materials must be submitted to the FDA in the form of a premarket approval application (PMAA).

In 1990, only 47 of the over 7,000 devices approved for marketing by the FDA went through the PMAA process (*4*). Of these 47 PMAA devices, 9 were considered to be significant breakthroughs. The other 7,000 or so were cleared through the premarket notification ("510K") provision of the Medical Device Amendments. This provision exempts a device from the more rigorous PMAA process if it is judged to be "substantially equivalent" to a device that was marketed in the United States prior to May 28, 1976. Substantial equivalence means that the device performs the same function as its predecessor and that it possesses similar technical and performance characteristics. Under the 510K process, examination is confined primarily to differences between the earlier and new devices to determine whether they might affect the safety and effectiveness of the device.

Clearance for marketing through the 510K provision is understandably preferred by manufacturers because it eliminates the need to develop primary data and an extensive application in support of the safety and effectiveness of the device. The FDA has interpreted the 510K provision liberally in recognition of its limitations of staff and the need to get devices to market in a timely fashion. In 1988, the average time for PMAA review was 262 days compared with 78 days for review of a 510K application (*5*).

Implementation of the regulatory controls mandated in the Medical Device Amendments has proceeded fairly well. However, in recent years there has been some congressional sentiment that the FDA should have a more restrictive interpretation of the 510K provision and that more devices should be subjected to the full PMAA process. This concern has been translated into action with the passage of the Safe Medical Devices Act of 1990, which explicitly provides the FDA with the authority to require as part of a 510K submission a summary of available data and information on the safety and effectiveness of the device. In practice, the FDA had already begun to occasionally require submission of safety and effectiveness data for a device submitted under the 510K process.

PET provides an excellent illustration of variation in controls over medical devices in recent years. Prior to November 20, 1990, PET instrumentation was considered to be instrumentation that was available before the May 28, 1976 deadline imposed by the Medical Device Amendments. Thus, marketing of the device did not fall under the requirements of either a 510K or PMAA process. However, on November 20, 1990, the FDA published a final rule (*6*) classifying the positron camera as a Class I device, thus making positron cameras subject to submission under the 510K provision. For purposes of the notice, a positron camera is considered to include "signal analysis and display equipment, patient and equipment supports, radionuclide anatomical markers, component parts, and accessories (*6*).

In addition to the device itself, the FDA classifies the imaging agents used in PET as pharmaceuticals. Thus, these agents will required passage through the FDA drug approval process. As indicated above, the approval of a new drug application (NDA) requires the submission of convincing data regarding the safety and effectiveness of the application of a technology for a specific indication. These data must be derived from well-controlled clinical trials.

Thus, the introduction of PET technology to the health care market is controlled under both the drug and device provisions of the Food, Drug and Cosmetic Act. Presently, permission to use imaging agents is granted by the FDA on an investigational basis through an exemption for use known as an IND (Investigational New Drug). However, it must be remembered that the FDA only has regulatory control over those drugs that are subject to interstate commerce. Confinement of the use of imaging agents produced by a local cyclotron to intrastate commerce places such use beyond the *purview* of the FDA.

Over the long haul, the production and distribution processes for imaging agents can be expected to become more efficient. As such, distribution across state lines will become an increasing reality and eventually approval of a NDA for specific imaging agents will be required. The problem then will be to find a sponsor willing to invest the time and resources to generate sufficient safety and effectiveness data for the FDA. When FDA approval is indeed accomplished, attention will then focus on the next imposing hurdle, the coverage decision-making process.

COVERAGE

Cost-containment forces have caused third-party payors to adopt a variety of strategies to retard the rate of increasing health care expenditures. One mechanism has been the application of technology assessment in the coverage-decision making process for important new technologies. The rationale for this is that intensity of services, of which utilization of new technology is considered to be the major component, is viewed as the most controllable factor contributing to increases in health care expenditures.

In applying technology assessment processes, the major payors have focused initially on "big-ticket" devices and

procedures. For devices, payors are becoming increasingly familiar with the differences in the FDA approval processes for devices and drugs. They also realize that devices may be cleared for marketing through the 510K process without consideration of primary data directed to safety and effectiveness. Indeed, payors have learned that pre-1976 devices can be marketed without any consideration at all. Payors understand that requirements for the approval of a PMAA may be less rigorous than those required for approval of a new drug. They also may consider the clinical indication for utilization of a device to be an intermediate health outcome, such as imaging of particular anatomic structures, measurement of blood flow, or temporary relief of pain. The contribution of this intermediate outcome to a specific health result (e.g., a specific diagnosis or curative therapy) may not always be certain.

