Executive Summary

BACKGROUND

Clinical trials have become an essential component of modern medical care. The breakneck speed of medical advances and the increased effort to base clinical decisions on reliable evidence place clinical trials in an ever more prominent position between medical innovation and medical practice. Expanding the evidence base for health care interventions is clearly in the interest of both taxpayers who support Medicare and beneficiaries who receive services.

The impression is widespread that some patient care in clinical trials is not reimbursable under Medicare. But except in the case of certain investigational medical devices and a few instances of "coverage with conditions," the Health Care Financing Administration (HCFA) has never explicitly laid out exactly what should and should not be reimbursed. This omission has led to varying interpretations of HCFA's intent by its fiscal intermediaries and carriers who process claims, as well as by providers submitting claims.

A large proportion of patient care provided in clinical trials is routine—care that would be eligible for reimbursement if delivered outside of a trial. Although the evidence is limited, it appears that claims for much of this care are submitted to HCFA (and other insurers, for non-Medicare patients) without acknowledgment that the patient is in a clinical trial, and they are paid in the normal course of business by HCFA's contractors. But not all such costs for clinical trial patients are paid.

Increasingly over the past five years, uncertainty about reimbursement for routine patient care has been suspected as contributing to problems enrolling people in clinical trials. Clinical trial investigators cannot guarantee that Medicare will pay for the care required, and they must disclose this uncertainty to potential participants during the informed consent process. Since Medicare does not routinely

"preauthorize" care (as do many commercial insurers) the uncertainty cannot be dispelled in advance. Thus, patients considering whether to enter trials must assume that they may have to pay bills that Medicare rejects simply because they have enrolled in the trial.

This report recommends an explicit policy for reimbursement of routine patient care costs in clinical trials. It further recommends that HCFA provide additional support for selected clinical trials, and that the government support the establishment of a national clinical trials registry. These policies (1) should assure that beneficiaries would not be denied coverage merely because they have volunteered to participate in a clinical trial; and (2) would not impose excessive administrative burdens on HCFA, its fiscal intermediaries and carriers, or investigators, providers, or participants in clinical trials. Explicit rules would have the added benefit of increasing the uniformity of reimbursement decisions made by Medicare fiscal intermediaries and carriers in different parts of the country. Greater uniformity would, in turn, decrease the uncertainty about reimbursement when providers and patients embark on a clinical trial.

CONTEXT OF THE CURRENT STUDY

In the Balanced Budget Act of 1997 (P.L. 105-33, Section 4108), Congress directed HCFA to enter into a contract with the National Academy of Sciences for a "Study on Preventive and Enhanced Benefits" under Medicare. Five specific items were to be studied:

1. nutrition therapy services, including parenteral and enteral nutrition and the provision of such services by a registered dietitian;
2. skin cancer screening;
3. medically necessary dental care;
4. *routine patient care costs for beneficiaries enrolled in approved clinical trial programs;*
5. elimination of time limitation for coverage of immunosuppressive drugs for transplant patients.

Three committees were established to carry out the tasks, including this one to focus exclusively on the clinical trial question.

The clinical trial committee is aware that the question of reimbursement for care in clinical trials is not a new issue. Clinical trial investigators, patients, and potential volunteers have increasingly seen as a problem the lack of coverage for routine patient care that would be covered if the patient were not in the trial. Cancer activists and organizations, including cancer centers, were the most active agents in bringing this issue into public view. Several draft bills have mandated that Medicare cover routine care costs in clinical trials. Some have

named only "cancer trials," while others have pointed to "cancer and other life-threatening diseases." Agreements to pay for treatment in cancer trials have been drawn up between the National Cancer Institute (NCI) and the departments of Defense (DoD) and Veterans Affairs (VA); and United Healthcare, a major managed care organization, does pay for treatment (at varying levels) in selected cancer trials.

CLINICAL TRIALS

In this report, we define the term "clinical trial" as a formal study carried out according to a prospectively defined protocol. Clinical trials are intended to discover or verify the safety and effectiveness in human beings of interventions to promote well-being, or to prevent, diagnose, or treat illness. Other definitions are more expansive, including even the first use of a new intervention without a formal plan or any type of comparison. Our definition is limited to the activities that could be eligible for having at least some patient care costs reimbursed under Medicare. This definition includes:

- interventions to prevent, diagnose, and treat disease;
- drugs and devices; surgical, manipulative, and other procedures; diagnostic laboratory tests, scans, and examinations; dietary, behavioral, and psychological techniques;
- interventions associated with any illnesses or conditions (not limited to specific ones such as cancer, AIDS, and heart disease);
- new interventions, as well as "standard" interventions that have been used in a limited way (or extensively, but about which not enough reliable information is available).

This definition does not include a new intervention applied by a single practitioner to a single patient in what might be the earliest phase of innovation. It applies only after a protocol describing the intervention, the types of patients, the endpoints, and other details has been developed to find out whether an intervention is safe and effective for a given condition. For all types of interventions, the definition encompasses the comparative trials that are needed to produce definitive evidence, and for drugs and devices, in particular, the definition also includes early trials that may be focused mainly on safety and have only one intervention group ("single-arm trials," i.e., they do not compare outcomes in one group versus another; they simply observe what happens when the intervention is given).

The central importance of research to medical practice is relatively new. In the past, when few effective medical interventions were available and most cost relatively little, the lack of precise information about their effects made less difference to the public's health or wealth (although people were adversely af-

fected by interventions that were not only ineffective but harmful). What is often cited as the first deliberately randomized clinical trial took place in the late 1940s to determine the efficacy of treating tuberculosis with a newly invented antibiotic, streptomycin. Over the years, occasional tragic complications associated with new drugs or devices led Congress to authorize regulatory agencies to mandate clinical trials to determine safety and efficacy before drugs and devices could be marketed in the United States. Although at least a minimal level of evidence from clinical trials is required for the legal marketing of drugs, biologics, and medical devices, information on whether a new drug or device works better than an old one is not required by law. And there is no such legal requirement to demonstrate safety or efficacy, to say nothing of superiority over existing procedures, for a new procedure that does not involve new commercial products. As a consequence, although many decisions are being made on the basis of sound evidence from clinical trials, the use of many medical interventions, old and new, does not rest on solid evidence. The new emphasis on evidence reflects the realization that intelligent decisions require substantial information that properly conducted clinical trials can provide.

CURRENT MEDICARE REIMBURSEMENT RULES RELATING TO INVESTIGATIONAL MEDICAL SERVICES AND CLINICAL TRIALS

The legislation establishing the Medicare program states:

> Notwithstanding any other provisions of this title, no payment may be made for items or services which are not reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member.

Since the inception of the Medicare program in the mid-1960s, the phrase "reasonable and necessary" has guided Medicare reimbursement. Although little explicit policy has been issued on the topic, this clause has been the basis for excluding reimbursement for at least some routine patient care in clinical trials. This Medicare interpretation has historical roots in the private insurance sector, whose policies in the 1960s and still, in 1999, exclude coverage of services in clinical trials (GAO, 1999). Most private insurance plans have excluded coverage of services in clinical trials on the basis that the treatment is "experimental" or "investigational," although the language does not explicitly mention clinical trials (GAO, 1999).* However, Medical Directors report that they often approve

*The language regarding experimental and investigational treatment in most health insurance contracts is similar to the following, which is taken from a current Group Service Agreement of CIGNA Healthcare of New York, Inc.: "By way of example, but not limita-

payment for care in clinical trials on a case-by-case basis. In addition, private insurers have been involved in supporting specific trials (e.g., the Blue Cross/Blue Shield Association was instrumental in initiating a trial of high-dose chemotherapy with bone marrow transplant rescue for women with advanced breast cancer).

Despite the lack of an explicit Medicare policy excluding reimbursement for routine care in clinical trials, HCFA has signaled its intent in several ways in recent years. In 1993, HCFA asked the Office of the Inspector General (OIG) of the Department of Health and Human Services (DHHS) to investigate whether hospitals were billing Medicare "improperly for millions of dollars worth of surgical procedures involving unapproved medical devices," specifically investigational pacemakers, defibrillators, and other cardiac devices in clinical trials. In a 1996 hearing of the Subcommittee on Investigations of the Senate Committee on Governmental Affairs, an official of the OIG reported their finding that most of the 130 hospitals they investigated had, in fact, improperly billed Medicare for implanting investigational devices. The Inspector General urged HCFA to recover these "overpayments" from the hospitals (Hartwig, 1996).

What might not be clear from the OIG account is that it was not only payment for the investigational devices themselves, but for the implantation *procedures*, as illustrated by comments of others, including at least one HCFA official.*

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tion, the following are specifically excluded services and benefits: "Medical, surgical or other health care procedures and treatments which are experimental or investigational, as determined by the HEALTHPLAN Medical Director in accordance with consensus derived from peer review medical and scientific literature and the practice of the national medical community, including (1) any procedures or treatments which are not recognized as conforming to accepted medical practice; (2) any procedures or treatments in which the scientific assessment of the technique, or its application for a particular condition, has not been completed or its effectiveness has not been established; and (3) any procedures or treatments for which the required approval of a government agency has not been granted at the time the services are rendered." GAO (1999) confirmed in interviews with health plan Medical Directors that this language is interpreted to exclude routine care in clinical trials. Most Medical Directors interviewed by GAO also stated that they make exceptions and do cover clinical trial costs on a case-by-case basis.

*This point was made clearly by a HCFA official testifying at the same hearing (Ault, 1996), who stated:

> Medicare's program instructions on medical devices, which were governing until November 1, 1995, were added to the Medicare Hospital Manual, the Carrier Manual, and the Intermediary Manual in 1986. These instructions stated clearly that "medical devices which have not been approved for marketing by the FDA are considered investigational by Medicare and are not reasonable and necessary." The instructions went on to explain that payment would not be made either for the devices or the procedures and services performed using the devices. Additional instructions in these manuals dealing more generally with

By the time of the hearing, HCFA had already changed its policy to allow reimbursement for patients in certain trials involving investigational devices (FDA "Category B" devices, which are refinements of, or very similar to, approved devices) but not for trials of other types of interventions. The clearest indication that routine patient care is not reimbursable in other types of trials is found in a 1997 report by the General Accounting Office (GAO, 1997) on reimbursement by HCFA for Medicare beneficiaries in cancer clinical trials. GAO found that reimbursement was, indeed, occurring without HCFA's knowledge. In responding to GAO's draft report, HCFA reported that their actuaries had "nearly doubled their estimates of the extent to which Medicare mistakenly reimburses claims for routine patient care costs. Under HCFA's current policy, any reimbursement for care associated with a cancer clinical trial would be made in error" (GAO, 1997).

