The Controversy Over High-Dose Chemotherapy With Autologous Bone Marrow Transplant For Breast Cancer

A cautionary tale about allowing politics and legal pressures to overwhelm science in evaluating new therapies.

by Michelle M. Mello and Troyen A. Brennan

ABSTRACT: In the 1990s more than 41,000 patients underwent high-dose chemotherapy plus autologous bone marrow transplant (HDC-ABMT) for breast cancer, despite a paucity of clinical evidence of its efficacy. Most health plans reluctantly agreed to cover the treatment in response to intensive political lobbying and the threat of litigation. The results of five recent major randomized trials showed that HDC-ABMT offers no advantage over standard-dose treatment for breast cancer. Our experience with HDC-ABMT coverage cautions against allowing politics to overwhelm science in the area of evaluating experimental procedures, and against relying on the courts as a means of resolving disagreements about coverage of these interventions.

HIGH-DOSE CHEMOTHERAPY plus autologous bone marrow transplant (HDC-ABMT) is a cancer treatment procedure through which bone marrow or stem cells from the blood are extracted from the patient and then reinfused following the administration of high doses of chemotherapy. HDC gives the patient a concentrated dose of cancer-fighting drugs that have the effect of destroying the patient's immune system. ABMT replaces the bone marrow and restores the patient's ability to fight infections, enabling the patient to withstand chemotherapeutic doses that otherwise would be lethal.

In April 2000 the *New England Journal of Medicine* reported the results of a major randomized controlled trial of HDC-ABMT for the treatment of metastatic breast cancer.[1] Edward Stadtmauer and col-

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leagues found no survival advantage to HDC-ABMT relative to standard-dose chemotherapy, corroborating the results of four other recent randomized trials.[2] An accompanying editorial concluded that based on these findings, "to a reasonable degree of probability, this form of treatment for women with metastatic breast cancer has been proved to be ineffective and should be abandoned in favor of well-justified alternative approaches."[3] The American Society of Clinical Oncology reached a similar conclusion in a recent consensus statement: "Given the lack of persuasive data demonstrating superior effectiveness of this very toxic therapy," HDC-ABMT for breast cancer "should be performed only in the context of a high quality clinical trial."[4]

This verdict signals a denouement to the controversy over HDC-ABMT's efficacy for breast cancer that has enveloped the medical, legal, and insurance communities for the past decade. Health maintenance organizations (HMOs) and other insurers initially resisted breast cancer patients' demands for coverage of the $80,000 treatment, arguing that the clinical evidence, derived from Phase II trials, was insufficient to support a conclusion that HDC-ABMT was superior to standard-dose chemotherapy. Their refusals led to an avalanche of litigation, accompanied by intensive political lobbying by patient advocacy groups. These legal and political pressures led most health plans to capitulate and pay for the treatment by the mid-1990s. And so, despite the weakness of the clinical evidence and the high cost and toxicity of the therapy, more patients underwent HDC-ABMT in the 1990s for breast cancer than for any other disease.[5]

Now, with the arrival of Stadtmauer's results, it appears that the insurers were correct in asserting that there were no data to support the use of HDC-ABMT for breast cancer. However, with public sentiment heavily tilted against managed care plans (due, in part, to numerous other cases in which coverage denials have not been justified), there has been little public acknowledgment of that fact.

The HDC-ABMT controversy contains two important lessons for future disputes over coverage of investigational procedures in the age of managed care. First, it serves as a cautionary tale about the dangers of allowing political pressures to overwhelm science in evaluating new therapies and rationing scarce health care resources. Second, it raises questions about the proper forum for resolving such controversies. The variability in litigation outcomes in the HDC-ABMT cases, and the number of verdicts for plaintiffs when strong scientific evidence of HDC-ABMT's effectiveness for breast cancer did not exist, forces us to think hard about the institutional competence of courts in resolving coverage disputes involving experimental treatments and to search for better alternatives.

