The Impact of Medical Technology on Future Health Care Costs

Final Report

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PREFACE

This report was prepared by the Project HOPE Center for Health Affairs under a grant from the Blue Cross and Blue Shield Association and the Health Insurance Association of America. The authors are grateful for the substantive input made by expert panel members Alan Garber, Scott Gazelle, Craig Henderson, John Inadomi, William McGivney and Earl Steinberg. Helen Lazenby, from the Health Care Financing Administration's Office of the Actuary, was particularly gracious in providing us with 30 years of health spending data. In addition, reports provided by Naomi Aronsen of the Blue Cross and Blue Shield Technology Evaluation Center and Karl Matuszewski of the University HealthSystem Consortium served as an invaluable foundation for the preparation of our case studies. We also are indebted to the careful review and comments provided by industry representatives and clinical experts too numerous to mention. However, the generous assistance of all of these people does not imply their complete agreement with the content of this report. As usual, the opinions, estimates, and errors made here are those of the authors alone.

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Executive Summary

Introduction

Medical technology has sometimes been called the "culprit" behind the rise in health spending in the U.S. – which increased to $3,632 per person in 1998 up from $297 in 1970 (Cowan et al., 2000). This study examines the role technology has played, relative to other factors such as inflation and the aging of the population, and its likely influence in the future.

Medical technology encompasses all aspects of medicine: devices, pharmaceuticals, surgeries and the organization of medical practice itself. An earlier study sponsored by BCBSA and HIAA focused on the impact of pipeline pharmaceuticals on drug spending; this study recognizes the complex interrelationships between drug and non-drug innovations and takes a broad view of health care technology and its impact on spending. However, we focus on non-drug interventions in discussing illustrative examples.

Approach

In general, researchers have used two approaches to examine the technology-expenditures link.

The more common is the "*top-down*" or "*residual*" approach, which involves estimating the impact of determinants of spending, such as inflation and population aging, and then isolating the "residual," as the unique contribution of medical technology. The second is a "*bottom-up*" or "*technology-specific*" approach, which involves examining the impact of individual technologies.

Because each strategy has advantages and downsides, we rely on both to provide a more complete portrait of technology's overall impact. In particular, we supplement our review of trends and forecasts of the "residual," with nine detailed case studies of new and emerging technologies. A six-member expert panel, comprised of specialists in several clinical fields, guided our selection of the following case studies:

- ✓ Coronary stents for restenosis of the arteries
- ✓ Drug inhalation devices for delivery of insulin
- ✓ Electron beam computed tomography to screen for coronary artery calcification
- ✓ Genetic testing for colorectal cancer
- ✓ Low-dose helical computed tomography for lung cancer screening

- ✓ Monoclonal antibodies for cancer
- ✓ Positron emission tomography in the diagnosis and staging of cancer
- ✓ Screening for colorectal cancer
- ✓ Thin-layer cytology (Thinprep) for cervical cancer screening

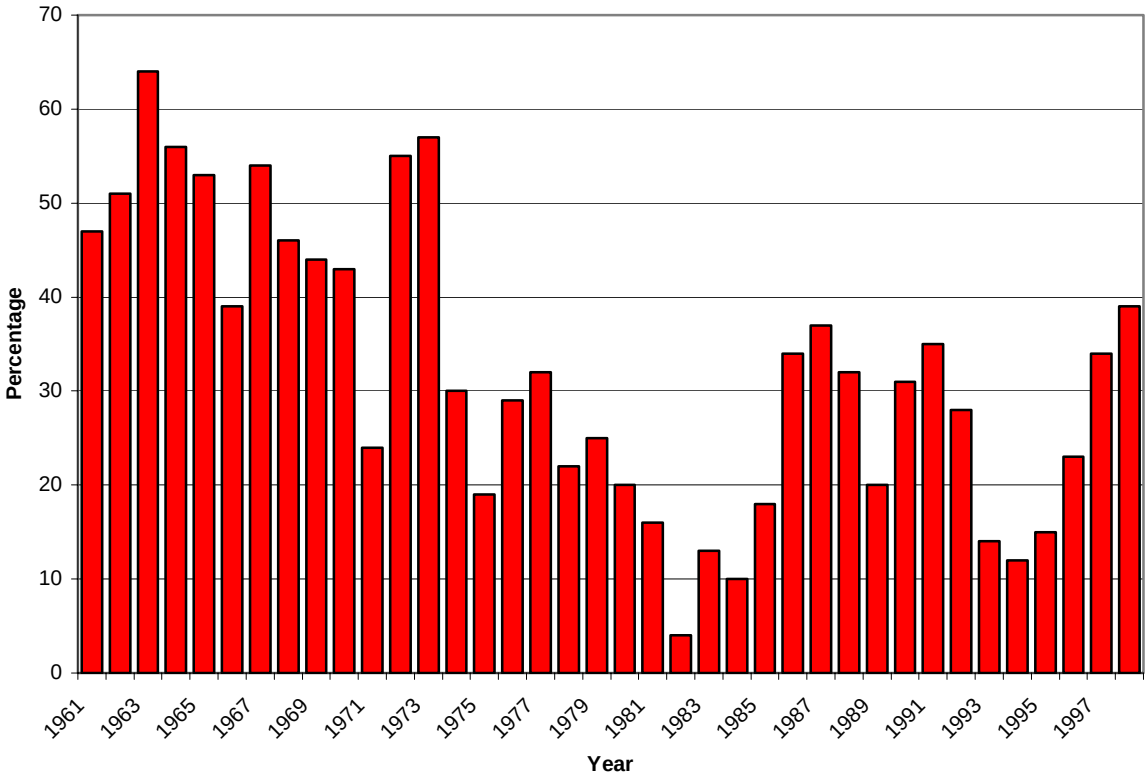
Findings

Prior research. Previous studies have shown that medical advances increase health costs
(Fuchs, 1972; Schwartz, 1987; Scitovsky, 1985, Showstack et al., 1982; Mueller and Weisblatt 1993; Mueller et al., 1993; McLaughlin et al., 1991; Center for Health Economics Research, 1988; PPRC, 1993; Newhouse, 1993; Cowan et al., 1999; Berndt et al., 1999; Cutler et al., 1999). New technology adds to costs because it increases the "intensity" of care – i.e., it expands the opportunities for providing services to patients. Even where a new technology can reduce unit costs for particular patients, it often increases net health expenditures by increasing overall volume – i.e., diffusing into patients with mildly symptomatic disease, or those who were previously too ill for treatments (Schwartz, 1994; Goldsmith, 1994).

Analysis of the residual. As a percentage of total health spending, the residual has varied considerably since 1960 (Figure 1). In the 1990s, this percentage declined during the first part of the decade, but increased steadily thereafter, from 12% in 1994 to 39% in 1999.

The data suggest that technology's impact on costs is influenced by systemic changes in health care reimbursement. For example, the residual reached its nadir during the mid-1980s with the advent of the Medicare prospective payment system (which presumably mitigated the influence of technology relative to inflation and other factors). It declined again in the early 1990s during a rapid expansion of managed care. Notably, in both cases, the residual rose sharply after temporary declines, suggesting that attempts to contain medical technology are difficult to sustain.

Figure 1. Residual as a Percent of Growth in Personal Health Spending



Projections

Between 2001 and 2005, we project that personal care expenditures will grow at 6.0 to 7.0 percent per year, and that the residual will account for 25 to 33 percent of the growth. This projection is based on several sources, including projections of HCFA's Office of the Actuary, a review of past trends, and discussions with experts responsible for making economic forecasts.

Notably, HCFA projected growth in total health care expenditures of 6.1 percent annually during 2001-2008, with the residual accounting for about 12 percent of the increase. Our estimates are somewhat higher, based on changes in baseline health spending forecasts made by the Congressional Budget Office and the effects of recent legislative changes in BBRA and BIPA, and not accounted for in HCFA's estimates.

Also, in the last 30 years, the residual has only twice attained the low values that were forecast by HCFA – once in the mid 1980s with the introduction of PPS, and again in the early-mid 1990s, during a period of aggressive cost containment by managed care. As noted above, in both cases the period of low residuals was short lived.

We believe it unlikely that such a low residual will be attained or sustained, and more probable that the period will be marked by less restrictive models of managed care

(though the repercussions of the Balanced Budget Act will preclude a period of particularly high residuals as well).

Case Studies

While our case studies focus on very different kinds of technologies, collectively they shed light on several important points:

"Cost-saving" technologies often spread in cost-increasing ways. Some technologies reduce costs if their use is restricted to narrowly defined indications or populations, but increase costs as their use expands. Positron emission tomography (PET) for diagnosing and staging cancer provides an example. Among other things, PET could help avert surgery for non-resectable or benign tumors, and preclude the use of prolonged chemotherapy for treatment failures, both of which may reduce costs. But because a PET scanner has relatively high acquisition costs and low operating costs, there are strong incentives for hospitals to expand its use to broader populations where it will add to overall health spending.

Technologies exert their influence through both volume and price effects. Some technologies have a small target population, but a high price tag. Monoclonal antibodies, for example, can add $8,000 to $30,000 per year to the costs of treating selected cancers, but fewer than 30,000 additional patients will receive treatments per year for the next five years. In contrast, other technologies may have a small price tag, but may be used by a large number of people. ThinPrep for cervical cancer screening adds only an estimated $8 to the cost of conventional Pap smears, but may be used by as many as 12 million new users in 2001. As a result, ThinPrep is expected to add approximately $100 million to aggregate health spending in 2001– about two-thirds that of monoclonal antibodies, despite having a considerably smaller price tag.

Technologies cannot be separated from the systems in which they are used. Medical technology does not increase costs by itself. Rather, the health care system and the incentives it contains are critical. The use of coronary stents provides an illustration. Under the per-procedure reimbursement used by private payers, stents diffused rapidly, with some physicians implanting 5 or 6 at a time, despite potentially adverse clinical consequences. In contrast, under the Medicare prospective payment system, hospitals pressured interventional cardiologists to reduce procedure costs and this practice has moderated. Aggressive price competition among producers has also helped hospitals reduce costs for stents.

The key question is not whether technologies increase costs, but what benefits are achieved for the resources consumed. While medical technologies tend to increase health costs, they also tend to improve health outcomes, at least for some segments of the population. A key challenge is to better measure the health effects of new technologies and to reimburse them in ways commensurate with their added costs and benefits. The

problem is that it is not always easy to discriminate between cost-effective and cost-ineffective technologies. More research in this area in the future would be worthwhile.

Caveats and Limitations

Several limitations are worth emphasizing. First, there is no perfect way to measure the impact of new medical technologies on costs. As noted, the residual captures all changes in the practice of medicine, not attributable to inflation and demographics. Second, our case studies are not intended to be representative to all technologies, but rather to complement the data analysis with illustrative examples.

Conclusion

Historically, new medical advances have exerted an upward impact on health care costs. We expect this to continue in the coming five years, at perhaps a slightly higher pace than the average trend for the 1990s. Increased pressure to buy new medical technology will result as consumers and providers resist efforts on the part of public and private payers to control costs in the near term. Policy changes on the horizon, such as a Medicare drug benefit, may accelerate technology's influence toward the latter half of our forecast period.

Any discussion of the costs of new medical technologies raises a crucial question about the benefit side of the equation. The key question from a societal perspective is not how much technology costs, but whether investments in medical technology are worth the health gains produced. A growing body of research suggests that Americans strongly support medical innovation and are willing to pay for technology. Among many new technologies, there is evidence they may be cost effective if used in appropriately selected individuals.

The challenge to policymakers and the insurance community is to put in place the incentives for more appropriate use of technology. The challenge for the research community is to enable policymakers and users to better understand the circumstances in which a new technology adds value.

1 OBJECTIVES

Over the past few decades, health expenditures have increased considerably. Personal Health Care (PHC) expenditures – an accounting total that excludes expenditures for research and construction and administration and public health expenditures – increased from $297 per person in 1970 to $3,632 per person in 1998 (Cowan et al., 2000). Increases in health care costs over time can be attributed to a number of factors, including inflation in the general economy, inflation in the health care sectors in particular, growth and aging of the population, and to advances in medical technology. Some observers have focused on technology as a culprit behind the cost increases. The adoption and spread of new technologies may be more susceptible to policy influence and controls, e.g., limits on benefits and use by third party payers, than demographic trends and inflation, particularly inflation that comes from outside of the health sector. Technology is also easy to fault as a culprit because measurement of its contributions to expenditures has traditionally been presented solely in terms of cost, with little mention of benefits and how benefits associated with applications of technology might offset costs.

The Project HOPE Center for Health Affairs (CHA) was asked by the Health Insurance Association of America (HIAA) and Blue Cross and Blue Shield Association (BCBSA) to review the historical influence of technology on health care costs and to project its likely influence in the next five years. The purpose of this research is to inform policy makers, the press, and the public about medical technology's role as a health care cost driver at a conference jointly sponsored by the HIAA and BCBSA. This conference will be the second in a series of conferences that focus on health care cost drivers. The first conference focused on the impact of pipeline drugs on pharmaceutical spending (Mullins et al., 2000).

Although CHA was asked to focus on non-pharmaceutical advances in order to not duplicate this earlier work, we felt it was difficult, if not impossible, to disentangle the effect of drug from non-drug innovations on costs. There are clear synergies between pharmaceutical and non-pharmaceutical innovations, which will be apparent in the report that follows. In some cases, beneficial devices may not have diffused had they not been accompanied by pharmacologic improvements. Our report, while not focusing on pharmaceuticals, examines a broad view of health care technology and its interface with health care spending.

We begin with a discussion of our methods to forecast the relationship between medical advances and health expenditures. We next review evidence on the relationship between technology and expenditures for health care in a non-technical and objective manner. We start this discussion with a definition of technology and a brief summary of the market-based framework that underlies interrelationships between technology and health care costs. Our discussion emphasizes approaches rather than completeness of literature because it is important that users of findings understand the underlying

limitations. Estimates of the "residual" measure of technology's contribution to expenditures, produced by the Health Care Financing Administration (HCFA), are also presented and interpreted. Next, we present a critique of residuals based on projections by HCFA staff and indicate how we believe the residual will change through the year 2005. This discussion is followed by a summary of the findings from our case studies. In this discussion, we are concerned not only with understanding how these technologies will influence costs, but also how they will affect health outcomes. The interplay between technology diffusion and other characteristics of a health care system is also illuminated. We conclude with a discussion of the cost-effectiveness framework and the importance of considering the contribution of new medical technologies to health outcomes as well as costs.

2 METHODS

a) Overview of Approach

Medical technology encompasses practically all aspects of medicine: medical devices, pharmaceuticals, the way physicians perform surgeries and practice medicine, and its organization (Rettig, 1994). Because of its complexity, the science of measuring the influence of medical advances on health care spending is in not well developed. Nevertheless, health care researchers have used a variety of methods to try to understand its impact on health care costs. These can be categorized into two broad approaches: a "residual" approach and a technology-specific approach (Garrison and Brown, 1991). In the residual approach, one attempts to measure all the factors that might account for health spending increases, such as price inflation and growth in the aging population at the national level. Unexplained changes (or the "residual") are attributed to technological change. Technology-specific approaches analyze the changes in the use of specific technologies and therapies over time and attempt to aggregate their impact.

Each of these methods has its own advantages and limitations. The advantage of the residual approach is that it focuses on changes in health spending at the national level. A conceptual weakness is that other factors that are poorly measured but influence health spending, such as changing insurance coverage, may be falsely attributed to technological change. The technology-specific approach is appealing in that it treats technologies at an identifiable, descriptive level, rather than as a residual. Another advantage to studying specific technologies is that analyses can be tailored to accommodate unique aspects of medical advances, such as their impact on quality of life and patient outcomes. The obvious limitation of this approach, in terms of measuring aggregate impact, is that the set of technologies chosen for analysis may not be a representative sample of all medical treatment.

Our approach combines a review of the historical context of technology's influence on health care costs, an analysis of trends in and forecasts of the "residual" in health care spending, and the conduct of nine case studies. Technologies selected for the case studies were anticipated to be future "cost drivers" for health care spending. These are meant to shed light on how technology influences costs, and also to better understand its impact on health outcomes. By combining approaches, we hope to inform our audience about the issues raised as new medical advances diffuse, as well as to shed light on the likely future influence of selected medical advances on health care spending.

b) Selection and Use of Advisory Panel

We used a six-member expert panel, comprised of specialists in the fields of cardiovascular medicine, diagnostic imaging, oncology, gastroenterology, and technology assessment, to help us select our case study technologies and provide

feedback on draft reports. In addition to assisting us with these aspects of the study, clinical advisors also assisted us in understanding specific issues related to the application of our case study technologies

We selected panel members to represent specific disease areas where there is a high pace of technological change, as evidenced by the focus of technology assessment organizations in recent years, and where there is high disease prevalence. We also felt it was important to include at least two panelist who were active participants in technology assessment. Our panel members are some of the most respected names in this field. Their names and affiliation are listed in Appendix 1. However, our report does not necessarily reflect the views of individual panelists.

c) Identification of Medical Technologies for Study

Due to the large numbers of new medical procedures that enter the market every year, it is difficult and extremely costly to keep abreast of change. There are no comprehensive lists of new medical procedures and devices that could be used in the selection of case study technologies. Project HOPE staff compiled a list of more than 400 new and emerging medical devices, procedures, and pharmaceuticals under study by some of the more prominent technology assessment organizations in the United States. Summary information on these organizations and the technologies that they studied is provided in Appendix 2. Expert panel members and a representative from AdvaMed, a device manufacturers' association, were then invited to add to this list.

Because the focus of an earlier conference was on pharmaceuticals and their role in health care cost increases, we omitted prescription drugs from our list of technologies to consider. However, we retained drugs that were administered by physicians, such as monoclonal antibodies and those administered in the hospital, such as antiplatelet therapy, as these are not commonly considered to be prescription drugs. The BCBSA and HIAA also specifically requested that we not consider information technologies in our selection.

Case study technologies were then selected from this list with the assistance of the expert panel using a two-round Delphi-panel technique. Panel members were asked to consider the following criteria in making their recommendations for case study technologies:

- Technologies should be expected to have widespread diffusion or have a high per case cost impact (either cost decreasing or cost increasing) in the next five years; and
- Technologies should have diffused to at least 5 percent of their potential market, but should not have yet reached 50 percent of their potential.

The criteria used should direct us to technologies that are expected to have substantial impact on health care expenditures. However, diffusion is hard to measure and is continuously evolving as the target population changes. Furthermore, data that

would enable us to determine a technology's impact were collected as part of the study, so we cannot assume the ones we selected are the most important technology cost drivers. In fact, because we selected only a handful, we can be sure there are technologies we overlooked that could have as big, if not bigger, impact, on aggregate health spending. Nevertheless, each case study provides an illustration into how a new medical technology diffuses and influences both costs and outcomes.

In each round of voting, panelists were asked to list their ten top choices of technologies that were likely to be cost drivers in the next five years. Some panelists provided slightly more than 10 choices and some provided fewer, but all votes were counted in the selection process. Final votes after the two rounds, including the list of all technologies that received at least one vote, are presented in Table 1.

Despite the large number of medical technologies on the list, there was unanimous agreement among panel members that colorectal cancer screening, positron emission tomography (PET) for cancer, and cardiac stents and related devices were likely to be cost drivers in future years. The remaining technologies selected for study all received votes from at least half the panel members. They are low dose spiral computed tomography (CT) for lung cancer, genetic testing for cancer, drug inhalation devices, fast cardiac CT to screen for coronary artery disease, immunotherapy, and ThinPrep Pap smears[1].

d) Data Collection Procedures for the Case Studies

For each case study, data were collected on the evidence of effectiveness, recent patterns of diffusion, expected rate of future diffusion and factors likely to influence the course of diffusion. Data were also collected on technology costs.

To gather these data, Project HOPE staff reviewed the clinical, cost-effectiveness, and medical technology literature and conducted interviews with industry analysts, manufacturers' representatives, laboratory and imaging center administrators, and clinicians. Summary reports prepared by technology assessment organizations were

[1] Panelists voted to include testing for humanpapillovirus, or chlamydia, both of which are potential applications of ThinPrep Pap smears.

TABLE 1. RESULTS OF DELPHI PANEL SELECTION OF TECHNOLOGIES

Technology	Disease Area	Technology Area	Final votes
Colorectal cancer screening	Malignant neoplasms	Screening/imaging technologies	6
PET for cancer (staging and diagnosis)	Malignant neoplasms	Imaging technologies	6
Cardiac stents and related devices	Cardiovascular disease	Devices for cardiac surgery	6
Low dose spiral CT for lung cancer	Malignant neoplasms	Imaging technologies	4
Genetic testing for cancer	Malignant neoplasms	Genetic testing for disease	4
Inhalation devices to deliver medication	Respiratory disease/Diseases of the endocrine system	Drug delivery systems	4
Fast cardiac CT screening (including screening for coronary artery disease)	Cardiovascular disease	Screening/imaging technologies	4
Immunotherapy	Malignant neoplasms	Cancer Therapy	3
ThinPrep PAP smears (including testing for HPV; screening for chlamydia)	Diseases of the reproductive system	Screening technologies	3*
Non-surgical procedures to decrease GERD	Gastrointestinal disease	Sclerotherapy	2
Digital mammography	Malignant neoplasms	Screening/imaging technologies	2
Photodynamic therapy for macular degeneration	Disorders of the eye	Photodynamic therapy	2
Brachytherapy of coronary disease	Cardiovascular disease	Radiation Therapy	2
Transplantation in orthopedics	Diseases of the muscoloskeletal system	Transplantation	1
Cardiac applications of laser surgery	Cardiovascular disease	Laser surgery	1
Bioartificial organs	Organ failure	Transplantation	1
Non-myeloablative high dose chemotherapy	Malignant neoplasms	Cancer Therapy	1
Growth factors	Wounds	Growth factors	1
Minimally invasive cardiac bypass	Cardiovascular disease	Minimally-invasive surgery	1
Coronary angiography	Cardiovascular disease	Imaging technologies	1
Bone mineral density testing	Diseases of the muscoloskeletal system	Screening technologies	1

*Recommended by BCBSA with wide agreement by panel members.

Technologies in **bold** text were selected for study.

found to be particularly useful, as were industry forecasts reported in *Biomedical Business International*, *Health Technology Trends*, and *MedPRO Month.* Experts who provided information are listed in Appendix 2.

e) Cost Estimation Procedures

Incremental cases, that is the number of "new" patients who would not have used the technology in the proceeding year are estimated for each year from 2001-2005. As an illustration, if 100,000 persons are forecasted to use the technology in 2001 and 110,000 persons are expected to use the technology in 2002, the incremental number of cases in 2002 is 10,000. Multiplying these estimates by the incremental cost per case results in the total increase in health spending that can be attributed to the diffusion of a particular technology. To the extent possible, costs are defined from the perspective of national health accounts, that is payments for services by either third party entities or consumers.

Cost estimation procedures varied depending on the nature of the technology and its use. We relied heavily on existing cost-effectiveness studies, where available. To estimate the incremental cost impact of a new technology, expenditures for substitute technologies are netted out and those for complementary procedures are added in. Downstream costs are considered only to the extent that they occur within the five-year period of our forecasts. For example, coronary stents and angioplasty procedures are now being used to replace coronary artery bypass graft surgeries. Based on a recent cost-effectiveness analyses, the total health care costs incurred in the first year for these two substitute procedures were roughly equivalent (Yock et al., 2000), but repeat angioplasties and subsequent need for bypass surgeries added costs in future years. These were included for the relevant years of our forecast.

Often cost-effectiveness studies report incremental lifetime costs, and Project HOPE staff contacted the authors to obtain shorter-term, discrete estimates, when possible. When cost-effectiveness studies were unavailable, we constructed simple models drawing our assumptions from summary literature, or clinical users. Unlike most cost-effectiveness studies, we do not discount costs in future years. This is because we are estimating the net contribution of these technologies to health spending in the aggregate, which is estimated in nominal terms (including inflation).

Because divining the future is difficult, and there is often controversy surrounding the effectiveness of new medical technologies and their influence on costs, we often provide a range of high and low estimates, as well as our "best" estimate.

3 MEASURING EFFECTS OF TECHNOLOGY ON HEALTH EXPENDITURES

We begin this section with a definition of medical technology and a brief description of a framework for considering the roles of technology in the health care delivery system. In subsequent sections, we review approaches of study that have been used to estimate the relationship between technology and expenditures on health care. We summarize technology-specific approaches and some empirical estimates of the relationship between medical technology and expenditures. This section concludes with a discussion of the residual approach as an estimate for the health care sector as a whole. Recent estimates from the HCFA are presented and used as a basis for projections by our research team.

a) Defining Medical Technology

At the outset of this analysis, it is important to define medical technology. We often think of technology as referring primarily to equipment or hardware. But technology also refers to ways or processes of delivering health care and encompasses the ways that various inputs, including human capital and information, are used to deliver health care. The old, but widely used definition of technology adopted by the now defunct Congressional Office of Technology Assessment (OTA) recognizes this breadth: technology is defined as "drugs, devices, medical and surgical procedures used in medical care, and the organizational and supportive systems within which such care is provided" (OTA, 1982). Recognition of the roles of “organizational and supportive systems” is especially relevant today because of the variety of settings within which medical care is provided. This definition also recognizes that technology includes management information systems, a technology that promises to affect significantly health care delivery in future years (Institute for the Future, 2000).

b) Framework

The framework that underlies our perspective is that medical technology and health expenditures are determined simultaneously by market forces. A key element of their determination is that technological change and the demands for health care and health insurance are interdependent (Weisbrod, 1991). Technological change affects the demands for medical care and insurance, and the levels and terms of coverage (e.g., copayment rates, deductibles, etc.) affect the nature of technological development and its diffusion over time. Technological change also affects supply by its impacts on production and productivity, and ultimately the costs of care. Together, these demand and supply-side factors determine aggregate expenditures. In practical terms, this means that changes in demand for medical care, fueled by changes in advertising to consumers by drug or device manufacturers or by technological developments that promise improved quality-of-life, for example, may increase demand for insurance. If this

increased demand leads to purchase of more or better insurance, the consumer's ability-to-pay for new drugs and devices improves and aggregate health expenditures increase. Meanwhile, increased earnings by manufacturers of new technologies stimulate research and production of the next generation of products, and the cycle begins anew.

In the same way, this perspective accommodates decreases in demand for insurance and changes in payment policies under public programs, such as Medicare and Medicaid. As health insurance premiums increase, the quantity of insurance demanded by some employers will decrease. Demand for managed care products with lower premiums, possibly achieved by managed limits on access to newer technologies, may increase, which will lower demand for and economic returns from the development and sale of new drugs, devices, and processes. By changing economic incentives of providers of outpatient services and procedures, replacement of cost-based with prospectively determined prices under Medicare reduces demand for the tools of new, cost-increasing technologies, which should ultimately constrain cost and expenditure increases in the future.

c) Technology-Specific Approaches

As we mentioned in our overview, one approach to examining the technology-expenditure link is the "bottom-up" or "technology-specific" approach, under which the expenditure impacts of individual technologies are studied. A variation of this approach is the "cost-of-illness" study, within which an "average" cost of treatment is estimated from information on the cost of inputs used to treat the illness of interest. The costs of alternative approaches to treatment are reflected in the average estimate.

Both the Prospective Payment Assessment Commission (ProPAC) and the Physician Payment Review Commission (PPRC), for example, have employed technology-specific approaches to generate estimates of the expenditure implications of the diffusion of new technologies. Such information on why expenditures are increasing is needed in deciding whether policy action is appropriate. Over several years, analysts of the Project HOPE CHA studied a number of new and diffusing technologies for ProPAC (e.g., Mueller and Weisblatt, 1993; Mueller et al., 1993; McLaughlin et al., 1991). The goal of these studies was to estimate incremental costs of applying the new technology in treatment of Medicare patients. In the 1993 studies, for example, study technologies included telemetry patient monitoring systems, cardiac catheterization laboratories, gamma knife radiosurgery, and PET. Estimation of cost impacts required data on the numbers of Medicare patients who would receive the new technology (including patients who would and would not have otherwise received the "older" technology), the unit cost of using the technology, and the cost of the technologies that were substituted against or that would be received as complements to the new technology. Although cost estimates varied from year to year, depending on the number of technologies of interest, results suggest that new and diffusing medical technologies are responsible for annual cost increases of less than 1 percent of hospital costs for Medicare beneficiaries.

The technology-specific approach adopted by PPRC was designed to supplement the Commission's work toward meeting its requirement of making annual recommendations on updating Medicare Part B physician fees and setting the Volume Performance Standard rate of increase for physician expenditures under Part B in the early 1990s (PPRC 1993, 1991). "New" technologies were identified each year, based on recommendations from technology experts and physician specialty societies. Using claims data for the Medicare population provided by HCFA, Commission analysts calculated historical growth rates for all procedures and for procedures corresponding to new technologies. All procedures were identified using codes assigned by HCFA for billing purposes. The difference in growth rates was interpreted as representing the share of total growth in volume that was attributable to new technologies. Results from data from 1990 and 1991indicated that that new technologies accounted for only about 12 percent of annual growth in the volume of physician services, but a larger portion – 25 percent – of all new service volume (PPRC 1993).

Studies conducted by Scitovsky, a number of years ago, are often cited as seminal applications of the "cost of illness" approach (e.g., 1967, 1985). Scitovsky studied treatments for seven conditions, including appendicitis, breast cancer, and myocardial infarction, with data from the Palo Alto Medical Clinic. In her earlier work, she concluded that ancillary services, including lab tests and x-rays, were sources of increases in expenditures; expenditure effects in her later studies were attributed more to "big ticket" items and the costs of sophisticated procedures, e.g. in the treatments of myocardial infarction and breast cancer.

In a recent study of the impacts of managed care on the spread of hospital-based technologies, Baker and Spetz (1999) studied several technologies, including cardiac catheterization, neonatal intensive care units, and diagnostic radioisotope units. The extent to which managed care had penetrated into urban areas affected acquisition of these technologies differently.

An advantage of the bottom-up approach is that it focuses on identifiable processes or techniques, and can be selectively applied to unusually expensive medical devices or procedures. By studying a specific technology, information on the technology's pattern of diffusion, speed of adoption, and its influence on clinical practice, and expenditures can be acquired, and this information may shed light on new technologies and lead to better understanding of the technology-cost relationship in the future (CHA 1990). Approaches adopted by Berndt et al. (2000) and Cutler et al. (1999) represent significant advances in the analysis of the cost of treatment that is not captured by simpler price indices. Results of these studies may be used in certain contexts as bases for drawing inferences or generalizations about expenditures over a broader range of technologies or health conditions. Given these advantages, cost implications of nine new technologies were studied by CHA as part of this report.

On the other hand, an obvious disadvantage of the bottom-up approach is that results may have only limited applicability to other technologies and populations that were not targeted in the studies. Since costs and the rates at which they are incurred

differ by technology and disease, it is often difficult to generalize from the studied technology or disease to other technologies and conditions of interest. Application of the approach to numerous technologies in a comprehensive fashion is likely to be costly.

d) The Residual Approach

Methodology. Another more common strategy in studying the technology-expenditure relationship is the "top-down" or "residual" approach. Under this approach, the analyst attempts to use empirical techniques to calculate the contributions of all hypothesized determinants of expenditures, thereby isolating the "residual." This is the approach used by Davis (1974) and Feldstein (1977) in their searches for factors underlying hospital cost changes. It is also the approach periodically used by HCFA's Office of the Actuary to determine factors accounting for growth in the PHC component of National Health Expenditures (Smith et al., 1999; Cromwell and Beaven, 1994; Sonnefeld et al., 1991).

The model that underlies HCFA's approach is an accounting identity that decomposes changes in expenditures into several parts, including parts due to changes in the following:

- population
- prices, economy-wide
- prices in the health sector, in excess of general inflation
- the age/sex composition of the population
- the residual measure of real expenditures, per unit of service

(Cromwell and Beaven, 1994; Sonnefeld et al., 1991). The residual is the portion of expenditures that represents real changes in the per capita use of health care services. Broadly, speaking, it thus reflects the effects of technology.

Use of this methodology is appealing because in theory, and unlike the technology-specific approach, the residual reflects the total impact of all of the myriad technological changes that affect the population, including both "big-" and "little-ticket" items, technically enhanced procedures, and changes in technology that affect the organization and delivery of care.