HCFA has not issued any new language to change clinical trial reimbursement policy since the 1995 change for trials involving Category B medical devices, and no HCFA statements contradictory to what is presented here were found in the course of this study.

The 1995 agreement between HCFA and FDA constitutes the only formal statement of policy about reimbursement of routine patient care costs in clinical trials, authorizing reimbursement for those costs in most trials of investigational medical devices.

THE STATUS QUO IN REIMBURSEMENT

There is relatively little information about how the costs of patient care in clinical trials are actually paid, and the extent to which insurers are paying these costs, either knowingly or unknowingly. What information is available suggests that a sizable proportion is paid for by insurers, including HCFA. This conclusion derives from:

- direct evidence from one study that HCFA has paid unknowingly for most routine care of Medicare beneficiaries in certain cancer trials (GAO, 1997),
- evidence that, in the past (before the 1995 change in policy) HCFA unknowingly paid millions of dollars in reimbursement for Medicare beneficiaries in medical device trials (Hartwig, 1996),
- interviews with clinical trial investigators conducted for this study, in which they uniformly acknowledged submitting claims for reimbursement to HCFA and other insurers for routine patient care in trials and getting them paid,

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all noncovered services also state that any services related to a noncovered service are excluded from coverage.

The official also made clear in his testimony that Medicare would have paid for patients in the trials to have the standard device implanted.

- interviews with private-sector clinical trial sponsors conducted for this study who stated that, while they do cover the costs of "protocol-induced" services, in general they do not provide money to pay for routine patient care; they expect providers to bill insurers for those costs,
- deduction, given the lack of another obvious source of payment for most routine care in trials, and
- lack of evidence from any source that HCFA and other insurers are *not* reimbursing for this care.

Providers violated no clear rules in billing for routine patient care costs in clinical trials because no such rules were ever codified. But the gap between the *impressions*—and statements of responsible HCFA officials—regarding reimbursement rules on the one hand, and reimbursement *practices* on the other hand, should be ended.

RECOMMENDATIONS

RECOMMENDATION 1. Medicare should reimburse routine care for patients in clinical trials in the same way it reimburses routine care for patients not in clinical trials.

This principle applies to payments for physicians and other providers, routine laboratory and other diagnostic tests, and any other services that comprise routine care for a given patient. All coverage and medical necessity rules and all other restrictions that apply to patients not in clinical trials would apply to care in clinical trials.

The committee recommends a broad definition of clinical trials—including all phases and legitimate designs and all sources of sponsorship (government, industry, or other)—all of which should be equally eligible for reimbursement. This definition does not mean, however, that any treatment simply called a "clinical trial" would qualify for reimbursement. To qualify, a clinical trial must have a written protocol that describes a scientifically sound study and have been approved by all relevant IRBs before participants are enrolled. HCFA should articulate criteria for an acceptable trial and IRB review, which investigators would apply to determine whether their studies are eligible for reimbursement. (HCFA could state the criteria in terms of "current NIH standards," e.g., rather than stating specific study characteristics.) The committee recognizes that controversies surround both the quality of current clinical trials and IRBs, but holds that these issues are being addressed in various ways by DHHS and other sectors of government, and should not be addressed routinely in HCFA's reimbursement decisions.

Medicare should reimburse *routine patient care* costs, but not *all* costs in clinical trials. Medicare should *not reimburse* the costs of experimental inter-

ventions (except category B devices for which reimbursement is allowed under agreement with FDA, and certain procedures as described in recommendation 2), of data collection and record keeping that would not be required but for the trial, or of other services to clinical trial participants necessary solely to satisfy data collection needs of the clinical trial ("protocol-induced costs"). These costs should remain the responsibility of research sponsors, private and public.

Medicare should continue its current practice of reimbursing costs of treating conditions that result as unintended consequences (complications) of clinical trials.

RECOMMENDATION 2. HCFA should reimburse surgeons (or other practitioners) for treating patients in randomized clinical trials involving procedures that are variations or modifications of accepted procedures, or new uses for accepted procedures.

Under the current interpretation of Medicare reimbursement rules, the committee believes that surgeons and others performing surgical or other procedures in trials might not be eligible to be reimbursed for those services. Therefore, the committee recommends that procedures that have become widely accepted as a part of standard medical practice, but which, as part of a clinical trial, are being rigorously evaluated, or are being modified or applied for new indications to determine the incremental risks and benefits, should be eligible for reimbursement at the rate for the standard procedure. Conversely, *types* of procedures for which initial questions of safety and efficacy have not been resolved would not be eligible for reimbursement.

Unlike the basic recommendation regarding routine patient care costs, which applies to *all* clinical trials, this recommendation would limit reimbursement to *randomized* trials (the equivalent of "phase 3" trials for drugs and devices). The committee believes this limitation is appropriate in order to avoid providing reimbursement for uncontrolled experimentation by practitioners. The introduction of new drugs and devices is governed by FDA under a formal system that involves phased trials. In contrast, the introduction of new procedures is not governed by any regulatory authority. In their early phases, procedures are modified or tried for different indications in clinical practice, but rarely in formal trials. However, once a new or modified procedure has been defined and developed to the point that it is distinct enough from the predicate procedure, it may be tested against the standard treatment (the predicate procedure or other accepted treatment) in a formal randomized trial. Medicare should provide reimbursement to the surgeon or other practitioner for treating patients in such trials.

Further clarification may be needed to make clear the committee's intent with regard to reimbursement for procedures on patients in clinical trials. The committee is expressing no judgments about when trials of procedures should or should not be carried out, or who should be involved in them if they are. This

recommendation is not intended to influence the criteria or processes HCFA uses to decide on *coverage* of new procedures under usual medical care. It applies only when a trial of a procedure is being done—for all the reasons that trials are done—and claims for *reimbursement* for the procedure are submitted by practitioners.

HCFA's initial task in implementing this recommendation will be to develop definitions for classifying procedures analogous to "category A" and "category B" devices. These definitions describing what is and is not allowed will be applied in the field when claims are submitted. HCFA should *not* be required to rule routinely on the eligibility of procedures before bills may be submitted. In the same way that providers are responsible for following reimbursement rules for all services under Medicare, they will be responsible for applying the rules appropriately in the case of procedures in clinical trials. Fiscal intermediaries and carriers audit these interpretations by providers in clinical trials, as they now audit bills from providers who are not in clinical trials. Advice or an interpretation could, of course, be requested of HCFA at any time. In addition, HCFA would retain the right to initiate its own review, without being asked, if it believes there is an issue to be explored, to carry out a random check, or for another reason.

The committee recognizes that creating definitions that neatly separate "category A" and "category B" procedures will not be simple, and disagreements are inescapable about where the line between "A" and "B" should be drawn in specific cases.

Wherever the separation lies, some procedures will fall into a "gray zone." HCFA can narrow the gray zone by applying the definitions to a wide range of real and hypothetical procedures, and stating whether the procedures would or would not be eligible for reimbursement. To deal with cases in which uncertainty remains, HCFA should set up a process to rule quickly on reimbursement eligibility. With accumulated experience, the number of gray zone cases should decline, as has been the case with FDA classification of devices into categories A and B.

The committee has not attempted to specify an institutional mechanism under which HCFA might carry out the tasks required by this recommendation. However, the committee notes that the new Medicare Coverage Advisory Committee* might provide the needed expertise for the task of defining categories A and B and ruling quickly on "gray zone" cases that arise.

RECOMMENDATION 3. For claims submitted in accordance with both the fundamental recommendation (No. 1) and the special

*The Medicare Coverage Advisory Committee (MCAC) was established by HCFA to provide guidance on coverage issues. The 120-member committee will function through specialty panels of not more than 15 members each. The MCAC had its first meeting in September 1999.

recommendation for procedures (No. 2), no special precertification by HCFA, or any other administrative process, should be required of clinical trial researchers or providers participating in trials before they submit claims for covered services. Claims should be submitted in the same way they are for treatment outside of trials.

Practitioners and institutions would be expected to submit reimbursement claims for services to patients in clinical trials under rules outlined in Recommendations 1 and 2. With a clear statement of reimbursement policy, such claims should pose difficulties no different from those arising in the administration of coverage and reimbursement rules for claims for care outside of trials.

Investigators and providers would not be routinely required to submit documentation about the trial to HCFA, but HCFA could, at any time, request such documentation to confirm that the clinical trial meets current standards for scientific merit and has the relevant IRB approval.

RECOMMENDATION 4. If Medicare or trial sponsors fail to cover clinical care costs, patients should not be billed for those costs above what they would pay if they were not in a trial.

This recommendation is not one that can be enforced as part of a reimbursement policy by HCFA; however, the committee believes it is an important principle that could be adopted by clinical trial sponsors and investigators. It also could be incorporated in any legislation passed to implement the committee's recommendations.

RECOMMENDATION 5. Medicare members of managed care plans should have the same reimbursement eligibility for care in clinical trials as those enrolled in fee-for-service Medicare, but not *beyond the limits of the managed care contract.*

Nearly one Medicare beneficiary in five belongs to a capitated plan—an HMO or some other form of managed care. That number is likely to increase over time. It is vital, therefore, that the committee's recommendations carry over to patients served outside traditional Medicare. Managed care plans must provide all benefits offered under traditional Medicare. (Most offer additional benefits, including coverage of outpatient drugs.) Accordingly, the committee recommends that managed care plans be required to offer Medicare beneficiaries access to clinical trials involving services available within their networks. If, for example, a plan routinely covers a particular drug, it should cover it in a trial, as well. If the plan limits the choice of drugs to those listed on a formulary, the plan should not be required to cover a nonformulary drug in a trial.

Under point-of-service plans, patients should have the right to go outside the managed care network to participate in a trial, under the terms stipulated in the plan for point-of-service care, but no such right should be inferred under plans that limit enrollees to the plan's providers. This recommendation is not comprehensive, but is suggestive of a policy for managed care. Full implementation will require additional thought when HCFA adopts a clinical trial reimbursement policy, but the committee urges that the new policy not create obstacles to clinical trial enrollment for beneficiaries in managed care.

RECOMMENDATION 6. In addition to providing routine coverage through the proposed policy, the committee urges HCFA to use its existing authority to support selected trials and to assist in the development of new trials. In selected clinical trials, the committee believes that HCFA should do more than pay for routine patient care according to the recommendations already stated. Medicare should (1) provide additional reimbursement in a limited number of trials and (2) identify emerging or current methods of care of particular importance to the Medicare population and work with other organizations to initiate trials.