In an era in which the technological imperative is one of the most powerful drivers of health care costs, these are crucial lessons. New drugs, medical devices, and other treatment modalities are emerging at a rapid pace. In 1999 the Food and Drug Administration (FDA) approved eighty-three new drugs, ninety-seven new or expanded use of existing drugs, and fifty-three premarket approval applications for new medical devices. The National Institutes of Health (NIH) received "dramatic and unprecedented" 15 percent budget increases in 1999 and 2000, bringing its 2000 budget to $17.8 billion. Advances in medical technology give rise to both great hope and great conflict over costs and coverage. A heightened commitment to technology assessment—by government bodies and managed care organizations, we believe, rather than courts—is required to channel these advances toward socially efficient uses.

The Science

The central question in assessing the reasonableness of insurers' refusals to cover HDC-ABMT for breast cancer is the extent to which that decision accurately reflected the available scientific knowledge about the treatment's efficacy at the time. To paraphrase Sen. Howard Baker's probing query during the Watergate investigations, what did the HMOs know and when did they know it? A review of the medical literature from 1990 to 2000 reveals that while public and physician enthusiasm for HDC-ABMT increased steadily over the course of the decade, the clinical evidence of the treatment's effectiveness went from promising to equivocal to disappointing.

■ **Early findings.** HDC-ABMT first attracted interest as a therapy for breast cancer following observations in the 1980s of dramatic improvements in complete and partial response rates (tumor shrinkage). These findings were soon followed by reports of improved survival rates. In 1990 William Peters released the preliminary results of a Phase II study in which patients with ten or more positive lymph nodes who were treated with HDC-ABMT experienced a 40 percent improvement in three-year survival rates compared with historical controls treated with standard-dose chemotherapy.[6]

While researchers were justifiably excited by these findings, several major insurers that had a strong commitment to basing coverage decisions on reliable evidence of therapeutic benefit balked at extending coverage for HDC-ABMT in the absence of evidence from well-controlled trials. The insurers and academic commentators noted a number of methodological shortcomings of Phase II HDC-ABMT trials. Most prominent was selection bias. The selection criteria for such trials generally were much stricter than those for standard-dose chemotherapy studies; therefore, the use of historical

controls from standard-dose trials was seen as problematic. Of particular concern was the requirement that HDC-ABMT trial participants have demonstrated an objective response to previously administered standard-dose chemotherapy, since prospects are better for treating responsive disease than for nonresponsive disease regardless of the treatment modality used. Other sources of concern about the trials included the publication bias in favor of positive results, lead-time bias, short follow-up time, and small sample size.[7]

Literature reviews published in the early to mid-1990s found the preliminary Phase II results promising but noted that the ability to draw inferences from these studies was limited by several factors including selection bias, and that consequently the superiority of HDC-ABMT over standard-dose therapy had not been conclusively shown. Also, David Eddy's 1992 review noted that the improvements in response seen in most Phase II studies lasted only a few months and came at the price of a markedly increased risk of serious morbidity compared with the risk attending standard-dose therapy.[8]

■ **Randomized controlled trials.** Eddy's paper was controversial among oncologists and researchers but contributed to the advancement of clinical research on HDC-ABMT. Prior to his review, researchers had objected to insurers' calls for randomized controlled (Phase III) trials on the basis that the tumor shrinkage evidence was sufficient to prove a therapeutic benefit from HDC-ABMT, and thus subjecting patients to randomization would be unethical. Eddy's review of the existing clinical series concluded that there was no proven survival advantage to HDC-ABMT. This finding provided a sufficient ethical and scientific basis for pursuing randomized trials.

Several years passed before Eddy's paper was followed by other reviews drawing pessimistic conclusions about HDC-ABMT for breast cancer. In the interim, randomized trials of HDC-ABMT were initiated. Interestingly, the Blue Cross Blue Shield Association (BCBSA), which had been active in performing technology assessments of HDC-ABMT, took the unusual step of approaching the National Cancer Institute and offering to fund the patient care costs associated with the trials.