Employing this approach with real-world data, however, is not problem-free. The validity of the residual as a measure of technology's contributions to expenditure changes depends on the extent to which expenditure changes can be attributed to their determinants. Application of the method requires that "clean" measures of the determinants of expenditures be used in the analysis. Consider, for example, the measurement of inflation. How should inflation be measured? As noted above, HCFA's application of the residual methodology distinguishes between general inflationary pressures over the economy at large, and medical care inflation, which has tended to exceed general inflation. The Consumer Price Index, or CPI, can be used to measure general inflation, but this index is a fixed weight index. This means that it tracks price

changes for the same basket of commodities over time. The mix of commodities that defines the index does not change without a re-basing of the index, when in fact purchasers may change the mix of commodities purchased in the short-run in response to changes in relative prices of commodities within the basket. As a means of dealing with this problem, HCFA uses more sophisticated "chain-linked" price indices that measure changes in prices of a mix of commodities that changes over time. Similar problems arise in the measurement of inflation within the health sector. Consider, for example, estimation of the residual for physician services. For what type of service or mix of services is the price measure defined? Once the service or mix is identified, how should the "transaction" price be defined? Presumably, the transaction price is the amount that is paid to the provider for delivering the service (Neumann and Juday, 1994). But is this the charge to an uninsured patient, or the discounted price facing a member of a preferred Provider Organization? Different persons face different prices, depending on their insurance coverage. Strategies to deal with this problem become even more complex as the nature of the commodity becomes less well-defined, e.g., hospital-based care, hospital outpatient department surgeries, etc., and when the components of PHC expenditures are aggregated. HCFA occasionally publishes values of the residual for PHC expenditures.[2]

Another challenge in measuring price changes is accounting solely for price changes, and not for changes in technology that may be reflected in price changes. We may observe, for example, that the price for a two-day hospital stay is higher in 1995 than in 1990. Although room and board components of the two-day hospital stay may cost more due to inflation, the prices of other components of the stay that are imbedded in the price measure may have increased because of technological changes in the components. Evidence from the Berndt et al. (2000) and Cutler et al. (1999) studies suggests that price indices overstate the effects of inflation. A consequence is that the magnitude of the residual is underestimated (and the magnitude of inflation is overestimated) when price changes embody technological changes because a portion of the change in expenditures that is attributed to inflation is in fact due to a change in technology.

The validity of the residual as an indicator of real changes in expenditures requires a complete accounting of its determinants, in addition to clean measures of the determinants of expenditures. There is a temptation to ascribe the entire residual to technology, but other unaccounted factors may be reflected in its value. An example is the effect of changing disease patterns. During the AIDS epidemic of the 1980s, hospitals adopted more stringent infection control standards. Adoption of these standards increased costs and are reflected as part of the residual during the 1980s because it was not possible to separate these costs from national account totals. Whether these expenditures should be viewed as new technology is debatable, but their inclusion in the residual should be kept in mind.

[2] The "price" measure used to remove excess inflation in the health sector from PHC expenditures is a weighted average of the prices used to value output for each component of PHC expenditures. Components include hospital care, physician services, nursing home care, and others.

Historic Trends. Between 1960 and 1998, nominal National Health Expenditures increased from $27 billion to $1.1 trillion (Table 2); on a nominal per capita basis, National Health Expenditures increased by a factor of 29 -- from $141 to $4,094 per capita. During the same period, Gross Domestic Product (GDP) increased 16-fold, from $527 billion to $8.5 trillion. Clearly, health expenditures have accounted for an increasing share of GDP. Five percent of GDP was spent on health care in 1960, versus over 13 percent in 1998.

Personal Health Expenditures increased at double-digit annual rates during the 18 year period 1965 to 1983, except for 1970-1971, when the increase was 9.8% (Table 3). Annual rates of increase bounced between 9 and 11 percent between 1984 and 1989. The annual rate of increase for 1990 – 11.7 percent – was the largest since 1981. From 1990 to 1997, however, rates of increase have fallen. In 1990, PHE increased by 11.7 percent; by 1997, the rate of increase had fallen to 4.8 percent. In 1998, expenditure growth had increased slightly to 5.2 percent.

As a percentage of total health spending, the residual has varied considerably since 1960 (Table 3), ranging from 4 percent to 64 percent of the increase. In the 1990s, this percentage declined during the first part of the decade, but increased steadily thereafter, from 12% in 1994 to 39% in 1998. By 1998, more of the expenditure growth was accounted for by the residual than by any of the other three factors (inflation, medical prices, and population), which hasn't been the case since 1987.

Neumann and Juday (1994) examined trends in the residual during the 1980s. During that time, inflation was the dominant factor accounting for increases in Personal Health Expenditures. As data presented here indicate, between 29 and 60 percent of expenditure increases (Table 3), or between 2 and 10 percentage points of the annual rate of increase in PHC expenditures (Table 4), were due to general, economy-wide inflation. Additional inflation in the health sectors accounted for another 13 to 40 percent of expenditure increases (Table 3), or between 2 and 4 percentage points in the annual growth rate of Personal Expenditures (Table 4). Population accounted for about 1 percentage point of expenditure growth each year (Table 4). The residual, or the remainder of the annual increase in expenditures, accounted for 20 and 37 percent (Table 3), or between 0.5 and 3.6 percentage points of increases in Personal Expenditures. In the early 1980, the residual accounted for 1 to 3 percentage points; between 1985 and 1990, the residual was at least 3 percent during four of the six years.

Since 1990, inflation has accounted for most of the annual increases in expenditures, as was the case between 1980 and 1990. In 1994 and 1995, general inflation accounted for over 40 percent of the increases in expenditures (Table 3). Its absolute contribution, however, has decreased throughout the decade. In 1990, 4.4 percentage points of the 11.7 percent increase in expenditures were attributed to general inflation. This contribution decreased to 1 percentage point of the 5-percentage point increase in 1998 (Table 4). The contribution of medical care inflation relative to general inflation has been erratic since 1990. In 1992 and 1993, medical care inflation accounted

for over 2 percentage points in expenditure increases. Since 1996, however, annual contributions of medical inflation have been 1.2 percentage points or less (Table 4).

Growth in the US population continues to have effects in the neighborhood of 1 percentage point per year. Estimates by HCFA are not adjusted for changes in the age composition of the population, even though their conceptual model recognizes the potential importance of this factor.

Interpretation. Historic trends in the residual suggest that technology's impact on costs is influenced by systemic changes in health care reimbursement. For example, the residual reached its nadir during the mid-1980s with the advent of the Medicare prospective payment system (which presumably mitigated the influence of technology relative to inflation and other factors). It declined again in the early 1990s during a rapid expansion of managed care. Notably, in both cases, the residual rose sharply after temporary declines, suggesting that attempts to contain medical technology are difficult to sustain.

We focus specifically on trends during the 1990s, because recent history may inform our forecasts of the near future. The values of the residual through the 1990s suggest that technology accounted for a decreasing share of the increase in expenditures in the early half of the decade, but that technology may have had increasing effects on expenditures since 1995. Does evidence from the 1990s question the validity of the residual as a measure of technology? What environmental factors might help explain effects of technology on expenditures during this decade?

Service mix. During the 1990s, there was a significant change in the nature of services provided by the US health care system. There has been a shift away from acute care services provided to hospital inpatients, stimulated in part by financial incentives of the inpatient prospective payment system implemented in the mid-1980s under the Medicare program (see below). Between 1990 and 1998, PHC expenditures grew by 66 percent, while expenditures for hospital care – the biggest health care expenditure component -- grew by only 49 percent. This aggregate masks rapid growth in the provision of outpatient services relative to inpatient hospital care.

TABLE 2. NATIONAL HEALTH EXPENDITURES, U.S. POPULATION AND GROSS DOMESTIC PRODUCT: SELECTED CALENDAR YEARS 1960-98

Item	1960	1970	1980	1985	1990	1991	1992	1993	1994	1995	1996	1997	1998
						Amount in Billions							
National Health Expenditures	$26.9	$73.2	$247.3	$428.7	$699.4	$766.8	$836.5	$898.5	$947.7	$993.3	$1,039.4	$1,088.2	$1,149.1
						Amount in Millions							
U.S. Population [1]	190	215	235	247	260	263	266	268	271	273	276	278	281
						Per Capita Amount							
National Health Expenditures	$141	$341	$1,052	$1,734	$2,689	$2,918	$3,151	$3,351	$3,501	$3,637	$3,772	$3,912	$4,094
						Amount in Billions							
Gross Domestic Product	$527	$1,036	$2,784	$4,181	$5,744	$5,917	$6,244	$6,558	$6,947	$7,270	$7,662	$8,111	$8,511
						Percent of Gross Domestic Product							
National Health Expenditures	5.1	7.1	8.9	10.3	12.2	13.0	13.4	13.7	13.6	13.7	13.6	13.4	13.5
						Average Annual Percent Growth from Previous Year Shown							
National Health Expenditures	--	10.6	12.9	11.6	11.0	9.6	9.1	7.4	5.5	4.8	4.6	4.7	5.6
U.S. Population	--	1.2	0.9	0.5	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9
Gross Domestic Product	--	7.0	10.4	4.1	7.5	3.0	5.5	5.0	5.9	4.6	5.4	5.9	4.9

[1] July 1 Social Security area population estimates for each year, 1960-98.

NOTE: Numbers and percents may not add to totals because of rounding.

SOURCE: Health Care Financing Administration, Office of the Actuary: National Health Statistics Group. *Highlights -- National Health Expenditures, 1998.* http://www.hcfa.gov/stats/nhe-oact/hilites.htm.

TABLE 3. GROWTH IN PERSONAL HEALTH CARE EXPENDITURES AND DISTRIBUTION BY SOURCE: UNITED STATES, 1960-98

Year	Average annual percent increase	Growth attributed to			
		Inflation[1]			
		Economy-wide	Medical	Population	Intensity[2]
		Percent			
1960-98	10.4	42	16	10	32
1961	6.1	20	6	27	47
1962	7.6	17	11	21	51
1963	9.3	13	7	16	64
1964	9.9	15	15	14	56
1965	8.6	23	9	15	53
1966	10.4	29	21	11	39
1967	13.7	25	13	8	54
1968	12.9	35	11	8	46
1969	12.8	38	10	8	44
1970	13.5	40	8	8	43
1971	9.8	54	11	11	24
1972	11.4	39	-3	9	55
1973	11.6	50	-15	8	57
1974	14.7	62	1	6	30
1975	14.7	66	9	6	19
1976	14.0	44	21	6	29
1977	13.2	50	11	7	32
1978	11.6	64	5	9	22
1979	13.7	64	4	7	25
1980	15.8	60	13	7	20
1981	16.1	60	17	7	16
1982	12.4	52	35	9	4
1983	10.0	44	32	11	13
1984	9.6	39	40	11	10
1985	10.2	36	36	10	18
1986	9.0	29	26	11	34
1987	9.6	33	19	11	37
1988	11.0	34	24	10	32
1989	10.2	42	27	11	20
1990	11.7	38	21	9	31
1991	10.6	39	16	10	35
1992	9.0	32	28	12	28
1993	6.7	39	32	15	14
1994	5.5	45	25	18	12
1995	5.4	43	25	17	15
1996	5.1	38	22	18	23
1997	4.8	39	7	20	34
1998	5.2	20	23	18	39

[1]Total inflation is economy-wide and medical inflation is the medical inflation above economy-wide.

[2]The residual which cannot be attributed to price increases or population growth represents changes in use or kinds of services and supplies.

SOURCE: Table 117 of *Health, United States, 2000 with* Adolescent *Health Chartbook, 2000,* National Center for Health Statistics, citing National Health Statistics Group, Office of the Actuary. National health expenditures, 1998. Health Care Financing Review vol 21 no 2. Health Care Financing Administration. Washington: U.S. Government Printing Office, Winter 1999.

TABLE 4. PERCENT GROWTH IN PERSONAL HEALTH CARE EXPENDITURES AND DECOMPOSITION BY SOURCE UNITED STATES, 1960-98

Period	Average annual percent increase	Growth attributed to			
		Inflation[1]			
		Economy-wide	Medical	Population	Intensity[2]
		Percent			
1960-98	10.4	4.4	1.7	1.0	3.3
1961	6.1	1.2	0.4	1.6	2.9
1962	7.6	1.3	0.8	1.6	3.9
1963	9.3	1.2	0.7	1.5	6.0
1964	9.9	1.5	1.5	1.4	5.5
1965	8.6	2.0	0.8	1.3	4.6
1966	10.4	3.0	2.2	1.1	4.1
1967	13.7	3.4	1.8	1.1	7.4
1968	12.9	4.5	1.4	1.0	5.9
1969	12.8	4.9	1.3	1.0	5.6
1970	13.5	5.4	1.1	1.1	5.8
1971	9.8	5.3	1.1	1.1	2.4
1972	11.4	4.4	-0.3	1.0	6.3
1973	11.6	5.8	-1.7	0.9	6.6
1974	14.7	9.1	0.1	0.9	4.4
1975	14.7	9.7	1.3	0.9	2.8
1976	14.0	6.2	2.9	0.8	4.1
1977	13.2	6.6	1.5	0.9	4.2
1978	11.6	7.4	0.6	1.0	2.6
1979	13.7	8.8	0.5	1.0	3.4
1980	15.8	9.5	2.1	1.1	3.2
1981	16.1	9.7	2.7	1.1	2.6
1982	12.4	6.4	4.3	1.1	0.5
1983	10.0	4.4	3.2	1.1	1.3
1984	9.6	3.7	3.8	1.1	1.0
1985	10.2	3.7	3.7	1.0	1.8
1986	9.0	2.6	2.3	1.0	3.1
1987	9.6	3.2	1.8	1.1	3.6
1988	11.0	3.7	2.6	1.1	3.5
1989	10.2	4.3	2.8	1.1	2.0
1990	11.7	4.4	2.5	1.1	3.6
1991	10.6	4.1	1.7	1.1	3.7
1992	9.0	2.9	2.5	1.1	2.5
1993	6.7	2.6	2.1	1.0	0.9
1994	5.5	2.5	1.4	1.0	0.7
1995	5.4	2.3	1.4	0.9	0.8
1996	5.1	1.9	1.1	0.9	1.2
1997	4.8	1.9	0.3	1.0	1.6
1998	5.2	1.0	1.2	0.9	2.0

[1]Total inflation is economy-wide and medical inflation is the medical inflation above economy-wide.

[2]The residual which cannot be attributed to price increases or population growth represents changes in use or kinds of services and supplies.

SOURCE: Calculations based on Table 117 of Health, United States, 2000 with Adolescent Health Chartbook, 2000, National Center for Health Statistics, citing National Health Statistics Group, Office of the Actuary. National health expenditures, 1998. Health Care Financing Review vol 21 no 2. Health Care Financing Administration

Physicians have maintained control over resource use in both inpatient and outpatient settings. There has been relatively little change in the share of expenditures for physician services, the second largest component of Personal Health Expenditures. Physician service expenditures increased by 57 percent between 1990 and 1998 (relative to an increase of 66 percent in health care expends overall), and accounted for 24 and 23 percent of expenditures in 1990 and 1998 overall (Cowan et al., 1999).

By contrast, drug expenditures increased by 140 percent. This increase has been attributed to more rapid drug approvals by the Food and Drug Administration, increased consumer demand, fueled by the drug industry's targeting of advertising to consumers, and facilitated access to care under managed care plans which has increased demand for prescription drugs (Cowan et al., 1999). The share of PHC expenditures for hospital care decreased from 42 percent in 1990 to 38 percent in 1998, while the share of expenditures for purchase of prescription drugs increased from 6.1 percent to about 9.0 percent during this time period.

At the same time, the home health care component of health expenditures has increased in absolute and relative size. Home health services are often viewed as low cost alternatives to post-acute care provided in hospitals and nursing facilities. Expenditures for home health care more than doubled during the 1990-98 period.

Hence, the current environment favors drugs and other technologies that more efficiently make use of the inpatient hospital environment, and technologies that favor care offered in outpatient settings including the home. Recent increases in the residual may reflect this environment, especially the increasingly important role played by prescription drugs.

Cost containment. Cost containment efforts that began during the decade of the 1980s with the implementation of the Medicare Prospective Payment System (PPS) for hospital inpatient care continued during the 1990s with attempts to control remuneration for services provided by physicians and other health professionals. Between 1980 and 1990, Medicare hospital expenditures increased by a factor of 2.6, while expenditures for physician services grew by a factor of 3.6. In response, research supported by HCFA and recommendations to Congress by the Physician Payment Review Commission (PPRC 1990, 1989) culminated in legislation that replaced cost-based payments for physician services provided to Medicare patients with payments based on the cost of the physician's time and effort, as measured by the Resource-Based Relative Value Scale (RBRVS). The new Medicare Fee Schedule was phased in during the early 1990s. During this time, fundamentals of the RBRVS were adopted by state Medicaid programs and by private payers, so effects of payment reforms extended well beyond the elderly segment of the population. Later in the decade, the second phase of physician payment reform -- which
changed the portion of the fee for practice expense (the non-physician costs of services) – occurred. The Balanced Budget Act of 1997 (BBA), legislated changes in the method of calculating the portion of payments for physician services that covered the non-

physician costs of providing services. Resource-based practice expense payments have since replaced payments based on the costs of practice.

Physician payment reform constrained expenditure increases to levels less than those that would have been experienced had payments remained cost-based. Payments that were most constrained by the new payment methodology were for medical and surgical procedures provided in physician offices and for surgical procedures provided primarily to inpatients; payments for evaluation and management services, most often provided by primary care physicians, were the least affected. Under the hospital inpatient PPS, incentives facing hospitals were fundamentally altered. The PPS fixed payments for each Medicare diagnosis, thereby replacing the incentive to increase volume with the incentive of minimizing resource use. By contrast, the Medicare resource-based Fee Schedule changes relative payments, but payments are still service-based: the more that are provided, the greater the provider's revenue, even though the service's payment may have fallen relative to payments for other services. Thus, it is not clear that implementation of the Medicare Fee Schedule would change the residual so long as distortions in fees are not introduced and physicians do not depart from behavior that is profit-maximizing. For some time, HCFA has been concerned that physicians will react to price reductions by increasing volume as a means of maintaining their income levels. Thus, one might expect to see an increase in the residual during the early 1990s, when the largest fee changes were introduced. During the early 1990s, however, the residual declined, contrary to expectations. The residual began to increase after 1995, during the period when fees were changing to reflect recalibrations in practice expense components of cost – a period when changes were not as great as earlier in the decade. It is possible that these changes, on top of earlier changes, were sufficient to cause physicians to increase volume. Whatever incentives were introduced by changes in Medicare fees probably extended beyond Medicare patients, as private payers have adopted Medicare's payment principles over time. And because the Physician Care component of Personal Care expenditures is relatively large, effects of the Medicare Fee Schedule may have increased the residual during the second half of the decade.

Managed care. During the 1990s, there was also significant growth in the number of persons enrolled in managed care plans. Enrollment increased from 9.1 million in 1980 to 33 million by 1990, and then to 81.3 million by 1999. The latter estimate contains 10.4 million persons enrolled in a Medicaid managed care program, up from 1.2 million in 1990, and 6.5 million Medicare managed care beneficiaries, up from 1.8 million beneficiaries in 1990 (NCHS 2000).

The slowdown in the growth of health expenditures during the 1990s has been attributed in part to competitive pressures of managed care (Cowan et al., 1999). In fact, a growing body of literature suggests that managed care has helped to contain medical care expenditures (Zwanziger and Melnick, 1996). Incentives implicit in managed care models – to minimize cost, given payments from enrollees that are only weakly related to quantity and intensity of prescribed use -- help contain expenditures by lowering demands for expensive, high technology services. These reductions in demand will, over time, reduce economic returns to investments in development of new technologies.

Ultimately, it is argued that as managed care's share of the insurance market grows, changes in the behaviors of physicians and other providers will "spill over" into other insurance markets, further dampening the spread of new technologies. Technologies most likely to be affected are most likely used in the inpatient and outpatient hospital settings and would involve higher payments to physicians. Thus, managed care's effects might have helped reduce the residual during the 1990s.

Some evidence is consistent with hypotheses that managed care has weakened the link between new technologies and expenditures. Evidence suggests that managed care's share of the health insurance market is negatively related to the availability of MRI equipment and its use (Baker, 1998) and the availability of angioplasty in community hospitals (Cutler and McClellan, 1996). Cutler and Sheiner (1998) also suggest that Health Maintenance Organizations (HMOs) may slow rates of growth in the adoption of new technologies.

Baker and Spetz (1999) studied the relationship between availability of hospital-based technologies and insurance market penetration by HMOs from the 1980s through the early 1990s, and report that managed care may have limited the availability of technology to some extent. Availability of technology was measured using an index, developed by the authors, that measures hospital acquisition of "rare" technologies. The authors find that that metropolitan areas with a strong HMO presence in the early 1980s also ranked relatively high with respect to technology availability, but technology index values for these areas had been surpassed by values in cities with a smaller managed care presence by the early 1990s – the time by which the size of the contribution of the residual to PHC expenditures (Table 3) began to decline.

A review of the evidence reported by Baker and Spetz, however, indicates that the role of managed care in the relationship between technology and cost is not clear. The authors emphasize that the technology index measures availability and not the cost of using rare technologies. Baker and Spetz also find that managed care penetration has not affected the rate of growth in the availability of technology in recent years. Furthermore, any impacts of managed care do not appear to be levered through traditional, competitive channels. Although one might hypothesize that a hospital's competition for HMO contracts might affect the hospital's technology position, Baker and Spetz find no evidence of a relationship between the extent of hospital competition and HMOs' influences on the availability of technology.

e) Bottom Line

Although investigators have used a variety of methods to measure the impact of technology on health care spending, most have shown medical advances have a net upward impact on costs (Fuchs, 1972; Schwartz, 1987; Scitovsky, 1985, Showstack et al., 1982; Mueller and Weisblatt 1993; Mueller et al., 1993; McLaughlin et al., 1991; Center for Health Economics Research, 1988; PPRC, 1993; Newhouse, 1993; Cowan et al., 1999; Berndt et al., 1999; Cutler et al., 1999). As our case studies in the following section will illustrate, new technology adds to costs because it increases the "intensity" of

care – i.e., it expands the opportunities for providing services to patients. Even where a new technology can reduce unit costs for particular patients, it often increases net health expenditures by increasing overall volume – i.e., diffusing into patients with mildly symptomatic disease, or those who were previously too ill for treatments (Schwartz, 1994; Goldsmith, 1994).

Reviewing past research, the magnitude of technology's influence on health care spending varies greatly and depends on how, and when, technology's influence is measured. Even when a common metric such as the residual is used, historic data show wide variation in its contribution to total health spending, ranging from a low of less than 5 percent to over 60 percent. However, changing economic incentives for providers does appear to influence estimates of technology's share of the increase. As we postulated at the beginning of this section, the public's demand for new technology is intricately woven into the fabric and design of the health care system.

4 FORECAST OF TECHNOLOGY'S FUTURE INFLUENCE

A goal of this analysis is to project the impact of new technology on health expenditures for the next five years. Between now and the year 2005, we project that the residual, a measure of the contribution of new technology to health care expenditures, will range from 25 to 33 percent, and that personal care expenditures will increase between 6.0 and 7.0 percent per year during this time period. In other words, increases in volume and intensity will account for between 25 and 33 percent of the annual increase in health care expenditures, or between 1.5 and 2.2 percentage points of the increase in expenditures annually between now and the year 2005.

This projection is based on projections made by staff of the HCFA Office of the Actuary, as reviewed by authors of this report and informed by a review of the literature cited in this report and by discussions with experts on various health technologies. We summarize HCFA's projections and our critique below.

a) HCFA's projections

Each year, HCFA's Office of the Actuary projects health care spending for the subsequent 10-year period. We reviewed their most recent published expenditure projections and projections on changes in volume of care and intensity that were not accounted for by changes in economy-wide and health care inflation and population growth (Smith et al., 1999). The Smith et al. projections are for the period 1998-2008; projections are based on data through 1997, even though their analysis was published at the same time as the Cowan et al. analysis of data that included the year 1998.

Smith et al. expected health care spending to increase at an annual average rate of 6 percent per year over the period 1997-2001 and 6.1 percent average annual growth during the period 2001-2008. This projected expenditure increase is less than the historical average . By 2005, the year of interest in this analysis, national health expenditures were expected to be about 15 percent of GDP, versus 13.5 percent in 1998.

Implied residuals, net of HCFA estimates of excess inflation in the health sector, are displayed graphically in the Smith et al. text for the periods 1997-2001 and 2001-2008. HCFA predicted residuals of 30 percent during the period 1997-2001, and 12 percent for the period 2001-2008. In other words, volume and intensity were expected to account for an average 30 percent of the annual expenditure increase from 1997-2001, and for 12 percent of the average annual expenditure increase between 2001 and 2008. Thus, the residual was expected to account for 1.8 percent of the 6 percent average annual increase for 1997-2001, and about 0.7 percent of the 6.1 percent average annual expenditure increase during the period 2001-2008.

Smith et al. note that their projections for the earlier period are larger than for the later (2001-2008) period. During the earlier period, the authors forecasted increasing demand for health services and slower growth in enrollment in managed care plans. Furthermore, the authors predicted that during this period of increasing demand, there

will be a shift in managed care enrollment toward less restrictive models of managed care that permit, for example, more choice among providers and out-of-plan use. During the later period, however, the authors anticipated reductions in volume and intensity as income increases will moderate, health insurance premiums will increase, and demand for more restrictive forms of managed care will rebound.

b) Critique

The HCFA projections are based on an actuarial model and professional judgment. General economic and demographic factors that are mentioned as affecting HCFA's expenditure and residual projections include trends in per capita income, inflation, and population growth and aging; attributes of the health sector that affect projections include managed care penetration, private health insurance premiums, the uninsured population, and the impact of the BBA. We reviewed published arguments supporting the projections and based our projections on recent and anticipated legislation and a review of recent evidence.

First, we project two scenarios for growth in personal health spending. Given the current state of the economy, we anticipate that personal health care expenditures will increase between 6.0 and 6.5 percent annually between the present and the year 2005. However, spending growth could be higher (6.5 percent to 7.0 percent) with somewhat increased inflation. Under both scenarios, we expect growth in personal health spending will likely be higher than HCFA forecasts. This modification is based on our views of the effects of recent legislative changes.

Under our first scenario, we considered effects of several legislative changes. First, projections by Smith et al. were based on a review of the BBA, which legislated numerous reductions in Medicare expenditures over the 1998-2002 period. These reductions, estimated to produce savings of $112 billion during the 1998-2002 period, affected payments for inpatient hospital, outpatient, home health, and skilled nursing services (MedPAC, 2000a). After the HCFA forecast was made, the Congressional Budget Office (CBO) markedly altered their forecasts for Medicare baseline spending. They projected Medicare spending reductions that were more than double what had been anticipated. In fact, between 1998 and 1999, there was a small negative growth in Medicare spending, which has been observed only one other time in the history of Medicare. Much of this dramatic slowdown probably occurred because of changes in provider billing (e.g., undercoding or lack of billing) in response to concerns about Federal anti-fraud and abuse strategies, as opposed to the BBA per se. Indeed, evidence from HCFA shows slower personal health spending in 1998. The *projected* increase in expenditures by HCFA, for 1998, was 5.8 percent, whereas *actual* expenditures increased by 5.6 percent. The projected increase in public expenditures was 5.6 percent, whereas public expenditures for 1998 increased by 4.1 percent (Smith et al., Table 1). The net effect is lower base public spending than expected.

There has already been pressure to increase the rate of spending over this lower base. Two recent legislative changes have occurred that were not taken into account in HCFA's projections that support this view. A part of the savings from the BBA was returned to providers by the Balanced Budget Refinement Act of 1999 (BBRA). Under the BBRA, Medicare spending is increased by $16 billion during the period 2000-2004, primarily by either delaying implementation of the BBA provisions or reducing the size of BBA payment reductions (MedPAC, 2000a). In addition, the Benefits Improvement and Protection Act (BIPA) legislation represents a second part of the "give back." The total impact of BIPA is estimated to be about $35 billion over five years. BIPA increases Medicare payments to hospitals, payments to Medicare+Choice plans, and offers other savings to Medicare beneficiaries (RUPRI, 2001). There is some indication that the rate of increase in Medicare spending is growing more rapidly now, albeit from a lower base. The Congressional Budget Office also predicts the rate of Medicare spending will range between 6 and 10 percent over the 2001 to 2005 period, which can be compared with a 3 percent rate of growth in 2000.

If inflationary pressures-- general or medical sector -- increase in the future, growth in personal health spending may be more in the range of 6.5 to 7.0 percent over the forecast period.

It should be noted that although we anticipate some form of Medicare drug benefit will be legislated prior to the year 2005, we do not expect to observe significant expenditure effects during this time period. Estimates of the cost of a benefit proposed during the campaign by the Bush administration are around $65 million over five years, which is small in comparison to annual changes in Medicare spending. Even if a drug benefit of larger magnitude is enacted, we would expect a substantial time lag between legislation and implementation. Thus, any expenditure effects are not likely to be felt until the end of our forecast period.

Second, we project that the residual will be within the range of 25 to 33 percent annually between now and the year 2005. Based on our review of 30 years of trends in the residual, it has rarely attained the low values forecast by HCFA (12 percent). Within the last decade, this low level was observed only during the period when the influence of managed care on cost containment was particularly aggressive (the early 1990s) and this dramatic slowing of the residual was only achieved for a short period (two years) at high cost to public opinion. We believe the public will resist further movement toward less restrictive models of managed care seen in the early 1990s.

The residual reached its lowest level during the implementation of Medicare's inpatient PPS. While the effect of the BBA is potentially greater than inpatient PPS, its effect on the residual is not expected to be sustainable over the long term. Three years after the implementation of PPS, the future five-year average for the residual climbed to 30 percent from a low of 12 percent; this is in line with our forecasts.

At the other extreme, we also believe the repercussions of the Balanced Budget Act will continue to be felt in the near term and there will be pressure to moderate spending in the private sector given recent increases in insurance premiums (as HCFA

had anticipated). Thus, we do not anticipate the residual will reach the high levels observed in the late 1990s (34-39 percent).

Even under our second scenario of higher growth in personal health care spending, we expect the residual will range between 25 and 33 percent. We anticipate that higher general and medical price inflation, rather then increases in the residual, will account for growth in personal health care spending.

5 INSIGHTS FROM TECHNOLOGY CASE STUDIES

Stepping away from the macro perspective, we now examine a handful of case study technologies to shed light on how technology is likely to influence health care costs in the future and to examine the impact of potential cost drivers on future health spending. They include devices (coronary stents, drug inhalation devices), non-prescription drugs (monoclonal antibodies), imaging technologies (colonoscopies, PET, electron beam CT, spiral CT), laboratory procedures (ThinPrep Pap smears), and genetic tests (genetic testing for colon cancer). These cases exhibit diverse patterns of diffusion and each raises unique issues with respect to why and how a technology diffuses and influences health care system costs.

In this section, we introduce our case study technologies by comparing them along various dimensions, such as their function, the relative intensity of resources consumed, and setting of use. Next, we examine their influence on health care costs and outcomes. We conclude with some general insights about technology's influence on health care spending. Case studies for each of these technologies are included in Appendix 4.

a) Characteristics of Study Technologies

Technologies may be used to prevent or cure disease; they may be used to improve our capacity to diagnose disease, or they may help extend survival, even if only briefly, for persons with life-threatening conditions. Technologies can be used for rehabilitating the ill, or simply to serve as a palliative to reduce the pain and suffering of a chronic or terminal illness (Rosenthal, 1977).

Notably, more than half of our study technologies is intended to *prevent* disease through mass screening programs (see Table 5). Of our remaining technologies, one is diagnostic (PET), two are palliative (coronary artery stents and inhaled insulin) and one focuses on extending survival (monoclonal antibodies). Notably, none are curative. The selection of such a large number of screening technologies may be indicative of more global trends in technological change. As we have become more proficient at treating disease, through the development of antibiotics and other interventions, the focus overall may be on earlier, preventive intervention. Certainly, private and public insurers have broadened their coverage of preventive services, such as screening mammographies, Pap smears, and influenza vaccines in recent years.

Technologies may also be classified according to their impact on resource consumption. Battista et al. (1991) identified three broad groups according to the intensity of resources each technology consumes: high, medium, and low. High technologies require not only a large investment in capital equipment, but major human, physical and administrative commitments, as well. PET for cancer is an example of a high technology. Medium technologies require substantial resources to develop, but far

fewer physical and human resources to administer, such as monoclonal antibodies. By contrast, low technologies such as Pap smears, require even fewer resources to develop and administer. A similar typology classifies technologies into "big ticket" (similar to the high technologies) and "small ticket" (similar to low technologies) groups (Scitovsky, 1967). Most of our technologies could be considered medium or high technologies, but one (ThinPrep Pap smears) is a "small-ticket" item, which nevertheless has potential application to a large number of persons in the United States (Table 5).