Researchers should be able to apply to HCFA for reimbursement above routine rates in cases meriting special treatment. Such trials could include some interventions that do not qualify under the basic recommendations, such as "category A" procedures, primary and secondary screening, diagnostics, and interventions not usually covered by Medicare (e.g., behavioral interventions). The rationale for extending coverage is straightforward. HCFA has a large stake in determining whether more effective or less costly alternatives to current interventions may exist, preventing ineffective procedures from becoming common practice, and facilitating the identification of innovations that would benefit the Medicare population.

For example, a behavioral intervention, which normally would not be covered, might replace a more expensive drug or surgical intervention to the benefit of both patients' health and Medicare finances. HCFA should have sole authority to decide whether to extend coverage and should make such determinations expeditiously. The committee assumes that only a few trials would be appropriate for such exceptional treatment each year.

In the case of interventions of particular importance to the Medicare population, HCFA should collaborate with the National Institutes of Health (NIH) or others to see that appropriate trials are fielded. HCFA should cover routine patient care costs for these trials along the lines of the committee's basic recommendation. It could also fund other costs as well, under the exceptions procedure described in the preceding paragraph. But the objective is to encourage trials, not necessarily to pay for them. Such an active role would not be new for HCFA. This recommen-

dation follows the model of the ongoing study of lung volume reduction surgery, which grew out of collaboration among HCFA, NIH, and the Agency for Health Care Policy and Research (AHCPR), at HCFA's initiative.

RECOMMENDATION 7. Every trial for which some Medicare reimbursement is sought should be entered into a national registry of clinical trials.

Reimbursement claims should bear an identification number assigned by the registry. A registry will facilitate *ex post* audits of reimbursement claims, HCFA's main tool for monitoring clinical trial coverage and detecting potential abuse. But identification of a claim as part of a clinical trial should not be relevant to the reimbursement decision.

The committee recognizes that implementation of this recommendation will necessarily take some time. Therefore, the committee's recommendations regarding reimbursement of routine patient care costs do not hinge on the existence of a clinical trials registry. Until a registry is in operation, reimbursement claims for interventions associated with a clinical trial should be denoted on the form, in a manner HCFA specifies. However, a registry would contribute to uniform administration and permit HCFA and others to carry out analyses of clinical trials and the costs of implementing the recommendations put forward here. It should, therefore, be put in place as quickly as possible.

Ideally, such a registry should include all publicly and privately sponsored trials before they begin accruing patients, thereby providing a link to all claims for Medicare patients in clinical trials. If the goal of creating such a registry is accepted, the practical question of how best to achieve it must be addressed. It would be possible to build upon the registry currently under development at NIH by broadening the definition of trials to be included and consulting widely on how to present data. Or a separate registry could be created.

Whether the registry should operate within NIH or elsewhere merits consideration. The design of the NIH registry has been underway for some time. Its designers claim that it will be functioning, at least in part, by early 2000. Redirecting any ongoing effort will be difficult for reasons that are well understood. If it were concluded that converting this limited registry into an inclusive national registry would be needlessly cumbersome, the creation of a separate comprehensive registry, serving objectives beyond those of NIH, or even of HCFA, should be explored. The committee urges the Secretary of DHHS to examine this issue promptly, set a timetable for completion of a registry, and seek adequate funding for it.

ADMINISTRATIVE AND COST IMPLICATIONS

Implementation of the committee's recommendations would likely cause some increase in administrative costs to HCFA. In making its recommendations, the committee strove to minimize potential administrative burdens. It is the committee's assertion that any added administrative costs required by institution of this reimbursement policy will be small.

Effects of the committee's recommendations on benefit costs are more important and far more uncertain. For several reasons, the cost impact of these recommendations is likely to be quite small. First, the recommended reimbursement policy is designed to limit payments for an individual to roughly the cost of "standard care" for which he or she would be eligible if not enrolled in the trial. This limitation does not imply that each individual would have chosen standard care that cost the same as the care in the clinical trial, so in individual cases, the cost of actual care in the trial might be higher or lower than forgone care outside the trial. Although the incremental cost of routine care in clinical trials is not known with certainty, it is almost surely small in comparison to the costs otherwise incurred by Medicare. Some clinical trial groups claim that the costs of treating patients in some trials may be less than treating them outside of trials. Second, clinical trials hold the long-term prospect of identifying ineffective interventions, which would fall out of favor in the clinical community, or could be excluded from coverage, in some cases saving Medicare dollars.

Finally, only a tiny fraction of Medicare patients participate in clinical trials. No accurate count of clinical trial participants at any point in time exists, but the Lewin Group has estimated that about 265,000 people in the United States participate in clinical trials each year, including about 161,000 Medicare beneficiaries—less than 0.5 percent of the 38 million Medicare enrollees in 1997 (Dobson and Sturm, 1999). Clearly, the proportion of Medicare beneficiaries in clinical trials is quite small. The available evidence suggests that Medicare already pays 50 to 90 percent of routine patient care in such trials. These estimates take into account both costs for which no reimbursement is sought, and claims that are submitted and rejected.

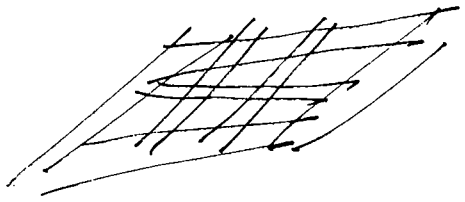
The largest effect on Medicare costs could come from the speedier determination of the efficacy of innovative or experimental procedures, drugs, and devices. Some will be cost increasing. Others will be cost reducing. Whether the net effect is to raise or lower total Medicare spending, the speedy determination of what works and what does not work will benefit the Medicare population and the nation as a whole.

CONCLUSION

Clinical trials are integral to modern medical care and to the progress of medical science. Although HCFA has issued little explicit policy about pay-

ment for routine care for patients in clinical trials, the Medicare statute has been widely interpreted to exclude reimbursement for such care. However, evidence is ample to suggest that providers submit claims for routine care for Medicare beneficiaries in trials without noting the existence of the clinical trial, and HCFA's financial contractors usually pay them. The thrust of the committee's recommendations is that nothing should be done that would materially curtail Medicare's reimbursement for routine patient care costs for patients in clinical trials. On the contrary, HCFA should encourage such trials and even extend reimbursement in a limited number of specifically approved exceptional cases. To achieve these goals, the committee believes that HCFA should assure patients in clinical trials the same reimbursement of routine patient care that is available to patients who are not in trials. Extending reimbursment to certain procedures that represent modifications of current practice and distinguishing those from procedures for which risks and benefits are largely unknown will require some additional effort by HCFA, but it is an essential component of the committee's recommendations. The fundamental recommendation—reimbursement independent of trial participation—should be implemented relatively easily.

bypass budget



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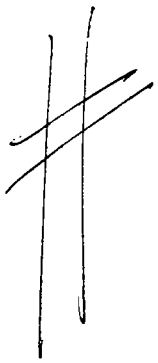

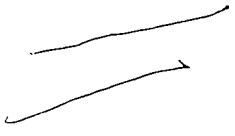

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TITLE: Better Fundamentals -- Not "Razzle Dazzle" -- Needed in Cancer Research on the Elderly

AUTHOR: Laurent Castellucci

TEXT:

Cancer is a disease of aging. Over 60% of all newly diagnosed cancers and 69% of all cancer deaths in the United States occur in people over 65 years of age. Americans over 65 are 10 times as likely to get cancer as are younger Americans.

But despite the disease's age-related aspects, researchers know surprisingly little about cancer treatment in the elderly and the elderly appear to be vastly underrepresented in **clinical trials.**

Kathy Albain, M.D., professor of medicine of Loyola University Medical Center and chair of the Committee on Women and Special Populations at the Southwest Oncology Group presented study results at the May meeting of the American Society of Clinical Oncology, that showed just how underrepresented the elderly are.

SWOG, a cooperative **clinical trial** group headquartered in San Antonio, Texas, concluded that the elderly represented only 25% of the 15,500 trial participants studied, despite representing some 63% of the cancer patient population at that time -- the mid-1990s.

The SWOG study was originally designed to look at the **participation rates** of African-Americans and women in **clinical trials,** special populations who have often been underrepresented, to improve their enrollment rates in trials.

"I don't think that in general people think of the elderly as a special population," Albain said. But as the data came in, the researchers noticed that while there wasn't significant underrepresentation for either of those two populations, the numbers on the elderly were striking.

"There is no active effort to exclude the elderly," Albain said, "But obviously something is going on. Why are so few being accrued?"

It is a question the SWOG study was not designed to answer, and one that very little research has addressed. It is a question Albain wants to explore in the future.

Barriers and Biases

Hymand Muss, Ph.D., associate director of the Vermont Cancer Center in Burlington, said there are probably many reasons why the accrual rates are so low.

Some of the barriers the elderly face are the same ones that others face concerning **clinical trials,** but are are just more pronounced. Many of the elderly no longer earn a steady income, and depend on Medicare for health insurance. Medicare does not cover the drugs and only covers standard care, not experimental techniques. Even examining standard treatments in elderly patients can be difficult, Muss said.

"You write it into a protocol, and it automatically becomes 'experimental' and Medicare doesn't want to touch it," said Muss.

Other Hurdles

Both Albain and Muss pointed out that there are barriers restricting a doctor from accepting elderly patients into some **clinical trials.** Many protocols have exclusion criteria based on the overall health of the patient. Elderly patients are far more likely to be suffering from some additional disease besides cancer that would exclude them from these trials. The presence of this comorbidity makes things difficult for researchers. It weakens the patients and can add confounding factors to any analysis.

But there are also biases held by both patient and doctor that can prevent the elderly from participating in trials, said Muss. Many patients are unclear on what goes on in a **clinical trial,** and assume they will be taking an unnecessary risk. Some do not wish to be a burden to their families, or doubt that any treatment will do them much good.

The attitude that it may not do much good anyway is one that doctors can succumb to as well, but is less and less true. Census data from the Department of Health and Human Services show that the life expectancy of a 70-year-old woman is 15.5 years. That of an 80-year-old, 9.2 years.

Teasing out the real reasons and how to address them will be complex research. "You can't snap your fingers and just get answers," Albain said.

The lack of elderly participation in **clinical trials** has created a vicious circle. There are few data on how older patients respond to most therapies, even the conventional ones. Meanwhile, many treatment studies are of aggressive treatments, such as bone marrow transplants and strong chemotherapy, not focused on elderly patients. Without firm knowledge of how elderly patients react, Muss said, "a lot of doctors are, with good reason, nervous about including them."