A report in 1995 of favorable results from the first randomized trial for patients with metastatic breast cancer temporarily buoyed enthusiasm for HDC-ABMT.[9] However, the results of this one small, relatively short trial were deemed insufficient to establish the treatment as superior. In 1996 the National Comprehensive Cancer Network, after studying the available evidence, explicitly decided not to include HDC-ABMT in its guidelines for the care of high-risk breast cancer patients. In the discussion following the presentation of these guidelines, a representative of the guidelines panel stated that

HDC-ABMT was considered "controversial, with people voting in different ways in terms of whether it's appropriate or not outside the confines of a trial."[10] A U.S. General Accounting Office (GAO) report issued in the same year reached essentially the same conclusion: "Current data indicate ABMT may be beneficial for some breast cancer patients but that there is not yet enough information to establish that it is more effective than standard chemotherapy."[11]

In the past five years, as additional Phase III trial results have come in, the outlook has gone from guarded to bleak. In 1997 Peters and colleagues at Duke University reported a survival advantage to HDC-ABMT for metastatic breast cancer patients relative to observation only but could not demonstrate the superiority of HDC-ABMT over standard therapy since that modality was not used as a control.[12] A randomized trial by researchers at the Netherlands Cancer Institute, which did compare HDC-ABMT with standard treatment, produced unequivocally negative results in 1998.[13] Three more major randomized studies reported over the next year confirmed these findings.[14] Two of these (the Peters and Scandinavian studies) were multicenter trials with sufficient power to detect even modest differences in outcome. A fourth study, by W.R. Bezwoda, reached a dramatically different conclusion about the efficacy of HDC-ABMT but was discredited after Bezwoda admitted scientific misconduct. In short, a review of clinical studies in the 1990s shows that as the science of studying HDC-ABMT advanced, hope that the treatment would benefit breast cancer patients receded.

■ **Practice versus clinical evidence.** While skepticism in the research community about HDC-ABMT's efficacy grew during this time, the perceptions of the public and of most oncologists remained quite positive. A survey of oncologists conducted in 1989 found that 79 percent believed that it would be appropriate to offer HDC-ABMT to patients with locally advanced breast cancer.[15] Over the next decade the number of breast cancer patients receiving HDC-ABMT increased more than tenfold, from an estimated 680 in 1990 to an estimated 8,200 in 1999.[16] The disparity between oncologists' practices and the clinical evidence is striking but not out of step with studies suggesting that oncologists may systematically overestimate the therapeutic benefits of chemotherapeutic modalities.[17]

■ **Insurers' dilemma.** The divergence between physicians' and patients' perceptions of HDC-ABMT and the clinical trial findings left HMOs and other insurers in a difficult position. Principles of fair resource allocation suggest that if a particular intervention is expensive and unproven, a health plan should steadfastly decline to pay for it as a therapy, regardless of how vocally the affected patient group protests. Paying for patients to receive the intervention in a clinical

trial, on the other hand, may be quite justifiable if the intervention and the standard treatment stand in a state of clinical equipoise. On this point there is reason to take a critical view of insurers' behavior. A 1994 study found that while insurers approved 77 percent of breast cancer patients' requests for coverage of HDC-ABMT clinical trial participation, the approval process appeared to be highly arbitrary, such that similarly situated patients were treated differently even by the same insurer.[18] This variability suggests that insurers' decision-making processes relating to clinical trials bore little relation to available medical or scientific information.

The Politics

Coverage for HDC-ABMT outside of a clinical trial setting became common in the 1990s as a result of both political and legal forces. A powerful breast cancer lobby succeeded in persuading or, in some states, forcing insurers to provide coverage for HDC-ABMT at a time when research into the treatment's effectiveness was still in its early stages. Several factors contributed to the group's success.

■ **Powerful lobbying group.** First, the degree of political organization and mobilization among breast cancer patients and their advocates is high. Approximately 400 support, advocacy, and care provider groups are organized under the aegis of the National Alliance of Breast Cancer Organizations (NABCO), which engages in large-scale educational and lobbying activities. Partnerships with several large corporations greatly augment NABCO's resources, and the organization's total revenue in 1999 approached $7 million.[19]

■ **Great public appeal.** Second, breast cancer, because of its prevalence and mortality rate, rightly commands great public attention. The American Cancer Society projects that 182,800 new cases of female invasive breast cancer will be diagnosed in 2001, resulting in 40,800 deaths, and that American women have a one-in-eight lifetime risk of developing breast cancer.[20] Also, the afflicted patients—overwhelmingly middle-aged and elderly women—are a particularly sympathetic group in the eyes of the public.