Notably, all but one of our case study technologies will be used in an outpatient or home setting (Table 5). This is consistent with our observation of aggregate trends where the market for new medical advances is now favoring drugs and other technologies that affect care offered in outpatient settings including the home. Even the one case study that is currently used in an inpatient setting – coronary stents – has seen rapid decreases in post-surgical lengths of stay and may become an outpatient procedure in the near future (Topol, personal communication).

b) Influence on Health Care Spending

Despite trying to select cost drivers, after further investigation not all of the case study technologies are expected to have a big influence on future spending (Table 6). Although there was unanimous agreement among panelists that coronary artery stents would be a large cost driver in the future, we found the market for stents is quite mature. Nevertheless, adjunct therapies being developed to reduce the associated risks of stent placement, such as the platelet inhibitor, GP IIb/IIIa, and embolic capture devices, are expected to add to costs of stent procedures, at a magnitude similar to the costs of stents themselves. Thus, stent procedures are still expected to be cost increasing in the future, but mainly due to technologies other than the coronary stents. Lack of insurance coverage for EBCT to screen for coronary artery disease and spiral CT to screen for lung cancer disease has constrained diffusion of these technologies. Recent evidence suggesting EBCT may be not as effective and less cost effective than alternative strategies is expected to substantially slow the diffusion of this technology in the future (O'Rourke, 2000). Several randomized trials are being conducted to examine the effectiveness of spiral CT for lung cancer screening, but the results are not expected to be available within the next five years. Given the large potential costs of this technology and the controversy surrounding its use, diffusion will likely be slow in the near term (Table 7).

Also, genetic testing is unlikely to be the cost driver sometimes suggested; although susceptibility-conferring genotypes have been found for colon and some other cancers, these genotypes remain rare, accounting for less than three percent of all cases (Holtzman and Marteau, 2000). Given the confidentiality concerns that arise with positive results, genetic testing is likely to be constrained to the high-risk population, rather than used in the healthy general public.

TABLE 5. CLASSIFICATION OF STUDY TECHNOLOGIES

Technology	Function	Relative impact on resource use	Setting
Coronary stents	palliative	medium	inpatient
with GP IIb/IIIa	survival	medium	inpatient
with capture devices	survival	medium	inpatient
Colorectal cancer screening	preventive	medium	outpatient
Fast cardiac CT screens	preventive	high	outpatient
Genetic testing for colon cancer	preventive	medium	outpatient
Spiral CT for lung cancer	preventive	high	outpatient
Immunotherapy	survival	medium	outpatient
Inhaled insulin	palliative	medium	home
PET for cancer	diagnostic	high	outpatient
Thin-Prep Pap smears	preventive	low	outpatient

TABLE 6. IMPACT OF STUDY TECHNOLOGIES ON COSTS AND QUALITY

Technology	Short-term cost impact (1 year)	Long-term cost impact	Quality impact	Additive, replacement, or new
Coronary stents	cost-neutral	cost-increasing	quality-enhancing	replacement
with **GP IIb/IIIa**	cost-increasing	cost-increasing	life-saving	replacement
with **capture devices**	cost-increasing	cost-increasing	life-saving	new
Colorectal cancer screening	cost-increasing	cost-neutral or cost-decreasing	life-saving	replacement
Fast cardiac CT screens	cost-increasing	cost-increasing	unproven benefit	additive
Genetic testing for colon cancer	cost-increasing	cost-decreasing	quality-enhancing	additive
Spiral CT for lung cancer	cost-increasing	cost-increasing	unproven benefit	new
Immunotherapy	cost-increasing	cost-increasing	life extending	additive
Inhaled insulin	cost-increasing	cost-decreasing	quality-enhancing	replacement
PET for cancer	cost-increasing	cost-increasing	quality-enhancing	additive
Thin-Prep Pap smears	cost-increasing	cost-increasing	quality-enhancing	replacement

Cost drivers are indicated by **bold** text.

TABLE 7. ESTIMATED INCREMENTAL COSTS FOR STUDY TECHNOLOGIES (BEST CASE SCENARIO)

	Incremental Costs by Year (Millions of US$)				
Technology	**2001**	**2002**	**2003**	**2004**	**2005**
Coronary stents	$17	$30	$46	$62	$67
Colonoscopy (screening)	$156	$171	$188	$208	$239
Fast cardiac CT screens	$49	$25	$13	$7	$0
Genetic testing for colon cancer	$1	$2	$3	$4	$6
Spiral CT for lung cancer screening	$11	$15	$19	$19	$19
Immunotherapy	$172	$211	$260	$321	$396
Inhaled insulin	$0	$0	$95	$460	$887
PET for cancer	$224	$199	$225	$248	$273
Thin-Prep Pap smears	$96	$40	$40	$40	$40
All case study technologies	$726	$693	$889	$1,369	$1,927
Growth in personal health spending[1]	$76,400	$82,700	$87,900	$90,700	$97,800
As a % of growth in personal health spending	1.0%	1.0%	1.0%	2.0%	2.0%

Cost drivers are indicated by **bold** text.
[1]Annual increase in personal health spending from Project HOPE calculations of HCFA, Office of the Actuary, 1997 forecasts.

- ✓ Nearly all of our case study technologies are expected to increase costs in the short term.

All but one of our case study technologies is expected to add costs to the health care system in the short term (Table 6). Under our "best case" scenario, the collective nine study technologies could add between $700 million to $1.9 billion to health care spending in a given year. Although this amount seems large, when compared with personal health spending growth these nine technologies will likely contribute to no more than 1-2 percent of the overall increase in health care spending. Nevertheless, if the residual accounts for between 25 to 33 percent of the growth in personal health spending, as we anticipate, these technologies may account for 3 to 8 percent of that increase; this is a relatively large magnitude considering the hundreds, and perhaps thousands, of new technologies that are being adopted today.

Screening technologies, which account for half of our case studies, are more likely to be cost drivers than other types of technologies for several reasons. First, their use is targeted to a large number of persons. There are an estimated 80 million people age 50 or older who could benefit from colorectal cancer screening; over 100 million women are candidates for regular pap smear screens and an estimated 92 million current and past smokers in the United States could potentially benefit from a more effective lung cancer screening test. Second, screening technologies often add to costs, because they may avert disease many years in the future, but not in the short term. The development of cancer from a polyp in the colon, for example, is slow, estimated from 10 to 20 years, although lung cancer is considerably more aggressive. Finally, new screening technologies may be adopted because they are more sensitive than existing alternatives, with a corresponding decrease in specificity. Thus, false positive results may give rise to further diagnostic testing and procedures that are themselves expensive. For example, estimates range from 20 to over 95 percent of suspicious lesions found in the lung with spiral CT may turn out to be benign (National Cancer Institute, 2000; Alberle, personal communication; Kolata, 2000).

New diagnostic technologies often add costs because they are used in addition to the existing battery of tests (additive), rather than replacing them (Eisenberg et al., 1989). As an illustration, although PET could supplant other imaging techniques, such as computed tomography (CT) or magnetic resonance imaging (MRI), it is most likely to be used in a sequence after other diagnostic procedures. This is because it adds different anatomical rather than functional -information, to the diagnostic process.

- ✓ Some technologies may reduce costs in the short term if their use is restricted to an appropriately selected population, but in the aggregate they are likely to increase costs.

The use of positron emission tomography (PET) for the diagnosis and staging of cancer, for example, could avoid surgery for non-resectable tumors and for benign tumors

in the short term. PET may also help to avoid prolonged chemotherapy for patients who are not responding to treatment. For lung cancer diagnoses, if restricted to those patients with proven lung cancer and no involvement of the lymph nodes, rather than earlier in the diagnostic algorithm, PET may be cost saving (Mitchell et al, 1998). Because a PET scanner has relatively high acquisition costs and low operating costs, there are strong incentives for hospitals to expand the use of PET to a broader population. New Medicare policies allow coverage for the use of PET in diagnosing six cancer indications, including lung, colorectal, lymphoma, melanoma, esophageal, and head and neck, but are not explicit about when in the diagnostic algorithm PET should be used. Coverage policies for private payers are expected to follow suit.

- ✓ While most of our study technologies are likely to increase costs in the short term, a few have the potential to save costs in the long run.

It is projected (although not proven), screening colonoscopies could reduce colorectal cancer costs by up to 75 percent (Lewis, 2000). The advantage of colonoscopies is achieved more through prevention of cancer than early detection, by removing polyps before they have a chance to become malignant. For patients who use inhaled insulin, improved compliance with scheduled therapy and lowered levels of complications resulting from poor glucose control, could avert some of the costly complications of diabetes.

- ✓ Technologies exert their influence through both volume and price

Some of our case study technologies are what could be considered "big ticket" items; their use will add substantial costs to the health care system largely because of the high costs associated with their use. Monoclonal antibodies, for example, may add $8,000 to $30,000 per year to the costs of treating selected cancers, but their use is expected to expand to fewer than 30,000 new persons each year for the next five years (Table 8). Overall, this technology is expected to add more than $170 million to health care spending in 2001. By contrast, ThinPrep Pap smears, may add only $8 above the cost of a conventional Pap smear, and would be a considered a "little ticket" item. Yet, their use may expand to 12 million new users next year. Despite the considerably smaller price tag, ThinPrep Pap smears may add nearly $100 million to health care spending in 2001.

On the other hand, the price of a new technology, may decline, improving its relative value over time. In the device market, at least, competitive influences often lead to price competition. Prices for coronary artery stents, for example, decreased by 25-50 percent over the five-year period when growth in their use was particularly strong. We anticipate seeing similar competitive pressures for the pricing of embolic capture devices. In the pharmaceutical market, such as for monoclonal antibodies, longer patent protection keeps their price more resilient, and such price reductions are

TABLE 8. ESTIMATED INCREMENTAL CASES FOR STUDY TECHNOLOGIES (BEST CASE SCENARIO)

	Existing Cases	Incremental Cases by Year				
Technology	2000	2001	2002	2003	2004	2005
Coronary stents*	700,000	43,400	96,400	107,000	118,800	131,800
with **abciximab**	70,000	23,500	24,500	26,100	27,700	29,400
with **capture devices**	limited to clinical trials	9,300	10,000	11,500	19,300	32,400
Colonoscopy (screening)	750,000	225,000	258,800	297,600	342,200	393,500
Fast cardiac CT screens	218,000	103,000	53,000	28,100	15,600	0
Genetic testing for colon cancer	2,500	600	1,000	1,500	2,500	3,900
Helical CT for lung cancer screening	22,500	22,500	22,500	22,500	22,500	22,500
Immunotherapy	55,000	13,000	16,100	19,900	24,700	30,600
Inhaled insulin	limited to clinical trials	0	0	188,000	375,000	563,000
PET for cancer	284,000	287,000	256,000	289,000	319,000	350,000
Thin-Prep Pap smears	17.2 million	12 million	5 million	5 million	5 million	5 million

Cost drivers are indicated by **bold** text.

not anticipated. The average effective patent life of a new pharmaceutical is around 12 years in the United States (Grabowski and Vernon, 1996), whereas in the device industry new products can be easily copied and incremental changes are often made in order to bring a "new" competitor more quickly to market (Holmes, 1992).

c) Influence on Health Outcomes and the Value per Benefit

Most of the technologies we studied are quality-enhancing for at least a segment of the population: reducing the need for invasive surgery; improving patient quality of life; or improving life expectancy. To summarize some of the potential benefits of the case study technologies:

- ✓ Coronary stents can halve the rate of restenosis of the artery and lower rates of repeat surgery compared with angioplasty alone; when compared with coronary artery bypass graft surgery, good outcomes can be obtained without the risks of open heart surgery;
- ✓ Screening colonoscopy can be used to detect and remove more polyps before they become malignant than sigmoidoscopy, preventing the development of cancer;
- ✓ Genetic testing among persons at high risk for two types of hereditary colon cancer can reduce the need for family members who test negative for specific mutations to undergo the pain and expense of routine colonoscopies;
- ✓ Immunotherapy as either an adjunct or replacement for standard chemotherapy can improve cancer survival;
- ✓ Inhaled insulin shows the potential to achieve similar glucose control as subcutaneous delivery without the pain of injection; its use could improve compliance with scheduled therapy and lower the incidence of diabetic complications;
- ✓ PET can provide new, anatomical, information in the diagnoses and staging of cancer, potentially averting unnecessary surgery and chemotherapy;
- ✓ ThinPrep Pap smears can improve the detection of cervical cancer; their dual use as a screening tool for human papillovirus (HPV) offers the opportunity for earlier detection of cervical neoplasms.

Most of these technologies have some evidence of being cost-effective, at least for some population groups (see Appendix 4), although results of cost-effectiveness analyses varied substantially depending on underlying assumptions of relative costs, relative efficacy, and effects on long term prognosis.

The relative value of these technologies in the future will depend on how well their use is targeted to those who would most benefit from them, and whether their anticipated long-term benefits are realized in practice.

d) Additional Insights

- ✓ Incentives are still lacking for the appropriate use of technology in the US health care system.

As an illustration, in one study about 40 percent of physicians used GP IIb/IIIa during stenting of the saphenous vein graft population, despite evidence it had limited benefit in that subgroup. The use of EBCT to screen for coronary artery disease is continuing to expand even in the face of evidence that the technology may not be as efficacious as current less costly alternatives.

Spiral CT for lung cancer screening provides another example of an unproven technology that is actively being promoted. Lung cancer is among the most lethal cancers, with a five-year survival rate of 14 percent (Kolata, 2000). The survival rate for cancer detected in the presymptomatic state is 80 percent, but only a small proportion are diagnosed early (National Cancer Institute Biomedical Imaging Program, 1999). Initial studies show spiral CT may detect disease earlier than other imaging techniques, even though its effect on survival is unproven (Health Technology Trends, 2000). Many hospitals are now considering spiral CTs, which cost upwards of $1million, standard equipment, and are actively promoting its use for lung cancer screening. Current and future smokers, concerned about the possibility of getting lung cancer, have responded in large numbers (Kolata, 2000), despite the fact that insurance does not cover lung cancer screening and there are risks of unnecessary biopsies recommended for suspicious lesions, such as partial lung collapse, bleeding, and infection. While a long-term randomized controlled trial may definitively resolve the controversy surrounding this technique, results are not expected within the next five years and its use is expected to continue to grow in the absence of evidence of its effectiveness. Pressure to bring lawsuits against tobacco companies will also encourage its diffusion.

- ✓ There is a strong synergy between device, procedure, and pharmacologic innovation.

Early in their diffusion, coronary stents were associated with high rates of adverse events, such as excessive bleeding that sometimes required transfusion. As a result, lengths of hospital stays with stent placements were more than 50 percent greater than angioplasties where stents were not placed (Cohen et al., 1995). As the use of stents has diffused, success rates have improved and vascular complication rates and hospital lengths of stay have been reduced dramatically. Hospital stays are now about equivalent to angioplasties without stents. Much of the decline in adverse events related to stent use have been attributed to changes in anticoagulation management after the stent procedure and better delivery systems during stent placement (Peterson et al., 2000). There was substantial “learning-by-doing” among interventional cardiologists. Also, it is very

likely if corresponding advances in pharmacologic management had not taken place, stents may not have diffused. Clearly, it is difficult, if not impossible to separate out the influence of drug innovation from device innovation on health spending under these circumstances.

- ✓ The influence of a technology on health care costs cannot be divorced from the system in which it is used.

Coronary stents can also be used to illustrate this point. Private payers often reimburse for both the stents and the angioplasty procedure. When per procedure reimbursement is in place, the incentive is to use as many stents as possible. At the height of stent diffusion, some physicians were implanting 5 or 6 at a time, colloquially known as placing a "full metal jacket" (Kolata, 1998). Apart from the added expense, there are serious clinical drawbacks to this practice, as the ability to perform bypass surgery is lost. Medicare, however, pays on a per discharge basis through Diagnosis Related Groups. Because Medicare accounts for about half of all stent procedures, hospital staff have put pressure on interventional cardiologists to reduce procedure costs and this practice has moderated.

- ✓ The influence of technology on costs in a moving target.

As a technology diffuses, users may become more proficient, adjunct therapies may develop to reduce the associated risk, price can change, alternative technologies may enter the market, and a technology may be applied to very different clinical indications. All of these factors influence the relative cost impact of a new technology. Today, stents are probably no more costly than angioplasty without stents and provide better outcomes. Because the availability of stents makes high-risk percutaneous transluminal coronary angioplasty (PTCA) safer, the combination procedure is increasingly used as a substitute for coronary aretery bypass graft (CABG) in high-risk patients eligible for both procedures. Their use in this population is probably cost increasing at this time (Yock et al., 2000). However, stent prices and lengths of stay for angioplasty procedures are continuing to decline. On the other hand, the costs and effectiveness of CABG surgery are also changing, and new alternatives, such as intracoronary radiation are on the horizon.

All of these factors make our forecasts at best a guess, but we hope, an informed one, and one that can illustrate how technologies may influence future costs.

6 DISCUSSION

Any discussion of the costs of new medical technologies raises a crucial question about the benefit side of the equation. The key question from a societal perspective is not how much technology costs, but whether investments in medical technology are worth the health gains produced. A complete accounting of benefits includes reductions in mortality and morbidity associated with the technology and the various enhancements to quality of life, including improvements in functioning, e.g., as measured by activities of daily living and instrumental activities scales. Assessing the costs and benefits of medical technologies has been an extremely active area of research during the past few decades. Increasingly, health care providers and policy makers are seeking measures of the benefits associated with technology. Before discussing measures of the links between technology and expenditures, it is helpful to review the state of the art in assessing technologies benefits.

Traditional Cost Analyses. Formal economic evaluations of health care interventions, which formally measure the costs and benefits associated with an intervention, can take a number of forms. Some analyses are "cost-" or "cost-identification analyses," which simply estimate and compare the net costs of different strategies. For example, analysts might compare the net cost (costs of the drug and associated side effects, minus any cost offsets) of medications for the management of angina versus a surgical intervention. A limitation of the approach, however, is that it does not explicitly consider health outcomes.

Another form of evaluation, termed "cost-consequences analysis," involves computing and listing components of costs and consequences of alternative programs, without any attempt to aggregate results into a single metric. Researchers conducting an economic evaluation of a new drug for clinical depression, for instance, might evaluate the net costs and health effects (in terms of the percent change on a validated depression scale), compared to an alternative treatment strategy. A limitation of this approach is that it does not permit comparisons across diverse diseases or conditions. For example, how can one compare the value of a drug for depression to a drug that manages angina?

An alternative approach is cost-benefit analysis, in which all costs and benefits are measured and compared in dollar terms, but the requirement for monetary valuation of health benefits raises measurement difficulties and often political objections.

Cost-Effectiveness Framework. In recent years, cost-effectiveness analysis has emerged as the recommended analytic technique for conducting economic evaluation of health and medical interventions (Gold et al. 1996). The appeal of this approach is that it allows a convenient means of quantifying both economic and health benefits with a single ratio. Cost-effectiveness analyses involve comparisons between two alternatives, or between the presence and absence of an intervention; the cost per effect (C/E) ratio

reflects the difference in the interventions' costs, divided by the difference in their health effectiveness (Gold et al., 1996).

While cost-effectiveness analyses can measure health effects in disease-specific terms (i.e., costs per number of cancer cases prevented), a growing trend is to evaluate interventions using a standard metric, which permits comparisons across diverse interventions and diseases. One way to standardize ratios is to measure health effects in terms of life expectancy -- the cost-effectiveness ratio for each alternative would reflect the costs per *year of life gained*. A limitation of this approach is that life expectancy alone does not take into account the quality of additional time that is gained (e.g., an added month of life with disability or pain is valued the same as an added month without disability or pain). Ideally, an analysis would capture such effects.

The approach recommended by the U.S. Public Health Service Panel on Cost-Effectiveness in Health and Medicine, as well as other consensus groups, is to measure health outcomes in terms of "quality-adjusted" life years (QALYs) (Gold et al., 1996; Drummond et al,. 1997). QALYs represent the benefit of a health intervention as time in a series of "quality-weighted" health states, where the quality weights reflect the desirability of living in the state, typically from "perfect" health (weighted 1.0) to death (weighted 0.0). Once the quality weights are obtained for each state, they are multiplied by the time spent in the state; these products are summed to obtain the total number of quality- adjusted life years. The advantage of using QALYs is twofold: they capture in a single measure gains from both prolongation and quality of life, and they incorporate the value or preferences people place on different outcomes (Gold et al. 1996).

The Panel on Cost-Effectiveness in Health and Medicine was charged with "assessing the current state of the science of the field, and with providing recommendations for the conduct of studies in order to improve their quality and encourage their comparability." (Gold et al. 1996). Among other recommendations, the Panel proposed the use of a "reference case," a standard set of methodological practices that an analyst would seek to follow in a cost-effectiveness analysis if results from different studies are to be compared. The Panel recommended that the reference case use QALYs to identify and value health outcomes. The idea is that incremental cost-utility ratios from reference case analyses can be ranked in "league tables," as a way of furnishing information about how to allocate health resources efficiently across many competing health interventions -- lower C/E ratios reflect more efficient ways to produce QALYs. The Panel also made numerous recommendations on all aspects of conducting and reporting cost-effectiveness analyses.

Relevance of the Framework. Abundant research using cost-utility analyses and a "societal perspective," has found that many new drugs and devices are cost-effective from a societal standpoint (Neumann et al. 2000). Examples include warfarin therapy to prevent stroke in those with atrial fibrillation, immunosuppressive drugs for those with kidney transplants, and treatment with mood-altering drugs for those suffering from depression (Neumann et al. 2000; Chapman et al 2000). These interventions provide

good value in the sense that they produce health benefits for relatively little cost, or may actually save money for the health care system.

Moreover, research suggests that investments in medical technology may offer greater gains per dollar expended than investments in other sectors of the economy. One recent investigation of over 500 published cost-effectiveness ratios of life saving interventions found that the median medical intervention had a cost of $19,000 per life-year saved, while the median injury reduction intervention had a cost of $48,000 per life-year saved, and the median toxin control intervention had a cost of $2,800,000 per life-year saved (Tengs et al. 1995). While attempts have been made to tell this "value" story in the past, a more focused and sustained effort, drawing upon recent scholarly work in the field, is warranted.

A growing body of research also suggests that Americans strongly support medical innovation and are willing to pay for technology. A number of threads of research are relevant in supporting this message. Some studies attempt to capture Americans' overall preferences to pay for medical technology or to fund health research. The research shows that Americans state that they are willing to pay for medical technology and for more funding of medical research. Moreover, Americans' support for medical innovation and research is considerably higher than support in other countries.

In addition, a number of recent studies have highlighted the fact that – in contrast to the situation in the earlier part of the 20th century – recent gains in life expectancy are attributable largely to medical interventions. Reductions in life expectancy in the early 20th century in the U.S. were due largely to reductions in infant mortality, attributable to improved sanitation, diet, and education and housing. But the ensuing gains were more closely tied to medical interventions. The introduction of antibiotics and vaccines in the 1920s through 1950s led to reductions in mortality due to syphilis, diphtheria, whooping cough, measles, polio, influenza, and pneumonia.

Gains in the latter part of the century were associated with declining mortality among the elderly, attributable in large part to declines in cardiovascular disease. The reduction in coronary mortality was in turn explained by improvements in treatments for patients with coronary disease (Hunink et al. 1997). Changes in acute treatment, such as the use of aspirin and beta blockers, and in part invasive procedures, account for a substantial part of the improvement (Cutler et al. 1999).

How can such gains be valued? Recently, some prominent economists have attempted to estimate the gains by appealing to the willingness-to-pay literature showing that the value of a statistical life is in the neighborhood of $3 to $7 million. Based on these estimates, the researchers have estimated that the value to society of gains in life expectancy in the 1975-1995 period equal an astonishing $57 trillion, equal to the tangible consumption as measured by national income during this period (Funding First 2000). Such valuations raise methodological questions and are somewhat controversial.

Still, they highlight the tremendous gains to society that medical technology has produced through increasing longevity.

Finally, none of the gains noted above include the value of improving quality of life. The policy community needs to be apprised of the societal benefits of medical innovations in terms of improving patient well being, apart from declines in mortality. Patients and family members may be much better off as the result of access to new treatment modalities in ways that are sometimes difficult to quantify and express in monetary terms. But recent years have seen strides in our ability to capture patient-based outcomes, such as reduced pain, return to work, satisfaction with care, and quality of life in addition to conventional measures of safety and efficacy.

7 CONCLUSION

Historically, new medical advances have exerted an upward impact on health care costs. We expect this to continue in the coming five years, at perhaps a slightly higher pace than the average trend for the 1990s. Increased pressure to buy new medical technology will result as consumers and providers resist efforts on the part of public and private payers to control costs in the near term. The repercussions of broad policy changes, such as the Balanced Budget Act, will nevertheless continue to be felt throughout the health sector.

Any discussion of the costs of new medical technologies raises a crucial question about the benefit side of the equation. The key question from a societal perspective is not how much technology costs, but whether investments in medical technology are worth the health gains produced. A growing body of research suggests that Americans strongly support medical innovation and are willing to pay for technology. Among many new technologies, there is evidence they may be cost effective if used in appropriately selected individuals.

The challenge to policymakers and the insurance community is to put in place the incentives for more appropriate use of technology. The challenge for the research community is to enable policymakers and users to better understand the circumstances in which a new technology adds value.

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Appendix 1. Expert Panel Members

EXPERT PANEL MEMBERS

Alan M. Garber, M.D., Ph.D., Staff Physician, Department of Veterans Affairs; Professor Director, Center for Health Policy and Center for Primary Care and Outcomes, Department of Medicine, Stanford University

G. Scott Gazelle, M.D., M.P.H., Ph.D., Associate Professor of Radiology, Harvard Medical School; Associate Professor of Health Policy and Management, Harvard School of Public Health

I. Craig Henderson, M.D., Adjunct Professor, University of California, San Francisco

John M. Inadomi, M.D., Chief, Gastroenterology Section, VA Ann Arbor Healthcare System, Assistant Professor of Medicine, University of Michigan Medical Center

William McGivney, Ph.D., Chief Executive Officer, National Comprehensive Cancer Network

Earl P. Steinberg, M.D., M.P.P., Senior Vice President of Industry Affairs and R & D, Resolution Health Strategies; Adjunct Professor of Medicine and Health Policy and Management, Johns Hopkins University

Appendix 2. Technologies Studied By Technology Assessment Organizations

Organization: Agency for Healthcare Research and Quality (formerly the Agency for Health Care Policy and Research – AHCPR)

Evidence-based Practice Centers
Center for Practice and Technology Assessment
6010 Executive Boulevard, Suite 300
Rockville, Maryland 20852

Contact: Jacqueline Besteman
EPC Project Officer
301-594-4017
jbestema@ahcpr.gov

Purpose:

The Agency for Health Care Policy and Research, now the Agency for Healthcare Research and Quality (AHRQ) in 1997 awarded 12 five-year contracts to institutions in the US and Canada to serve as Evidence-based Practice Centers (EPCs) to review scientific literature on assigned clinical care topics and produce evidence reports and technology assessments, conduct research on methodologies and the effectiveness of their implementation, and participate in technical assistance activities. The Centers are part of the AHRQ initiative to promote evidence-based practice in everyday care, to improve the quality, effectiveness, and appropriateness of clinical care by facilitating the translation of evidence-based research findings into clinical practice.

Selection Criteria:

Topics for EPC evidence reports and technology assessments are routinely solicited through notices in the Federal Register. Topic nominations also are accepted on an ongoing basis. Specific information accompanying nominations includes the potential questions to be answered by the report or assessment, availability of scientific data, disease prevalence and/or severity, practice variation patterns, and descriptions of plans for using the evidence report or technology assessment to improve quality of care.

Selection criteria for clinical topics include:

- High incidence or prevalence in the general population or in subpopulations, including racial or ethnic minorities
- Significance for the needs of the Medicare, Medicaid, and other Federal health programs.
- High costs associated with a condition, procedure, treatment, or technology, due to the number of people needing care, high unit cost of care, or high indirect costs.
- Controversy or uncertainty about the relative effectiveness of available clinical strategies or technologies.
- Potential to inform and improve patient or provider decision making
- Potential to reduce clinically significant variations in the prevention, diagnosis, treatment, or clinical management of a disease or condition, in the use of a procedure or technology, or in the health outcomes achieved.
- Availability of scientific data to support the study or analysis of the topic.
- Potential opportunities for rapid implementation.

- Complimentarity to other evidence reports to support AHCPR's effort to build a balanced portfolio of evidence reports and technology assessments.
- Indication that the nominating organization and/or relevant professional organizations would use the report or assessment on the topic nominated to develop or update a clinical practice guideline, other quality improvement tools, or coverage decision policies.

Selection criteria for organization and financing topics include:

- Uncertainty about the impact of the subject organizational or financing strategy.
- Potential for the organizational or financing strategy or the proposed research synthesis to significantly affect aggregate health care costs, outcomes, or quality.
- Policy-relevant to Medicare, Medicaid, and/or other Federal and State health programs.
- Relevant to vulnerable populations, including racial and ethnic minorities, and particular communities, such as rural areas.
- Available scientific data to support the study or analysis of the topic.
- Potential for rapid incorporation into managerial or policy decisionmaking

Primary Focus:

Prevention, diagnosis, treatment and/or management of a particular condition or an individual procedure, treatment, or technology as well as issues related to the organization and financing of care

Stage of Technology:

Technology/Conditions Reviewed: Listed by the 12 Evidence-based Practice Centers

Blue Cross and Blue Shield Association. Technical Evaluation Center (TEC), Chicago, Il.
1998: Use of erythropoietin in hematology and oncology
1999: Management of chronic asthma

Duke University, Durham, NC
1998: Management of acute chronic obstructive pulmonary disease
1999: Treatment of pulmonary disease following spinal cord injury
Treatment of fibroids

ECRI, Plymouth Meeting, Pa.
1998: Criteria for determining disability in patients with end-stage renal disease
1999: Treatment of degenerative lumbar spinal stenosis

Johns Hopkins University, Baltimore, Md.
1998: Treatment of acne
Anesthesia management during cataract surgery
1999: Treatment of coexisting cataract and glaucoma (anti-fibrosis agents, trabeculectomy vs. endoscopsic laser vs. deep sclerectomy/viscoanulostomy, nuclear expression/phacoemulsification)

McMaster University, Hamilton, Ontario, Canada
1998: Criteria for weaning from mechanical ventilation
1999: Management of neurogenic/neuropathic pain following spinal cord injury
MetaWorks, Inc., Boston, Ma.
1999: Criteria for the referral of patients with epilepsy
Sentinel node biopsies for management of breast disease

New England Medical Center, Boston, Ma.
1998: Management of cancer pain
1999: Evaluation of technologies for identifying acute cardiac ischemia in the emergency department

Oregon Health Sciences University, Portland, Or.
1999: Bone mass measurement techniques such as quantitative ultrasound for diagnosis and management of osteoporosis
Medical informatics and telemedicine coverage under the Medicare Program

Research Triangle Institute and University of North Carolina at Chapel Hill, NC.
1998: Management of pre-term labor (tocolytics, antibiotics, and home uterine monitoring)
1999: Efficacy of behavioral dietary interventions to reduce cancer risk

Southern California Evidence-based Practice Center – RAND, Santa Monica, Ca.
1998: Management of acute otitis media in children (treatment with antibiotics)
Prevention of venous thromboembolism after injury
1999: Management of otitis media with effusion

University of California, San Francisco and Stanford University, Stanford, Ca.
1998: Prediction of Risk for Patients with unstable angina (ECG/exam, troponin, chest pain units)
1999: Refinement of HCUP Quality Indicators

University of Texas Health Science Center, San Antonio, Tx.
1998: Management of chronic hypertension during pregnancy
1999: Use of garlic for cardiovascular disease
Use of silybum marianum in treatment of liver disease and cirrhosis

2000 Management of Allergic Rhinitis
Autopsy as the Ultimate Outcomes Measure
Bioterrorism: Training for Rare Public Health Event
Bioterrorism: Role of Decision Support Systems in Disease Management Following Bioterrorism Event
Blood Pressure Monitoring Outside the Clinic Setting
Impact of Cancer-related Decision Aids
Defining and Managing Chronic Fatigue Syndrome
Diagnosis and Treatment of Congestive Heart Failure
Criteria to Determine Disability of Infant/Childhood Impairments

Diagnosis and Management of Parkinson's Disease
Management of Post-term Pregnancy
Diagnosis and Treatment of Repetitive Motion Disorders
Criteria to Determine Disability of Speech/Language Disorders
Effectiveness and Cost-Effectiveness of Echocardiography and Carotid Ultrasound in Evaluation and Management of Stroke
Study: Utilization of Physician Services
Study: Methods to Rate Strength of Scientific Evidence

Current Projects:

Child and adolescent health
Maternal health
Geriatrics
Dental health
Mental health
Substance abuse
Rehabilitation
Preventive care

Organization: Blue Cross and Blue Shield of America
Technology Evaluation Center (TEC)
TEC/BCBSA
225 North Michigan Avenue
60601-7680

Contact: Naomi Aronsen, Director
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naomi.aronson@bcbsa.com

Purpose:

The assessments issued by TEC are intended to provide objective information to those who deliver and manage medical care. They are based on clinical and scientific evidence and evaluate whether a technology improves health outcomes, such as length of life, quality of life and ability to function. TEC assessments are not recommendations for coverage decisions by health insurance companies.