Muss argued that what needs to be done are studies that can give baseline data on the elderly. Before getting to the cutting edge treatments, researchers need to amass data on the treatments that are known to save lives: adjuvant therapy for colon cancer and breast cancer chemotherapies that are known to work. Muss would like a cohort of elderly patients that have been studied so that doctors can say, "Look, here is what they can handle; here are the toxicity problems; here's what isn't effective."

"We need the Vince Lombardi touch. Fundamentals. We don't need the razzle dazzle," said Muss.

There has been a move to start providing those fundamentals. The National Cancer Institute and the National Institute on Aging have begun attempts to stimulate further work in this area. Both institutes announced in October 1998 a joint program to make available $ 2.5 million a year for the NCI's **Clinical Trials** Cooperative Groups to conduct trials that will increase knowledge on the elderly and in May 1998 began a program on cancer pharmacology and treatment in older patients.

The "Right Place"

Rosemary Yancik, Ph.D., chief of the cancer section of the geriatrics program of the NIA, is encouraged with the response. "We would not have the wherewithal and expertise to do it alone. NCI had the right people in the right place at the right time."

Yancik said that the principle behind all of these programs is to help gather the kind of data needed to make best use of treatments for the elderly. "They must recognize the heterogenicity among the elderly," Yancik said. Like other patients, the elderly can't simply be lumped together and generalized about.

Muss also sees the issue of comorbidity as all the more reason to do studies.

"We need to know a lot more about the interaction of comorbidity," Muss said. "If you have bad heart disease and then you get breast cancer, how do we figure out the trade offs? What do I tell you if you're sitting in my office? Is it worth it giving you 6 months of chemotherapy if you've had two by-passes? We need models, and data, to figure this out."

An Aging Population

The population of the United States is living longer, and healthier. A study by the U.S. National Center for Health Statistics released in late 1998 put the U.S. life expectancy at an all-time high of 76.5 years. As the population ages, the elderly are going to be an even larger proportion of the cancer patient population than they are now.

"We're a country that's been blessed, despite complaints, with a pretty good health care system," Muss said, "As people get older and healthier, we will have less comorbidity among the aged." But an increasingly fit elderly population currently presents problems for clinicians who simply do not have good data to work with.

"You have a healthy 72-year-old woman with breast cancer in front of you," Muss asked, "What do you tell her?"

GRAPHIC: Picture 1, Dr. Kathy Albain; Picture 2, Dr. Hymand Muss

J Natl Cancer Inst 1999; 91: 114-117

January 20, 1999

SECTION: NEWS

LENGTH: 1466 words

TITLE: What Ever Happened To . . .?: A 10-year Retrospective

AUTHOR: Nancy J. Nelson

TEXT:

One way to measure the progress of cancer research is to begin at some past point in time and see if things have changed. 1988 is the year that the *News* section of *Journal of the National Cancer Institute* began. What has happened in the 10 intervening years to the stories first reported back then?

Some issues don't seem to go away. In May 1988, the *News* reported that the U.S. Surgeon General C. Everett Koop, M.D., after releasing a U.S. Public Health Service report on American nutritional habits, encouraged Americans to reduce their consumption of cholesterol, fat, and alcohol, and to increase the amount of fiber in their diets.

Likewise, in this year's Oct. 1 issue of *Cancer*, Susan M. Krebs-Smith, Ph.D., of the National Cancer Institute's Cancer Surveiliance Research Program in Bethesda, Md., reporting on trends in American dietary habits from 1971 through 1995, found American dietary habits wanting. For example, data from the most recent survey showed that the 16 grams of dietary fiber that adults consumed each day remain well below the recommended 20 to 30 grams per day. Equally discouraging was a study reporting that 50% of the energy in children and adolescents diets came from fat and added sugars.

Another 1988 *News* item had a familiar ring: A forum of oncologists met to discuss **low participation** in **clinical trials** at the annual meeting of the American Society of Clinical Oncology in May. The *News* section wrote, "This **low participation** rate of 2.5% hampers the development of new cancer therapies according to several oncologists at the meeting." Today, the rate is about 3.0%.

Prevention Trials

Another "same-old, same-old" story discussing the feasibility of prevention trials appeared as a commentary in the Nov. 16, 1988, issue of the Journal. The author, M. Zelen, Ph.D., from Harvard's School of Public Health, in Boston, was opposed to conducting prevention trials unless intermediate end points could be found. He argued that the size and length of these trials will be very expensive. "Using incidence as a primary end point will require much larger numbers of participants than therapy trials and will need long-term follow-up," said the author.

Similarly, at a recent American Association of Cancer Research meeting, Frank L. Meyskens. M.D., director of the University of California Irvine Clinical Cancer Center, reported that "the major limitation in the development of micronutrients [vitamins and minerals] as chemoprevention agents has been the unavailability of intermediate biomarkers of cancer, making phase III trials very long and expensive."

"So far a validated marker predictive for subsequent cancer development is not available for any cancer," said Meyskens.

Knowledge has been advanced, however, in several areas. Studies to look for a link between silicone gel implants and breast cancer were just getting under way in 1988. Now with the completion of nine studies, Louise A. Brinton, Ph.D., of NCI's Division of Cancer Epidemiology and Genetics in a review article in the Sept. 17, 1997, issue of the Journal, commented that the accumulated epidemiological evidence suggests that breast cancer risk might actually be reduced among women with implants.

Although she cautioned that the data will become clearer when several ongoing follow-up studies, including one being conducted by NCI, are complete, she concluded that "there is currently little evidence to support the notion that breast implants increase the risk of subsequent breast cancer."

Gene Therapy

And the answers are now in for two more cancer treatments. In 1988, the National Institutes of Health's Recombinant DNA Advisory Committee approved the first gene therapy protocol for transferring genetic material into humans. Researchers were trying to correct a single gene defect in a gene, adenosine deaminase (ADA), in two girls, by adding copies of a normal gene to the patients' T cells. However, time has shown that neither of the patients could make enough of the normal enzyme with the gene therapy alone.

Similar results have been found in the 100 U.S. gene therapy trials launched since then involving therapeutic approaches to cancer. These results led a blue-ribbon panel of scientists to conclude (in a 1996 report to assess NIH's investment in gene therapy research) that the most common approach for delivering genes to cells, viral vectors, cannot yield high enough levels of protein expression for therapeutic benefit and there is no flexibility to change the level of expression once the gene is in the target cell.

In July 1988, NCI's National Cancer Advisory Board approved funding for the completion of phase III trials for another type of cancer treatment, high energy neutron therapy -- that is, instead of treating tumors with x-ray radiation, researchers were treating them with high energy nuclear particles. Frank J. Mahoney, Ph.D., acting chief of NCI's Radiotherapy Development Branch, said the results are interesting, but "nothing spectacular . . . . It seems to work for a small number of rare tumors. For example, for some reason neutrons are better for salivary gland tumors. There's also some controversy over whether they're better for prostate cancer at certain stages."

He said that there are now three places to receive treatment with neutrons; the University of Washington in Seattle, the Fermi Laboratory outside Chicago, and the Gershen Radiation Oncology Center at Harper Hospital in Detroit.

Also, the *News* in July 1988 announced the launching of an intense anti-smoking intervention trial known as COMMIT (Community Intervention Trial for Smoking Cessation). The findings, reported in the February 1995 issue of the *American Journal of Public Health*, showed that the intervention -- using the media, community events, worksite programs and smoking cessation resources -- helped light-moderate smokers stop smoking, but were unable to help heavier smokers end their addiction. Currently, NCI's anti-smoking programs are directed more toward policy changes on a state-wide level; creating smoke-free facilities, restricting youth access, and advertising.

In spite of the success of the COMMIT program, the current smoking trends in the U.S. do not augur well. Donald Shopland, from NCI's Smoking and Tobacco Control Program noted that the smoking rate for adults had been declining for over 20 years until 1991. "But since 1991 smoking prevalence among adults has not changed, and among kids it has been going up."

Shopland said that the adult prevalence has been pretty steady at 25% during the 1990s and among high school age children, the rates are as high as 20%. "A lot of things are not too encouraging," he mused.

Sequencing Genes

Finally, the *News* reported in November 1998 that after 3 years of extensive debate, the NIH established the Office of Human Genome Research. At a cost of $ 200 million per year for 15 years, the Genome Project announced it would sequence the entire human genome and make the data freely available to everyone.

Looking back over those 10 years, Elke Jordan, Ph.D., deputy director of the now National Human Genome Research Institute seemed very pleased with how well things have worked out.

The sequencing is still within budget and is expected to be finished 2 years ahead of schedule.

"At the same time that it's gone well, it's more complicated than we expected," said Jordan. "The rapid growing interest of industry in carrying out mapping and sequencing for their own purposes has been a surprise. They are soaking up skilled people and, not suprisingly, in many cases, want to patent and protect the information in proprietary ways."

However, one of the most gratifying innovations, Jordan said, was the genius of Nobel laureate James D. Watson, Ph.D., the first associate director of the Office of Human Genome Research, in announcing even before the program began, that 3% of the project would be spent in addressing the ethical, legal, and social implications of the research. Because of that program, known as ELSI, the Working Group on the Ethical, Legal and Social Implications of Human Genome Research, the issues have become clearer and the debate better informed.

"Initially the public was concerned that we were going to clone people or create monsters, which at the time seemed unreal," said Jordan. "Now the public realizes that the real issues are more practical ones -- issues of privacy, confidentiality, protection from discrimination, how the information will be used in a clinical setting, and educating professionals and the public who will use the information. Because of the ELSI program, we have all matured in our thinking about these problems."

GRAPHIC: Picture 1, Dr. C. Everett Koop; Dr. Louise A. Brinton

1988, U.S. Department of Health and Human Services;
Journal of the National Cancer Institute

J Natl Cancer Inst 1988; 80: 619-620

July 6, 1988

SECTION: NEWS

LENGTH: 1261 words

TITLE: Recruiting Patients for **Clinical Trials**

TEXT:

Of the nearly 1 million newly diagnosed cases of cancer each year, only 25,000 patients become involved in National Cancer Institute (NCI)-sponsored clinical treatment trials. This low **participation rate** of 2.5% hampers the development of new cancer therapies within a reasonable time frame, according to several oncologists at the annual meeting of the American Society of Clinical Oncology (ASCO) in May.