■ **Impetus from AIDS lobby.** Third, the breast cancer lobby was energized by the success of the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) lobby in pressuring the FDA to expedite its review of potentially life-prolonging new AIDS drugs and to expand preapproval access to the drugs. This victory gave impetus to other single-disease advocates, including cancer groups. In response to their lobbying, the FDA implemented its "cancer drug initiative" in 1996 to provide increased access to experimental cancer medicines. For breast cancer activists, winning state-mandated insurance coverage for those and other

therapies was the logical next step. Bolstered by the support of oncologists and clinical investigators, they achieved this goal in a number of states.

■ **Support of researchers.** Fourth, lobbyists for HDC-ABMT greatly benefited from the enthusiastic and aggressive support of a handful of prominent oncology researchers. The investigators, who also had an interest in getting HDC-ABMT covered by insurance, encouraged breast cancer patients and their advocates to take their cases to the courts. They then provided strong testimony on behalf of the plaintiffs, which contributed much to their success at trial.

■ **Media coverage.** Fifth, the mass media has provided major assistance to the breast cancer lobby's efforts. In 1991 the television news show *60 Minutes* aired a piece decrying Aetna's decision to deny coverage for HDC-ABMT for breast cancer. In 1993 the media widely publicized a staggering $89 million jury verdict in the Nelene Fox case, a suit brought by a California breast cancer patient against HealthNet for failure to provide coverage for HDC-ABMT. State-level publicity of sympathetic local cases spurred several state legislatures to pass laws mandating that insurers doing business in the state cover HDC-ABMT for breast cancer. In Massachusetts, for example, the *Boston Globe* publicized the battle of Charlotte Turner, a forty-seven-year-old nurse and mother, against her HMO for its refusal to pay for HDC-ABMT. The Massachusetts legislature passed a mandated benefit law for HDC-ABMT in late 1993 in response to intensive lobbying by Turner's friends and relatives and public pressure generated by the media coverage of her predicament.

Even in states without mandated benefit laws, the politicization of the HDC-ABMT issue impelled many large health plans to reconsider their position that HDC-ABMT for breast cancer was excluded from coverage as an experimental treatment. Those that continued to deny coverage found themselves embroiled in litigation. For most insurers, the economic pressures of litigation forced a change in their coverage policies, even where political pressures had not.

The Litigation

Breast cancer patients began suing recalcitrant health plans for coverage of HDC-ABMT in the early 1990s. To date, there have been more than 100 published state and federal court decisions in such cases. This number underestimates the number of claims filed, since it does not include claims that were settled, claims still pending, and cases decided by a jury in state courts and not appealed.

■ **Fox case.** The judgment in the Nelene Fox case, with its $77 million punitive damages component, was extremely unsettling to insurers. That case was factually atypical in that there was an ele-

ment of hypocrisy involved in the plan's coverage decisions: HealthNet paid for a relative of its chief executive officer (CEO) to receive HDC-ABMT but denied the treatment to Fox and other plan subscribers. This made the plan's behavior toward Fox seem particularly blameworthy, leading to a high punitive damages award. Other insurers may have taken comfort in the unique facts of the Fox case; however, the judgment must still have been worrisome to plans that maintained a policy of excluding coverage for HDC-ABMT.