Selection Criteria:

TEC uses five criteria for evaluating technologies:

- The technology must have final approval from the appropriate government regulatory bodies;
- The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
- The technology must improve the net health outcome;
- The technology must be as beneficial as any established alternatives; and
- The improvement must be attainable outside the investigational settings.

Notably, TEC does not consider the effect of a technology on costs in analyzing a technology.

Primary Focus:

devices, surgical procedures, medical procedures, pharmaceuticals

Stage of Technology:

new and emerging medical technologies

Technology/Conditions Reviewed:

1998: Monolayer Slide Preparation and Automated Slide Reading Systems for Cervical Cancer Screening – Clinical Effectiveness Analysis

Special Report: Comparative Efficacy of Different Types of Pneumatic Compression Pumps for the Treatment of Lymphedema

Special Report: Pressure-Reducing Support Surfaces in the Prevention and Treatment of Pressure Ulcers: Group 1 Technologies

Partial Left Ventriculectomy

Pelvic Floor Stimulation in the Treatment of Adult Urinary Incontinence

High-Dose Chemotherapy with Autologous Stem-Cell Support for Epithelial Ovarian Cancer

Pancreas Transplantation

"Tandem" High-Dose Chemotherapy with Autologous Stem-Cell Support for Newly Diagnosed or Responsive Multiple Myeloma

Chronic Vagus Nerve Stimulation for Treatment of Seizures

Genetic Testing for Inherited Susceptibility to Colorectal Cancer: Part I – Adenomatous Polyposis Coli Gene Mutations

Genetic Testing for Inherited Susceptibility to Colorectal Cancer: Part II – Hereditary Nonpolyposis Colorectal Cancer

Special Report: Pressure-Reducing Support Surfaces in the Prevention and Treatment of Pressure Ulcers: Group 2 Technologies

Special Report: Pressure-Reducing Support Surfaces in the Prevention and Treatment of Pressure Ulcers: Group 3 Technologies and Continuous Rotational Devices

Intravenous Immune Globulin for Recurrent Spontaneous Abortion

Minimally Invasive Coronary Artery Bypass Graft – Update

External Counterpulsation for Treatment of Chronic Stable Angina Pectoris

Intra-Articular Hyaluronan Injections for Treatment of Osteoarthritis of the Knee

Sacral Nerve Stimulation for the Treatment of Urge Incontinence

Intravenous Immune Globulin for Multiple Sclerosis

Ketogenic Diet for the Treatment of Children with Medically Refractory Epilepsy

Radioimmunoscintigraphy for Prostate Cancer – Update

Fetal Surgery for Prenatally Diagnosed Malformations

Transmyocardial Revascularization for the Treatment of Coronary Artery Disease

High-Dose Chemotherapy with Autologous Stem-Cell Support in the Treatment of High Risk, Primary Breast Cancer

Transurethral Radiofrequency Needle Ablation of the Prostate

Single or Tandem High-Dose Chemotherapy with Autologous Stem Cell Support for Resistant Multiple Myeloma

Diagnosis and Screening for Coronary Artery Disease with Electron Beam Computed Tomography

Special Report: Stereotactic Radiosurgery for Intracranial Lesions by Gamma Beam, Linear Accelerator, and Proton Beam Methods

TEC Special Assessment Program (1998):

- The Cost-Effectiveness of Three New Technologies to Enhance Pap Testing

1999: Lung Volume Reduction Surgery for Severe Emphysema
Intracoronary Radiation to Prevent Restenosis
Lipid Apheresis in the Treatment of Severe, Refractory Hypercholesterolemia
Phototherapy for the Treatment of Seasonal Affective Disorder
Becaplermin for Wound Healing
Off-Label Uses of Trastuzumab
Genetic Testing for Alzheimer's Disease: *APOE* Epsilon 4 Allele
Ambulatory Blood Pressure Monitoring for Diagnosis of Hypertension in Adults
Small Bowel Transplants in Adults and Multivisceral Transplants
Salivary Estriol for the Assessment of Spontaneous Preterm Labor
Salvage High-Dose Chemotherapy with Allogeneic Stem Cell Support for Relapse Following High-Dose Chemotherapy with Autologous Stem Cell Support for Non-lymphoid Solid Tumors
Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease: ANCA for Ulcerative Colitis and ASCA for Crohn's Disease
Hyperbaric Oxygen Therapy for Wound Healing – Part I
Bilateral Prophylactic Mastectomy in Women with an Increased Risk of Breast Cancer
Hyperbaric Oxygen Therapy for Wound Healing – Part II
Hyperbaric Oxygen Therapy for Wound Healing – Part III
Uterine Artery Embolization for Treatment of Symptomatic Uterine Fibroids

a) External Counterpulsation for Treatment of Chronic Stable Angina Pectoris

Ultrasonography of the Heel for Diagnosing Osteoporosis and Selecting Patients for Pharmacologic Treatment
High-Dose Chemotherapy with Autologous Stem Cell Support for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
Cranial Orthosis for Plagiocephaly without Synostosis
Sensory Integration Therapy
In Utero Fetal Surgery for Prenatally Diagnosed Sacrococcygeal Teratoma
Monitoring of Bone Density to Assess Active Treatment of Osteoporosis
FDG Positron Emission Tomography in Colorectal Cancer
FDG Positron Emission Tomography in Lymphoma
FDG Positron Emission Tomography in Melanoma
FDG Positron Emission Tomography in Pancreatic Cancer

TEC Special Assessment Program (1999):
Cost-Effectiveness of Diagnosis and Screening for Coronary Artery Disease with Electron Beam Computed Tomography

2000: High-Dose Lymphoablative Therapy (HDLT) with or without Stem Cell Rescue for Treatment of Severe Autoimmune Diseases
Pelvic Floor Electrical Stimulation in the Treatment of Urinary Incontinence in Adults

Biofeedback in the Treatment of Urinary Incontinence in Adults

FDG Positron Emission Tomography in Head and Neck Cancer

Intradiscal Electrothermal Therapy for Chronic Low Back Pain

Special Report: Relative Effectiveness of Treatment Programs and Components of Treatment for Anorexia Nervosa

Sacral Nerve Stimulation for the Treatment of Refractory Urinary Urgency/Frequency in Adults

Magnetic Stimulation in the Treatment of Urinary Incontinence in Adults

Salvage High-Dose Chemotherapy with Allogeneic Stem-Cell Support for Relapse or Incomplete Remission Following High-Dose Chemotherapy with Autologous Stem-Cell Transplantation for Hematologic Malignancies

Magnetic Resonance Imaging of the Breast: Differential Diagnosis of a Breast Lesion

Chemotherapy Sensitivity and Resistance Assays

Current Projects:

Autologous Chondrocyte Transplantation

Cryosurgical Ablation of Liver Tumors

Magnetic Resonance Imaging for Breast Cancer – Staging

Photodynamic Therapy for Suboveal Choroidal Neovascularization

Radiofrequency Ablation of Liver Tumors

Radiofrequency Volumetric Tissue Reduction for the Treatment of Snoring and Obstructive Sleep Apnea

Treatment of Twin-to-Twin Transfusion Syndrome with Aggressive Amnioreduction and/or Fetoscopic Laser Therapy

Organization: Emergency Care Research Institute (ECRI)
5200 Butler Pike
Plymouth Meeting, Pa. 19462-1298

Contact: Vivian Coates, (610) 825-6000
Don Cummins (610) 825-6000 extension 5170
dcummins@ecri.org

Purpose:

ECRI is a nonprofit, private organization whose mission is to improve the safety, quality, and cost effectiveness of healthcare. ECRI provides information and technical assistance to the health care community to support safe and cost –effective patient care. To accomplish its mission ECRI's clearinghouse:

- Collects and disseminates information on studies undertaken by academic medical centers, hospitals, health plans, integrated delivery systems, medical device and pharmaceutical companies, professional and specialty societies and associations, healthcare provider organizations, financial and investment analysts, and government agencies worldwide.
- Evaluates the scientific methods used in these studies and their strengths and weaknesses.
- Maintains a comprehensive International Health Technology Assessment database of citations and abstracts covering the peer-reviewed literature, as well as proprietary documents, technical reports, newsletters, and other sources (the "gray" literature) from around the world.
- Summarizes information related to specific technologies or their applications, based on available evidence, either for publication or on request.
- Publishes the results of selected studies for Member and public benefit, including patients and their families.

ECRI is one of 12 Evidence-based Practice Centers (EPC) for the US Agency for Healthcare Research and Quality (AHRQ). ECRI is also a World Health Organization Collaborating Center. ECRI provides information about technology-related hazards; disseminates the results of medical product evaluations and technology assessments; gives expert advice on technology acquisitions, staffing, and management; reports on hazardous materials management policy and practices, and supplies authoritative information on risk control in healthcare facilities and clinical practice guidelines and standards.

ECRI produces several types of products, among them:

Comprehensive Technology Assessment Reports – Comprehensive report on the sue of a given technology for a given application(s) and comparison to other technologies used to diagnose or treat the same condition; includes review and discussion of the known issues that have an impact on the use of the technology

Windows on Medical Technology – Short-form evidence reports of drugs, devices, and procedures that provide a rapid and accurate overview of emerging medical technologies

Hotline Titles – A response letter to a telephone or e-mail inquiry about a technology. The response includes a summary letter about what the literature searches found, a full description of the search strategies and terms, a copy of the abstracts found in the search

TARGET (Technology Assessment Resource Guide for Emerging Technologies) Reports – Web-based database about new and emerging healthcare technologies (devices, drugs, biotechnologies, procedures, and information systems) including those technologies still in development plus information on new uses for more mature technologies

Selection Criteria:

ECRI responds to requests from AHRQ as an EPC. ECRI also selects topics in response to member interest expressed as Hotline responses, membership polls, and requests. Topics are also provided by internal committee members.

Primary Focus:

Healthcare technology (drugs, devices, procedures), healthcare risk quality management, healthcare environmental management

Stage of Technology: New and emerging

Type of Technology: Drugs, devices, procedures

Technologies/Conditions Reviewed:

1998: **Technology Assessment Reports**

Gynecology

Cost-Effectiveness Analysis of In Vitro Fertilization (January 1998)

9 ONCOLOGY

High-Dose Chemotherapy for the Treatment of Multiple Myeloma (June 1998)

Pain Management

Spinal Cord Stimulation for Relief of Neuropathic Pain (June 1998)

Wound Care

Growth Factors for the Treatment of Chronic Dermal Wounds (April 1998)

Windows on Medical Technology

Diagnostic Imaging

Doppler Flow Testing of Vascular Access Grafts (October 1998)
FDG SPECT for Diagnosing Ischemic Heart Disease (January 1998)

Endocrinology

Recombinant Human Growth Hormone for AIDS Wasting (June 1998)

Gastroenterology

Biofeedback for the Treatment of Fecal Incontinence (October 1998)
Urea Breath Tests for Detecting Helicobacter Pylori (March 1998)

Neurology and Neurosurgery

Vagus Nerve Stimulation for the Treatment of Intractable Epilepsy (December 1998)

Oncology

CA 27.29 Radioimmunoassay (RIA) for Detecting and Monitoring Recurrent Breast Cancer (January 1998)
Proton Beam Radiation Therapy for Prostate Cancer (November 1998)

10 PAIN MANAGEMENT

Oxygen Therapy for Cluster Headaches (September 1998)

i) Pediatrics

Biofeedback for the Treatment of Constipation in Children (September 1998)

TARGET (Technology Assessment Resource Guide for Emerging Technologies)

11 CARDIOLOGY

Angioscopy for diagnosis of cardiovascular disease (8/25/98)
Coronary stents for coronary artery stenosis (7/10/98)
Heart volume reduction surgery for end-stage heart disease (8/7/98)
Low-density lipoprotein (LDL) apheresis for the treatment of atherosclerosis and related disorders (8/25/98)
Radiofrequency (RF) catheter ablation for supraventricular tachycardia (8/7/98)

12 CLINICAL LABORATORY-HEMATOLOGY

Automated reticulocyte analyzers (ARAs) (8/12/98)

13 DIABETOLOGY

Implantable insulin infusion pumps for diabetes (8/25/98)

14 DIAGNOSTIC IMAGING

Broadband ultrasound attenuation (BUA) for osteoporosis screening (9/9/98)
Doppler ultrasound for evaluation of vascular access (8/27/98)
Dual-energy x-ray absorptiometry (DXA) for osteoporosis screening (7/10/98)
Dual-photon absorptiometry (DPA) for osteoporosis screening (8/12/98)
Magnetic resonance angiography (MRA) for diagnosis of abdominal vascular abnormalities (7/10/98)
Magnetic resonance angiography (MRA) for diagnosis of peripheral vascular disease (7/10/98)
Positron emission tomography (PET) for diagnosis and staging of lung cancer (8/27/98)
Quantitative computed tomography (QCT) for osteoporosis screening (7/10/98)
Single-energy x-ray absorptiometry (SXA) for osteoporosis screening (7/10/98)
Single-photon absorptiometry (SPA) for osteoporosis screening (7/10/98)
Ultrasound mammography for diagnosis of suspicious breast lesions (7/10/98)

15 ENDOCRINOLOGY

Recombinant human growth hormone for AIDS wasting (8/25/98)

16 GASTROENTEROLOGY

Biofeedback for constipation (8/27/98)
Biofeedback for fecal incontinence (8/27/98)
Urea breath test for detection of Helicobacter pylori (H. pylori) infection (8/7/98)

17 GYNECOLOGY

Assisted reproductive technologies (ARTs): gamete intrafallopian transfer (GIFT) (8/25/98)

Assisted reproductive technologies (ARTs): in vitro fertilization (IVF) embryo transfer(8/25/98)

Assisted reproductive technologies (ARTs): intrauterine insemination (IUI) (8/25/98)

Assisted reproductive technologies (ARTs): zygote intrafallopian transfer (ZIFT) (8/25/98)

Cryosurgical endometrial ablation for excessive uterine bleeding (7/10/98)
Hydrothermal endometrial ablation for excessive uterine bleeding (7/10/98)
Laparoscopic-assisted vaginal hysterectomy (LAVH) (8/18/98)
Laser endometrial ablation for excessive uterine bleeding (7/10/98)
Uterine artery embolization for excessive uterine bleeding (7/10/98)
Uterine balloon therapy (UBT) for excessive uterine bleeding (7/10/98)

Wire-loop or rollerball electrosurgical endometrial ablation for excessive uterine bleeding (7/10/98)

18 MATERIALS MANAGEMENT/CENTRAL SUPPLY

Plasma sterilizers (8/25/98)

19 MENTAL HEALTH AND SUBSTANCE ABUSE

Chemical aversion therapy for alcoholism (8/25/98)

20 NEUROLOGY

Botulinum toxin for cervical dystonia (10/14/98)
Botulinum toxin for spasticity, rigidity, and tremors (10/14/98)
Neuroprotective drugs for ischemic stroke (8/7/98)
Polysomnography (PSG) for diagnosis of hypersomnia (7/10/98)
Polysomnography (PSG) for diagnosis of insomnias (8/25/98)
Polysomnography (PSG) for diagnosis of narcolepsy (7/10/98)

Polysomnography (PSG) for diagnosis of periodic limb movement (PLM) disorder and restless leg syndrome (RLS) (7/10/98)

Polysomnography (PSG) for diagnosis of sleep apnea (7/10/98)

21 NEUROSURGERY

Occlusion coils for brain aneurysms (8/7/98)
Thalamic stimulation for tremor (7/10/98)
Vagus nerve stimulator for epilepsy (implantable) (8/7/98)

22 ONCOLOGY

Cancer antigen CA 125 tumor marker assay for detection of ovarian cancer (8/25/98)
Cancer antigen CA 15-3 tumor marker assay for detection of breast cancer (7/10/98)
Cancer antigen CA 27.29 tumor marker assay for detection of breast cancer (7/10/98)
High-dose chemotherapy (HDC) with autologous bone marrow transplantation (ABMT) and/or stem cell transplantation (SCT) for lung cancer (8/7/98)
Interleukin-2 (IL-2) for malignant melanoma (7/10/98)
Interleukin-2 (IL-2) for renal cell carcinoma (7/10/98)
Stereotactic breast biopsy for diagnosis of breast cancer (8/7/98)

23 OTOLARYNGOLOGY

Multichannel cochlear implant for profound deafness (8/10/98)

24 RADIATION ONCOLOGY

Hyperbaric oxygen (HBO) therapy for radiation tissue damage (8/7/98)

25 TRANSPLANTATION

Intestinal/liver transplantation or small bowel transplantation (8/7/98)

26 UROLOGY

Biofeedback for urinary incontinence (8/27/98)

27 WOUND CARE

Air-fluidized beds for decubitus ulcers (8/25/98)
Exogenous epidermal growth factor (EGF) for venous ulcers (7/10/98)
Exogenous fibroblast growth factor (FGF) for decubitus (pressure) ulcers (7/10/98)
Exogenous fibroblast growth factor (FGF) for diabetic (neurotrophic) ulcers (7/10/98)
Platelet-derived wound-healing formula (PDWHF) for diabetic (neurotrophic) ulcers (7/10/98)
Platelet-derived wound-healing formula (PDWHF) for ischemic (arterial) ulcers (7/10/98)

1999: **<u>Full-Length Technology Assessment Reports</u>**
Gynecology

Cost-Effectiveness Analysis of Screening for Cervical Cancer (April 1999)

Mental Health and Substance Abuse

Comprehensive Programs for the Treatment of Children with Autism (December 1999)

Neurology and Neurosurgery

Diagnosis and Treatment of Dysphagia/Swallowing Disorders in the Elderly (March 1999)

Oncology

Screening for Prostate Cancer: A Cost-Effectiveness Markov Decision Analysis (December 1999)

Pain Management

Long-term Spinal Infusion for the Management of Severe Chronic Pain (July 1999)

Surgery - General

Bariatric Surgery for Morbid Obesity (November, 1999)

Windows on Medical Technology

Gynecology

Alendronate for Prevention of Postmenopausal Osteoporosis (June 1999)

Automated Monolayer Slide Preparation Systems for Pap Smear Screening: ThinPrep® 2000 (September 1999)

Raloxifene, a Selective Estrogen Receptor Modulator (SERM) for Prevention of Osteoporosis (February 1999)

Neurology and Neurosurgery

Neural Surgery for Carpal Tunnel Syndrome (April 1999)

Thalamic Stimulation for Parkinson's Disease (March 1999)

i) Oncology

Permanent Prostate Brachytherapy for Localized Prostate Cancer (March 1999)

Laser Photodynamic Therapy (PDT) for the Local Palliation of Chest Wall Recurrence and Metastatic Cutaneous Breast Cancer (August 1999)

Tamoxifen for Prevention of Breast Cancer in Healthy Women at High Risk (December 1999)

ii) Orthopedics

Autologous Chondrocyte Transplantation for Knee Cartilage Defects (updated, November 1999)

b) Surgery—General

Lung Volume Reduction Surgery (Update of full TA Report, July 1999)

i) Transplantation

Islet Cell Transplantation for Type 1 Diabetes (October 1999)

TARGET (Technology Assessment Resource Guide for Emerging Technologies)

28 ALLERGY AND IMMUNOLOGY

Needleless injection technology for immunization/vaccination of adults and children (11/23/99)

Ultrasound-enhanced latex agglutination test (USELAT) for diagnosis of bacterial meningitis and meningococcal septicemia. (10/4/99)

29 ANESTHESIOLOGY

Iontophoresis for local anesthesia (2/19/99)

30 CARDIOLOGY

External counterpulsation for relief of angina (3/9/99)

Stents for carotid artery stenosis (5/27/99)

Transmyocardial revascularization (TMR) for intractable ischemic heart disease (4/23/99)

31 DIAGNOSTIC IMAGING

Cineless imaging for cardiology applications (4/21/99)

Scintimammography for diagnosis of suspicious breast lesions (2/19/99)

32 GASTROENTEROLOGY

Proton pump inhibitor based triple therapy for peptic ulcer disease (PUD) (5/27/99)

Standard bismuth triple therapy for peptic ulcer disease (PUD) (5/27/99)

33 GYNECOLOGY

Alendronate for prevention of osteoporosis (6/24/99)

Alendronate for treatment of osteoporosis (6/24/99)

Automated monolayer slide preparation systems for Pap smear screening (12/1/99)

Automated Pap smear rescreening devices (12/1/99)

Etidronate for prevention of osteoporosis (4/13/99)

Etidronate for treatment of osteoporosis (4/13/99)

Human papillomavirus (HPV) DNA testing for assessing cervical cancer risk (12/1/99)

Raloxifene for prevention of postmenopausal osteoporosis (3/31/99)

34 MATERIALS MANAGEMENT/CENTRAL SUPPLY

Endoscope reprocessors (3/22/99)

35 NEUROLOGY

Ketogenic diets for prevention of epileptic seizures in children (2/19/99)

36 ONCOLOGY

Cryosurgery for prostate cancer (5/25/99)

Genetic testing for BRCA1 and BRCA2 for assessing breast cancer risk (11/29/99)

Genetic testing for BRCA1 and BRCA2 for assessing ovarian cancer risk (11/29/99)

Permanent brachytherapy for localized prostate cancer (5/25/99)

Proton beam radiation therapy for prostate cancer (5/28/99)

37 OTOLARYNGOLOGY

Continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (9/7/99)

38 PAIN MANAGEMENT

Oxygen therapy for cluster headache (5/25/99)

Spinal cord stimulation (SCS) for intractable angina (5/27/99)

Spinal cord stimulation (SCS) for peripheral vascular disease (6/3/99)

39 PULMONARY MEDICINE

Extracorporeal membrane oxygenation (ECMO) for adult respiratory failure (7/16/99)

High-frequency jet ventilation (HFJV) for respiratory distress syndrome (RDS) in premature infants (11/17/99)

Lung surfactant for prevention of respiratory distress syndrome (RDS) in premature infants (11/29/99)

40 TRANSPLANTATION

Extracorporeal porcine-based bioartificial liver (BAL) for acute liver failure (9/24/99)

41 UROLOGY

Sildenafil for erectile dysfunction (7/20/99)

Transurethral microwave thermotherapy (TUMT) for benign prostatic hyperplasia (BPH) (12/22/99)

42 WOUND CARE

Alternating current (AC) electrical stimulation for the treatment of decubitus ulcers (1/7/99)

Alternating current (AC) electrical stimulation for the treatment of diabetic ulcers (1/7/99)

Exogenous platelet-derived growth factor-BB (PDGF-BB) for decubitus (pressure) ulcers (7/7/99)

Exogenous platelet-derived growth factor-BB (PDGF-BB) for diabetic (neurotrophic) ulcers (7/7/99)

Pulsed current (PC) electrical stimulation for the treatment of decubitus ulcers (1/7/99)

Pulsed electromagnetic induction (PEMI) for the treatment of decubitus ulcers (1/7/99)

Pulsed electromagnetic induction (PEMI) for the treatment of venous ulcers (1/7/99)

2000: **Full-Length Technology Assessment Reports**

Cardiology

Biofeedback for Cardiovascular Disorders (in progress)

Dentistry and Oral Surgery

Surgical and Injection Treatment of Temporomandibular Joint Disorder (TMJ) (in progress)

Obstetrics

Fetal Fibronectin Assay for Prediction of Preterm Birth and Neonatal Morbidity (March 2000)

Pain Management

Biofeedback for Migraines and Tension Headaches (in progress)

Wound Care

Occlusive Dressings for the Treatment of Chronic Wounds (March 2000)

Windows on Medical Technology

Cardiology

External Counterpulsation for the Treatement of Stable Angina (June 2000)

Left Ventricular Assist Devices for Long-term Bridge to Transplantation (in progress)

Minimally Invasive CABG on the Beating Heart for Coronary Artery Disease (in progress)

Transmyocardial Laser Revascularization for Intractable Ischemic Heart Disease (Update of June 1998 in progress)

Gene Therapy for Intractable Ischemic Heart Disease (June 2000)

43 DIAGNOSTIC IMAGING

Bone Mineral Density Screening for Osteoporosis (Update of December 1995 in February 2000)

MRI for Diagnosing and Staging Breast Cancer (in progress)

Ultrasound Bone Densitometry for Diagnosis of Osteoporosis (February 2000)

Pediatrics

Growth Hormone Therapy for short Stature (Update of April 1994 in progress)

Surgery - General

Lung Reduction Surgery for Emphysema (Update of May 1996 in progress)

Gynecology

Automated Pap Smear Screening Technologies: The AutoPap® System (Update April 2000)
Thermal Uterine Balloon Endometrial Ablation Therapy for Treatment of Benign Menorrhagia (April 2000)
Uterine Artery Embolization for Fibroids (in progress)
Laparoscopy in Hysterectomy for Benign Conditions (Update of October 1995 in progress)

Neurology and Neurosurgery

Interferon Beta-1a and Interferon Beta-1b for the Treatment of Relapsing/Remitting Multiple Sclerosis (in progress)

Oncology

Capromab Pendetide (ProstaScint™) for Staging of Prostate Cancer in Patients at High Risk for Metastasis (in progress)
Chemotherapeutic Hyperthermia for Colorectal Cancer (in progress)
Cryosurgery for Prostate Cancer (Update of February 1996 in progress)
Her2/Neu Gene Amplification as a Prognostic and Therapeutic Indicator for Breast Cancer Recurrence (in progress)

Immunotherapy Treatment with IL-2, GMCSF and TAA for Breast Cancer (in progress)

Sentinel Node Biopsy for Staging Breast Cancer (March 2000)
Trastuzumab (Herceptin) for the Treatment of HER2/Neu Positive Metastatic Breast Cancer (in progress)

a) Ophthalmology

Confocal Scanning Laser Ophthalmoscope for Diagnosing Glaucoma (July 2000)

i) Orthopedics

Meniscal Allograft Transplantation for Damaged or Removed Meniscus (in progress)
Hyaluronan-Based Therapy for Osteoarthritis of the Knee (in progress)

- **Pain Management**

Oral Transmucosal Fentanyl Citrate for the Treatment of Breakthrough Cancer Pain (January 2000)
Percutaneous Vertebroplasty for Pain from Spinal Compression due to Osteoporosis (in progress)

44 PEDIATRICS

Growth Hormone for Idiopathic Short Stature (Update of full TA Report)

a) Pulmonary Medicine

High Frequency Chest Compression (ThAIRapy) Device for Cystic Fibrosis (in progress)

i) Transplantation

Intestine and Intestine/Liver Transplantation (Update of full TA Report, May 2000)
Living-related Donor Liver Transplantation in Adults (in progress)
Living Donor Lung Transplantation for Cystic Fibrosis (in progress)

b) Urology

Implantable Sacral Nerve Stimulation for the Treatment of Idiopathic Urinary Dysfunction
Sacral Nerve Stimulation for Urinary Urge Incontinence
Transurethral Needle Ablation (TUNA) for Benign Prostate Hyperplasia

i) Wound Care

Vacuum-assisted (VAC) Wound Closure Devices for Wound Healing

Hotline Titles Current to six months

c) Allergy and Immunology

Enzyme Potentiated Desensitization for Allergic Rhinitis
Immunotherapy for Allergens
Intravenous Infusion of Sandoglobulin for the Treatment of Common Variable Immunodeficiency
Repeated Intravenous Immunoglobulin (IVIG) and Plasmapheresis for Systematic Lupus Erythematosus (SLE) and Lupus Cerebritis
Sublingual Drops for Treating Allergies

d) Anesthesiology

Iontophoresis for Drug Delivery (Update of full TA Report)

e) Cardiology

Alcohol Ablation of the Septum for Hypertrophic Obstructive Cardiomyopathy
Cholesterol-Lowering Therapies for Hypercholesterolemia
Cost Benefit Analysis for Treatment of LDL in Patients with Cardiac Disease
Endarterectomy, Angioplasty and Stents for Carotid Stenosis
Endovascular Stents for Treatment of Abdominal Aortic Aneurysms
Enhanced External Counterpulsation for the Treatment of Chronic Angina
Enoxaparin (Lovenox) for Aspirin-Intolerant Coronary Stent Patients
Gene Therapy for Cardiovascular Disease
Homografts for Heart Valve Diseases
Intracranial Artery Angioplasty
Laser Angioplasty for Coronary Artery Blockages
Left Ventricular Assist Devices for Failing Hearts

The Maze (surgical procedure) for Chronic Atrial Fibrillation

Measurement of T-Wave Alternans Using the CH 2000 Cardiac Diagnostic System for Prediction of Arrhythmias

Minimally Invasive Direct Coronary Artery Bypass Graft (MIDCAB) Surgery

Off-Label Uses of Low Molecular Weight Anticoagulants

Outpatient Infusion Therapy with Milrinone (Primacor) and Dobutamine (Dobutrex) for Congestive Heart Failure

Percutaneous Transluminal Angioplasty for the Carotid Arteries

Port Access Coronary Artery By-Pass Surgery

Sclerotherapy for the Treatment of Varicose Veins

Signal-Averaged Electrocardiographs for Diagnosis of Heart Attack, Syncope, and Ventricular Tachycardia

Stress as a Risk Factor for Restenosis after Coronary Artery Bypass Grafts

Tilt Table Testing for Syncope

Transcatheter Closure of Atrial Septal Defects in Adults

Transmyocardial Laser Revascularization

VNUS Closure Procedure for Varicose Veins and Venous Insufficiency

f) Clinical Laboratory

Coagulation Monitoring utilizing the CoaguChek and Protime Microcoagulation Systems

Immediate Response Mobile Analysis (IRMA) System for Home Use Electrolyte Monitoring

Irradiation Indicators (RAD-SURE) for Visual Confirmation of Gamma Irradiated Blood Products

g) Dentistry and Oral Surgery

Dental Appliances for Sleep Apnea

Orthognathic Surgery (Update of full TA Report)

Temporomandibular Joint Arthroscopy (Update of full TA Report)

h) Dermatology

Laser Surgery for Rosacea

Laser Treatment for Keloids

Pemphigus Treatment with Intravenous Immunoglobulins

Diabetology

Continuous Glucose Monitoring System (MiniMed) for Type I Diabetes Patients

Continuous Subcutaneous Insulin Pumps for Diabetes

Cost Benefits of Diabetes Disease Management

i) Diagnostic Imaging

Cardiac Ultrasound Devices
Computer Assisted Design (CAD) Mammography Using the ImageChecker for Breast Neoplasms
Dedicated Cardiac MRI
Dynamic MRI for Evaluation of Pelvic Floor Prolapse
Electron Beam Computed Tomography (Ultrafast CT) for Diagnosis of Coronary Artery Disease
FDG SPECT Scans for Diagnosing Cardiac Disease and Myocardial Viability
Gamma Cameras and Positron Emission Tomography for the Diagnosis of Cancer
Helical Computed Tomography for Detection of Calcium for Diagnosis of Coronary Artery Disease
Helical (Low Dose) Computed Tomography for Early Stage Lung Cancer Screening
Magnetic Resonance Spectroscopy for Prostate Cancer and Benign Prostatic Hyperplasia
Positron Emission Tomography (PET) Coverage in the US
Position Emission Tomography (PET) for Ovarian Cancer
Positron Emission Tomography for the Heart (Update of full TA Report)
Reimbursement Issues for Magnetoencephalography (MEG)
Retinal Screening Imaging Devices Comparison
Scanning LASER Polimeters for Diagnosing Glaucoma
Sonohysterography for Gynecologic Conditions
Spinal Discography for Disk/Back Pain
Technetium Tc 99m Sestamibi (Miraluma) Imaging Agent Kit for Diagnosis of Breast Cancer
Three Dimensional Quantitative Computed Tomography Scanners for Bone Densitometry
Three Dimensional RODEO Imaging for Detection of Breast Cancer
Telethermography as a Diagnostic Tool
Ultrasound for Peyronie's Disease
Virtual Colonoscopy for Diagnosing Colon Diseases

- Endocrinology

Growth Hormone Therapy for Hypopituitarism
Growth Hormone Therapy for Adults with Non-Pituitary Related Growth Hormone Deficiencies
Recombinant Human Growth Hormone for AIDS Wasting
For additional related titles, please see the listings under Diabetology.