"It is reasonable to assume that 10% of the patients with common tumors, e.g., breast and colon cancers, could go on **clinical trials,**" NCI Director Vincent T. DeVita Jr., M.D., said during a press conference. "It would allow us to accrue enough patients to open and close a study within a year and then have a 5-year follow-up and be able to answer questions fairly emphatically at that time."

Currently, less than 2% of the breast cancer patients and only about 1% of those with colorectal cancer participate in **clinical trials.**

In the past, treatment studies generally have needed at least 3 to 5 years to accrue patients and another 5 years to find out whether a new treatment is better than standard care.

According to Robert E. Wittes, M.D., chief of the NCI's Cancer Therapy Evaluation Program, the field of cancer research has never been so rich in opportunity to develop new cancer treatments as it is now, not only in the rare tumors but also in common epithelial tumors of adults. "We're excited about the opportunity to make a real difference in outcome for cancers that affect large numbers of Americans," he said.

Calling patient accrual a high priority area, scientists discussed during an ASCO forum the problem of too few participants in **clinical trials** and proposed ways to resolve the problem. The speakers agreed that part of the accrual problem lies in physicians' unwillingness to enroll their patients in **clinical trials.** "We need to work with physicians to encourage those who already enroll patients in **clinical trials** to enroll more patients," stated ASCO President Charles Coltman, M.D., chairman of a major consortium of physicians and cancer centers who collaborate on a wide variety of patient studies. "In addition, we need to work to increase the overall number of physicians who enter their patients in studies."

According to Bernard Fisher, M.D., of the University of Pittsburgh, there are a lot of factors contributing to the reluctance of physicians to participate in these studies.

"What (physicians) learn in medical school and in their early practice stays with them. This is a very fast moving period in medical history. These physicians are busy taking care of patients and busy trying to give them good care. They can't afford to have their system interfered with," said Dr. Fisher, who heads the National Surgical adjuvant Breast and Bowel Project, one of the largest NCI-sponsored groups conducting **clinical trials.**

Time Consuming

Other speakers pointed out that **clinical trials** are often time-consuming for physician participants and

sometimes expensive for both physicians and patients. Particular problems with financing occur when third-party insurance carriers refuse to reimburse patients for expenses incurred as a result of participation in **clinical trials.**

According to Bruce A. Chabner, M.D., director of NCI's Division of Cancer Treatment, benefits for physicians exist and include educational advantages of group membership, intellectual stimulation, the discipline of doing studies on protocol, and the satisfaction and recognition of having participated in positive trials. "All of these are very tangible benefits," he said.

Dr. Wittes praised those physicians who participate in **clinical trials** on an unfunded basis, which he said is commonly done. "You people are really the unsung heroes of the program because you do it out of belief," he stated.

The problem of financing **clinical trials** is one that ASCO and NCI hope to solve by expanding the role of third-party insurance carriers and Health Maintenance Organizations in the research, the speakers said, adding that discussions with these groups are currently under way. "We need a national effort to better educate the private insurors," said Gary A. Ratkin, M.D., chairman of ASCO's Clinical Practice Committee.

The NCI also will work to reduce the paperwork involved for physicians. Says Dr. Wittes, "A major problem for physicians is that **clinical trials** take time, time to explain the trial to patients and to keep up with the paperwork. We're working on ways to help physicians deal better with both."

"However, the first step in solving the problem of poor patient accrual is to increase the number of patients who participate," Dr. DeVita said.

At a press conference, Dr. DeVita and other scientists announced NCI's new special initiative to increase the number of patients in **clinical trials.** The initiative is an educational and informational program aimed at increasing awareness of **clinical trials** among health professionals, patients, and the public.

Because it hopes to double the number of patients in **clinical trials** by 1992, NCI is identifying certain patient trials for special emphasis, based on how common that particular cancer is, the relative importance of the medical issue addressed by the trial, and the potential impact of a new treatment on cancer patient survival.

Target Trials

Five trials on colon, rectal, bladder, and non-Hodgkin's lymphoma are currently designated "highest priority." Each trial is based on small pilot studies, with small numbers of patients, which suggests that a new treatment might be better than standard treatments. To determine if this is true, NCI must initiate large-scale trials.

Hundreds of cancer centers and community hospitals nationwide have signed on to participate in these studies. Each study has a set of eligibility criteria that indicate the kinds of patients a study can accept, so that results can be compared and have scientific validity. There can be benefits for patients participating in trials. "If you're looking for a guarantee of a standard of care, the best way to get it is to go into a **clinical trial,**" Dr. DeVita said.

In designing studies in which treatments are compared, clinical investigators have two concerns: that all patients who participate receive the highest quality medical care and that rigorous scientific principles are followed to allow meaningful conclusions from the study. Not all patients in every study receive a new treatment. Some are in a group that may receive standard care (the best treatment generally available) for comparison to the new approach. Patients are assigned randomly to receive new or standard treatment.

"There's a vast, untapped resource of patient material out there," Dr. DeVita said. "We cannot put all patients in the country on **clinical trials** nor do we need to put all patients in the country on **clinical**

trials, but 10% would be enough to make some impact and would allow us to translate benefits more effectively."

A 23-page NCI booklet for patients, *What Are **Clinical Trials** All About?* is available free of charge by calling NCI's Cancer Information Service (1-800-4-CANCER).

Physicians can obtain information on **clinical trials** that are currently accepting patients through NCI's Physician Data Query (PDQ), a computerized cancer treatment database that is updated monthly. Access to PDQ can be gained through physicians' personal computers, through medical libraries, or by calling 1-800-4-CANCER.

The New York Times

June 2, 1988, Thursday, Late City Final Edition

SECTION: Section B; Page 13, Column 3; National Desk

LENGTH: 1475 words

HEADLINE: HEALTH: EXPERIMENTAL TREATMENTS;
Cancer Agency Seeks Patients for **Clinical Trials**

BYLINE: By PHILIP M. BOFFEY, Special to the New York Times

DATELINE: WASHINGTON, June 1

BODY:

The National Cancer Institute has begun a four-year drive to double the number of patients who receive experimental treatments, providing an opportunity for far more patients than ever before to receive the most advanced therapies for many forms of cancer.

The institute said that it was undertaking special recruiting to find more patients to participate in **clinical trials** to evaluate new therapies "because the current level of patient participation is inadequate for maximizing progress."

"We are not getting enrolled anywhere near the number of patients we need to get answers within a reasonable period of time," Dr. Vincent T. DeVita Jr., director of the cancer institute, said at a meeting of the American Society of Clinical Oncology in New Orleans last week.

The target by 1992 is to enroll 50,000 new patients in trials each year. While a major expansion, the trials would involve only a small fraction of the estimated one million Americans who develop cancer each year.

Such trials typically compare the effectiveness of an experimental treatment for a cancer, such as a new drug, a biological agent, or radiation therapy, with the effectiveness of the best standard therapy in use.

Patients Assigned Randomly

The main purpose of the trials is to find better treatments that will benefit all patients. But, from an individual patient's perspective, an important byproduct is the opportunity to receive the most advanced care available. The patients are assigned randomly to groups that receive either the best of the standard treatments or an experimental treatment that has given scientists some reason to believe it might be better.

Although cancer experiments are typically among the largest **clinical trials** conducted at medical institutions, only a small fraction of cancer patients participate. Currently about 25,000 patients a year enter the large **clinical trials** sponsored by the National Cancer Institute in which many institutions take part.

Thousands of additional patients participate in smaller trials sponsored by the institute or in trials sponsored by individual medical centers or drug companies. But even if all these patients are added, "You still end up with a very small percentage of the nation's cancer patients in **clinical trials,**" said Dr. Robert E. Wittes, the institute's associate director for cancer therapy evaluation.

Enrollment in Trials Varies

The percentage of available patients currently enrolled in **clinical trials** varies greatly from one type of

cancer to another, ranging from about 1 percent for colon and breast cancer, to 3 percent for acute non-Hodgkin's lymphoma, to 25 percent for leukemias and lymphomas, to 80 percent for one rare tumor, according to Government estimates.

Some cancers for which new treatments are most promising, such as colon and rectal cancers for which experimental drugs can be used in addition to surgery, have the lowest **participation rates** in **clinical trials.** Many of the trials the institute is beginning involve not simply testing a new drug, but rather testing the effectiveness of various new combinations of drugs, radiation and surgery.

Dr. Wittes said it was unclear whether patients, doctors or the system of conducting **clinical trials** was chiefly responsible for the low enrollment rates. "We think that patients and doctors could both stand some education," he said.

Dr. DeVita also expressed concern that the public is confused. "They think they are guinea pigs, that they will get nothing and we'll just watch their tumors grow," he said. "That's not the case."

Virtually all cancer patients have the option of applying to participate in **clinical trials** but few are aware of it, officials say. The cancer institute is urging all patients to consider, in consultation with their doctors, participating in **clinical trials.**

Patients Carefully Monitored

An advantage, the institute says, is that patients will receive the most advanced care, will have the satisfaction of helping themselves and future patients and will be carefully monitored. Patients may withdraw from the study at any time for any reason.

But the officials point out to patients that an experimental treatment could be worse than the standard treatment and could produce unanticipated side effects. Moreover, patients who want the experimental treatment may not get it because of the random assignment of patients to the new therapy or the standard therapy, and those who do get the experimental treatment may find that their insurance does not cover all costs.

Each study has eligibility criteria that may prevent some patients from participating. Other patients may find that there is no relevant study in their area of the country.

Cancer institute officials believe that doctors are often a major impediment to enrolling patients in trials. Some doctors fear they will lose their patients to other doctors. Others prefer to determine what treatment their patients receive instead of leaving it to the random process. And many doctors are reluctant to do the paperwork or take time to explain the trial to patients.

Promising Approaches Await

"Some physicians don't want to be bothered," Dr. Wittes said.

The prime reason for seeking more patients, officials say, is that "an extraordinary number of promising approaches" is waiting to be tested, including new drugs and biological agents, as well as new surgical procedures and new radiation therapy.

Moreover, the current testing program is taking far too long to provide useful answers, officials say. A recent important study of rectal cancer treatments took nine years to enroll 555 patients, and a colon cancer study took five and a half years to enroll 1,166 patients, the institute said.

In its recruiting drive, the institute will focus initially on enrolling more patients for studies of treatments for bladder cancer, colon cancer, rectal cancer and non-Hodgkin's lymphoma. The agency also has plans to seek breast cancer patients once a suitable trial is available. These cancers were given priority either because they affect large numbers of people or because they are "extremely responsive" to the latest therapies.