■ **Inconsistent court judgments.** Another source of concern for health plans was the inconsistency with which courts resolved HDC-ABMT claims. Across the judicial circuits, the judgments were highly variable, and the lack of uniformity was not easily explained.[21]

The ERISA factor. One source of variation was the standard of review applied. When a plaintiff who is insured by a plan not covered by the Employee Retirement Income Security Act (ERISA) of 1974 sues for breach of contract under state law, he or she is permitted to introduce new expert testimony about the treatment in dispute, and the judge or jury will render an independent judgment about whether the treatment should have been covered. In contrast, federal courts deciding coverage disputes involving ERISA plans will only consider the information that the plan actually considered when it made its coverage decision. Moreover, where the terms of an ERISA plan policy give the plan discretion to determine eligibility for benefits, the court will not make an independent judgment about the treatment but will only determine whether the plan's decision was so lacking in foundation as to be considered "arbitrary and capricious." Plaintiffs whose ERISA plans have not explicitly reserved this discretion fare better, as the courts are willing to determine their eligibility for coverage *de novo*, or as if no decision previously had been rendered.

Ambiguous language. Another source of variation was judges' willingness to deem exclusionary language in the insurance policy "ambiguous" and, according to standard principles of insurance law, construe the ambiguity in favor of the insured. For example, in *Bailey v. Blue Cross & Blue Shield of Virginia*, the Fourth Circuit Court of Appeals found the policy's statement that "autologous bone marrow transplants or other forms of stem cell rescue (in which the patient is the donor) with high dose chemotherapy or radiation are not covered" to be ambiguous and entered judgment for the plaintiff.[22] Similarly, in an unusual display of numerical exactitude, the federal district court in *Bucci v. Blue Cross-Blue Shield of Connecticut* ordered the insurer to pay for HDC-ABMT on the basis that its contractual definition of "experimental" as "not recognized as acceptable medical practice" was impermissibly vague because it did not specify the

number of cases that would be required to establish acceptance.[23] In contrast, in *Peruzzi v. Summa Medical Plan* the Sixth Circuit Court of Appeals upheld the insurer's exclusion of treatments of an "experimental or of a research nature," where that term was interpreted by the insurer to mean not "generally accepted medical therapy."[24]

Impact. The inconsistency in judicial decisions made it difficult for insurers to estimate the degree of financial risk involved in continuing to deny coverage for HDC-ABMT. Where an economic actor subject to tort liability operates under conditions of uncertainty as to the probability of a large adverse judgment, the tort liability system will have the effect of overdeterring risky behavior, resulting in inefficiency. As rational economic actors, potential defendants conduct a cost-benefit analysis to determine what level of precaution to take in conducting their affairs. Where they cannot conduct this analysis with certainty because they cannot estimate the probability of being sued, the likelihood of an adverse verdict, or the size of the damages award against them, they will tend to err on the side of avoiding litigation. This decision can be viewed as socially inefficient if it involves a decision to cover a treatment that is not medically efficacious (much less cost-effective).

■ **"Judge-made insurance."** Health plans in the 1990s continued to insist that HDC-ABMT was unproven as a treatment for breast cancer and was rightly classified as experimental and therefore excluded from coverage. But because of a widespread perception of extreme vulnerability to litigation, many insurers chose to cover HDC-ABMT notwithstanding their doubts about its benefits. As Mark Hall and Kenneth Abraham have noted, perceived exposure to costly litigation gives rise to the phenomenon of "judge-made insurance"—the mandating of coverage that informed consumers in a private marketplace would not have chosen to purchase.[25] This carries social costs in terms of higher insurance premiums, which price some consumers out of the market. The GAO study found that nine of twelve large health plans surveyed about their decision to cover HDC-ABMT named the threat of litigation as a major factor in their decision.[26] With the benefit of 20-20 hindsight, we can now say that this decision was a socially inefficient one.