- Gynecology

Alendronate (Fosamax) for the Treatment of Osteoporosis
Automated Pap Smear Rescreening Devices for Cervical Cancer Screening
Effects of Age on In vitro Fertilization Success Rates
Embryo Toxicity Factor L Assay for Recurrent Pregnancy Loss
Endometrial Ablation for Menorrhagia (Update of full TA Report)

Female Breast Reduction Surgery (Update of full TA Report)
Partial Colpoclesis for Treatment of Uterine Prolapse
Prophylactic Mastectomy to Prevent Breast Cancer
Reconstructive Breast Surgery for Tubular Breast Deformities
Ultrasound for Bone Mineral Density Measurement
Uterine Balloon Therapy Systems (UBT) for Endometrial Ablation
Uterine Artery Embolization (UAE) for Fibroids

- Infectious Disease

Amplicor HIV-1 Monitor Ultrasensitive Test for HIV Viral Loads
Effect of Stress on HIV Disease Progression
HIV Genotypic and Phenotypic Testing for Anti-Retroviral Drug Resistance
Interleukin-2 for the Treatment of HIV/AIDS
Interleukin-2 for the Treatment of HIV/AIDS - associated with Kaposi's Sarcoma
Intravenous Ceftriaxone for Treatment of Lyme Disease
LYMErix, A Vaccine Against Lyme Disease
Polymerase Chain Reaction (PCR) Test for Hepatitis B
Rapid Flu Tests for Detecting Influenza A and B
Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) Testing for Hepatitis C RNA
Sensitivity and Specificity of Serologic Tests in the Diagnosis of Lyme Disease
Zanamivir (Relenza) for Treatment of the Influenza Virus

- Internal Medicine

Alglucerase Treatment for Gaucher's Disease
Complex Decongestive Physiotherapy for Lymphedema
Extracorporeal Membrane Oxygenation for Pediatric Population
Gastric Pacemakers for Gastric Paralysis (Gastroparesis)
Guidelines for Dialysis for End Stage Renal Disease
Interferon Injections for Myelofibrosis
Jaw Wiring for Obesity Management
L-Carnitine for Treatment of Carnitine Deficiency
Massage Therapy for Lymphedema
Phototherapy for Delayed Sleep Phase Syndrome
PUVA Therapy for the Treatment of Alopecia
Radiotherapy High-Dose Chemotherapy with Autologous Bone Marrow
Transjugular Intrahepatic Portasystemic Shunt (TIPS) for Refractory Ascites
Transplantation for the Treatment of Amyloidosis

- Mental Health and Substance Abuse

Biofeedback for Attention Deficit Disorder
Cognitive Therapy and Community Reintegration Therapy for Traumatic Brain Injury
Eye Movement Desensitization and Reprocessing for Post-Traumatic Stress Disorder
Intensive Narcotic Detoxification (Rapid Detox) for Opiate Addiction
Lovaas Therapy for Autism

Relapse Rates of Recovering Substance Abusers when Re-Exposed to Abused Substances in the Work Environment

Sexual Reassignment for Gender Identity Disorders

Vision Therapy for Learning Disabilities

- Neurology and Neurosurgery

Botulinum Toxin (Botox) for Treatment of Migraines and Tension Headaches

Botulinum Toxin for the Treatment of Various Ophthalmologic and Neurologic Conditions

Fetal Brain Cell Implants for Treating Huntington's Chorea

High Voltage Galvanic Stimulation for Cervical (Dorsal) Radiculopathy

Hippotherapy for Multiple Sclerosis

Hyperbaric Oxygen Therapy for Brain Injury, Stroke, Multiple Sclerosis and Cerebral Palsy

Neuromuscular Electrical Stimulation for Cerebral Palsy and Spina Bifida

Neuromuscular Electrical Stimulation for Paralysis Due to Stroke

Neuromuscular Electrical Stimulation for Paralyzed Facial Nerves

Neuromuscular Electrical Stimulation for Peripheral Nerve Injuries

Neuromuscular Electrical Stimulation for Spinal Cord Injuries

Neuromuscular Electrical Stimulation for Muscle Paralysis by Functional Motor Disease

Pharmacologic Treatment for Multiple Sclerosis

Plasmapheresis for Multiple Sclerosis

Sensory Integration Therapy for Fragile X Syndrome, Autism, Attention Deficit Disorder and Developmental Delay

Stereotactic Radiosurgery for Treating Epilepsy

Suboccipital Craniotomy using DRES Technique for the Treatment of Cluster Headaches

Thalamic Stimulation for Parkinson's Disease

Therapeutic Electric Stimulation for Spina Bifida

Thoracic Outlet Syndrome

Vagal Nerve Stimulation for Epilepsy

Video EEG Monitoring for Epilepsy/ Seizures

- Obstetrics

Enoxiparin (Lovenox) and its Safety in Pregnancy

Prevention of Congenital Disorders using Preimplantation Genetic Diagnosis and Sperm Sorting

Prevention of Deep Vein Thrombosis during Pregnancy Using Compression Stockings

- Oncology and Hematology

Allogeneic Adoptive Immunotherapy for Glioblastoma

Allogeneic Bone Marrow Transplantation for Chronic Lymphocytic Leukemia

Antineoplaston Therapy for the Treatment of Cancer at the Burzynski Research Institute

Autolymphocyte Therapy (ALT) for Non-Metastatic Renal Cell Carcinoma
Bone Marrow Transplantation for the Treatment of Hurler's Syndrome
CA 125 for the Detection of Ovarian Cancer (Update of full TA Report)
CA 15-3 for the Detection of Breast Cancer (Update of full TA Report)
Cryosurgery for Liver Cancer
Cryosurgery for Prostate Cancer (Update of full TA Report)
Donor Lymphocyte Infusion for Relapse after Bone Marrow Transplantation
Doxorubicin Liposomal (Doxil®/Caelyx®) for Treatment of Leiomyosarcomas
Endocavitary Radiation for Rectal Cancer
Extracorporeal Photophoresis for Treatment of Cutaneous T-Cell Lymphoma
Frameless Stereotactic Radiosurgical Systems for Cancer Therapy
Gene Therapy for End-Stage Carcinoma
Genetic Screening for BRCA1 and BRCA2
Genetic Testing (Microsatellite Instability and DNA Sequencing) for Colorectal Tumors
Herbal Tonics for the Treatment of Adenocarcinoma of the Lung with Brain Metastasis
Her-2/Neu Testing for Breast Cancer
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Breast Cancer (Update of full TA Report)
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Lung Cancer (Update of full TA Report)
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Medulloblastoma (Update of full TA Report)
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Neuroblastoma
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Non-Hodgkin's Lymphoma
High-dose Chemotherapy with Autologous or Allogenic Stem Cell or Bone Marrow Transplantation for Testicular Cancer
High-dose Chemotherapy with Autologous Bone Marrow or Stem Cell Transplantation for Ovarian Cancer (Update of full TA report)
High-dose Chemotherapy/Autologous Peripheral Stem Cell Harvest and Transplantation for the Treatment of Systemic Lupus Erythematosus
High-dose Chemotherapy with Stem Cell Infusion for Recurrent Anaplastic Astrocytoma
Hyperthermia with Chemotherapy for Rectal and Colorectal Cancers
Hyperthermic Lavage with Chemotherapy Agents for the Treatment of Gastric and Other Intraperitoneal Cancers
Immunoaugmentative Therapy for Cancer Patients
Intralesional I131 Therapy for Glioma
In Vitro Chemosensitivity Assays for Predicting Tumor Response to Chemotherapy
Leuprolide Acetate (Lupron) for Treatment of Ovarian Cancer
Monoclonal Antibodies for Diagnosing Colorectal cancer
Monoclonal Antibodies (Rituximab and Tositumomab) for Treatment of Non-Hodgkin's Lymphoma

New Castle Therapy (Poultry Virus) for the Treatment of Adenocarcinoma of the Lung with Brain Metastases

Non-Myeloablative Allogeneic Bone Marrow Transplantation for Acute Lymphocytic Leukemia (ALL)

Octreoscan for the Diagnosis/Detection of Neuroendocrine Tumors

Paclitaxel (Taxol) and Carboplatin for the Treatment of Thymus Cancer

Photodynamic Therapy for Esophageal Cancer

Poly-(styrene-co-maleyl-half-n-batylate)-neocarzinostatin (SMANCS) for the Treatment of Recurrent Gastric Cancer

Prophylactic Use of Tamoxifen for Women at High Risk for Breast Cancer

ProstaSinct for Detection of Prostate Cancer Metastases

Prostate Cancer (see Treatments for Localized Prostate Cancer)

Proton Beam Radiation Therapy for Prostate Cancer

Radiofrequency Ablation for Metastatic Liver Tumors

Sentinel Node Biopsy for Breast Cancer

Sentinel Node Biopsy for Malignant Melanoma

Shark Cartilage for the Treatment of Cancer

Stereotactic Radiosurgery for Extracranial Tumors

Stereotactic Radiosurgery for Intracranial Tumors

Tandem Bone Marrow Transplantation for Multiple Myeloma

Temporary Brachytherapy with HDR-Ir192 for Prostate Cancer

Transoral Laser Surgery for Supraglottic Carcinoma

Treatments for Localized Prostate Cancer (Update of full TA Report)

Tumor Necrosis Factor Receptor (TNFR) Ultrapheresis for Metastastasized Breast Cancer

Umbilical Cord Blood Transplantation

Vaccines for Malignant Melanoma

- Ophthalmology

Amniotic Membrane Transplantation for Corneal Injuries

Laser Iridotomy for Narrow Angle Glaucoma

MTI Photoscreener for Amblyopia

Pachymetry for Diagnosis and Monitoring of Keratoconus

Photodynamic Therapy with Visudyne for Age-Related Macular Degeneration

Vision Therapy for Eye Disorders

- Orthopedics

Autologous Chondrocyte Transplantation for the Knee

Carpal Tunnel Syndrome and its Relationship to Repetitious Work Activities

Copes Brace for Scoliosis

Electrical Bone Growth Stimulation for the Lower Leg (Update of full TA Report)

Electrical Bone Growth Stimulation for the Wrist/Short Bones (Update of full TA Report)

Electrothermal Arthroscopy (specifically, Electrothermal Repair of the Anterior Cruciate Ligament using the Oratec Arthroscopy System)

Foot or Shoe Orthotic Devices for the Treatment of Foot Conditions

MedX Lumbar Extension Machine for Testing Back Strength

Meniscal Allograft Transplantation for Damaged/Removed Meniscus

Osteochondral Allograft Transplantation for the Knee
Osteochondral Autograft Transplantation for the Ankle
Shock Wave Therapy for Orthopedic Indications
Taylor Spatial Frame for Fracture Healing
Vascularized Fibular Grafting for Avascular Necrosis

- Otolaryngology

Canalith Repositioning Maneuver (CRM) of Epley for the Treatment of Benign Paroxysmal Positional Vertigo (BPPV)

Clinical Criteria for Surgical Treatments of Obstructive Sleep Apnea

Continuous Positive Airway Pressure (CPAP) and Bi-Level Positive Airway Pressure (BiPAP) for Adult Sleep Apnea
Effectiveness of the Vorteq Device to Diagnose Central and Peripheral Vertigo
Habituation Therapy for Chronic Tinnitus

Laser-Assisted Uvulopalatoplasty (LAUP) for Sleep Apnea and Obstructive Snoring (Update of full TA Report)

Laser Tonsil Ablation for Treatment of Cryptic Tonsillitis

OtoLAM (Laser Assisted Myringotomy) Laser Device for Treatment of Middle Ear Infections

Radiofrequency-Mediated Tongue Tissue Reduction (Sommnoplasty) for Sleep Apnea
Serum Protein Antibodies for the Diagnosis of Ménière's Disease

- Pain Management

Baclofen Infusion Pumps for Muscle Spasticity and Back Pain
BAK and Ray Threaded Spinal Fusion Devices (Cages) for Back Pain
Cervical Traction Devices for Neck Pain
Chemonucleolysis for Herniated Disk
Electrical Stimulation Therapy for Edema

Electric Stimulation Using the Micro Z Stimulator and Electro- Mesh Garments for Treatment of Diabetic Neuropathy, Ulcers and Pain
Epidurolysis Procedure Using Racz Catheter for Low Back Pain
Facet Joint, Epidural, and Trigger point Injection Therapies for Pain
H-Wave Electrical Stimulation Therapy for Neuropathy and Ischemic Diseases
Implantable Pumps for Intractable Back Pain
Infusaid 400 Implantable Pumps
Intradiscal Electrothermal Catheterization (using SpineCATH™) for Back Pain
Interferential Current for Pain Management
Multiple Epidural Blocks for Pain
Neuroplasty for Back Pain
Oxygen Therapy for Cluster Headache
Pelvic Sacral Bone Stimulation for Pain or Fracture Healing
Percutaneous Laser Disk Decompression for Herniated Disk
Percutaneous Vertebroplasty for Treatment of Spinal Compression due to Osteoporosis
Prolotherapy for Pain
Radiofrequency Ablation (Lesioning) for Low Back Pain

Sacroiliac Joint Denervation with Electrocoagulation
Transcutaneous Electrical Nerve Stimulation (TENS) for Back Pain
VAX-D Therapy for Herniated Disk

- Pediatrics

Automated Auditory Brainstem Response System for Universal Screening of Newborns for Hearing Deficiency

Dynamic Orthotic Cranioplasty for Infants with Plagiocephaly
Enuresis Alarms for Nocturnal Bed-Wetting
Exchange Transfusion for the Treatment of Sickle Cell Anemia in Infants
Growth Hormone for Children with Heart Disease
Home Phototherapy for Treating Neonatal Jaundice
RespiGam for the Prevention of Respiratory Syncytial Virus in Infants
Physical Medicine and Rehabilitation
Continuous Passive Motion Devices
Pulmonary Medicine
Airwatch System for Anesthesiology and Asthma Monitoring
Color Corrected Lighting to Detect Cyanosis
Emphysema Statistics: What percent of emphysema patients are over 65?
Epoprostenol (Flolan) to Treat Pulmonary Hypertension with Scleroderma
Extracorporeal Membrane Oxygenation in Pediatric Populations
Flutter Device for Treatment of Cystic Fibrosis
High Frequency Chest Compression for the Treatment of Cystic Fibrosis
Inhaled Nitric Oxide to Treat Pulmonary Diseases
Insufflators for Pneumonia and Other Pulmonary Diseases
Outpatient Pulmonary Rehabilitation Programs for Chronic Obstructive Pulmonary Disease and Other Lung Diseases
Use of Pulse Oximetry in the Home

- Rheumatology

Hyaluronic Acid Derived Synovial Fluid (Synvisc and Hyalgan) for the Treatment of Osteoarthritis of the Knee
Protein A Separation (PROSORBA) Columns for Treatment of Rheumatoid Arthritis

45 SURGERY—GENERAL

Anti-Adhesion Barrier Gel (ADCON-L) for Use During Laminectomy or Laminotomy Surgery
Autotransfusion Using the OrthoPAT System for Orthopedic Surgery
Electric Stimulator (CaverMap) to Identify Nerve Bundles During "Nerve Sparing" Prostatectomy
Endoscopic Carpal Tunnel Release
Endoscopic Thoracic Sympathectomy for Palmar Hyperhydrosis
Fibrin Glue for Tissue Adhesion
Fobi Pouch Gastric Procedure for the Surgical Treatment of Obesity
In Utero Surgical Treatment for Fetal Malformations

Surgical Treatment of Morbid Obesity
Thyroplasty for Vocal Cord Paralysis

- Transplantation

Bowel and Bowel/Intestine Transplantation for Small Bowel Syndrome (Update of full TA Report)
Heart Transplantation for Idiopathic Cardiomyopathy
Liver Assistance Technologies as a Bridge to Liver Transplantation
Liver Tansplantation for Primary Liver Tumors
Living Donor Liver Transplantation for Adults
Living Donor Lung or Pancreas Transplantation
Lung Transplantation (Update of full TA Report)
Oxygen Consumption at Peak Exercise (VO2Max): A Prognostic Variable for Heart Transplant Candidates
Pancreas Transplantation Alone (Update of full TA Report)
Prevention of Hepatitis B Infection Recurrence after Liver Transplantation for Chronic Hepatitis B
Segmental Pancreas Transplantation, Specifically with Living-Related Donors
Simultaneous Pancreas/Kidney Transplantation (Update of full TA Report)

- Urology

Extracorporeal Magnetic Innervation (NEOCONTROL) for Urinary Incontinence
Holmium: YAG Lasers for Urologic, Neurologic and Orthopedic Conditions
Electric Stimulation Device (Medtronic's InterStim) for Urinary Incontinence, Urinary Retention and Urgency/Frequency
Male Infertility - Intracytoplasmic Sperm Injection
Pelvic Floor Stimulation for the Treatment of Urinary Incontinence
Penile Drug Delivery Implants for Erectile Impotence
Portable Lithotriptors for Gallstones and/or Kidney and Urinary Stones
Sildenafil (Viagra) for Male Erectile Dysfunction
Tension Free Vaginal Tape for Female Stress Urinary Incontinence
Transurethral Microwave Therapy (TUMT) for Benign Prostatic Hypertrophy
Transurethral Needle Ablation (TUNA) for Benign Prostatic Hyperplasia

- Wound Care

Procuren for Wound Healing (Update of full TA Report)
Skin Substitutes (Apligraf, Dermagraft, Integra) for Treatment of Ulcers and Burn Wounds
Topical Hyperbaric Oxygen Therapy for Chronic Wounds
Vacuum-Assisted Wound Closure Therapy

- Other

Alternatives to Ethylene Oxide Sterilization
Antisense Oligonucleotides as Drug Therapy
Credentialing for Acupuncture
Volume-Based Credentialing

TARGET (Technology Assessment Resource Guide for Emerging Technologies)

46 ANESTHESIOLOGY

Electroencephalographic (EEG) bispectral analysis systems for monitoring of intraoperative awareness (2/23/00)

47 CARDIOLOGY

Commercial fibrin sealant for cardiovascular surgery (2/21/00)

Ventricular assist devices (VADs) for heart failure (short-term bridge to recovery) (3/13/00)

Ventricular assist devices (VADs) for heart failure (long-term bridge to heart transplantation) (2/29/00)

48 CLINICAL LABORATORY-HEMATOLOGY

Laboratory automation (Updated 8/15/00)

49 DIABETOLOGY

Islet cell transplantation for insulin-dependent (type 1) diabetes mellitus (7/27/00)

50 DIAGNOSTIC IMAGING

Digital radiography using amorphous silicon flat-panel detectors (2/21/00)

Full-field digital mammography (3/30/00)

Magnetic resonance angiography (MRA) for diagnosis of carotid artery disease (6/29/00)

Magnetic resonance angiography (MRA) for diagnosis of coronary artery disease (CAD), bypass graft stenosis, and congenital abnormalities (7/27/00)

Magnetic resonance angiography (MRA) for diagnosis of intracranial vascular disease and tumors (7/27/00)

Magnetic resonance angiography (MRA) for diagnosis of pulmonary embolism (6/29/00)

Mammography computer-aided detection (CAD) systems for breast cancer screening (8/31/00)

Multislice computed tomography (CT) scanners (6/29/00)

Virtual colonoscopy for detection of colorectal cancer and polyps (2/21/00)

51 GYNECOLOGY

Bilateral prophylactic mastectomy for women at moderate or high risk of breast cancer (7/27/00)

52 INFECTIOUS DISEASE

Antimicrobial Foley catheters to minimize risk of catheter-related infection (5/10/00)

Antimicrobial-impregnated central venous catheters to minimize risk of catheter-related infection (3/29/00)

Vaccine for Lyme disease (3/21/00)

53 INTERNAL MEDICINE

Enzyme replacement therapy (ERT) for Gaucher disease (6/29/00)

54 ONCOLOGY

High-dose chemotherapy (HDC) with autologous bone marrow transplantation (ABMT) and/or stem cell transplantation (SCT) for metastatic breast cancer (4/21/00)

Photodynamic therapy (PDT) for cutaneous metastasis or chest wall recurrence of breast cancer (4/21/00)

Tamoxifen for prevention of breast cancer in healthy women at high risk (4/21/00)

55 OPHTHALMOLOGY

Photodynamic therapy (PDT) for wet age-related macular degeneration (AMD) (8/3/00)

56 ORTHOPEDICS

Autologous chondrocyte implantation (ACI) for knee cartilage defects (7/28/00)

57 OTOLARYNGOLOGY

Digital hearing aids for sensorineural hearing loss (5/10/00)

58 PAIN MANAGEMENT

Intradiscal electrothermal therapy for discogenic pain (3/29/00)
Oral transmucosal fentanyl citrate (OTFC) for breakthrough cancer pain (3/29/00)

59 PULMONARY MEDICINE

Lung volume reduction surgery (LVRS) for emphysema (2/21/00)
Nitric oxide therapy for primary pulmonary hypertension (PPH) or acute respiratory distress syndrome (ARDS) in adults (5/12/00)

60 UROLOGY

Implantable sacral nerve stimulator for urinary urge incontinence (4/21/00)

Laser prostatectomy for benign prostatic hyperplasia (BPH) (2/8/00)

Transurethral balloon dilatation (TUBD) therapy for benign prostatic hyperplasia (BPH) (3/21/00)

Transurethral needle ablation therapy for benign prostatic hyperplasia (BPH) (2/23/00)

61 WOUND CARE

Vacuum-assisted closure therapy for wound healing (4/12/00)

Organization: Hayes Incorporated
157 S. Broad Street
Suite 200
Lansdale, PA 19446

Contact: Diane Hayes, PhD
VP of Technology Assessment and Editor-In-Chief
215-855-0615

Purpose:

Hayes, Inc., a small, privately held company, was founded and incorporated in 1989 by President and CEO Dr. Winifred S. Hayes. It produces a range of medical technology assessment reports and publications that specialize in evidence-based analyses of a variety of health care technologies. Hayes, Inc. also publishes legal/medical reports that assess and analyze the legal status of medical technologies and managed care issues specific to insurance coverage, medical malpractice, and legislative trends. Hayes, Inc mission is to support clients in their efforts to improve health outcomes, while ensuring patients receive high-quality, safe and effective healthcare. Hayes, Inc. works with professionals in clinical research, medicine, and law.

Selection Criteria:

Topic are selected in two ways: customer requests and information reviewed for the monthly newsletter based on tracking several sources including FDA, HCFA, multiple peer-reviewed journals, newspapers, and other health-related sources. Topics are prioritized based on the importance of the study published or regulation approved.

Primary Focus:

Safety, efficacy, patient selection criteria

Stage of Technology:

Hayes, Inc. primarily looks at new, emerging, and leading edge technologies. However, the company also considers pre-established and outmoded technologies

Type of Technology:

Medical and surgical procedures, including transplants; drugs and pharmaceuticals; diagnostic and screening tests; alternative therapies; medical devices/equipment

Technologies/Conditions Reviewed:

1998: Acupuncture and Acupressure for the Treatment of Nausea and Vomiting.
04/14/1998

Acupuncture for Addictive Behavior 04/02/1998
Allergy Testing, In Vitro, Rast and Other Immunoassays 04/23/1998
Allergy Testing, In Vivo 05/14/1998
Allogeneic Bone Marrow Transplantation for Aplastic Anemia 12/02/1998
Ambulatory Blood Pressure Monitoring (ABPM) with Fully and Semi-Automatic Portable Monitors 06/01/1998
Biochemical Markers of Bone Mass for Postmenopausal Women 04/23/1998
Biofeedback, Management of Pain BIOF1501.01 02/20/1998
Boron Neutron Capture Therapy for Glioblastoma Multiforme 12/16/1998
Brachytherapy for Prostatic Carcinoma 06/26/1998
Chemotherapy for Malignant Glioma Using Biodegradable Polymers 12/10/1998
Chronic Fatigue Syndrome Treatment 04/23/1998
Cochlear Device Implantation 07/15/1998
Computer-Assisted Rescreening of Pap Smears 05/12/1998
Coronary Artery Bypass Grafting 08/12/1998
Coronary Stent Implantation 10/08/1998
Donor Leukocyte Infusion for Relapsed Leukemia after Allogeneic Bone Marrow Transplantation 12/28/1998
Electrical Bladder Stimulation for the Treatment of Urinary Incontinence 07/13/1998
Epidural Steroid Injections for Low Back Pain and Sciatica 02/26/1998
Facet Blocks for Treatment of Low Back Pain 02/28/1998
Genetic Carrier Testing for Cystic Fibrosis 05/01/1998
Genetic Testing for Susceptibility to Alzheimer's Disease 05/18/1998
Genetic Testing for Susceptibility to Familial Adenomatous Polyposis 03/05/1998
Genetic Testing for Susceptibility to Hereditary Nonpolyposis Colorectal Cancer 03/05/1998
Genetic Testing for Tay-Sachs Disease 12/10/1998
Growth Hormone Treatment in Adults 07/17/1998
Heart Transplantation, Adult 02/24/1998
Heart Transplantation, Pediatric 02/24/1998
Heart-Lung Transplantation 04/22/1998
Heart-Lung-Liver Transplantation 04/29/1998
HER-2 Genetic Testing System 11/30/1998
High Dose Chemotherapy With Autologous Stem Cell Support for Low-Grade Non-Hodgkin's Lymphoma 09/01/1998
High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Acute Leukemia 10/15/1998
High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Breast Cancer 07/06/1998
High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Chronic Leukemia 10/15/1998
High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Epithelial Ovarian Cancer 07/02/1998

High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Germ Cell Testicular Cancer 10/02/1998

High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for Hodgkin's Disease 09/01/1998

High-Dose Chemotherapy with Autologous Stem Cell Support, Treatment for I/H Grade Non-Hodgkin's Lymphoma 07/27/1998

Home Uterine Activity Monitoring 11/30/1998

In Vitro Chemosensitivity Assays in Cancer Treatment 03/09/1998

Interleukin-2 Therapy for Acute Leukemia 03/04/1998

Interleukin-2 Therapy for Lymphoma 02/25/1998

Interleukin-2 Therapy for Other Malignancies 03/04/1998

Interleukin-2 Therapy for Renal Cell Carcinoma 10/09/1998

Laparoscopic Hysterectomy 09/16/1998

Laser In Situ Keratomileusis 11/06/1998

Lung Volume Reduction Surgery for Chronic Obstructive Pulmonary Disease 02/24/1998

Lyme Disease Vaccine 12/03/1998

Magnetic Resonance Angiography, Abdominal Applications 07/08/1998

Magnetic Resonance Angiography, Cardiac Applications 07/08/1998

Magnetic Resonance Angiography, Head and Neck Applications 09/24/1998

Magnetic Resonance Angiography, Peripheral Applications 07/08/1998

Magnetic Resonance Angiography, Thoracic Applications 07/13/1998

Magnetic Source Imaging for Neurologic Applications 09/25/1998

Minimally Invasive Coronary Artery Bypass Surgery 09/14/1998

Neonatal Hearing Screening 05/14/1998

Noninvasive Complex Lymphedema Therapy 10/12/1998

Pallidotomy for Treatment of Parkinson's Disease 03/05/1998

Paternal Leukocyte Immunization and Intravenous Immunoglobulin for Recurrent Spontaneous Abortion 03/11/1998

Percutaneous Transluminal Coronary Angioplasty 09/14/1998

Photorefractive Keratectomy 11/06/1998

Positron Emission Tomography (PET) for Central Nervous System Tumors 03/10/1998

Positron Emission Tomography (PET) for Lung Cancer 03/17/1998

Positron Emission Tomography (PET) for Non-Central Nervous System Head and Neck Tumors 03/17/1998

Positron Emission Tomography (PET) for Other Malignancies 03/17/1998

Presacral Neurectomy for Chronic Pelvic Pain, Endometriosis, Dysmenorrhea, and Dyspareunia 05/07/1998

Prophylactic Oophorectomy 11/17/1998

ProstaScint 03/04/1998

Prostate-Specific Antigen Ratio 03/17/1998

Proton Beam Therapy 09/01/1998

Radial Keratotomy 11/06/1998

Radionuclide Therapy for Palliative Management of Bone Metastases, Prostatic Carcinoma 09/11/1998

Spinal Cord Stimulation for the Treatment of Pain 04/28/1998
Stereotactic Radiosurgery 10/12/1998
Taxol Treatment for Non-Small-Cell Lung Cancer 12/22/1998
Taxol Treatment for Small-Cell Lung Cancer 12/22/1998
Therapeutic Uses of Inhaled Marijuana and Oral Tetrahydrocannabinol (THC) 07/17/1998
ThinPrep Pap Smear Test for Detecting Cervical Cancer 05/12/1998
Transcutaneous Electrical Nerve Stimulation for the Treatment of Pain 04/15/1998
Transurethral Needle Ablation Therapy 12/03/1998
Ultrasound versus Dual Energy X-Ray Absorptiometry for Osteoporosis Diagnosis and Screening 04/22/1998
Umbilical Cord Blood Stem Cell Transplantation 12/04/1998
Vacuum-Assisted Closure for Wound Healing 06/30/1998
Viagra 10/15/1998

1999: Allogeneic Bone Marrow Transplantation for Rare Genetic Diseases 05/10/1999
Allogeneic Bone Marrow Transplantation for Severe Combined Immunodeficiency 01/07/1999
Allogeneic Bone Marrow Transplantation for Sickle Cell Disease and Thalassemia 02/03/1999
Antibiotic Treatment for Initial and Recurrent Otitis Media 08/26/1999
Autologous Chondrocyte Transplantation 05/05/1999
Botulinum Toxin for Neurological and Ophthalmic Disorders 03/10/1999
Botulinum Toxin for Spasticity and Gastrointestinal Disorders 01/28/1999
Cardiac Rehabilitation Programs 03 10/18/1999
Chiropractic Treatment of Low Back Pain 05/26/1999
Computer-Assisted Diagnosis for Mammography 06/22/1999
Continuous Passive Motion 11/04/1999
Cryoablation for Prostate Cancer 10/20/1999
Deep Brain Stimulation for Parkinson's Disease and Essential Tremor 11/29/1999
Electrical and Ultrasound Bone Growth Stimulation 09/14/1999
Electron Beam Computed Tomography (EBCT) 07/12/1999
Endometrial Laser Ablation 08/16/1999
Endoscopic Sympathectomy Treatment of Hyperhidrosis 01/08/1999
Enhanced External Counterpulsation for Chronic Stable Angina 10/11/1999
Etanercept for Rheumatoid Arthritis 06/07/1999
Fetal Fibronectin Test 02/19/1999
Fine-Needle Aspiration Biopsy for Breast Cancer 09/07/1999
Growth Hormone Treatment in Children 05/25/1999
Homeopathy for Skin Conditions 05/21/1999
Hybrid Capture HPV Testing for Cervical Cancer 08/16/1999
Hyperbaric Oxygen Therapy for Burns, Infections, and Wounds 06/01/1999
Hyperbaric Oxygen Therapy for Carbon Monoxide Poisoning 06/01/1999
In Utero Fetal Surgery 10/28/1999
Infliximab for Crohn's Disease 03/08/1999

Interferon Beta for Multiple Sclerosis 03/10/1999
Interferon/Ribavirin Therapy for Hepatitis C 04/26/1999