"We thought we'd get the system up and running with these and then broaden the whole issue to other cancers," Dr. Wittes said.

THE ACCELERATED SEARCH FOR NEW CANCER CURES

The National Cancer Institute is making special efforts to recruit patients for five high-priority trials of therapies against four kinds of cancer. The cancers were chosen because they affect large numbers of people and show signs of being especially responsive to these specific new treatment approaches.

RECTAL CANCER

Study 1, the treatment: Chemotherapy plus radiation therapy after surgery.

Goals: To evaluate a radiosensitizer, a drug given with radiation therapy to make the rectal cancer cells more sensitive to radiation, and two ways of administering it; and to compare a two-drug therapy with a single drug.

Study Size: Up to 450 patients.

Study 2, the treatment: Chemotherapy with and without radiation therapy after surgery.

Goals: To evaluate whether radiation therapy used with a combination of anticancer drugs is more effective than the drugs alone and to compare two different combinations of drugs, used both with and without radiation.

Study Size: Up to 750 patients.

COLON CANCER

Treatment: Chemotherapy after surgery.

Goals: To compare two different drug combinations, one of two drugs and one of three, used after surgery.

Study Size: About 200 patients have been enrolled and up to 655 more may be enrolled.

NON-HODGKIN'S LYMPHOMA

Treatment: Chemotherapy

Goals: To compare three newly developed multiple-drug regimens with the multiple-drug treatment most commonly used in this country, considering side effects as well as effectiveness in prolonging life.

Study Size: Up to 800 patients, with 300 already enrolled.

BLADDER CANCER

Treatment: Chemotherapy followed by surgery.

Goals: To compare one of the standard treatments, surgical removal, with a combination of four drugs followed by surgery.

Study Size: Up to 298 patients.

PATIENT TRIALS

Patients who want to participate in a cancer treatment study may ask their doctors about treatment options or they call (800) 4-CANCER, an information service sponsored by the National Cancer Institute. It offers a computerized listing of trials sponsored by the institute.

Physicians can obtain information on what **clinical trials** are accepting patients by contacting the Physician Data Query, or PDQ, a computerized listing operated by the cancer institute. Physicians can gain access to PDQ through their own computers, a commercial vendor or medical libraries.

GRAPHIC: photo of Dr. Vincent T. DeVita Jr. (UPI)

LANGUAGE: ENGLISH

2000, U.S. Department of Health and Human Services;
Journal of the National Cancer Institute

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March 15, 2000

SECTION: NEWS

LENGTH: 1435 words

TITLE: Wanted: Senior Citizens for Cancer Treatment Trials

AUTHOR: Steve Benowitz

TEXT:

Cancer is primarily a disease of the elderly. Yet **participation** by the elderly in **clinical trials** is not nearly proportional to their representation in the population with cancer.

According to a Southwest Oncology Group study published Dec. 30 in the *New England Journal of Medicine*, 63% of all cancer patients are older than 65, but they only make up 25% of those enrolled in studies. The numbers get worse for breast cancer: The elderly make up 49% of breast cancer patients, but only 9% of patients 65 or older are in **clinical trials** for the disease.

Several years ago, federal rules mandated that **clinical trials** be made up of both women and minorities in proportion to the percentage of the population that has the disease. And in fact, the SWOG study found that these goals have been met.

But those same federal guidelines said nothing of the elderly.

"We need to determine the best cancer therapies for elderly patients as well as for younger patients, which may not be the same," said Lawrence N. Shulman, M.D., vice chair for clinical services in the Department of Adult Oncology at Dana-Farber Cancer Institute in Boston. "The biology of cancers is sometimes different in elderly patients, and the toxicity profile of the treatments we use may be different for elderly patients as well."

While few researchers were surprised by the findings, the question remains, why do so few elderly participate in cancer trials?

In some cases, the problem starts with physicians.

A previously published survey of U.S. oncologists found that while 80% thought that patients had better results when treated in **clinical trials,** roughly half said they would not recommend patients for **clinical trials** based on age alone.

One reason may be the belief that those cancer patients 65 and up cannot stand up to the rigors of potentially toxic drugs.

"There's a tendency among oncologists to say, 'They're older, why bother them,'" said Lee Rosen, M.D., director of the Cancer Therapy Development Program at the University of California at Los Angeles Jonsson Comprehensive Cancer Center. "There's no question that some drugs can help the elderly. If we had studies that randomly assigned patients to low dose versus supportive care, and show the benefit to quality of life, that might support a lot more people to be more aggressive," he said.

What's more, the elderly are more likely to have other illnesses and conditions, such as heart disease, high blood pressure, and diabetes. This "noise" compromises the integrity of the **clinical trial** comparing the efficacy of two drugs. How can researchers tell how effective a drug is if the patients have other

complicating illnesses and are taking other medications with unknown interactions?

But excluding the elderly misses the point of a trial in the first place -- to find out how well a particular drug will work in all patients, including the 65-and-older set, said Maurie Markman, M.D., chairman of the Taussig Cancer Center at the Cleveland Clinic. "We need to make sure that we're including all the conditions in the real world for patients," he said.

"If you're not capturing this patient population in trials, it's a problem in terms of generalization of results, knowledge, and understanding of how to deal with these situations. I think it's important that the elderly are included in trials to make sure you have enough experience with dealing with side effects and find out if you have to give certain dose modifications," he said. "Because most research is done on younger patients, treatments may not be appropriate or may be ineffective in the group most likely to develop cancer."

To some degree, the under-representation of the elderly owes to the realities and business of conducting cancer **clinical trials,** said John Wasson, M.D.

"You can follow younger individuals for a longer time, and the drug manufacturer is able to recoup money because those patients will live longer," said Wasson, who is the director of the Center for Aging at Dartmouth Medical School in Hanover, N.H.

"That doesn't work when you have an 85-year-old with many different conditions and limited life expectancy," he said. "It's hard to do a study on a group of such individuals because results are difficult to interpret -- there's so much data noise." As a result, oncologists "need more of them because 'competing hazards' -- other diseases -- will take so many out of the study, and you likely can't follow them for long."

Elderly Don't Enroll

In some cases, it is the patients who are reluctant players. While younger patients may be more aggressive in seeking out trials and treatments, older patients may be more likely to wait to be asked. Aminah Jatoi, M.D., assistant professor of oncology at Mayo Clinic Cancer Center, Rochester, Minn., believes a major reason the elderly don't enroll in trials is because they are not asked to.

"If you ask an oncologist how a certain patient will do in chemotherapy, most oncologists would predict a particularly elderly patient would not do well," she said.

"How many elderly want to embark on trial with the potential for significant toxicity?" asked Samuel Taylor, M.D., medical director of the Creticos Cancer Center at the Illinois Masonic Medical Center in Chicago. Many older adults decide they are not willing to undergo potentially grueling treatments to extend their lives.

"Quality becomes more important," said Georgia Sadler, Ph.D., associate director of the University of California at San Diego Cancer Center and director of community outreach. Some elderly patients simply cannot or will not keep up with the study regimen and are more likely to drop out than are younger patients. Still others have trouble getting to a medical center to see the doctor.

Insurance reimbursement is also a problem. "For children, **clinical trials** are the standard care," Sadler said. "For adults, they're experimental care." Many insurance companies and Medicare won't pay for experimental treatments, though sometimes the therapy costs differ little from that outside a trial, noted Edward Trimble, M.D., head of the surgery section of the Cancer Therapy Evaluation Program at the National Cancer Institute.

Social and family support also play a tremendously important role in a senior's **participation,** Trimble said. The elderly tend to become more isolated as they age. Family and friends help influence treatment decisions and are more likely to encourage younger patients to enroll in trials.

Specialized Trials

While the researchers who conducted the SWOG study and others have called for greater **participation** of the elderly in **clinical trials,** some, such as UCSD's Sadler, advocate specialized trials for the elderly.

Whereas younger patients seek the most aggressive treatments, such trials would employ milder treatments for people who probably will not live much more than 10 to 20 years.

"We have to have standard **clinical trials** to know whether a drug works or not," Sadler said. "But we need additional studies because we need to know what happens when we introduce this new drug in someone taking a number of other medications for other health problems. These types of trials will become more important as we age as a society.

"The question is, is it better to give a woman a full dose of chemotherapy for her cancer although she has diminished kidney function, or is it better to give a lower dose, which overall provides a better quality of life?"

Some existing trials focus exclusively on the elderly, though they are by far the exception. The North Central Cancer Treatment Group is conducting a multi-institutional 40-patient phase II trial of carboplatin and taxol for non-small-cell lung cancer for patients 65 and older. Because of potential toxicity, researchers have made dose modifications.

Other groups have begun similar studies. The Cancer and Leukemia Group B is conducting a randomized study of women over 65 comparing intravenous and oral chemotherapy for stage II breast cancer.

Getting the elderly to take part in trials will continue to be increasingly important, researchers agree. "Cancer in the elderly has not been carefully studied," said Richard Schilsky, M.D., chairman of CALGB and associate dean for clinical research at the University of Chicago. "When it has, it's not clear it's different in the elderly than in younger people."

"There's a certain pressure on all oncologists to investigate the elderly," Jatoi said. "It's inevitable that we will have to face the questions of treating the geriatric cancer patient."

GRAPHIC: Picture 1, Dr. Lee Rosen; Picture 2, Dr. Georgia Sadler; Picture 3, Dr. Richard Schilsky

3

Recommendations for Medicare Clinical Trial Reimbursement

Clinical trials have become an essential component of modern medical care because they are the best means of finding out which health care interventions work and which do not. Trials produce information of value to future patients, and frequently benefit the people enrolled in them. Medicare beneficiaries and taxpayers have a shared interest in the development of reliable information about health care interventions, because such information provides the basis for rational health care and resource allocation decisions by providers and patients.

Although neither regulations nor specific policy directives have been issued about the reimbursement of routine patient care costs in clinical trials, the impression is widespread that the Medicare statute excludes from reimbursement all or some such costs (see chapter 2). This impression is apparent from the nature of legislation introduced in Congress to assure reimbursement for routine patient care costs, from statements of HCFA officials, and from remarks of providers. In chapter 2, the committee also established that, in practice, Medicare reimburses many claims for routine patient care. Thus, a wide gap separates many people's impressions of HCFA's rules and the demonstrable facts of actual reimbursement.

The committee is recommending explicit policy to legitimize reimbursement for much—though not all—of the care rendered to participants in clinical trials. Reimbursement should not be denied solely because the care is delivered as part of a clinical trial. In addition, the recommendations apply to all clinical trials involving any type of intervention in any aspect of health care and for any illness, for care that would be eligible for Medicare reimbursement outside of trials. They apply whether government, industry, or other private sources support or sponsor the trial.