The Technology Evaluation Criteria of the National Blue Cross and Blue Shield Association illustrate the increasing rigor applied by third-party payors in the assessment and coverage process. A technology that meets all five of the following criteria is generally recommended for coverage:

1. The technology must have final approval from appropriate government regulatory bodies.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcome.
3. The technology must improve the net health outcome.
4. The technology must be at least as beneficial as all established alternatives.
5. The benefit must be attainable outside an investigational setting.

Criterion 1 establishes FDA approval as necessary for even consideration of the other four criteria and, indeed, supporting data beyond that required for FDA approval are often required for an affirmative coverage recommendation. Criterion 4 raises the issue of equivalent effectiveness that is not explicitly addressed in a PMAA, and criteria 4 and 5 may require data to support equivalent effectiveness under normal conditions of use. Acquisition of these data can significantly delay reimbursement and, therefore, the availability of an FDA-approved device to patients. Indeed, providers and manufacturers find themselves in a "catch-22" where an expensive device may be approved by the FDA as safe and effective, yet payors ask for more data before reimbursement. Without some form of payment, extensive utilization of expensive instrumentation to generate data supporting use under normal conditions is very difficult, if not impossible.

Magnetic resonance imaging (MRI) illustrates this conundrum that may pertain for PET as well. The first two MRI units were approved by the FDA on March 29, 1984 for marketing in the U.S. In February 1985, the National Blue Cross and Blue Shield Association recommended against coverage by stating "it is premature to accept MRI as a standard clinically effective diagnostic technique even for general applications to the central nervous system" (*7*). In June of 1985, Blue Cross/Blue Shield updated its assessment and recommended that MRI should be considered "generally accepted medical practice for diagnostic conditions of the posterior fossa (cerebellum and brain stem), and high (C_1 through C_3) cervical cord and demyelinating diseases of the brain" (*8*). The Health Care Financing Administration (HCFA) announced its affirmative coverage decision for MRI in November 1985. This delay in a decision by the HCFA also points out that approval by one government agency, the FDA, of a device as safe and effective does not ensure the availability of this device through coverage to patients enrolled in the government's own insurance program for the elderly. The delay in coverage for MRI has been suggested to have had a significant negative impact on the diffusion of MRI in the U.S. (*9*).

Presently, the coverage situation for PET resembles that seen for MRI in mid-1985. The HCFA is not covering the use of PET and is awaiting the results of an assessment being conducted by the Office of Health Technology Assessment (OHTA). Since the average length of time required for OHTA to conduct an assessment is 2.4 yr (*10*) and since OHTA initiated its assessment in April 1990, the decision by the HCFA on Medicare coverage for PET may still be some months away. Among the private payors, Travelers and Metropolitan cover some PET cardiologic applications. Prudential and Aetna do not. Aetna has indicated that it is leaning toward some limited coverage and will base its decisions upon the results of a recent conference sponsored by the Health Insurance Association of America. Florida Blue Cross and Blue Shield covers diagnostic workups for symptomatic heart patients. Among the HMOs, Kaiser Permanente in Oakland and the Health Insurance Plan of New York have no blanket policy but may provide coverage on an individual basis.

One interesting note is that the Technology Management Group of National Blue Cross and Blue Shield has not developed a coverage recommendation for individual plans. This decision is based upon the fact that there is no FDA-approved imaging agent and, thus, the first of their five criteria have not been fulfilled. This situation exemplifies the litany of regulatory and coverage factors that may constrain the utilization of PET. PET instrumentation can be marketed in the United States. Yet, the requisite imaging agents are classified as investigational by the FDA. An assessment critical to the coverage recommendation of "Blues Plans" throughout the country has not been forthcoming because a component technology of PET, the imaging agent, has not satisfied criterion 1 regarding the achievement of regulatory approval.

Level of Reimbursement

The setting of specific levels of reimbursement has become an increasingly effective means of controlling the

diffusion of technologies. Uncertainty over the eventuality of affirmative coverage compounded by uncertainty over adequate reimbursement contributes to difficult acquisition decisions and slower diffusion. For MRI, reimbursement levels were a controversial and significant factor in the technology's rate of diffusion (*11*).