■ **Domino effect.** As has been described elsewhere, individual private insurers' decisions to change their coverage policies had a domino effect throughout the industry.[27] Initially, many major insurers agreed to cover HDC-ABMT in the context of a clinical trial. In response to this action, the federal Office of Personnel Management (OPM) decided to mandate coverage of HDC-ABMT for all federal employees.[28] Because the OPM opted to mandate coverage outside the context of randomized clinical trials, private health plans soon

found it untenable to continue to limit their coverage to clinical trials. And so the herd migrated over time toward unconditional coverage for HDC-ABMT, with the result that only one in ten breast cancer patients who received HDC-ABMT in the 1990s did so within a clinical trial.[29]

The Lessons

The HDC-ABMT controversy bears two important lessons for resolving future disagreements about paying for experimental treatments. First, it underscores the importance of fidelity to good science as the primary basis for using and paying for a new medical intervention. Providing coverage for a costly and toxic intervention such as HDC-ABMT when its efficacy is unproven has serious ramifications for patients, clinical researchers, and the health care budget. Second, the controversy raises questions about the institutional competence of courts to resolve coverage disputes concerning investigational therapies. For a number of reasons, courts have not been able to answer questions about the appropriate scope of coverage in a manner that is consistent and mindful of public policy goals.

■ **Lessons for insurance coverage decision making.** The first lesson pertains to the way in which political and legal pressures may overwhelm science in the realm of rationing health care resources. We should be concerned whenever an interest group uses its political clout or the threat of litigation to coopt health care payers into covering unproven treatments, but that concern is particularly acute in the case of HDC-ABMT, for three reasons.

Cost of treatment. Most obvious is the high cost of the treatment. Although the cost has decreased somewhat in the past several years, it remains in the neighborhood of $80,000. An estimated 42,680 autologous bone marrow transplants were performed on breast cancer patients during the 1990–1999 period.[30] Estimating the cost at $80,000 per transplant, this means that the nation's health insurers spent more than $3.4 billion during that ten-year period on a treatment that turned out to offer no appreciable medical advantage over standard-dose chemotherapy, which can be had for less than half the price. These costs, of course, were passed on to the plans' subscribers and, in the case of public payers, to the taxpayers.

Burdens for the patient. Another cause for concern is that treatment with HDC-ABMT entails serious burdens for the patient. Acute-onset toxicities (in addition to vomiting and diarrhea) include sepsis, pulmonary failure, veno-occlusive disease, cardiac failure, nephrotoxicity, hemorrhagic cystitis, and cardiac toxicity. Among the chronic sequelae that may ensue are acute myelogenous leukemia or myelo-dysplastic syndrome, bone marrow insufficiency, psy-

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chosexual disorders, and heightened vulnerability to opportunistic infections in the first year after treatment. HDC-ABMT also can kill. The recent randomized clinical trials reported treatment-related mortality rates ranging from zero to 7 percent among HDC-ABMT recipients, while the standard-dose control arms of the studies had no such deaths.[31]

Impact on clinical research. Yet another problem is the collateral effects on clinical research of providing unconditional coverage for an investigational treatment. When health plans offered coverage for HDC-ABMT only in the context of participation in a clinical trial, this aligned patients' interest in receiving treatment with that of insurers and with society's interest in furthering scientific knowledge. When health plans began to cover HDC-ABMT outside of the setting of clinical trials, these interests fractured, and the clinical trials effort suffered severely. As noted above, nine out of ten patients chose to receive HDC-ABMT outside of clinical trials. This is not surprising given patients' level of faith in HDC-ABMT (a rational patient believing that it offers improved response rates relative to standard treatment would not risk being randomized to a control group). The impact on research is exemplified by the fact that the randomized trial reported in 2001 by Gabriel Hortobagyi and colleagues took eight years to accrue eighty eligible participants, rather than the planned three years.[32] Stadtmauer and colleagues, too, encountered difficulties with accrual; 28 percent of enrolled patients withdrew from the study rather than submit to randomization, with the result that the investigators were forced to modify their study design.[33] When political and legal pressures cause health plans to adopt coverage policies that not only jump ahead of science but impede it, we as a community concerned with the advancement of public health have taken a serious wrong turn.