Medicare reimbursement should not hinge on a judgment by HCFA about the quality of the trial. However, HCFA does have a legitimate interest in assuring that trials meet currently accepted standards for scientific merit and protection of research participants. The committee recommends limiting reimbursement to trials that have been reviewed and accepted by all relevant institutional review boards (IRBs). The committee does not believe that HCFA should evaluate every trial for which a reimbursement claim is submitted, but it should have access to documentation of a trial's scientific merit and the fact of IRB approval, upon request. The committee believes the need for such review would be quite rare.

A new reimbursement policy following these recommendations would satisfy two conditions the committee believes to be key: (1) beneficiaries would not be denied reimbursement merely because they have volunteered to participate in a clinical trial; (2) the new rules would not impose excessive administrative burdens on HCFA, its fiscal intermediaries and carriers, or investigators, providers, or participants in clinical trials. Explicit rules would have the added benefit of increasing the uniformity of reimbursement decisions made by Medicare fiscal intermediaries and carriers in different parts of the country. Greater uniformity would, in turn, decrease the uncertainty about reimbursement when providers and patients embark on a clinical trial.

The fundamental principle is that reimbursement decisions should be made independent of whether a beneficiary is receiving care in or out of a clinical trial. Reimbursement should be provided for all services to which the beneficiary would be generally entitled under Medicare. This rule would provide reimbursement for a large share of services to participants in clinical trials.

The fundamental rule would apply to routine care in all trials comparing standard approved interventions (drugs, devices, procedures, or other). It also would apply to routine care in trials of new versus standard drugs. No new reimbursement policy is needed for routine care in trials of most investigational medical devices. Under the 1995 agreement between FDA and HCFA, reimbursement for participants in trials of devices is allowed when the device is "investigational," but not when it is "experimental" (i.e., when the device itself is not a new type but is a modified version of an existing approved device or is being used for a new indication). For such devices the underlying questions of safety and effectiveness have already been answered. Such devices are classified in "category B." Devices for which initial questions of safety and effectiveness have not been answered are designated "category A."

The committee believes that reimbursement should be provided for procedures under rules analogous to those applied to medical devices; procedures that are modifications of, or new uses for existing procedures should be reimbursed at the same level as the existing, accepted procedure. Conversely, as with category A devices, Medicare should not pay routinely for procedures that are considered "experimental," although HCFA may (and should) choose to do so in specific trials. The committee recognizes that classifying procedures may be challenging. A "gray zone" in which a reimbursement decision is unclear will

require some special determinations by HCFA. Nonetheless, this provision is an essential component of the overall recommendation.

In addition to providing reimbursement through the proposed policies, the committee urges HCFA to use its existing authority to support selected trials and in two ways to assist in the development of new trials. First, HCFA should reimburse for care in selected trials that would not otherwise qualify, or reimburse at a higher rate than would otherwise be allowed for investigational interventions that are more expensive than the standard treatment. Second, HCFA should assist in the development of new trials of particular importance to the Medicare population.

In all cases, HCFA should provide clear guidance on how the recommended reimbursement policies should be implemented by providers and the entities that process Medicare claims. Such guidance would promote nationally uniform administration and minimize uncertainty for providers and patients about what will and will not be reimbursed.

Finally, although not a requirement of implementing a new policy, the committee recommends prompt completion of a national clinical trials registry. Such a registry will increase HCFA's ability to monitor reimbursement for services in clinical trials, in addition to serving its other functions.

RECOMMENDATIONS

RECOMMENDATION 1. Medicare should reimburse routine care for patients in clinical trials in the same way it reimburses routine care for patients not in clinical trials.

This principle applies to payments for physicians and other providers, routine laboratory and other diagnostic tests, and any other services that comprise routine care for a given patient. All coverage and medical necessity rules and all other restrictions that apply to patients not in clinical trials would apply to care in clinical trials.

The committee recommends a broad definition of clinical trials—including all phases and legitimate designs and all sources of sponsorship (government, industry, or other)—all of which should be equally eligible for reimbursement. This definition does not mean, however, that any treatment simply called a "clinical trial" would qualify for reimbursement. To qualify, a clinical trial must have a written protocol that describes a scientifically sound study and have been approved by all relevant IRBs before participants are enrolled. HCFA should articulate criteria for an acceptable trial and IRB review, which investigators would apply to determine whether their studies are eligible for reimbursement. (HCFA could state the criteria in terms of "current NIH standards," e.g., rather than stating specific study characteristics.) The committee recognizes that controversies surround both the quality of current clinical trials and IRBs, but holds that these issues are being addressed in various ways by DHHS and other sectors

of government, and should not be addressed routinely in HCFA's reimbursement decisions.

Medicare should reimburse routine patient care costs, but not all costs in clinical trials. Medicare should not reimburse the costs of experimental interventions (except category B devices for which reimbursement is allowed under agreement with FDA, and certain procedures as described in recommendation 2), of data collection and record keeping that would not be required but for the trial, or of other services to clinical trial participants necessary solely to satisfy data collection needs of the clinical trial ("protocol-induced costs"). These costs should remain the responsibility of research sponsors, private and public.

Medicare should continue its current practice of reimbursing costs of treating conditions that result as unintended consequences (complications) of clinical trials.

RECOMMENDATION 2. HCFA should reimburse surgeons (or other practitioners) for treating patients in randomized clinical trials involving procedures that are variations or modifications of accepted procedures, or new uses for accepted procedures.

Under the current interpretation of Medicare reimbursement rules, the committee believes that surgeons and others performing surgical or other procedures in trials might not be eligible to be reimbursed for those services. Therefore, the committee recommends that procedures that have become widely accepted as a part of standard medical practice, but which, as part of a clinical trial, are being rigorously evaluated, or are being modified or applied for new indications to determine the incremental risks and benefits, should be eligible for reimbursement at the rate for the standard procedure. Conversely, types of procedures for which initial questions of safety and efficacy have not been resolved would not be eligible for reimbursement.

Unlike the basic recommendation regarding routine patient care costs, which applies to all clinical trials, this recommendation would limit reimbursement to randomized trials (the equivalent of "phase 3" trials for drugs and devices). The committee believes this limitation is appropriate in order to avoid providing reimbursement for uncontrolled experimentation by practitioners. The introduction of new drugs and devices is governed by FDA under a formal system that involves phased trials (see chapter 1). In contrast, the introduction of new procedures is not governed by any regulatory authority. In their early phases, procedures are modified or tried for different indications in clinical practice, but rarely in formal trials. However, once a new or modified procedure has been defined and developed to the point that it is distinct enough from the predicate procedure, it may be tested against the standard treatment (the predicate procedure or other accepted treatment) in a formal randomized trial. Medicare should provide reimbursement to the surgeon or other practitioner for treating patients in such trials.

Further clarification may be needed to make clear the committee's intent with regard to reimbursement for procedures on patients in clinical trials. The committee is expressing no judgments about when trials of procedures should or should not be carried out, or who should be involved in them if they are. This recommendation is not intended to influence the criteria or processes HCFA uses to decide on coverage of new procedures under usual medical care. It applies only when a trial of a procedure is being done—for the all the reasons that trials are done—and claims for reimbursement for the procedure are submitted by practitioners.

HCFA's initial task in implementing this recommendation will be to develop definitions for classifying procedures analogous to "category A" and "category B" devices. These definitions describing what is and is not allowed will be applied in the field when claims are submitted. HCFA should not be required to rule routinely on the eligibility of procedures before bills may be submitted. In the same way that providers are responsible for following reimbursement rules for all services under Medicare, they will be responsible for applying the rules appropriately in the case of procedures in clinical trials. Fiscal intermediaries and carriers audit these interpretations by providers in clinical trials, as they now audit bills from providers for care outside of clinical trials. Advice or an interpretation could, of course, be requested of HCFA at any time. In addition, HCFA would retain the right to initiate its own review, without being asked, if it believes there is an issue to be explored, to carry out a random check, or for another reason.

The committee recognizes that creating definitions that neatly separate "category A" and "category B" procedures will not be simple, and disagreements are inescapable about where the line between "A" and "B" should be drawn in specific cases. Table 3-1 gives a few examples of how the definitions might work.

Wherever the separation lies, some procedures will fall into a "gray zone." HCFA can narrow the gray zone by applying the definitions to a wide range of real and hypothetical procedures, and stating whether the procedures would or would not be eligible for reimbursement. To deal with cases in which uncertainty remains, HCFA should set up a process to rule quickly on reimbursement eligibility. With accumulated experience, the number of gray zone cases should decline, as has been the case with FDA classification of devices into categories A and B.

TABLE 3-1. Reimbursement Eligibility for Procedures Under Recommendation 2

Standard Procedure and Indication	Innovation and/or Indication	Circumstances of Trial, Nature of Innovation	Reimbursement Eligibility: Yes/No/HCFA Review
Open cholecystectomy	Laparoscopic cholecystectomy	If neither this nor other "keyhole surgeries" were being reimbursed by HCFA, this would be considered a major departure from standard practice	No
Open cholecystectomy	Laparoscopic cholecystectomy	If other "keyhole surgeries" were already being reimbursed by HCFA, this would fall in the "gray zone"	HCFA review?
Mastectomy for early breast cancer	Lumpectomy for early breast cancer	Lumpectomy is a variation on mastectomy	Yes
Standard surgery for parathyroid disease: removal of some parathyroid glands with confirmation by pathology during surgery	Surgery for parathyroid disease with physiologic calcium measurement to determine surgical endpoint	The procedure is the same; only monitoring is different	Yes
Optic nerve decompression surgery (ONDS) for pseudotumor cerebrii	ONDS for nonarteritic ischemic optic neuropathy	New indication for standard procedure, but had been used and reimbursed for new indication outside of trial	Yes (this would qualify under recommendation 1, because Medicare had been paying for patients outside of trials)

Open CABG	Midline CABG (minimally invasive procedure)	Could be considered next-generation open CABG	Yes or gray zone
Human liver transplant	Pig liver transplant	Used only in experimental situations; significantly different from standard intervention	No
Heart transplant or aggressive medical treatment for congestive heart failure	Battista procedure: removal of damaged cardiac tissue	Completely new procedure.	No
Pharmacologic or no treatment	Fetal cell transplant for Parkinson's disease	Completely new procedure	No

NOTE: Procedures in the table are for illustration only and are treated as though they were new in 1999 and relevant to the Medicare population, even though that is not the case for all examples. In each instance, the judgment about reimbursement eligibility is made assuming that the trial was taking place before HCFA had begun "legitimate reimbursement " for the procedure for the specified indication. By "legitimate reimbursement," we mean that reimbursement was made for claims that disclosed the nature of the procedure and the indication for which it was performed.