Public controversy about MRI reimbursement occurred in 1986. In its annual report (*12*), the Prospective Payment Assessment Commission (ProPAC) recommended an additional payment for each MRI scan performed on an inpatient Medicare beneficiary. This recommendation proceeded from the recognition of MRI by ProPAC as an important new diagnostic technology. First, ProPAC recognized that hospital payment had not been increased to compensate adequately for the additional costs associated with the use of this new technology. Second, simple increases in payment in future years due to MRI would improperly increase payment under particular DRGs to cases where MRI was not utilized. Third, ProPAC felt that Medicare's payment mechanism would lead to inappropriate distribution and siting of MRI units in the outpatient setting.

ProPAC believed that it was inappropriate to have a significant new technology introduced and not provide hospitals with adequate reimbursement for that technology's operating expenses (*13*). The recommendation was based squarely on the issue of adequate payment since "ProPAC's goal is neither to encourage the use of MRI nor to discourage its availability and use" (*13*). The ProPAC recommendation for an add-on payment was not accepted by the HCFA.

The issue of adequate levels of reimbursement will persist and pertain to the evolving clinical applications of PET. Under Medicare, the lag time to recalibration has been cut by the implemention of annual adjustment of DRG levels. Thus, cost increases attending the use of PET would be more rapidly reflected in future Medicare payments. Distribution of PET across several DRGs may stimulate many of the concerns experienced with MRI (e.g., payment of equal amounts whether or not MRI was used). In general, the lessons learned from the introduction and diffusion of MRI may actually make setting of PET reimbursement levels easier. In the end, the actual decision to pay for specific clinical indications may be the most difficult hurdle for PET to surmount.

SUMMARY

The converging forces of the rapid proliferation of technology and its perceived contribution to continued escalation in health care expenditures have caused payors to establish specific mechanisms to evaluate the appropriateness of the utilization and payment for new technologies. FDA approval of a device deemed safe and effective for marketing to health care providers is now merely a threshold to signal initial consideration for coverage by payors. This is no more clearly illustrated than in the position of the HCFA that FDA approval of a device does not necessarily mean that the device and its labeled indication will be covered under Medicare. Rather, the safety and effectiveness of the technology may be subjected to further evaluation by OHTA. When coverage is finally achieved, the level of reimbursement established for the technology may be an incentive or disincentive for its utilization.

The travail and traversal of new expensive medical technologies through this tortuous path of regulatory and economic hurdles may have deleterious implications for future investment in the development of devices and drugs. The uncertainty created clearly confuses and prolongs the decision-making process of acquisition for health care facilities and physicians. Finally, it delays the availability of important new technologies to patients who need them.

The picture will only continue to get more complicated, however. For example, the HCFA has proposed to add the criterion of cost-effectiveness to its coverage process. In so doing, the HCFA became the first major third-party payor to explicity propose this. Whatever the final decision, it is clear that cost-effectiveness will become an increasingly important consideration in decisions about making technologies available for patients.

The other significant consideration will be increasing emphasis on the generation and analysis of primary health outcomes data. National Blue Cross and Blue Shield has announced its intention to generate outcome data on one controversial and expensive technology: autologous bone marrow transplantation in breast cancer. In order to receive payment for the procedure, patients must receive care under the National Blues Research protocol. Indeed, four of the five Blues criteria for coverage revolve around the generation, analysis, and evaluation of outcomes data.

How will society continue to foster the development of important new technologies such as PET? The answer may lie in a synergistic compromise between advocates of a technology and those who wish to carefully evaluate the technology. When some data are available to establish the promise of a technology in improving patient outcomes, a mechanism for adequate payment for its use in a carefully circumscribed population of patients could be made. In return, proponents and users of the technology would agree to participate in prospective studies to develop outcomes data regarding the technology's performance under normal conditions of use. When data appear adequate to make a definitive judgement, all affected constituents of the health care community could join together in a consortial arrangement to decide upon the future use and payment for this technology. In reality, one cannot expect parties to be totally bereft of individual interests. But face-to-face discussions should facilitate decisions that provide appropriate incentives for the continued development of important new technologies and enhance the appropriate and efficient utilization of our technologic resources.

Could PET serve as the prototype for this consortium?

DISCLAIMER

The views expressed in this paper represent those of the individual author and are not positions or policies of the American Medical Association.

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