Ethical considerations. While it is true that many other treatments have been fully covered by health plans without ever having been subjected to randomized controlled trials, we must use exceptional care when evaluating a treatment with the toxicity and high cost of HDC-ABMT. Widespread use and coverage of such treatments entail special ethical problems. The principles of beneficence and nonmaleficence dictate that a physician should not routinely recommend, with a health plan's implicit sanction, a treatment with high morbidity and mortality when the efficacy of that treatment is un-

proven. From a contributive justice standpoint (concerning fairness to those who have, through taxation, paid into a common pool of resources for the benefit of all), draining massive amounts of resources from the health care budget is difficult to justify in the absence of convincing evidence of medical benefit. With respect to distributive justice, uncoupling coverage decisions from their anchor in the treatment's proven efficacy and cost-effectiveness creates chaos in our efforts to ration health care resources fairly. In health care, money should not flow to the squeakiest wheel. It should flow where it can do the most good.

Differing standards. These principles should guide coverage decisions by insurers, but patients and their physicians may take a different approach to treatment decisions. Indeed, a crucial aspect of the disagreement about HDC-ABMT between insurers, on the one hand, and physicians and patients, on the other, was that the two sides appeared to apply different standards in judging the appropriateness of the procedure. To insurers, the relevant question was whether there was reliable evidence that HDC-ABMT did have therapeutic benefit. To desperately ill patients and their physicians and advocates, the question was whether the procedure might have benefit. HDC-ABMT is offered to breast cancer patients who have not responded to conventional treatment options—it is a last-chance intervention. It is understandable that patients and physicians contemplating the treatment from that perspective had a lower appropriateness threshold than insurers had. The controversy over HDC-ABMT, then, was not simply a case of one side using scientific evidence and the other side ignoring it; it was a fundamental disagreement about how much evidence is enough. The need to reconcile these competing views lies at the heart of the struggle over rationing in the age of managed care.

■ **Lessons for judicial decision making.** The second lesson of our experience with coverage for HDC-ABMT is that there are major limitations on the usefulness of litigation as a means of resolving disagreements about investigational treatments. It has been observed that socially efficient contractual arrangements, such as what scope of insurance coverage a group of healthy patients ought to purchase, cannot be generated *ex post facto* through litigation.[34] Courts' role in breach-of-contract disputes is not to consider group needs and allocate resources according to principles of distributive justice, but to adjudicate individual claims. As the U.S. Supreme Court recently stated in the context of evaluating HMO rationing mechanisms, "complicated factfinding and...debatable social judgment[s]" about optimum treatment levels and health care expenditures "are not wisely required of courts unless for some reason resort

cannot be had to the legislative process."[35]

The approach: contract law. In an HDC-ABMT coverage case, the court examines whether HDC-ABMT falls within the insurance contract's language governing the exclusion of experimental or investigational treatments and whether the procedure the HMO used to determine that the treatment was excluded meets basic legal standards of reasonableness and nonarbitrariness. Judges rarely inquire into whether an insurer's specific exclusion of HDC-ABMT is invalid on its face. The assumption of this classic contract-law approach to insurance disputes is that an insurance agreement freely entered into after arm's-length bargaining between two informed parties should not be disturbed merely because one of the parties later wants something not included in the agreement. Under this approach, an ambiguous insurance policy usually will be construed in favor of the insured, but if the policy provides reasonably clear notice to the insured that a particular treatment will not be covered, the court will not mandate that the insurer provide it.

The validity of many of the assumptions of the contract-law approach—such as informational symmetry, free choice, and parity of bargaining power—are highly questionable in the context of a contract between an HMO and an insured individual. But courts to date have given little consideration to this problem. They generally have not struck down contractual provisions that clearly exclude coverage for HDC-ABMT. On the other hand, they have in many cases been quite willing to find that an exclusionary provision is "ambiguous" and therefore inapplicable. As a result, courts have mandated coverage for HDC-ABMT even where there has been scant scientific evidence in support of the insured's argument that the treatment was not merely experimental. In these cases, the courts' usual approach to insurance contract disputes meant that coverage was extended where, in retrospect, it should not have been.