In this table, "HCFA review" means that the procedure falls in the "gray zone" (or for some other reason, the principal investigator is uncertain about reimbursement eligibility), and a determination of eligibility could be made by HCFA.

If a trial is initiated after reimbursement has become standard practice, the "fundamental" rule—that procedures that are covered in the course of usual medical practice would also be covered in clinical trials—would apply, and reimbursement would be allowed. For any procedure not eligible for reimbursement under the stated rule, investigators could apply to HCFA for reimbursement as an exception.

The committee has not attempted to specify an institutional mechanism under which HCFA might carry out the tasks required by this recommendation. However, the committee notes that the new Medicare Coverage Advisory Committee* might provide the needed expertise for the task of defining categories A and B and ruling quickly on "gray zone" cases that arise.

RECOMMENDATION 3. For claims submitted in accordance with both the fundamental recommendation (No. 1) and the special recommendation for procedures (No. 2), no special precertification by HCFA, or any other administrative process, should be required of clinical trial researchers or providers participating in trials before they submit claims for reimburseable services. Claims should be submitted in the same way they are for treatment outside of trials.

Practitioners and institutions would be expected to submit reimbursement claims for services to patients in clinical trials under rules outlined in recommendations 1 and 2. With a clear statement of reimbursement policy, such claims should pose difficulties no different from those arising in the administration of coverage and reimbursement rules for claims for care outside of trials.

Investigators and providers would not be routinely required to submit documentation about the trial to HCFA, but HCFA could, at any time, request such documentation to confirm that the clinical trial meets current standards for scientific merit and has the relevant IRB approval.

RECOMMENDATION 4. If Medicare or trial sponsors fail to cover clinical care costs, patients should not be billed for those costs above what they would pay if they were not in a trial.

This recommendation is not one that can be enforced as part of a reimbursement policy by HCFA; however, the committee believes it is an important principle that could be adopted by clinical trial sponsors and investigators. It also could be incorporated in any legislation passed to implement the committee's recommendations.

RECOMMENDATION 5. Medicare members of managed care plans should have the same reimbursement eligibility for care in clinical trials as those enrolled in fee-for-service Medicare, but not beyond the limits of the managed care contract.

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*The Medicare Coverage Advisory Committee (MCAC) was established by HCFA to provide guidance on coverage issues. The 120-member committee will function through specialty panels of not more than 15 members each. The MCAC had its first meeting in September 1999.

Nearly one Medicare beneficiary in five belongs to a capitated plan—an HMO or some other form of managed care. That number is likely to increase over time. It is vital, therefore, that the committee's recommendations carry over to patients served outside traditional Medicare. Managed care plans must provide all benefits offered under traditional Medicare. (Most offer additional benefits, including coverage of outpatient drugs.) Accordingly, the committee recommends that managed care plans be required to offer Medicare beneficiaries access to clinical trials involving services available within their networks. If, for example, a plan routinely covers a particular drug, it should cover it in a trial, as well. If the plan limits the choice of drugs to those listed on a formulary, the plan should not be required to cover a nonformulary drug in a trial.

Under point-of-service plans, patients should have the right to go outside the managed care network to participate in a trial, under the terms stipulated in the plan for point-of-service care, but no such right should be inferred under plans that limit enrollees to the plan's providers. This recommendation is not comprehensive, but is suggestive of a policy for managed care. Full implementation will require additional thought when HCFA adopts a clinical trial reimbursement policy, but the committee urges that the new policy not create obstacles to clinical trial enrollment for beneficiaries in managed care.

RECOMMENDATION 6. In addition to providing routine coverage through the proposed policy, the committee urges HCFA to use its existing authority to support selected trials and to assist in the development of new trials. In selected clinical trials, the committee believes that HCFA should do more than pay for routine patient care according to the recommendations already stated. Medicare should (1) provide additional reimbursement in a limited number of trials and (2) identify emerging or current methods of care of particular importance to the Medicare population and work with other organizations to initiate trials.

Researchers should be able to apply to HCFA for reimbursement above routine rates in cases meriting special treatment. Such trials could include some interventions that do not qualify under the basic recommendations, such as "category A" procedures, primary and secondary screening, diagnostics, and interventions not usually covered by Medicare (e.g., behavioral interventions). The rationale for extending coverage is straightforward. HCFA has a large stake in determining whether more effective or less costly alternatives to current interventions may exist, preventing ineffective procedures from becoming common practice, and facilitating the identification of innovations that would benefit the Medicare population.

For example, a behavioral intervention, which normally would not be covered, might replace a more expensive drug or surgical intervention to the benefit of both patients' health and Medicare finances. HCFA should have sole authority to decide whether to extend coverage and should make such determinations

expeditiously. The committee assumes that only a few trials would be appropriate for such exceptional treatment each year.

In the case of interventions of particular importance to the Medicare population, HCFA should collaborate with the National Institutes of Health (NIH) or others to see that appropriate trials are fielded. HCFA should cover routine patient care costs for these trials along the lines of the committee's basic recommendation. It could also fund other costs as well, under the exceptions procedure described in the preceding paragraph. But the objective is to encourage trials, not necessarily to pay for them. Such an active role would not be new for HCFA. This recommendation follows the model of the ongoing study of lung volume reduction surgery, which grew out of collaboration among HCFA, NIH, and the Agency for Health Care Policy and Research (AHCPR), at HCFA's initiative.

RECOMMENDATION 7. Every trial for which some Medicare reimbursement is sought should be entered into a national registry of clinical trials.

Reimbursement claims should bear an identification number assigned by the registry. A registry will facilitate ex post audits of reimbursement claims, HCFA's main tool for monitoring clinical trial coverage and detecting potential abuse. But identification of a claim as part of a clinical trial should not be relevant to the reimbursement decision.

The committee recognizes that implementation of this recommendation will necessarily take some time. Therefore, the committee's recommendations regarding reimbursement of routine patient care costs do not hinge on the existence of a clinical trials registry. Until a registry is in operation, reimbursement claims for interventions associated with a clinical trial should be denoted on the form, in a manner HCFA specifies. However, a registry would contribute to uniform administration and permit HCFA and others to carry out analyses of clinical trials and the costs of implementing the recommendations put forward here. It should, therefore, be put in place as quickly as possible.

Ideally, such a registry should include all publicly and privately sponsored trials before they begin accruing patients, thereby providing a link to all claims for Medicare patients in clinical trials. If the goal of creating such a registry is accepted, the practical question of how best to achieve it must be addressed. It would be possible to build upon the registry currently under development at NIH by broadening the definition of trials to be included and consulting widely on how to present data. Or a separate registry could be created.

Whether the registry should operate within NIH or elsewhere merits consideration. The design of the NIH registry has been underway for some time. Its designers claim that it will be functioning, at least in part, by early 2000. Redirecting any ongoing effort will be difficult for reasons that are well understood. If it were concluded that converting this limited registry into an inclusive national registry would be needlessly cumbersome, the creation of a separate comprehensive registry, serving objectives beyond those of NIH, or even of HCFA,

should be explored. The committee urges the Secretary of HHS to examine this issue promptly, set a timetable for completion of a registry, and seek adequate funding for it.

ADMINISTRATIVE AND COST IMPLICATIONS

Implementation of the committee's recommendations would likely cause some increase in administrative costs to HCFA. In making its recommendations, the committee strove to minimize potential administrative burdens. It is the committee's judgment that any added administrative costs required by institution of this reimbursement policy will be small.

Effects of the committee's recommendations on benefit costs are more important and far more uncertain. For several reasons, the cost impact of these recommendations is likely to be quite small. First, the recommended reimbursement policy is designed to limit payments for an individual to roughly the cost of "standard care" for which he or she would be eligible if not enrolled in the trial. This limitation does not imply that each individual would have chosen standard care that cost the same as the care in the clinical trial, so in individual cases, the cost of actual care in the trial might be higher or lower than forgone care outside the trial. Although the incremental cost of routine care in clinical trials is not known with certainty, it is almost surely small in comparison to the costs otherwise incurred by Medicare. Some clinical trial groups claim that the costs of treating patients in some trials may be less than treating them outside of trials. Second, clinical trials hold the long-term prospect of identifying ineffective interventions, which would fall out of favor in the clinical community, or could be excluded from coverage, in some cases saving Medicare dollars.

Finally, only a tiny fraction of Medicare patients participate in clinical trials. No accurate count of clinical trial participants at any point in time exists, but the Lewin Group has estimated that about 265,000 people in the United States participate in clinical trials each year, including about 161,000 Medicare beneficiaries—less than 0.5 percent of the 38 million Medicare enrollees in 1997 (Dobson and Sturm, 1999). Clearly, the proportion of Medicare beneficiaries in clinical trials is quite small. The available evidence suggests that Medicare already pays for a large proportion of routine patient care in such trials, including both costs for which no reimbursement is sought, and claims that are submitted and rejected.

The largest effect on Medicare costs could come from the speedier determination of the efficacy of innovative or experimental procedures, drugs, and devices. Some will be cost increasing. Others will be cost reducing. Whether the net effect is to raise or lower total Medicare spending, the speedy determination of what works and what does not work will benefit the Medicare population and the nation as a whole.

CONCLUSION

Clinical trials are integral to modern medical care and to the progress of medical science. Although HCFA has issued little explicit policy about payment for routine patient care for patients in clinical trials, the Medicare statute has been widely interpreted to exclude reimbursement for such care. However, evidence is ample to suggest that providers submit claims for routine care for Medicare beneficiaries in trials without noting the existence of the clinical trial, and HCFA's financial contractors usually pay them. The thrust of the committee's recommendations is that nothing should be done that would materially curtail Medicare's reimbursement for routine patient care costs for patients in clinical trials. On the contrary, HCFA should encourage such trials and even extend reimbursement in a limited number of specifically approved exceptional cases. To achieve these goals, the committee believes that HCFA should assure patients in clinical trials the same reimbursement of routine patient care that is available to patients who are not in trials. Extending reimbursement to certain procedures that represent modifications of current practice and distinguishing those from procedures for which risks and benefits are largely unknown will require some additional effort by HCFA, but it is an essential component of the committee's recommendations. The fundamental recommendation—reimbursement independent of trial participation—should be implemented relatively easily.