62 INTRATHECAL BACLOFEN FOR CEREBRAL PALSY 02/12/1999

Intrathecal Opioid Therapy for Chronic Nonmalignant Pain 10/07/1999
Intravenous Immunoglobulin for AIDS in Adults 02/25/1999
Intravenous Immunoglobulin for Multiple Sclerosis 02/25/1999
Laparoscopic Colon Resection for Benign Conditions 11/24/1999
Laparoscopic Hernia Repair 05/13/1999
Laser-Assisted Endoscopic Sinus Surgery 08/08/1999
Light Therapy for Seasonal Affective Disorder 08/31/1999
Liver Transplantation, Orthotopic, Adult 11/15/1999
Lung Transplantation 06/24/1999
Lymphoscintigraphy/Lymphatic Mapping for Breast Cancer 08/13/1999
Meniscal Allograft 11/02/1999
Magnetic Resonance Imaging for Myocardial Viability 08/06/1999
MOHS Micrographic Surgery for Basal and Squamous Cell Carcinomas 04/12/1999
Obesity Management, Pharmacologic Treatment with Orlistat or Sibutramine 09/07/1999
Obesity Management, Surgical Approaches 10/12/1999
Pancreas Transplantation Alone (PTA) 03/01/1999
Pancreas-After-Kidney Transplantation (PAK) 02/25/1999
Photodynamic Therapy for Esophageal Cancer 04/30/1999
Photodynamic Therapy for Head and Neck Cancer 07/06/1999
Photodynamic Therapy for Lung Cancer 03/08/1999
Plasmapheresis for Non-Renal Indications 02/16/1999
Plasmapheresis for Renal Indications 02/19/1999
Positron Emission Tomography (PET) for Cardiac Applications 07/12/1999
Procuren and Platelet-Derived Growth Factors for the Treatment of Chronic Nonhealing Wounds 05/05/1999
Prophylactic Mastectomy 05/05/1999
Prophylactic Medical Treatments for Breast Cancer 05/05/1999
Pulmonary Rehabilitation 09/13/1999
Radiofrequency Ablation for Low Back Pain 10/21/1999
Radiofrequency Ablation for Trigeminal Neuralgia and Cervical/Thoracic Pain 04/30/1999
Reverse Transcription Polymerase Chain Reaction for Hepatitis C 11/17/1999
Salivary Estriol Test for Preterm Labor 05/14/1999
Self-Monitoring of Warfarin Therapy 10/01/1999
Sentinel Node Biopsy for the Staging of Breast Cancer 08/13/1999
Sentinel Node Biopsy for the Staging of Malignant Melanoma 08/31/1999
Simultaneous Pancreas/Kidney (SPK) Transplantation 03/23/1999
Sleep Apnea Treatment, Devices 08/26/1999
Sleep Apnea Treatment, Surgical 02/25/1999

Sleep Apnea, Diagnosis, Adult 07/15/1999
Small Bowel Transplantation 03/12/1999
Stereotactic Directional, Vacuum-Assisted Biopsy and Minimally Invasive Percutaneous Excision Biopsy for Breast Cancer 11/08/1999
Stereotactic Fine-Needle Biopsy and Core-Needle Biopsy for Breast Cancer 11/08/1999
Testosterone and Other Anabolic Steroid Treatment for AIDS Wasting Syndrome 03/02/1999
Thermal Balloon Endometrial Ablation 08/16/1999
Transcervical Resection of Endometrium 08/16/1999
Transcutaneous Electrical Nerve Stimulation for the Treatment of Nausea and Vomiting 11/01/1999
Transmyocardial Laser Revascularization 10/21/1999
Uterine Artery Embolization for Treatment of Fibroids 09/29/1999
Vagus Nerve Stimulation for Epilepsy 02/16/1999
Ventricular Assist Devices 11/23/1999
Ventricular Reduction Surgery 03/16/1999
Vertebral Axial Decompression for Low Back Pain 05/05/1999
Vestibular Therapy for the Treatment of Vestibular and Balance Disorders 10/08/1999
Vision Therapy to Improve Visual Dysfunctions 03/03/1999

2000: Chelation Therapy, Non-Overload Conditions 02/27/2000
Chelation Therapy, Overload Conditions 02/21/2000
Cranial Orthotic Devices 01/21/2000
Estrogen Pellet Implants 02/17/2000
Helical CT for Coronary Artery Disease 02/07/2000
Hepatitis A Vaccine 02/24/2000
High-Dose Chemotherapy and Radiation Therapy Followed by Allogeneic Transplantation for Multiple Myeloma 03/06/2000
High-Frequency Chest Wall Compression 03/03/2000
Infliximab for Rheumatoid Arthritis 02/21/2000
Insulin Pumps, Implantable 02/22/2000
Intravenous Immunoglobulin for Hematological Diseases 03/03/2000
Intravenous Immunoglobulin for Neurological Diseases 01/10/2000
Intravenous Immunoglobulin for Pediatric AIDS 01/31/2000
Intravenous Immunoglobulin for Rheumatic Diseases 03/07/2000
Laparoscopic Colon Resection for Malignancy 01/06/2000
Lithotripsy for Pancreatic Stones and Gallstones 03/02/2000
Lithotripsy for Salivary Stones 01/31/2000
Outpatient Low-Molecular-Weight Heparin Therapy for Deep-Vein Thrombosis 02/11/2000
Percutaneous Vertebroplasty 01/27/2000
Preoperative Autologous Blood Donation (PABD) for Elective Hip Surgery 03/02/2000
Sensory Integration Therapy for Children with Learning Disability 01/03/2000

New Reports 1st Quarter 2000:

Chelation Therapy, Non-Overload Conditions
Chelation Therapy, Overload Conditions
Cranial Orthotic Devices
Estrogen Pellet Implants
Helical Computed Tomography for Coronary Artery Disease
Hepatitis A Vaccine
High-Dose Chemotherapy and Radiation Therapy Followed by Allogeneic Transplantation for Multiple Myeloma
High-Frequency Chest Wall Compression Update
Infliximab for Rheumatoid Arthritis
Insulin Pumps, Implantable Update
Intravenous Immunoglobulin for Hematological Diseases
Intravenous Immunoglobulin for Neurological Diseases
Intravenous Immunoglobulin for Pediatric AIDS
Intravenous Immunoglobulin for Rheumatic Diseases
Laparoscopic Colon Resection for Malignancy
Lithotripsy for Pancreatic Stones and Gallstones
Lithotripsy for Salivary Stones New
Outpatient Low-Molecular-Weight Heparin Therapy for Deep-Vein Thrombosis
Percutaneous Vertebroplasty
Preoperative Autologous Blood Donation (PABD) for Elective Hip Surgery
Sensory Integration Therapy for Children with Learning Disability

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64 UPCOMING TOPICS 2ND QUARTER 2000:

Automatic Defibrillators, Implanted
Brachytherapy for Breast Cancer
Brachytherapy for Lung Cancer
Chemotherapy Resistance Assays
Dorsal Rhizotomy
Electrical Stimulation for Urinary Incontinence
Endovascular Stents for Aortic Aneurysm Repair

65 FETAL FIBRONECTIN

HDC/AuSCT for Other Solid Tumors
HDC/AuSCT for Pediatric Solid Tumors
Insulin Pumps, External
IVIG for Pulmonary Disorders

a) Ketogenic Diet

Lipoprotein Analysis for Dyslopidemia
Meningococcal Vaccine
Radiofrequency Ablation for Liver Cancer
Sclerotherapy, Esophageal Varices
Sclerotherapy, Joint and Ligamentous Injections
Sclerotherapy for Varicose Veins

66 SLEEP APNEA DIAGNOSIS, PEDIATRIC

Syngis for RSV
TUNA for BPH
Transurethral Microwave Thermotherapy for BPH

Organization: Medicare Payment Advisory Commission (MedPAC)
1730 K Street Suite 800
Washington, DC 20006

Contact: Nancy Ray, Analyst

67 TELEPHONE: (202) 653-7220

a) Jack Ashby, Research Director

Telephone: (202) 653-7233

Purpose:

To estimate changes in resource use in the upcoming fiscal year due to the adoption of new technologies that affect hospital operating and capital cost. Data are used to update the scientific and technological advances component of the conversion factor for the Medicare inpatient Prospective Payment System.

Selection Criteria:

Technologies that are quality-enhancing but cost increasing. They must have diffused to 5% of their potential market, but not have yet reached 75% diffusion. Their selection of technologies is qualitative, not quantitative.

Primary Focus:

High cost procedures affecting hospital operating and capital costs for Medicare patients

Stage of Technology: new, emerging

Technology/Conditions Reviewed:

1998: Hospital services—

- information systems
  - on-line clinical data
  - telemedicine
  - reconfiguring computer systems to become Y2k compliant
- cardiovascular drugs and devices
  - stents and balloon dilatation catheters
  - magnetic resonance angiography
  - pharmacologic therapy
- biotechnology

platelet inhibitor abciximab

radiolabeled antibodies to detect spread of lung, prostate, and colon cancer and to identify myocardial injury

- radiology, imaging and nuclear medicine

improvements and further applications for MRI, PET, ultrasound, CT and radionuclides

image-directed therapy for vascular conditions

1999:

- information systems

telemedicine

clinical data repositories (electronic medical records)

multi-site integrated data networks (medical intranets)

Y2k computer problem

- cardiovascular drugs, devices, techniques

aptifibatide (anticoagulant) to treat acute coronary syndromes

tirofiban (anticoagulant) to treat acute coronary syndromes

transmyocardial revascularization (a laser treatment) to treat patients with coronary heart disease

fibrin sealants to control bleeding during cardiopulmonary bypass and colostomy operations

aterial-wound closing devices such as collagen protein plug to deal arterial punctures during procedures such as angiograms and angioplasties

direct-access minimally invasive mitral valve surgery

robotic arms in coronary bypass surgery

- Biotechnology

Biological markers to identify disease conditions, such as thrombogenesis during acute coronary syndromes

prognastic antibodies to detect spread of prostate and gastric cancers

genetically engineered protein (etanercept) to manage severe rheumatoid arthritis

monoclonal antibody (infliximab) to treat Crohn's disease

rituximab to treat low-grade b-cell non-Hodgkin's lymphoma

monoclonal antibody (daclizumab) to prevent acute kidney transplant rejection

- radiology, imaging, and nuclear medicine

solid-state sytems that combine ultrasound with balloon and stent placement

combined imaging atherectomy devices

high frequency imaging

improved methods for characterizing tissue

three-dimensional reconstruction techniques

new advanced computed tomography scanners (CAT?) for trauma, vascular and

cardiac scanning

MRI for cardiac conditions

New contrast agents ([1-11C]octanoate) for better liver imaging during MRI

New ultrasound device (agent-injectable microscopic gas bubbles) to diagnose osteoporosis

acoustic instrumentation with new contrast agents to diagnose cardiac conditions and evaluate cardiac functions

PET for detecting segmental and diffuse coronary artery disease
Improved PET for neuropsychiatric disorders
Augmented reality systems for pre-operative planning

- other devices and technology

robotics used during minimally-invasive cardiovascular and nuerosurgery
a monitor to measure the brain's response to anesthesia to monitor unconsciousness during surgery
fiber-optic laser surgery
laser treament for benign prostatic hyperplasia
devices for implanted drug delivery, including intelligent devices with biosensors to monitor body fluid concentrations and make adjustments
cardiac implants with antithrombogenic drugs

2000:

- information systems

telemedicine
clinical data repositories
multi-site integrated data networks
physician order entry
computer-assisted decision-making systems

- cardiovascular drugs, devices, techniques

2 platelet aggregation inhibitors to treat acute coronary syndromes
3 antiarrhythmics to treat irregular heartbeat
protease inhibitor to reduce perioperative blood loss in patients undergoing cardioplumonary bypass
quinolone derivative to treat intermittent claudication
agent to treat deep-vein thrombosis
laser treatments for severe angina
left ventricular assist devices to support patients waiting for heart transplants
fibrin sealants to control bleeding during cardiopulmonary bypass and colostomy operations
catheter-based devices to remove blood clots prior to angioplasty
endovascular devices to reinforce weakened, bulging sections of the abdominal aorta
laser angioplasty to ablate arterial plaque

- biotechnology

injectable, sustained release formulation to treat lymphomatous meningitis
a retinoid and fusion protein to treat lymphomas
genetically engineered protein to manage severe rheumatoid arthritis

recombinant thrombin inhibitor to treat anticoagulation in patients with heparin-induced thrombocytopenia
synthetic plasma expander to treat hypovolemia
bioengineered skin for treatment of venous leg ulcers

- radiology, imaging, and nuclear medicine
  digital mammography and breast imaging devices for clarification of ambiguous mammograms
  mini-magnetic resonance imaging to view internal body structures
  handheld ultrasound devices
  electron-beam computed tomography to detect blockages in arteries
  functional anatomic mapping systems
  PET to diagnose certain cancers and lymphomas
  Radiosurgery devices that direct radiation to treat certain solid tumors
  New imaging agents to detect certain lung tumors and brain and spinal lesions

- other devices and technology
  (4)anti-infectives that treat infections caused by susceptible strains of gram-negative bacteria, drug-resistant blood stream and skin infections, and certain acute bacterial infections
  (2)cox-2 inhibitors for rheumatoid arthritis
  anti-coagulant to prevent the formation of clots after surgery
  anti-neoplastics for certain cancers, and agents to reduce the side effects of some cancer therapies
  (3)agents for surgical anesthesia and sedation
  automated blood testing system
  electronic device for post-operative nausea
  cardiac and drug delivery implants
  robotics used during minimally-invasive surgery
  use of microchips in restoring vision in patients with diseases of the retina
  robotics for telesurgery
  robotics for the development of prosthetic limbs for paralyzed patients

Organization: National Institutes of Health, National Heart, Lung, and Blood Institute (NIH NHLBI)
Building 31, Room 5A03 MSC 2482
NHLBI, NIH
31 Center Drive
Bethesda, MD 20892-2482

Contact: Carl A. Roth, PhD, LLM
Associate Director for Scientific Program Operation
301-496-6331

Purpose:

Originally established in 1948, the NHLBI's mission is to provide leadership for a national program in diseases of the heart, blood vessels, lung, and blood; sleep disorders; and blood resources. The Institute plans, conducts, fosters, and supports an integrated and coordinated program of basic research, clinical investigations and trials, observational studies, and demonstrations and education projects related to the causes, prevention, diagnosis treatment of heart, blood vessel, lung, and blood diseases and sleep disorders conducted in its own laboratories and by scientific institutions and individuals supported by research grants and contracts. The programs of the NHLBI are implemented through five extramural units: the Division of Heart and Vascular Diseases, the Division of Lung diseases, the Division of Blood diseases and Resources, the Division of Epidemiology and Clinical Applications, and the National Center on Sleep Disorders Research, and one intramural unit, the Division of Intramural Research

Selection Criteria:

Approximately seventy percent of studies are investigator initiated grants. The remainder is initiated by the Institute. Each NHLBI initiative represents the outcome of discussions and reviews by representatives of the scientific community and by Institute advisory committees and special emphasis panels. Proposals are reviewed by the National Heart, Lung, and Blood Advisory Council and the NHLBI Director in the context of the Institute's budget, program priorities, review workloads, and the proposed mechanism. Responses to released initiatives are reviewed by NHLBI

Primary Focus:

Safety, efficacy

68 STAGE OF TECHNOLOGY:

69

70 ESTABLISHED, EMERGING/DEVELOPING

Type of Technology: Drugs, devices, procedures

Technologies/Conditions Reviewed (Institute Initiated Programs):

1998: Heart and Vascular Diseases
Magnesium in Coronaries (MAGIC), Initiated in Fiscal Year 1998

The multicenter trial will determine whether intravenous magnesium will reduce the short-term mortality of high-risk patients with suspected acute MI when it is administered sufficiently early to reduce reperfusion injury.

1999: Heart and Vascular Diseases
New Initiatives

- *Abdominal Aortic Aneurysms: Pathogenesis*

The objective of this RFA is to determine the etiology, pathophysiology, and clinical progression (or stabilization and/or regression) of abdominal aortic aneurysm. Research will focus on disease initiation and progression and on rupture that leads to thromboembolic events and sudden death.

Cardiovascular Complications From Cocaine Abuse in HIV Infection

The purpose of this RFA is to investigate the pathology and pathophysiology of cardiovascular complications associated with cocaine abuse in HIV patients. Research findings will enable scientists to establish a rational basis for developing prevention, diagnosis, and treatment strategies.

Decreasing Weight Gain in African American Preadolescent Girls

The purpose of this RFA is to develop and test interventions that involve decreasing excessive weight gain during the high-risk transitional period from prepuberty to puberty to prevent obesity in African American girls. Phase I studies include development of new interventions and a 12-week pilot test to determine their feasibility, acceptability, and potential impact. During Phase 2, a 2-year controlled trial will be conducted to evaluate the efficacy of the interventions.

Early Access to Defibrillation as Treatment for Out-of-Hospital Cardiac Arrest
Public Access Defibrillation (PAD) Community Trial

The purpose of this RFP is to evaluate whether survival of persons with out-of-hospital cardiac arrest can be significantly improved in a community by making automated external defibrillators (devices capable of automatically detecting and treating ventricular fibrillation) available to individuals (foremen, guards, police, and airline stewards) who are likely to react to a medical emergency. The primary objective of this program is to determine whether volunteers trained in the use of automatic external

defibrillators for out-of-hospital cardiac arrest victims will significantly increase survival to hospital discharge compared with community volunteers trained in standard life-saving techniques.

Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE)

The purpose of this RFP is to determine whether a pulmonary artery catheterization (PAC)-directed treatment strategy is more effective than a non-PAC treatment strategy in reducing morbidity and mortality in patients with advanced CHF. The study is designed to determine whether therapy specifically tailored to the individual, using hemodynamic monitoring, results in a better clinical outcome than current standard therapy without invasive monitoring.

Genesis of Cardiomyopathy With HIV Infection and Alcohol Abuse

The objective of this RFP is to elucidate the mechanisms responsible for additive or synergistic effects of alcohol abuse and HIV infection in the development of cardiomyopathy. The ultimate goal is to provide a rational basis for prevention, optimal diagnosis, and treatment of cardiovascular complications in patients with HIV infection and alcohol abuse.

Hemochromatosis: Genetic Prevalence and Penetrance

The purpose of this RFP is to initiate an epidemiologic study of the prevalence and genetic determinants of hereditary hemochromatosis (chronic iron overload toxicity) in a multiethnic population. Results will be used to determine the feasibility and public health benefits of presymptomatic screening and intervention for this condition.

Multi-Ethnic Study of Atherosclerosis (MESA)

The purpose of this RFP is to conduct a 10-year observational study of subclinical CVD in a diverse population. Investigators will determine the characteristic associated with progression of subclinical to clinical CVD, identify factors related to newer measures of subclinical disease, examine relationships between new and established measures, and develop population-based methods suitable for application in future screening and intervention studies to identify aymptomatic persons at highest risk of clinical events.

- **Prevention of Cardiovascular Disease in Diabetes Mellitus(PCDD)**

The purpose of this study is to evaluate three diabetic treatment strategies (intensive glycemic control, intensive lipid and blood pressure control, and insulin resistance-lowering therapy) to prevent major cardiovascular events in patients with Type 2 diabetes mellitus. . In addition, it will compare the current recommended treatment for blood pressure and lipids control with a more aggressive approach to treating these risk factors in non-diabetic patients. Outcome measures include CVD mortality and major morbidity (MI and stroke).

Study of Coronary Revascularization and Therapeutics Evaluations (SOCRATES)

The objective of this RFP is to assess benefits and risks associated with early revascularization compared with medical anti-ischemic strategies in patients with stable CHD and ischemia who are receiving intensive drug and lifestyle risk factor modifications according to current guidelines. Information obtained from the study will provide a rational basis for safe and effective therapy for patients with stable CHD and will provide insights into the role of ischemia in the long-term clinical outcome of CHD patients.

71

72 LUNG DISEASES

New Initiatives

- Airway Remodeling and Repair in Asthma

The purpose of this RFA is to understand at the cellular, subcellular, and molecular levels, the role airway injury and its abnormal repair have in airway remodeling and its consequences in the pathogenesis of asthma.

Obstructive Sleep Apnea in Children

The objectives of this RFA are to define abnormalities in airway structure and function responsible for obstructive sleep apnea (OSA) in children 3 to 12 years of age and to identify physiologic and clinical measures associated with increased morbidity. Research findings will provide new strategies for diagnosis and treatment of OSA in children.

Pediatric Asthma Clinical Research Network

The purpose of this RFA is to establish a net-work of interactive pediatric asthma clinical research groups to evaluate new and existing therapeutic approaches for children with asthma and to disseminate scientific findings to health care professionals, patients, and the public. The purpose of this study is to evaluate current and novel therapies and management strategies for children with asthma. Emphasis is on clinical trials that help identify optimal therapy for children with different asthma phenotypes, genotypes, and ethnic backgrounds and children at different developmental stages.

Retinoic Acid Treatment in Emphysema

The purpose of this RFP is to determine the feasibility of conducting a clinical trial on the efficacy of retinoic acid, a derivative of vitamin A, in the treatment of emphysema. Secondary objectives are to identify optimal patient populations, drugs, dosing schedules, and outcome measures. The purpose of this program is to conduct preliminary studies to identify optimal patient populations, drugs and dosing schedules, and outcome measures before conducting a larger clinical trial on retinoid treatment for emphysema.

Strategies to Augment Alveolization

The objectives of this RFA are to elucidate molecular and cellular processes that are involved in the formation and functional differentiation of lung alveoli and to determine whether similar principles apply to induction of alveolar regeneration. Research findings should lead to new strategies for interventions in aberrant development of lungs, lung injury, and diseases such as emphysema, diffused interstitial fibrosis, and bronchopulmonary dysplasia.

Blood Diseases and Resources Program

73 NEW INITIATIVES

Creutzfeldt-Jakob Disease (CJD) Assay Methods Development

The goal of this RFA is to develop assay methods for detecting CJD and other transmissible spongiform encephalopathies that can be used to screen donated blood and organs or tissues.

Developmental Processes in Differential Expression of Globin Genes

The purpose of this PA is to investigate developmental processes involved in differential expression of globin genes. Mutations in this gene cluster lead to common inherited diseases such as sickle cell anemia and thalassemia. Elucidation of molecular mechanisms responsible for developmental and tissue-specific control of the globin gene cluster could lead to new therapeutic approaches to treat hemoglobinopathies.

Stem Cell Transplantation to Establish Allochimerism

The objective of this RFA is to develop improved and novel preparative regimens that will enable successful incompatible hematopoietic stem cell transplantation in immunized patients with hemoglobinopathies such as SCD and Cooley's anemia.

Trans-NHLBI

New Initiatives

HIV in the Lungs, Heart, and Blood: Role of Chemokines and Their Receptors

The objective of this RFA is to investigate the role of chemokines (chemicals that stimulate cells) and chemokine receptors in the pathogenesis of HIV in the lungs and in the cardiovascular and hematopoietic systems. Ultimately, the goal is to determine whether chemokines or their derivatives can effectively block infection of tissue cells and transfer of virus and whether new antiviral agents based on these molecular interactions block cell infection.

Vascular and Hematopoietic Development and Disease

The goal of this PA is to elucidate the origins of blood and vessel formation and the fundamental processes of commitment and diversification during development. Investigators will apply innovative approaches to identify and characterize precursor cells, define regulatory mechanisms that determine and maintain diverse phenotypes, and explain how these developmental mechanisms might be involved in pathologic conditions of the mature animal. The ultimate goal is to provide the foundation for new therapies to treat cardiovascular, lung, and blood diseases based on morphogenetic principles.

TRANS-NIH

New Initiatives

Bioengineering Research Grants and Partnerships

The purpose of this PA is to foster bioengineering studies among interdisciplinary groups (bio-engineers, scientists, and clinicians) to advance health or health-related research within the mission of the NIH. Bioengineering integrates physical, chemical, mathematical, and engineering principles to develop innovative biologics, materials, processes, implants, devices, and informatics for prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health.

Centers for Mind/Body Interactions and Health

The purpose of this RFA is to encourage behavioral, psychological, social, and biomedical research on the interrelationships among cognition, emotion, biological processes, and physical health. The NHLBI is interested in research on the role of stress

in coronary heart disease and hypertension, the experience of pain due to a disease or condition, causes or precipitants of asthma, and sleep disorders.

Novel Approaches to Enhance Stem Cell Research

The purpose of this PA is to encourage research that enhances the use of stem cells as a model biological system. Studies of interest include isolating, characterizing, and identifying totipotent and multipotent stem cells from animal models, as well as generating reagents and techniques to characterize and separate stem cells from other cell types.

Organization: National Institutes of Health
Consensus Development Program
Office of Medical Applications of Research (OMAR)
Building 31, Room 1B03,
31 Center Drive
MSC 2082
Bethesda, MD 20892-2082

Contact: Barnett S. Kramer, MD, MPH
Director, 301-496-5641 kramerbs@mail.nih.gov
Jerry M. Elliott
Program Analyst, 301-435-5060 elliottj@od.nih.gov

Purpose:

The NIH Office of Medical Applications of Research (OMAR) manages the NIH Consensus Development Program for which it organizes major conferences that produce consensus statements and technology assessment statements on controversial issues in medicine. NIH Consensus Statements are prepared by a non-advocate, non-Federal panel of experts, based on (1)presentations by investigators working in areas relevant to the consensus questions during a 2-day public session; (2)Questions and statements from conference attendees during open discussion periods that are part of the public session; and (3)closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the NIH or the Federal Government.

Selection Criteria:

Consensus Development Conference topics may be suggested by an Institute, Center, or division within NIH, by other government agencies, by Congress, or by the public. An issue must have:

- Public health importance
- Controversy or a gap between current knowledge and practice
- An adequately defined and available base of scientific information
- Additional, desirable elements are:
- Health care cost impact
- Preventive impact
- Public interest

Primary Focus:

Safety, efficacy

Stage of Technology:

Emerging, existing

Type of Technology: Procedures, devices, drugs

Technologies/Conditions Reviewed:

1998: Consensus Statements:
Rehabilitation of Persons With Traumatic Brain Injury, October
Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder, November

1999: None Available

2000: Technology Assessment Statement:
Improving Medical Implant Performance Through Retrieval Information: Challenges and Opportunities, January

Consensus Statements:
Osteoporosis Prevention, Diagnosis, and Therapy, March
Antenatal Corticosteroids Revisited: Repeat Courses, August

Organization: University Health System Consortium
2001 Spring Road, Suite 700
Oak Brook, IL 60523-1890
630/954-1700

Contact: Karl Matuszewski
Telephone: (630) 954-1709

Purpose:

The University HealthSystem Consortium (UHC) is an alliance of the clinical enterprises of academic health centers. Its Technology Assessment staff conduct technology assessments to assist member organizations in making the best possible clinical resource management decisions.

Selection Criteria:

The following criteria are used to select topics for assessment:

- Use with large number of patients
- Variation in medical practice or outcomes
- Controversial use
- High cost
- Reimbursement issues
- Risk or unproven benefits
- Number of available alternatives

Primary Focus:

pharmaceuticals, devices, and procedures

Stage of Technology:

new, existing, and emerging

Technology/Conditions Reviewed:

1998: Anticoagulant options in heparin-induced thrombocytopenia
dapanaparoid sodium
lepirudin
argatroban
ancrod

Platelet transfusion guidelines

Results of the Intravenous Immunoglobulin Surveillance Study

1999: Electron beam computed tomography to detect coronary artery calcification

74 FIBRIN SEALANTS

Intravenous Immunoglobulin Preparations (off-label uses)
Solvent/detergent-treated Plasma
Transmyocardial Revascularization

Paclitaxel for:

a) Breast

Non-small cell lung cancers
AIDS-related Kaposi's sarcoma
Head and neck, esophageal, small-cell lung, endometrial and bladder cancers

2000: Medication expenditures: trends and management strategies
Intensity-modulated radiation therapy
Antimicrobial CV catheters
Albumin/NPC guideline revision
Cardiac stents

Current Projects:

Cardiac biomarkers
Drug development guide
Hemostatic closure devices
HIV therapy update
Minimally invasive CABG
Universal leukoreduction
MUEs on IV to PO antibiotics, albumin, GPIIb/IIIa

Organization: Department of Veterans Affairs
Technology Assessment Program
Management Decision & Research Center
VA Medical Center (152-M)
150 South Huntington Avenue
Boston, MA 02130 USA

Contact: Dr. Karen Flynn
Telephone: (617) 278 4469
Karen.Flynn@med.va.gov

Purpose:

To coordinate information from existing technology assessment and related activities within the VA and to assess the clinical use of selected technologies for the VA system.

Selection Criteria:

Based on requests from VA managers

Primary Focus:

Devices, drugs, medical and surgical procedures, systems of care, support systems, organizational and managerial systems

Stage of Technology:

new, emerging

Technology/Conditions Reviewed:

1998: Endovascularly placed grafts for infrarenal abdominal aortic aneurisms
Stereotactic pallidotomy for treatment of Parkinson's disease

1999: Treatments for male erectile dysfunction
vacuum constriction devices
penile prostheses implantation
vasoactive drugs (by injection or oral)
intraurethral (alprostadil) injection
intracavernosal injection (alprostadil monotherapy, papaverine and phentolamine, combination of all three therapies)
oral
yohimbine
sildenafil (Viagra)

Positron Emission Tomography
using 2-[F-18]-2-deoxy-D-glucose (FDG) in selected cancers (head and neck, lung cancer staging, solitary pulmonary nodules, breast, and colorectal) and Alzheimer's disease

2000: Optical lens fabrication system

75 TABLET SPLITTING

Computerized lower limb prosthesis
Case management programs

Current Projects:

Diagnosis and management recommendations on alpha-one antitrypsin deficiency
Brachytherapy for prostate cancer
Cryosurgery for prostate cancer
Cardioplegia monitoring during coronary artery bypass grafting

Appendix 3. List of Contacts

LIST OF CONTACTS

Denise Aberle, M.D. Chairman, Department of Radiological Sciences, U.C.L.A. Los Angeles

Ali Aminpour, Manager, Nuclear Medicine Department, Saint Joseph's Hospital, Marshfield, WI

Laurie Aro, Myriad Genetics, Inc., Salt Lake City, Utah

Ali Barrows, Coordinator and Genetic Research Associate, Department of Preventive Medicine, Creighton University, Omaha, Nebraska

Tom Bradley, Chief, Health Cost Estimates Unit, Congressional Budget Office

Adalsteinn Brown, Assistant Professor, Department of University of Toronto

Rosemary Brekke, Director of Reimbursement and Outcomes Planning, Boston Scientific

Mitchell Burkin, Medical Officer, HCFA, Coverage and Analysis Group

William Cefalu, M.D., Associate Professor, University of Vermont College at Burlington

Neil Cohen, Genentech, San Francisco, California

Myron Czuczman, M.D., Roswell Park Cancer Institute, Buffalo, New York

Bill Daltry, Director of Sales and Marketing, Eastern Isotopes, Sterling, VA

Dave Dawson, Genentech, San Francisco, California

Farrokh Dehdashti, M.D., Associate Professor of Radiology, Mallinkrodt University, Washington University Medical Center

George Desko, Operations Manager, PET Imaging Division, Massachusetts General Hospital

Paul Edwards, MEDTRONIC

Martin Erlichman, Ph.D., Senior Health Science Analyst AHRQ Center for Technology Assessment

Beth Francis, Account Executive, Cytyc Corporation

Frank Fujimura, Director, Clinical Molecular Diagnostic Laboratory, City of Hope National Medical Center, Duarte, California

Alan Garber, M.D., Ph.D., Director, Center for Health Policy and Director, Center for Primary Care and Outcomes Research, Stanford University

Jonathan Gasson, Director of Sales Strategy and Contracts, MEDTRONIC

G. Scott Gazelle, M.D., Associate Professor, Radiology, Harvard University

Milt Gross, M.D., VHA PET Registry, Ann Arbor, MI

Jan Healy, Program Manager, Alliance for Lung Cancer Advocacy, Support, and Education (ALCASE)

Stephen Heffler, Deputy Director, National Health Statistics Group, Office of the Actuary, Health Care Financing Administration

I. Craig Henderson, M.D., Adjunct Professor, University of California, San Francisco

Cindy Hoyle, Genetic Counselor, Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah

Martha Hutchinson, Ph.D., M.D., Professor of Pathology - Brown University Director of Cytopathology - Women & Infants' Hospital of Rhode Island

John Inadomi, Acting Chief, Gastroenterology, University of Michigan, Ann Arbor, Michigan.