Definitions of "experimental." One reason for both the prevalence of verdicts in favor of plaintiffs and the heterogeneity of judicial reasoning in HDC-ABMT cases may have been the lack of a shared understanding of the term "experimental." In some cases, the insurance policy provided an explicit definition. For example, in *Bucci* and *Peruzzi* the policy defined an "experimental" treatment as one not yet assimilated into generally accepted medical practice. In contrast, the policy in *Lewis v. Trustmark Insurance Co.* classified as "experimental" any therapy that was the "the subject of ongoing Phase I, II, or III clinical trials or under study to determine its maximum tolerated dose, its toxicity, its safety, its efficacy, or its efficacy as compared with the standard means of treatment or diagnosis."[36] Thus, some insurers defined "experimental" by reference to prevailing medical

practice, while others referred to the status of clinical trials.

Some insurance policies did not define the term at all, leaving courts to select a definition. Judges may have been inclined to opt for a prevailing-medical-practice approach because professional custom has long been the standard of care applied in medical negligence cases and thus is a benchmark with which courts are familiar and comfortable. This approach is problematic for the HDC-ABMT cases, however, because of the gap between oncologists' optimistic perceptions of HDC-ABMT and the relatively weak scientific evidence of the treatment's efficacy. Medical experts reasonably could have testified in the 1990s that HDC-ABMT represented the professional standard of care for high-risk breast cancer, but strong clinical trials evidence to support this practice did not exist.

Reliance on medical experts. There are other reasons to doubt courts' institutional competence to determine whether HDC-ABMT should be considered an experimental treatment for breast cancer. Judges, who are not trained in medicine or scientific research methods, typically rely on the opinions offered by one or two paid medical experts, who may not convey a full and accurate picture of the current state of clinical research. Particularly since there historically has been a divide between the opinions of clinical researchers and those of practicing oncologists, two different courts hearing testimony from different experts might receive very different reports. Even if the experts do give a comprehensive summary of clinical trial findings, judges and juries may well be unable to appreciate the methodological weaknesses of the Phase II studies relative to randomized controlled trials.

Improving Dispute Resolution

The two major lessons of the HDC-ABMT controversy interrelate in an important way. If health plans resist pressures to provide coverage for expensive new therapies that are not yet proven by well-designed clinical trials, inevitably more patients will turn to the courts for relief. Thus, the more faithful insurers are to good science, the more judicial participation in determining the medical appropriateness of experimental treatments we must accept.

Given the pace at which new medical and technological advances are occurring, this dilemma should cause us to think seriously about how we might improve judicial decision making—for example, whether a science panel of the kind used in the breast implant litigation might be more widely applied in cases involving complex issues of medical fact. An expert panel, perhaps one ostensibly set up to evaluate new therapies for Medicare coverage, could make the purely scientific determination of whether the available research

shows that a particular therapy falls within a standard definition of "experimental." This would leave courts to their special areas of expertise: interpreting contracts and laws and applying experts' general findings of fact to a dispute in a particular legal posture.

Removing judgments about what falls within the gray zone of investigational therapy from judges' hands would reduce the amount of coverage litigation and ensure more expeditious, accurate, certain, and just outcomes in the cases that remained. It would not, however, prevent all disputes about coverage for experimental treatments from arising. It would not resolve the fundamental divergence in the ways in which insurers, physicians, and patients approach decision making about care and coverage. At least in the realm of last-chance interventions, the question of "how much evidence is enough?" continues to be answered differently by those making coverage decisions and those making care decisions. The gap between these parties may have narrowed with respect to HDC-ABMT for breast cancer since the release of the negative randomized controlled trials findings, but it will persist for a host of other experimental interventions in the years to come.

PERHAPS THE MOST FUNDAMENTAL LESSON of the controversy over HDC-ABMT, then, is that we as a society still suffer from a degree of cognitive dissonance when it comes to insurance coverage. Most people believe that coverage policies should be set from behind a veil of ignorance as to what our own health care needs will turn out to be, and should be based on the efficacy and cost-effectiveness of the interventions at issue. But when we are confronted with identifiable cases of desperately ill patients' being denied a last-chance treatment, our decision rule may change. Until we resolve this basic conflict about coverage, attempts to "manage care" will continue to spark intense political and legal battles like those waged over HDC-ABMT.

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NOTES

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