Rick Jeffrian, Vice President of Marketing, PercuSurge

C. Daniel Johnson, M.D., Professor, Mayo Medical School, Rochester, Minnesota,

Robin Kelley, Investor Relations Manager, Imatron Inc., South San Francisco, California

David King, MD, Director of Clinical Services, Mount Sinai Cardiac Prevention Center, Miami Beach, Florida

Helen Lazenby, Health Insurance Specialist, Health Care Financing Administration

Bernard Levin, M.D., Professor, Vice President, Cancer Prevention, Anderson Cancer Center, Houston, Texas

Andrew McDonald, Marketing Director, Heart Savers, Irvine, California

Pamela M. Marcus, Ph.D., M.S., Epidemiologist, Biometry Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda

Frank Miller, Director, Gastroenterology Radiology, Northwest University, Chicago, Illinois

Matthew Mitchell, Analyst, ECRI, Plymouth Meeting, Pennsylvania

Susan Moore, Oncology Nurse Practitioner, Rush-Presbyterian - St. Luke's Medical Center, Chicago, Illinois

Sol Mussey, Carter Warfield - Office of the Actuary

Bill Radaj, American Marketing Manager, CT, G. E. Medical Systems

Will Richt, Public Relations Specialist, Institute for Clinical PET

Colleen Rogers, R.N., Department of Colon and Rectal Surgery, Lahey Clinic Medical Center, Burlington, Massachusetts

Geoff Rubin, MD, Associate Professor of Radiology, Stanford University Medical School, Palo Alto, California

Cindy Rundell, EBCT Technician, Cardiac Healthscan at Glenbrook Hospital, Glenview, Illinois

Beth Schreiber, Hereditary Colon Cancer Association, Sioux Falls, South Dakota,

Robert Silverman and Jeffrey Keene, Corporate Communications, Cytyc Corporation

Jay Skyler, MD, Professor of Medicine, the University of Miami

Michael Spieth, M.D., Nuclear Radiologist, St. Joseph's Hospital, Marshfield, WI

Yurgen Soldner, Siemens Medical Systems Nuclear Medicine Group

Nadine Stewart, VHA PET Registry, Ann Arbor, MI

Dee Strano, Marketing and Business Development, Generex Biotechnology Corporation of Toronto, Canada

Ann Thor, M.D., Professor of Pathology and Surgery, Northwestern University School of Medicine

Eric Topol, M.D., Chief of Cardiology, Cleveland Clinic Foundation

Bert Vogelstein, Professor, School of Medicine, Johns Hopkins University, Baltimore, Maryland

Peter Webner, Certified Nuclear Medical Technician, Eastern Isotopes

Chris Wyatt, Research Assistant, Wake Forest University, Winston-Salem, North Carolina

Cynthia Yock, Research Associate, Center for Primary Care and Outcomes Research, Stanford University School of Medicine

Appendix 4. Technology Case Studies

CORONARY STENTS FOR RESTENOSIS OF THE ARTERIES

Description and Indications for Use

Stents are tiny flexible mesh cylinders that open the arteries and flatten plaque against the vessel wall. They are primarily used to prevent recurrence of the arterial narrowing after balloon angioplasty but are also important for treating arterial damage done during angioplasty procedures. There are several varieties of stents on the market, which produce similar outcomes (Noorani, 1997). Since their introduction, stents have become more flexible, and improvements in stent deployment and medical management after insertion have reduced complications from stent placement and expanded the types of lesions they can safely be used to treat (Suwaidi et al., 2000; Weintraub, 2000).

Revascularization is most commonly performed for patients with progressive or unstable angina (*WebMD*, 1999); some physicians also use the technique for patients who are asymptomatic, but have a positive stress test. There is some controversy about the appropriate indications for the use of stents. Stents can either be placed in all patients undergoing revascularization (elective stenting) or their use can be reserved for patients who have poor angiographic outcome of a conventional procedure (provisional stenting). While the majority of European clinicians practice provisional stenting (Eeckhout et al., 1999), elective stenting has become widespread in the United States

76 EVIDENCE ABOUT EFFECTIVENESS

Several large randomized controlled trials have demonstrated that stents can reduce restenosis rates and the need for repeat vascularization when compared with PTCA or balloon angioplasty alone in carefully selected patients. Without stents, up to 50 percent of coronary narrowings treated with PTCA are expected to restenose within six months, and the use of stents has approximately halved this rate (*MDI Online*, 1997). These benefits persist at one year (Macaya et al., 1996), but there is no evidence that the benefit extends beyond that time. In general, stents have shown the best results among patients with single vessel disease in the larger arteries (> 3.0 cm) and are not recommended for use in small arteries, long lesions, treatment of diffuse disease, or clogging where vessels branch (Holmes et al., 1998; Suwaidi et al., 2000). Several long term trials have recently completed that show clinical and angiographic outcomes are as good or better for an elective rather than provisional stenting approach (Suwaidi et al., 2000), although the cost-effectiveness of this practice remains a question particularly given the added risks of stent placement. A small trial in Spain suggested a provisional stenting strategy can achieve most of the clinical benefits with a large cost savings over elective stenting (Rodriguez et al., 1998).

Stent placement increases the risk for the formation of blood clots and particulate matter during the procedure, which could result in infarct. Also in-stent stenosis, where there is an overgrowth of the elastic membrane inside the artery, occurs in about 15-20

percent of patients (*WebMD,* 1999) and is difficult to treat. Moreover, the placement of stents may narrow future clinical options. When symptoms are not adequately reduced, stent patients may require open heart surgery rather than a further percutaneous intervention (Meads et al., 2000).

77 COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

Alternatives to stent placement are medical management, angioplasty without stents, and coronary artery bypass graft (CABG) surgery. During the 1990s, stents have most often been used as an adjunct to balloon angioplasty to maintain the opening and reduce failure rate of angioplasty. Because the availability of stents makes high-risk PTCA safer, the combination procedure is increasingly used as a substitute for CABG in high-risk patients eligible for both procedures.

Once the decision to place a stent has been made, a two-week course of antithrombotic therapy (aspirin plus antiplatelet therapy –ticlopidine or clopidogrel) is routinely used to reduce associated bleeding complications. Clopidogrel has fewer side effects than ticlopidine and has become the treatment of choice in the United States. The cost for a 28-day treatment regimen is estimated to be $84 (Susman, 1999). Some clinicians feel long-term antiplatelet therapy may be warranted, which would increase the long-term costs of stent placement.

Although stent placement can increase the risk of thrombosis or myocardial infarction, prophylactic therapy with the recently-approved platelet Glycoprotein (GP) IIb/IIIa blockers (abcximab, eptifibatide, tirofiban) can reduce this risk by 40 to 50 percent (Suwaidi et al., 2000). GP IIb/IIIa is administered by bolus prior to the angioplasty, and is followed by a continuous infusion for 12 hours. The use of GP IIb/IIIa has been shown to have a net impact of around $300 over a six-month period among

high-risk candidates (Mark et al., 1996). The current controversy is whether to reserve the use of this relatively-high cost, but potentially life-saving, therapy for high-risk candidates or for all stent candidates. Among primary stent candidates, the use of abciximab adds a net cost of $544 per discharge, according to industry sources (Lilly Research Laboratories, no date). Clinical experts estimate 35 percent of stent patients receive GP IIb/IIIa as routine adjunct therapy and this is expected to grow steadily over the next five years.

Emboli protection devices in development are also expected to reduce the risks of myocardial infarction or death in high risk patient subgroups, such as for stent placements in saphenous vein grafts or patients undergoing acute myocardial infarction. There are no devices currently on the market in the United States, however, at least one is expected to enter the market this year. According to the unpublished results from the Saphenous Vein Graft Free of Emboli (SAFER) trial, major adverse cardiovascular events were reduced by more

than 50 percent by using a capture device during the angioplasty procedure (Gibson, 2000). These may become routinely used in the saphenous vein graft population and may add as much as $1000 to the cost of a stent procedure (Topol, personal communication). Although these devices potentially could substitute for GPIIb/IIIa for patients with saphenous vein grafts, because the latter is used prophlylactically industry spokespersons suggest it may be very difficult to get interventional cardiologists to change their practice in this area. According to industry sources, 60 percent of clinicians in one of their trials routinely used GP IIb/IIIa in saphenous vein graft procedures, despite limited evidence of its effectiveness in this population.

In-stent restenosis remains a major complication of stents. Several advances in adjunctive therapy are seeking to reduce this risk. These include drug-coated stents, intracoronary radiotherapy, photodynamic therapy, cryotherapy, and intravascular ultrasound (IVUS). Early results from a

*recent trial showed stents coated with rapamyacin, which is an anti-inflammatory, may substantially reduce scarring. Drug coated stents are likely to be cost-saving (Yock, personal communication), but this will depend on the final price established for these technologies. Pivotal trials have also shown radiotherapy can reduce instent restenosis by as much as 50 percent (*Medical Industry Today*, 2001). However, its use can triple the cost of a stent procedure (Topol, personal communication). The use of intravascular ultrasound to maximize stent deployment has also been shown to be effective, although similar results have been shown with high pressure deployment and no IVUS.*

Emerging alternatives to stent placement include angioplasty with intravascular ultrasound, intra-arterial radiation, chemotherapy, and pharmacologic regimens. Trials using IVUS with PTCA and drug or radiation therapy show stent use may be avoided, with similar clinical results. Studies showing the use of intravascular ultrasound in combination with angioplasty can

dramatically improve results, may mean such a strategy would be more cost-effective than stenting (need citation).

78 RECENT PATTERNS OF USE

The growth of the use of coronary stents has been explosive during the last decade. Worldwide, stent procedures were performed in only ten percent of PTCA cases in 1994, but this had grown to an estimated 52 percent by 1997 (*MDI Online*, 1997). Recent accounts suggest they are now used in 80 percent of percutaneous coronary revascularization procedures. In the last calendar year, an estimated 700,000 Americans received stents. This growth has far exceeded the initial indications of FDA approval, for which 30 percent of all angioplasty patients would have qualified.

During the height of stent growth, there was a trend toward the increased placement of multiple stents during a revascularization procedure. On average, 1.4 stents are placed per procedure, but some physicans were implanting 5 or 6 at a time, colloquially known as placing a "full metal jacket" (Kolata, 1998). Apart from the added expense, there are serious clinical drawbacks to this practice, as the ability to perform bypass surgery is lost. Although there are still some clinicians who place more stents than may be clinically beneficial, this practice has moderated. Medicare, which reimburses for 50 percent of stent candidates, pays a single fee per procedure regardless of the number of stents placed. As a result, hospital staff has put pressure on interventional cardiologists to reduce procedure costs.

As the use of stents has diffused, success rates have improved and vascular complication rates and hospital lengths of stay have been reduced dramatically. Much of the decline in adverse events of stent use have been attributed to changes in anticoagulation management after the stent procedure and better delivery systems during stent placement.

79 EXPECTED FUTURE DIFFUSION AND FACTORS INFLUENCING THE COURSE OF DIFFUSION

The diffusion of the use of stents among patients undergoing angioplasty has probably reached its maximum growth. There are anatomical limits which will slow its further diffusion to these patients, although there is potential for greater use among the minority population; blacks are two-thirds as likely to have an angioplasty procedure as whites (Ford et al., 2000).

Most of the future growth in the use of stents is expected to occur in its expanded use in treating complex vascular disease, for which CABG is currently the preferred intervention. We have assumed angioplasty will continue to substitute for CABG, but at a slower rate in the future (1.5 percent per annum diffusion into that population), and stents will continue to be placed in about 80 percent of the angioplasty population. Historical trends (1995-1998) in the use of CABG and PTCA procedures were derived from the National Hospital Discharge Survey and projections made *by Cardiovascular Device Update* (2000).

The growth of angioplasty cases using adjunct GP IIb/IIIa and capture devices are also expected to add costs to the health care system. These incremental cases among the angioplasty population have been forecast separately below. GP IIb/IIIa is assumed to grow from 35 percent of cases to 46 percent of cases (Topol, personal communication). Growth of the use of capture devices is anticipated to be rapid and reach 80,000 cases per year within five years (industry estimates).

Table A4-1. Incremental Cases

	2001	2002	2003	2004	2005
CABG	29,500	28,700	29,400	30,100	30,900
GP IIb/IIIa	23,500	24,500	26,100	27,700	29,400
Capture Device	9,300	10,000	11,500	19,300	32,400

80 COSTS

Cost-effectiveness studies generally support the notion that initial higher costs of stents (longer hospital stays, increased transfusions) are at least partly offset by better long term outcomes (reduced restenosis and revascularization) than PTCA, but results should be treated with caution (Meads et al.,

2000). Studies are old and their conclusions limited to very specific stenting applications and protocols, and may not reflect the actual practice of interventional cardiologists. In particular, the cost-effectiveness of routine versus provisional stenting remains questionable. However, the costs for angioplasty with stents have been reduced dramatically as well since many of these cost-effectiveness studies were completed. Stent costs have fallen from around $1500-$2000 to $1000-$1250, and stents are now longer, reducing the need to place two stents rather than one for longer lesions. Lengths of stay are now about equivalent to angioplasty alone and the use of better anticoagulant management has led to a reduced need for transfusions.

Because stents are expected to diffuse to the bypass graft population, the relevant cost comparison is between CABG versus angioplasty with stent. Early studies based on preliminary data report lower costs with a stent strategy versus CABG in patients with multivessel or two vessel disease (Serruys et

al., 1998; Schwicker and Banz, 1997a and b). Recent estimates from the United States show elective stenting in patients with multivessel disease was more costly than coronary artery bypass graft surgery (Yock et al., 2000). Over four years, the primary stenting strategy resulted in costs that were $1,250 (2.5 percent) above CABG. Although the strategies were cost-neutral in the first year, most of this cost difference occurred after one year. Assuming this cost difference is spread equally in the last three years, and not discounting (our cost estimates are nominal for the US economy), new cases of stents would add the following costs over CABG in four years:

Year 1: $0
Year 2: $464
Year 3: $464
Year 4: $464

The cost-effectiveness of stenting over alternative strategies may become even more questionable as the use of expensive complementary technology, such as GP IIb/IIIa and capture devices, become routine. GP IIb/IIIa is projected to add $544 per

discharge. Data on the cost-effectiveness of capture devices are not available, but assuming they have a similar effect on outcomes as GP IIb/IIIa, a net increase in costs per case of $500 is not unreasonable. This is expected to decrease to $300 in future years due to anticipated price competition in the market for emboli capture devices.

i) Table A4-2. Incremental Costs of Coronary Stents to the

ii) U.S. Health Care System (millions)

	2001	2002	2003	2004	2005
CABG	$0	$13.7	$27.0	$40.6	$40.9
GP IIb/IIIa	$12.8	$13.3	$14.2	$15.1	$16.0
Capture Device	$4.7	$5.0	$5.2	$7.7	$9.7
Total	*$17.4*	*$32.0*	*$46.4*	*$63.4*	*$66.6*

81

82 KEY ASSUMPTIONS

Stent prices do not decrease any further over the next five years.

GP IIb/IIIa diffuses at a steady rate to reach two-thirds of angioplasty cases using antiplatelet therapy in five years.

The use of intravascular ultrasound is cost neutral.

The use of drug-coated stents is cost neutral.

Trends in angioplasty substitution for CABG continue at a somewhat slower pace than has been seen in the last few years.

Incremental costs for multivessel disease population represent all new cases where a primary stenting strategy with angioplasty substitutes for CABG.

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DRUG INHALATION DEVICES FOR DELIVERY OF INSULIN

Description and Indications for Use

Inhalation devices to deliver drugs for asthma sufferers have become commonplace, and manufacturers are exploring numerous other medical conditions inhalers could be used to treat. To help circumvent the pain of daily insulin injections among diabetics, several manufacturers are developing similar systems for the delivery of insulin (Berg, 1999).

Drug inhalation therapy is expected to be adopted principally by insulin users, although persons with noninsulin dependent diabetes mellitus (NIDDM) whose glucose levels are poorly controlled with oral hypoglycemics are also candidates. Also, inhaled insulin may be used prophylacticly to prevent onset of insulin-dependent diabetes mellitus (IDDM) among close relations to IDDM patients who show beta-cell deterioration (*WebMD, 1998).* In 1997, there were an estimated 3.5 million insulin-using diabetics in the United States, including nearly all of the insulin-dependent diabetics and 40 percent of noninsulin dependent diabetics (Centers for Disease Control and Prevention, 1998). Estimates for 2000 could reach 4.3 million, as the prevalence of diabetes has been increasing rapidly with the aging population and increased obesity (Mokdad et al., 2000).

Inhaled systems under development include dry powder or liquid formulations of insulin and buccal-delivery or microprocessor-aided devices that may lead to more efficient and reproducible deposition of the inhaled drug (Gonda et al., 1998).

85 EVIDENCE ABOUT EFFECTIVENESS

The evidence about the efficacy of inhaled insulin compared with subcutaneous injection is limited mainly to Phase II trials. Short-term studies (three months) have shown inhaled insulin may be more rapid-acting than and as effective as injections (Gelfand et al., 1998; Skyler et al., 1998; Cefalu et al., 1998; Farr et al., 1998). Inhaled insulin is not as efficient as subcutaneous injection, however (Patton et al., 1999). Results from open-label follow-up with as much as 30 months experience suggest continued safety and efficacy of this mode of delivery (Cefalu, 2000). Longer term controlled trials are underway, which are expected to address such questions as continued efficacy during bouts with respiratory illness, consistency in insulin dose delivery, and the long-term effects of inhaled insulin on the lungs.

Anticipated benefits of these systems include improved compliance with scheduled therapy and lowered levels of complications resulting from poor glucose control. By enabling intensive insulin therapy without multiple injections during a day, patient satisfaction and quality of life are also expected to improve.

86 COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

Among patients with insulin-using patients, inhaled insulin is expected to be used to supplement long-acting insulin; thus its use will require fewer insulin shots, but will not replace them. Inhaled insulin may be used as a complete substitute or complementary therapy for oral hypoglycemics.

87 RECENT PATTERNS OF USE

None of the inhaled insulin systems have been on the market, yet, and their use has been restricted to patients enrolled in clinical trials. By May of 2000, a spray device had been tested in about 300 patients in the United States, and long-term trials began later that year (McKeown, 2000).

88 EXPECTED FUTURE DIFFUSION AND FACTORS INFLUENCING THE COURSE OF DIFFUSION

Clinical experts feel one or more of these systems will be on the market within the next two years (Mendosa, 2000). Some manufacturers expect a worldwide market potential of $32 billion (*MedPRO Month*, 1999). This is assuming that 90 percent of persons with IDDM and 20-25 percent of persons with NIDDM would benefit from inhaled insulin. These forecasts predict 4 million diabetics would use insulin inhalers once they become available. One clinical expert interviewed felt inhaled insulin is most likely to appeal to the NIDDM population, which would suggest a target market of 3 million users (or $24 billion).

Growth in use of inhaled insulin is likely to be constrained somewhat by the many competing alternatives that are now, or soon to be, on the market. These include new developments in oral antidiabetics, transdermal delivery systems, and continued diffusion of ambulatory insulin pumps. Ambulatory insulin pumps are expected to offer strong competition in the Type I diabetic market, where their efficacy in maintaining tight blood glucose control is likely superior.

Best forecasts below were obtained from industry sources. Our low forecasts assume diffusion into only the insulin-using NIDDM population, which is assumed to be stable over the five-year period, and the growth in inhaled insulin would reflect growth of other inhaled drugs, representing 5 percent of the market and increasing to 15 percent of the market in 2005 (*MDI Online*, 1997). High forecasts assume the prevalence of diabetes increases at the same rate as seen over the last decade, and that 20 percent of the

non-insulin-using NIDDM patients would also be candidates (U.S. Bureau of the Census, 2000).

Table A4-3. Incremental Cases

	2001	2002	2003	2004	2005
low	0	0	150,000	300,000	450,000
best	0	0	120,000	582,000	1,123,300
high	0	0	295,000	638,000	1,232,000

89 COSTS

Although inhaled insulin could be cost-saving in the long run, it is likely to be cost-increasing in the short run. This is because many of the potential benefits that can be attained with tighter blood glucose control, such as reduced incidence of diabetic retinopathy and neuropathy, are realized after more than three years of intensive therapy (Diabetes Control and Complications Trial Research Group, 1993). Thus, the short-term costs of inhaled insulin are its incremental costs over replacement technologies.

Inhaled insulin is expected to cost between $800 and $1200 per year (*MedPRO Month*, 1999; Skyler, personal communication). This can be compared with an annual cost of conventional insulin delivery of approximately $780. These estimates assume the following prices (http://www.hsc.colorado.edu/misc/diabetes/appen3.html):

- around $25 per 1000 units for the insulin;
- approximately 80 units per day for persons with NIDDM;
- approximately 40 units per day for persons with IDDM;
- $16.80 per case of one hundred monoject syringes;
- $2.50 per box of 100 alcohol spongese; and
- two injections per day on average for both types of diabetics.

The annual cost of oral antidiabetics ranges from $108 for glyburide (*Physicians GenRx*, 1998) to $850 for combined metformin/sulfonylurea therapy (Mohr, 1994). A mid-range cost for oral antidiabetics is $480, although the majority of patients probably use combined regimens, placing its annual cost closer to that of insulin therapy. Our low estimate assumes an incremental cost for inhaled insulin of $410 ($800-.50*($780)). Our high estimate assumes an incremental cost of $810. These estimates assume that none of the beneficial effects of potentially reduced complications would occur in the short term, and that one insulin shot will still be required among insulin users.

i) Table A4-4. Incremental Costs of Inhaled Insulin to the

ii) U.S. Health Care System (millions)

	2001	2002	2003	2004	2005
low	0	0	$62	$123	$185
best	0	0	$73	$355	$685
high	0	0	$239	$517	$998

90 KEY ASSUMPTIONS

Use of inhaled insulin does not avert any of the costly complications of diabetes in the short term.

Inhaled insulin principally is adopted by insulin-using persons.

Inhaled insulin will replace oral hypoglycemics in about half the cases, but will be used in combination with them in the other half.

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93 ELECTRON BEAM COMPUTED TOMOGRAPHY

94 TO SCREEN FOR CORONARY ARTERY DISEASE

95

96 DESCRIPTION AND INDICATIONS FOR USE

Electron Beam Computed Tomography (EBCT) is a non-invasive radiographic procedure used to detect and quantify coronary artery calcification (CAC), which is widely recognized as an indication of atherosclerosis. Using single-slice or multislice imaging, EBCT permits very rapid screening of the heart and coronary vasculature. EBCT scans establish a patient's calcium score, which is then used to assess the level of coronary atherosclerotic burden. As many as half of coronary events occur in asymptomatic people, so a non-invasive, reliable technique for detecting risk of coronary artery disease (CAD) could be an important tool for reducing the burden of the disease
(O'Rourke, 2000; Ratko, 1999).

Over the past ten years, EBCT has been used with increasing frequency in the United States for the diagnosis of CAD in symptomatic patients and more frequently for screening asymptomatic patients to assess their risk of developing CAD (O'Rourke, 2000). Screening centers and hospitals have been aggressively advertising EBCT screening and have experienced large volumes of predominantly self-pay, self-referral patients (King, McDonald and Rundell interviews). EBCT is also being proposed for assessing progression and regression of stenosis in patients undergoing risk factor treatment; however, to date, this research has not shown EBCT to be effective for this purpose (O'Rourke, 2000).

Despite the fact that EBCT has been heavily promoted for screening to assess CAD risk, there is substantial disagreement on its clinical value and appropriate roles. The American Heart Association (AHA) maintains that there is no role for EBCT in screening of asymptomatic patients with no risk factors (Aetna, 2000). However, EBCT is considered useful for determining low risk in older patients and for guiding therapy of asymptomatic patients who are at high risk (O'Rourke, 2000; Ratko, 1999).

97 EVIDENCE ABOUT EFFECTIVENESS

i)

Research has clearly indicated that EBCT is highly sensitive in detecting CAC in comparison to other types of CT (Ratko, 1999). Moreover, various studies have shown a strong correlation between EBCT calcium scores and quantities of atherosclerotic plaque (O'Rourke, 2000). However, there is skepticism about the relationship between EBCT calcium scores and the likelihood of coronary events because of the following factors:

- ✓ Calcium does not collect exclusively at sites with severe stenosis (O'Rourke, 2000)
- ✓ EBCT calcium scores do not identify the location of specific vulnerable lesions (Wexler, 1996)
- ✓ Substantial noncalcified plaque is frequently present in the absence of CAC (Davies, 1993)
- ✓ There is no proven relationships between CAC and the probability of plaque rupture (Furster, 1994; Falk, 1995)

Despite the limitations mentioned above, some consider EBCT screening reliable for demonstrating the absence of CAC in order to rule out stenosis. Several studies have concluded that a negative EBCT screen has a strong correlation with the absence of CAD and this result is most substantial in older populations (Berry, 1999; Bielak, 2000).

- **Various studies have concluded that EBCT scores could be an effective substitute for standard risk factors in predicting the risk of CAD. These studies show CAC to be correlated with significant risk factors such as age, male sex, tobacco use, hypertension, and diabetes. However, some do not consider this data conclusive in showing that EBCT alone can assess CAD risk (Ratko, 1999; O'Rourke, 2000). One study demonstrated that the addition of EBCT data provided no added value to the risk determined by the Framingham and National Cholesterol Education Program risk models (Detrano, 1999). EBCT is only recommended for providing supplementary information for the management of intermediate to high-risk asymptomatic patients.**

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- **Proponents of using EBCT for screening maintain that patient compliance with risk-reducing behaviors (such as exercise, modified diet, and smoking cessation) is greatly enhanced by knowing the results of and EBCT test. In fact, one study found that patients' calcium scores were directly related to new aspirin usage, new cholesterol medication, consulting with a physician, losing weight, and decreasing dietary fat (Wong, 1996).**

98 COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

Several imaging techniques that detect CAC are available. When studied simply for the ability to evaluate and quantify CAC, EBCT demonstrates better sensitivity and specificity than fluoroscopy, conventional CT, and spiral CT (Ratko, 1999). Recently, however, one study used an ordinary CT scanner in conjunction with an EKG machine to try and replicate the effects of ultrafast CT. The results were highly correlated to scores obtained with EBCT. If more research is done in this area, it could present a more widely available and less costly alternative to EBCT (Carr, 2000). Perhaps more significant, though, are improved fast helical CT scanners – also called multidetector row CT – that have been developed by various companies and are being promoted for CAD screening. Proponents claim that these fast helical scanners are comparable to EBCT, but others claim that EBCT is superior in speed and image quality. To date, only a few clinical studies comparing Multidetector fast CT to EBCT have been completed. One study showed a high correlation between EBCT and Multidetector CT scores, especially among patients with high levels of CAC, but another showed EBCT to be between 4 and 8 percent more sensitive than multidetector CT (Carrington, 2000; Bankhead, 1999). Many experts are skeptical about the lack of substantial findings and maintain that there is not enough evidence to disprove EBCT's superiority (Budoff, King, Mitchell, Radaj and Rubin interviews). Nonetheless, the multidetector CT scanners have the advantages of being used for screening and diagnosing other diseases and being less costly to use (Dhingra, 2000; Dakins 2000). Therefore, hospitals and facilities that purchase

multidetector CT scanners have an extra incentive to use them for CAD screening rather than investing in an EBCT machine.

- **Evaluations of the cost-effectiveness of EBCT in comparison with exercise treadmill testing (ETT) for screening to assess CAD risk are highly contingent on the sensitivity and specificity estimates used in each study. For this reason, two of the most commonly recognized studies in this area disagree – one concludes that EBCT is more cost-effective than ETT and the other concludes that EBCT is not superior to ETT (Hwang, 2000).**

Other alternatives for assessing risk in asymptomatic people include ankle-brachial blood pressure index and B-mode carotid Doppler ultrasound assessment of intimal-medial thickness. Both of these techniques have been demonstrated to add substantial value in risk prediction over Framingham scores, but neither have been compared to EBCT (O'Rourke, 2000).

a) Recent Patterns of Use

Sales of EBCT scanners by Imatron (the sole manufacturer of the equipment) have increased steadily over the past three years. The company sold 15 scanners in 1998, 19 in 1999, and 30 in 2000. Imatron administrators expect continuing increases of up to 30 percent in 2001. There are currently 70 scanners in use in the United States, up from 45 in 1999 (Imatron Interview; Ratko, 1999). EBCT scanners tend to belong to different types of users. Many are freestanding screening centers that market to self-referred

patients while others are associated with hospitals.

An assessment of the average number of scans performed at EBCT sites is unavailable; however, two institutions surveyed in 1999 reported performing 400 screens per year and 1,500 screens per year, respectively (Ratko, 1999). Currently, Imatron administrators estimate that sites with EBCT scanners generally perform between 15 and 30 scans per day (Imatron interview). Interviews with screening facilities suggest that between 10 and 40 screens are performed per day, and this number is increasing.

Increases in the number of EBCT scans are often attributed to advertising and media. EBCT has been advocated on popular television programs such as The Oprah Winfrey Show, 20/20, and NBC News. In addition, some screening centers aggressively advertise in the community. A director of one scanning site that does not currently advertise indicated that advertising could potentially

double the facility's patient volume (King and McDonald interviews).

Neither Medicare nor most private insurers reimburse for EBCT screening; almost all screening is self-pay. Therefore, most screening patients are what one industry expert called the "worried well." Patients are primarily self-referred. There are also corporate programs that contract with hospitals to provide screenings to their executives as part of "healthy employee" initiatives (King, McDonald and Mitchell interviews).

Expected Future Diffusion

The increase in the use of EBCT scanners is expected to slow in coming years due to competition from the new fast multidetector CT scanners mentioned previously. However, patient volumes and use of scanning for CAC in general are not expected to decrease due to the technology's publicity. Additionally, facilities that have purchased an EBCT scanner have a large incentive to strongly

promote scanning because of the potential for profit. The cost per scan is estimated at $233 while most facilities charge between $300 and $500 per scan (Ratko, 1999; Imatron interview).

To compute future diffusion estimates, we used 10 scans per day/per facility as our low estimate and 20 scans per day as our high estimate and assumed that scanners were used 260 days per year (5 days per week). We used the manufacturer's estimate of 30% sales growth in 2001 and then decreased sales by half each subsequent year in order to account for the expected competition from other types of fast CT scanners.

Table A4-5. Incremental Cases

	2001	2002	2003	2004	2005
Low	68,640	35,400	18,700	10,400	0
High	137,280	70,700	37,400	20,800	0

Factors Influencing the Course of Diffusion

As mentioned above, competitive scanners, media, and advertising are important factors influencing the diffusion of EBCT for screening to assess the risk of CAD in asymptomatic patients. Some physicians and medical groups advocate the use of EBCT scanning only on a referral basis and call for an end to advertising. However, these efforts have so far been unsuccessful at deterring media publicity. Although physicians may not be swayed by advertising, the number of scans performed will not be diminished as long as free-standing centers admit self-refered patients.

Definitive research comparing the other fast CT scanners and EBCT would have an effect on the acceptance of these scanners as an adequate substitute for EBCT. In June of 2000, the National Heart, Blood, and Lung Institute began a four-year, $60-million study comparing the two technologies that may generate more conclusive data (Dakins, 2000).

The completion of more conclusive research on the correlation between CAC

levels and the likelihood of a coronary event would also have a large impact on diffusion of the technology. Likewise, if EBCT is eventually accepted for screening and becomes reimbursable, the population able to access the technology would certainly increase. However, these factors may not be realized for several years.

b) Costs

Sources suggest that EBCT screening is primarily additive and not used to replace other tests or procedures. In addition, patients are not believed to undergo further surgeries directly as a result of high CAC scores; rather, procedures such as revascularization are performed as a result of already existing clinical indications (Arad, 1996). Therefore, the most significant costs of EBCT are primarily the scan itself and the costs of prescribing expensive lipid-lowering drugs, such as statins, to patients with high calcium scores who might not have otherwise used them.

One possible factor in reducing the costs of EBCT screening is an increase in risk-reducing habits among screened patients. However, this could only result in long-term future saving, if anything. Moreover, this effect could be balanced out by possible risk-increasing behaviors in patients with negative or false negative scans. A more immediate cost-reducing factor would be the patients with a borderline cholesterol level that might be taken off statins as a result of a low calcium score. However, we have estimated that this would have to occur in more than 50 percent of patients using EBCT screening in order for this practice to make EBCT screening cost-reducing overall. Moreover, the practice of taking patients off of statin therapy following an EBCT scan is not carried out by all phsycians. Therefore, we expect EBCT screening to be cost-increasing over the next few years.

Competition from other fast CT scanners and further research into the reliability of calcium scores could also affect EBCT costs,

but these will not be realized in the short-term.

Estimating the costs – apart from the cost of the actual scan – of EBCT screening over the next few years is difficult because the exact number of people put on and taken off of statins as a result of screening is unavailable. Screening facility managers estimate that 25 percent of patients have a high enough calcium score to be placed on statins as a result of the score. Many of these patients are already taking these medications to manage cholesterol levels. Therefore, we estimated that 12.5 percent of patients undergoing EBCT screening are subsequently put on a new regimen of statins. We also estimated that approximatly 5 percent of patients already using such medications might be taken off of them due to low calcium scores. Although the efficacy of statins is not yet definitively proven, they are expected to be highly effective; thus, we have presumed that very few patients would be taken off the drugs after a calcium test if they were given them for other clinical indications. The cost of a year

of treatments with statins was fixed at $1,000 (Hwang, 2000).

Table A4-6. Incremental Costs to the U.S. Health Care System (millions)

	2001	2002	2003	2004	2005
Low	$32.6	$16.8	$8.9	$4.9	$0
High	$65.2	$33.6	$17.8	$9.9	$0

c)

d) Key Assumptions

Other fast multidetector CT scanners will result in a decrease in the sale and use of EBCT scanners.

EBCT will continue to be additive and not replace other types of testing.

CAC will not result in hospitalizations that would not have occurred anyway.

If patients are more compliant with risk-reducing behaviors because of CAC, these health benefits and related cost changes will not be realized in the next few years.

Statin therapy may be modified as a result of EBCT scan results.

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GENETIC TESTING FOR COLORECTAL CANCER

Description and Indications for Use

Colorectal cancer, which includes cancers of the colon and rectum, is the third most commonly diagnosed cancer among American women and men. In 2000, more than 130,000 new cases were diagnosed; almost three-quarters of which will be cancers of the colon (American Cancer Society, 2000; BCBSA TEC, 1998a). More than 56,000 deaths in 2000 were attributable to colorectal cancer (ACS 2000; BCBSA TEC, 1998a). Inherited colorectal cancers account for 5 to 10 percent of all colorectal cancer cases (BCBSA TEC, 1998a).

There are two defined types of heredity colorectal cancer: familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC) (BCBSA TEC, 1998a; BCBSA TEC, 1998b; Cromwell et al., 1998).[3] While the lifetime risk for colorectal cancer is about 6 percent for Americans, for those with FAP or HNPCC the lifetime risks increases to 80 to 100 percent (BCBSA TEC, 1998a; BCBSA TEC, 1998b). Gene mutations that are linked to these two forms of hereditary colorectal cancer have been identified and commercial tests are available.

Familial Adenomatous Polyposis

FAP is characterized by the development of hundreds or thousands of adenomas during adolescence and young adulthood and, without treatment, 100 percent of persons with this condition will develop colorectal cancer in their lifetime. Consequently, most individuals who are aware of their condition undergo a complete colectomy (Hoyle personal communication; BCBSA TEC, 1998a; Cromwell et al., 1998). In the affected individual, FAP can usually be diagnosed clinically by the presence of dozens to hundreds of adenomatous polyps at a young age.[4] A mutation on the adenomatous polyposis coli (APC) gene has been identified as the source of FAP; commercial genotyping of the APC gene has been available since 1994 (Cromwell et al., 1998). After identification of an affected individual, family members are tested for FAP and begin colorectal cancer screening, using flexible sigmoidoscopy and other methods, starting at age 12. If no polyps are found, screening may be decreased to every second or every third year as the person ages. If no adenomatous polyps are found by age 50, then the individual is assumed to have the average risk for colorectal cancer (Cromwell et al., 1998). If polyps are found, then annual colonoscopy should be performed and prophylactic total colectomy should be considered (BCBSA TEC, 1998a). Other risks associated with FAP include an increased risk for tumors in the upper gastrointestinal

[3] There are other colorectal conditions related to genetic mutations, such as juvenile polyposis and Peutz-Jeghers Syndrome. These conditions are not considered in this analysis because they are rare and gene mutation testing is not commercially available (Hoyle, personal communication).

[4] An attenuated form of FAP has been identified. In this form of FAP, affected persons have a smaller number of adenomas along with a mutation in the APC gene (Hoyle, personal communication; BCBSA TEC, 1998a).

tract, thyroid, adrenal gland and pancreas (BCBSA TEC, 1998a; Hoyle personal communication).

Genotyping is an alternative to this intensive screening. First-degree relatives of persons with FAP have a 50 percent change of carrying the APC mutation[5] (BCBSA TEC, 1998a). Genetic testing avoids mass screening of relatives and allows targeting those family members at risk. If the specific APC mutation is not identified after testing the patient, then genotyping for family members is not recommended (Hoyle personal communication). Such relatives would instead undergo sigmoidoscopy testing. At-risk relatives who test negative for an identified APC mutation are determined not to have FAP and further screening is not needed (Cromwell et al., 1998; Hoyle personal communication).

Hereditary Nonpolyposis Colon Cancer

HNPCC is believed to account for 3 to 4 percent all colorectal cancers (BCBSA TEC, 1998b). Lifetime risk of developing colorectal cancer in people with HNPCC is 80 percent (BCBSA TEC, 1998b; Vasen et al., 1996; Jarvinen et al., 2000; Brown and Kessler, 1995). Median age at diagnosis is 40-45 years of age (Brown and Kessler, 1995). Other cancers associated with HNPCC include endometrial, ovarian, stomach, and small bowel[6] (Jarvinen et al., 2000; BCBSA TEC, 1998b; Hoyle personal communication). HNPCC-affected persons can be identified using the Amsterdam criteria which examines the family history of cancer by type and age at diagnosis. Changes in five genes (MLH1, MSH2, PMS1, PMS2, MSH6) have been identified and account for about 70 percent of HNPCC families (Hoyle personal communication; BCBSA TEC, 1998b; Lerman et al., 1999). Genetic tests are available for alterations in MLH1 and MSH2 using the in vitro synthesized protein (IVSP) assay. Use of this assay is typically preceded by the replication error (RER) or microsatellite instability (MSI) tests to identify at-risk patients (BCBSA TEC, 1998b). Current guidelines for at-risk persons call for annual or biennial colonoscopies starting at age 25 (Brown and Kessler, 1995).

99 EVIDENCE ABOUT EFFECTIVENESS

Evidence from a Dutch HNPCC registry suggests that frequent colonoscopy screening on these persons can increase life expectancy by 7 years (Lerman et al., 1999). Genetic testing identifies individuals who need intensive monitoring. In addition,

[5] A form of FAP related to a mutation of I140K codon has been identified among those of Ashkenazim Jewish decent. However, the value of genetic testing for this subpopulation is not known (BCBSA TEC, 1998a).

[6] There are two forms of HNPCC: Lynch 1, which is limited to an increased risk for colorectal cancer, and Lynch 2, which has an increased risk for other cancers. Currently, genetic testing cannot determine which form of HNPCC the affected person carries (Rogers, personal communication).

persons in at risk families who do not carry the mutation do not need intensive monitoring, thereby reducing cost and morbidity associated with monitoring.

For the genetic forms of colorectal cancer, first the affected person is tested. If a specific mutation can be identified, then family members are tested. Without the identification of the specific mutation, genetic testing of family members is not recommended because even a negative test would not eliminate the need for cancer monitoring (because of the risk of false negatives) (Hoyle, personal communication).

For FAP, the clinical phenotype is the gold standard. The sensitivity is 80-85 percent; specificity is unknown (Hoyle, personal communication; BCBSA TEC, 1998a). If the mutation is identified in the affected person, then testing for this mutation among family members has a sensitivity of 100 percent (Hoyle, personal communication).

Most HNPCC testing focuses on two genes – MLH1 and MSH2. The sensitivity of this assay is 65-80 percent (BCBSA TEC, 1998b; Cromwell et al., 1998). As with FAP, if a specific mutation is identified, then testing for that mutation in families members has a sensitivity of 100 percent (Cromwell et al., 1998; Hoyle, personal communication). False negative tests, absent family history information, may be as high as 50 percent (Cromwell et al., 1998). A new test, Colaris™, has recently been released. This test has a sensitivity and specificity of 99 percent (Aro, personal communication). Another new test has improved sensitivity to 85 percent (Vogelstein, personal communication).

100COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

For families believed to include a family member with FAP or HNPCC, intensive colorectal cancer surveillance is recommended at an early age (12 for FAP and 25 for HNPCC). Such testing has high cost and morbidity. The advantage of genetic testing for these syndromes is that family members with negative tests (assuming the mutation has been identified) are considered to be at average risk for colorectal cancer and therefore do not need intensive screening (BCBSA TEC, 1998a; BCBSA TEC, 1998b; Hoyle personal communication; Rogers, personal communication).

101RECENT PATTERNS OF USE

The estimated prevalence of HNPCC genetic mutations is estimated at 5 to 50 per 10,000 (Vasen et al., 1998). FAP accounts for about 1 percent of CR cancers or 1 in 10,000 births (BCBSA TEC, 1998a). Based on the estimated prevalence of FAP, there are approximately 27,000 Americans with this genetic defect. For HNPCC, prevalence estimates indicate between 135,000 and 1,350,000 Americans with this condition. Some estimates for HNPCC are higher, suggesting that 5 to 10 percent of the U.S. population has HNPCC. Because FAP is almost certain to lead to colorectal cancer without screening, and it has clear clinical indications, the majority of FAP affected persons are

likely to be identified and receive genetic testing (Rogers, personal communication). HNPCC is associated with a wide range of cancers and there are concerns about the insurance and employment implications after genetic testing. One genetic counselor estimates that only about half of family members of affected individuals opt to receive the test and that perhaps only 10 percent of all HNPCC cases are tested (Rogers, personal communication).

Laboratories offering these genetic tests are listed on the GENETESTS.ORG web site. We contacted the majority of the labs offering the clinical tests and ascertained the number of tests they completed in the last year. Our limited findings indicate about 500 FAP and 300 HNPCC assays. There are different types of tests, including full sequencing and testing for a specific mutation only (for family members if the affected person's mutation has been identified). It is important to note that testing may be done on a research basis. In addition, concerns about the insurance implications have led some genetic counselors to send tests out of state (Rogers, personal communication). Thus the true number of tests currently being performed is unknown. We have used 1500 FAP and 1000 HNPCC tests as our estimates for current testing levels.

102EXPECTED FUTURE DIFFUSION

It is likely that other colorectal cancers are hereditary since the relative risk of family members of persons with non-FAP and non-HNPCC colorectal cancer range from 1.7 to 8.0 (Frommer, 1998). In addition, research into genetic tests on sporadic colorectal cancers is ongoing (Inadomi, personal communication; Hoyle, personal communication). However it is not believed that additional genetic tests for these other mutations related to colorectal cancer are likely to be commercially available in the next 5 years (Inadomi, personal communication; Hoyle personal communication; Rogers, personal communication; Barrows, personal communication).

Therefore, future diffusion is expected to be related to testing for mutations associated with FAP and HNPCC. Since FAP affects a smaller population, is clinically identifiable, and has a 100 percent risk for colorectal cancer if not addressed, it is more likely to already be highly diffused (Rogers, personal communication). HNPCC genetic testing appears to have the potential for greater diffusion over the next 5 years. In addition to increased physician and public awareness of this condition, additional commercial testing for specific HNPCC testing may become available in the next 5 years (currently, commercial testing is focused on two genes). Genetic counselors report the greatest growth in testing has been in the HNPCC population. HNPCC testing for the general population has been investigated and the findings are mixed. In general, the cost effectiveness of such testing is dependent upon the prevalence of HNPCC (Brown and Kessler, 1995). Given the uncertainty of the benefit for the general population, it is assumed that testing will not be extended to the average risk population in the next 5 years.

For the low estimate of growth, we have assumed a 20 percent increase in the number of tests per year. For the high estimate, we have assumed that the level of HNPCC testing doubles each year. A new test for HNPCC, with a higher sensitivity and specificity, has recently been released. Though at the higher cost end, company representatives expect widespread diffusion, with growth perhaps at 100 percent per year (Aro, personal communication). The best estimate assumes a 60 percent growth rate.

Table A4-7. Incremental Cases

	2001	2002	2003	2004	2005
low	200	240	288	346	414
best	600	960	1536	2458	3932
high	1,000	2,000	4,000	8,000	16,000

103FACTORS INFLUENCING THE COURSE OF DIFFUSION

Four barriers to diffusion have been identified: physician awareness of the value of testing (especially for HNPCC); individuals' willingness to be testing, even with family evidence of the genetic mutation; insurance coverage for the testing; fears of insurance or employment discrimination as a result of testing. Since HNPCC may be related to several cancers, complete family history is an important step in identifying families who may be affected. Increased physician knowledge of the importance of such detailed history is needed to increase the diffusion of genetic testing (Rogers, personal communication). Research suggests that patients' expressed interest in genetic testing for cancer exceeds their actual use of such testing, with one estimate that 57 percent of people at risk for HNPCC declined the genetic test (Lerman et al., 1999). A genetic counselor who deals with HNPCC families has also estimated that about 50 percent of at-risk family members choose not to undergo genetic testing (Barrows, personal communication). Often individuals simply do not want to know their risk. For some family members, however, the benefits of knowing if they need to continue extensive cancer screening outweigh these concerns. Patients may be concerned about the impact on their employment and insurance options once testing is completed. As such testing becomes more common, and privacy and insurance concerns are addressed, diffusion will increase. Insurers vary in their coverage for genetic tests, though most cover the increased screening needed for families at risk. An issue is that insurers may be asked to cover the costs of genetic screening for uncovered persons (i.e., at risk family members).

104COSTS

The cost of these genetic tests vary depending on whether full sequencing is being done, specific mutations are being examined, and which gene is being tested (since the

length of the gene is a factor in cost). Some tests, such as the microsatellite instability testing, are considerably cheaper than full sequencing (Hoyle, personal communication). In addition, most genetic testing is accompanied by genetic counseling. Estimates for genetic testing and the associated counseling are around $2000 (Vasen et al., 1998; Brown and Kessler, 1995). For the first affected person to be tested, the genetic testing costs range from $500 to $2600. Testing for a known mutation ranges from $200 to $500 (Hoyle, personal communication; Cromwell et al., 1998; Barrows, personal communication).

Costs savings are primarily from avoided cancers, but also include savings from early diagnosis of cancer and reduced monitoring costs, since at-risk relatives with a negative genetic test (assuming the mutation is known) do not need intensive cancer screening. HNPCC is associated with increased risk for cancers other than colorectal, and therefore some individuals have additional screening include endometrial aspirations, CA125 test, and uterine ultrasound (barrows, personal communication). However, we have assumed that the only routine surveillance is biennial colonoscopy with an assumed cost of $1,100.

Cost savings come from reduced costs of treating colorectal cancer because of earlier diagnosis and avoided screening for family members determined not to have the gene mutation. Because colon cancer is slow growing, we are assuming in the five-year period of our forecast most cost savings will occur because genetic tests will also be offered to children of affected individuals. An estimated half of children of affected persons will not carry the mutation. These children can avoid biennial colonoscopies. Constructing a simple model, we make the following assumptions:

- the cost of a test is $2000 for a positive test result (including genetic counseling) and $1200 for a negative test result;
- genetic tests among first relatives would cost $300;
- 40 percent of first relatives would have accepted biennial colonoscopies;
- 85 percent of children undergoing a conventional screening strategy would accept a genetic test;
- there are 1.5 children per affected individual.

Some facilities report only 25 percent of persons requesting the genetic test have positive test results (Fujimura, personal communication); compared with the 90 percent reported by facilities serving the high-risk population. Using this assumption, plus assuming a higher proportion of family members (90 percent) would accept the genetic test if the initial patient at risk tested positive, and 60 percent of family members would have received biennial colonoscopies provides us with a low cost estimate. Assuming all persons receive genetic counseling and only 40 percent of family members would have received biennial colonoscopies provides us with our high estimate

These assumptions result in per case annual costs for a given cohort of:

Table A4-8. Additional Costs of Genetic Testing Over Conventional Colonoscopy Strategy Among First Relatives

	Year 1	Year 2	Year 3	Year 4	Year 5
low	$1,400	$0	-$70	$0	-$70
best	$1,800	$0	-$320	$0	-$320
high	$1,900	$0	-$250	$0	-$250

Multiplying these costs times the incremental cases results in our aggregate incremental cost estimates below:

Table A4-9. Incremental Cost of Genetic Testing for Colorectal Cancer to the U.S. Health Care System

	2001	2002	2003	2004	2005
low	$280,000	$336,000	$405,000	$488,800	$571,600
best	$1.1m	$1.7m	$2.6m	$4.1m	$6.4m
high	$1.9m	$3.8m	$7.3m	$14.7m	$29.2m

Because of the relatively small number of tests, the relatively low cost of genetic testing, and the cost savings associated with genetic testing, genetic testing for colorectal cancer is unlikely to be a large cost driver over the next five years. Toward the end of our forecast period, if persons with a lower risk profile commonly seek to have genetic testing, this technology could become a cost driver.

105KEY ASSUMPTIONS

No other genetic tests for colorectal cancer will be commercially available in the next 5 years.

Growth in testing is almost entirely among the HNPCC population.

Only colorectal cancer screening is assumed.

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107LOW-DOSE (SPIRAL) COMPUTED TOMOGRAPHY

108FOR LUNG CANCER SCREENING

109DESCRIPTION AND INDICATIONS FOR USE

In the U.S. there are approximately 164,000 new cases of and 157,000 deaths from lung cancer annually. This disease has the highest mortality rate of any cancer. The five year survival rate of 14 percent has remained virtually constant for the last 30 years (Kolata, 2000). The survival rate for cancer detected in the presymptomatic state is twice that of symptomatic disease. The survival rate is approximately 60 percent when lung cancer is detected in the early, localized stage. However, currently only about 15 percent of lung cancers are diagnosed at an early stage (National Cancer Institute Biomedical Imaging Program, 1999).

Efforts to develop a screening test for lung cancer have been ongoing. Chest x-ray and sputum cytology for mass screening were abandoned in the early 1980s after the Mayo

Lung Project, a randomized controlled clinical trial, found no reduction in mortality for screened individuals (Marcus et al., 2000). Studies from the United States, Canada, and Japan have shown that low dose spiral computed tomography (CT), a new technology, is more sensitive than traditional chest x-ray for detecting small, noncalcified nodules and early cancers in the lungs (Frame, 2000). However, CT is not very specific. Thus false-positive results requiring additional testing are common (Henschke et al., 2000). Approximately 50 percent of CT screenings will pick up abnormalities but only 2-10 percent will find cancer (Aberle, Marcus, personal communications).

The name spiral CT derives from the shape traced by the x-ray beam during scanning. The spiral path represents a continuous, contiguous volumetric data set that covers a specific volume of the patient's anatomy with no spatial or temporal gaps. Spiral scan technology allows scanning of the entire volume during a single breath-hold, and thus avoids the problem of involuntary

patient motion (Plunkett, 1997). CT technology is advancing rapidly, from a 4 to an 8 slice scanner and a halving of scanning time to ½ second. Soon 16 slice and then flat-plate scanners will become available (Gazelle, personal communication).

Most broadly defined, the primary population for lung cancer screening is some subset of current and former smokers, perhaps based on pack-year smoking history. There are approximately 92 million current and former smokers in the United States (Brown, 2001). Precise definition of the population awaits the outcome of ongoing studies (Gazelle, personal communication). Most lung cancers, over 80 percent, can be attributed to smoking (American Cancer Society, 2000). Other populations that may be appropriate for lung cancer screening include persons with exposure to secondhand smoke; persons with exposure to carcinogens (such as asbestos, arsenic, radon, or diesel fuel); persons with radiation exposure from occupational, medical, or environmental sources; persons with previous lung disease;

and persons with a family history of lung cancer (CancerNet,1999, American Cancer Society, 2000).

110EVIDENCE OF EFFECTIVENESS

Unlike some other cancers for which screening has been more successful, lung cancer is an aggressive disease that is difficult to diagnose and to treat. At present no major medical organizations in the United States recommend any form of routine lung cancer screening for either the general population or any subgroup (Mandel and Weinberger, 2000). Virtually no third party payers cover lung cancer screening (Alliance for Lung Cancer, 2000).

The effectiveness of spiral CT screening of asymptomatic individuals for lung cancer has not been established (National Cancer Institute, 2000). Although some studies have demonstrated increased detection of early stage lung cancers and increased 5-year survival rates in screened over unscreened groups, none has demonstrated a difference in cancer mortality. Because of biases such as lead time[7], length time[8], and overdiagnosis[9], apparent morbidity benefits from screening can be spurious. Thus reduced mortality is

[7] Tumors are detected earlier in their natural history causing longer survival from diagnosis even with ineffective treatment.

[8] Screening detects slower growing, indolent cancers more often than aggressive cancers.

[9] Screening may detect some indolent cancers that would never become symptomatic.

the gold standard for demonstrating the efficacy of screening (Frame, 2000).

Promising studies using spiral CT imaging have demonstrated that this technology is more sensitive than chest radiographs for identifying small lung nodules that may be cancer. However, nodule size is not an accurate surrogate for virulence of lung cancer (Aberle, personal communication; Patz, Rossi, Harpole et al., 2000). Because these studies do not address disease specific mortality (number who die of relative to number screened for the disease) they do not establish the utility of spiral CT screening. Although spiral CT scanning is definitive for diagnosis, its use for screening remains controversial (Frame, 2000).

At present several studies are planned to assess the role of spiral computed tomography in screening for lung cancer. The National Cancer Institute is using the infrastructure of the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) begun in 1992 to see if subjects are willing to be randomized into groups receiving CT versus conventional chest x-ray screening for lung cancer. The study will examine the lung cancer detection rate of each test, the amount and kind of medical follow up required for positive or ambiguous results, and the amount of contamination[10] of subjects receiving outside of study testing (National Cancer Institute, 2000).

Researchers who oversaw the Early Lung Cancer Action Project (ELCAP), the impetus for interest in CT screening for lung cancer, are organizing a study of 5,000 high risk older smokers[11] to document how many lives CT scanning might save. All subjects will get a base line CT scan and a one year repeat screening. Similar non randomized studies are underway in Germany, Israel, Florida, and Minnesota. Statistical analyses will be used to determine if outcomes improve as a result of screening in the absence of randomized assignment (Brice, 2000).

The American College of Radiology Imaging Network (ACRIN) is planning a study to determine if chest radiographs, sputum cytology, or spiral CT scanning can detect early stage lung cancer and if early detection can reduce surgical stage and tumor size. The study will also assess lung cancer screening costs. The five-year, multi-site enterprise will randomize participants[12] to either a screening or control, no intervention arm. Screening participants will receive chest radiographs, low-dose spiral CT, and sputum analysis for lung cancer associated molecular markers at six month intervals. Both groups will complete annual questionnaires on health status and behavioral

[10] Contamination or outside of study receipt of the intervention by the control group can attenuate the effects of the intervention.

[11] Eligibility criteria include: age 60 and above, 10 pack-years of smoking, no currently diagnosed cancers.

[12] Eligibility criteria include: age 55-70; current or prior heavy smokers; or individuals with a previous curatively resected Stage I lung cancer or an upper respiratory neoplasm.

practices (Aberle, personal communication, National Cancer Institute Biomedical Imaging Program, 1999).

The ELCAP and ACRIN studies reflect two alternative outlooks in the scientific community studying lung cancer screening. The ELCAP study presents the concept of screening as early diagnosis, leading to an assessment of aspects of health care practice. The ACRIN trial stresses the concept of screening as an intervention aimed at cause specific mortality reduction, requiring the use of long term randomized controlled trials to determine success. The decision to view screening research strategies as early diagnosis or mortality reducing interventions requiring randomized control trials will affect the speed of diffusion of spiral CT technology for lung cancer screening (Alliance for Lung Cancer Third International Conference, 2000).

111SUBSTITUTE AND COMPLEMENTARY TECHNOLOGY

Currently there is no recommended technology for lung cancer screening. No lung cancer screening technology has been shown to affect mortality. However, in addition to spiral CT scanning a number of nonradiographic technologies are being scrutinized for their potential to detect lung cancer at an early stage including: immunostaining of sputum for molecular tumor markers, automated image cytometry of sputum, fluorescence bronchoscopy, and analysis of exhaled gases for volatile organic compound that appear associated with lung cancer (Mandel and Weinberger, 2000).

Once a CT scan has been performed, additional testing will need to be done to distinguish false positive from true positive cases of malignancy. Henschke and her colleagues recommend more frequent CT scans for persons with small nodules. Biopsies would be performed only if the nodules grew over time or for larger nodules (Brown, 2001). Risks associated with biopsies recommended for suspicious lesions include partial lung collapse, bleeding, and infection. A concern among the policy and clinical community is due to the high false positive rate whether lung cancer screening with spiral CT does more harm than good. Estimates range from 20 to over 95 percent of suspicious lesions found with spiral CT may turn out not to be cancerous (National Cancer Institute, 2000; Alberle, Heschke et al., Kolata, 2000). False positives could also generate a large number of unnecessary surgeries. There is a 2-4 percent complication rate associated with the removal of lung nodules (D. Alberle, personal communication).

112RECENT PATTERNS OF USE

To date, instances of spiral CT screening for lung cancer have been the result of self pay, self referral responses of community members to advertisements by medical facilities and the participation of subjects in clinical trials. Spiral CT scanners have a number of uses distinct from lung cancer screening that make them an integral part of the

equipment of many hospitals. However, the possible increased utilization of spiral CT scanners to accommodate initial and follow up lung cancer screenings could overwhelm current resources.

Approximately half the hospitals in the United States own spiral CT scanners each costing upwards of $1 million. Although most insurers do not currently pay for lung cancer screening, some hospitals are providing spiral CT lung cancer scans directly to the community without physician referral, usually on a self pay basis (National Institutes of Health, 2000).

There are no good data on the volume of spiral CT lung cancer scans being done in the United States. ALCASE lists 12 CT sites that are currently providing screening scans, although it is likely there are more. One of these centers provided 1800 scans in 2000; another had completed 300 scans within the first six months of advertising the availability of spiral CT lung cancer screening (Kolata, 2000). Another center estimates they perform 10 scans per day (Brown, 2001). Assuming the average center performs 6 lung screening scans per day, as many as 22,500 scans may have been performed in 2000, although this

could range from 7,500 to more than 40,000 given the variation in average volume per day among centers. At lease one scan provider in California had to rescind its program because its facilities were overwhelmed by community response (Aberle, personal communication). Such pressures may cause changes in professional recommendations and practices in the absence of evidence of effectiveness or the outcome of evidence based medicine.

Expected Future Diffusion

The prospects for spiral CT screenings for lung cancer may depend on the outcome of current clinical trials. However, in the absence of definitive evidence of clinical efficacy, because of widespread voluntary and involuntary exposure to cigarette smoke and other carcinogens and the virulence of the disease there is general and medical community lobbying of third party payers and professional organizations to approve spiral CT screening. The Early Lung Cancer Action Program, an organization of radiologists has been particularly vocal in attempting to sway the American Cancer Society to accept

evidence from non-randomized trials as sufficient to recommend CT screening for lung cancer. Normally the ACS requires persuasive results from large long term trials with randomized assignment of subjects to recommend a change in procedure (Philipkoski, 2000).

In the past, promising technologies have been deployed without evidence that they work. Once they are widely available, it is difficult to withdraw them to await adequate data. They become de facto procedures without clinical evidence of their usefulness. Such was the case when a large grassroots movement, responding to early indicators of success, precipitated the use of autologous bone marrow transplants to treat metastatic breast cancer. Insurance companies began to pay for the procedure. However, subsequently a large randomized trial suggested the process was not useful(Philipkoski, 2000). Currently, the concentration of prostate-specific antigen (PSA) in the blood of asymptomatic males is used to screen for prostate cancer without

evidence that such screening saves lives. The National Cancer Institute supported Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial is only now examining screening procedures for prostate cancer (CancerNet, 1998).

Assuming spiral CT scans continue to expand at similar to the number seen in recent years into new centers, the incremental number of cases is projected below. Under our high estimates, less than one percent of the target population would have been screened in the following five years.

Table A4-10. Incremental Cases for Spiral CT Scans

	2001	*2002*	*2003*	*2004*	*2005*
low	***7,500***	***7,500***	***7,500***	***7,500***	***7,500***
best	***22,500***	***22,500***	***22,500***	***22,500***	***22,500***

high 37,000 37,000 37,000 37,000 37,000 37,000

Factors Influencing the Course of Diffusion

Diffusion will be affected by the results of current clinical trials. If the trials provide evidence of effectiveness, the demand for spiral CT screening for lung cancer could be enormous. The danger is that, due to community pressures, the technology could become a de facto standard of care before information about its usefulness is available.

The publication of Henschke's trial results in the Lancet (Henschke et al., 1999) and surrounding media publicity provoked thousands of phone calls to participating centers by current and former smokers seeking to get a scan (Grady, 1999). Legal pressures from those anxious to receive settlements from tobacco companies are also expected to spur future diffusion. A recent class action lawsuit in West Virginia is seeking reimbursement from four tobacco

*manufacturers to cover the costs of ongoing medical monitoring (*MSNBC News, 2001*). New York City also contributed $4 million from tobacco settlement money to help finance a large observational study of spiral CT (Zielbauer, 2000).*

Costs

*CT centers are providing screening scans for $300 to $1000 to interested individuals on a self-referral, self-pay basis (*Health Technology Trends*, 2000). According to the National Cancer Institute there are no current estimates of the cost of follow-up care that screening may require. There also have been no cost-effectiveness studies examining the implications of a spiral CT lung screening program in the United States. Interpretations of scans by different clinicians can vary leading to disagreement about appropriate responses to positive or ambiguous results. Possible medical responses include additional scans, biopsies, chest surgery or other diagnostic tests (National Cancer Institute, 2000). The hospital cost of diagnosing a lung*

nodule with open lung biopsy has been estimated at $12,900 (Yang et al., 1999). The cost for lung cancer diagnosis and treatment, under current conditions without screening, has been estimated to be $50,000 (1990 dollars) with a two year survival rate of 20 percent (Hillner et al., 1998).

Using the simplifying assumptions that the 20 percent with abnormal scans require 6 rescannings over the following two years to observe the course of lung changes (as was found in the ELCAP study) and that each scan costs $300, the incremental cost for spiral CT scanning for lung cancer is projected to be $480 in the first year and $180 in the second year. These numbers may underestimate the costs of a spiral CT screening program, because costs for biopsies and subsequent surgeries are not included. They may also overestimate the costs of screening because savings from averted cancer care are not considered. ELCAP investigators estimate a spiral screening strategy may not cost more than $200 per individual once these other factors are taken into consideration

(Miettinen, 2000). Our low estimate assumes this to be the case. Our high estimate assumes biopsies would be performed in 5 percent of positive scans, but does not consider future surgical intervention or averted cancer care. Incremental costs per case under these assumptions are $609 in the first year and $180 in the second year.

Table A4-11. Incremental Cost for Spiral CT Screening to the U.S. Health Care System (millions)

	2001	*2002*	*2003*	*2004*	*2005*
low	***$1.5***	***$1.5***	***$1.5***	***$1.5***	***$1.5***
best	***$10.8***	***$14.9***	***$18.9***	***$18.9***	***$18.9***
high	***$22.5***	***$29.1***	***$35.9***	***$35.9***	***$35.9***

The costs of screening all current and future smokers with spiral CT have been estimated by the National Cancer Institute to be $39 billion. However, if a CT lung cancer scan works, it could also save hundreds of thousands of lives (Kolata, 2000). This figure clearly indicates the risks associated with coverage decisions for this technology.

Key Assumptions

Dramatic increases in the use of spiral CT will not occur before more definitive results are available from the scheduled trials.

Cost savings due to averted treatment procedures because of early detection and cost increases due to false positives beyond the two year rescreening requirement are not considered.

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MONOCLONAL ANTIBODIES FOR CANCER

Description and Indications for Use

Monoclonal antibodies are highly specific antibodies which work by binding to a target antigen. After attaching to antigens on the cancer cells, these cells may then be destroyed by the body's immune system or prevent further growth of these cells. Monoclonal antibodies (Moabs or Mabs) may be used to disable the cancer antigens (so-called naked Mabs) or to deliver chemotherapy or radioactive particles to destroy the cancer cells (so-called conjugated Mabs) (American Cancer Society, 1999). In this brief, we focus on two naked Mabs which have been approved by the Food and Drug Administration for use in treatment of cancer – trastuzumab (Herceptin) for breast cancer and rituximab (Rituxan) for non-Hodgkin's lymphoma. One advantage of Mabs over standard cancer chemotherapies is that since they are targeted, rather than indiscriminately attacking rapidly-dividing cells as standard chemotherapies do, patients may experience fewer side effects.

Trastuzumab (Herceptin): Approved in September 1998 for the treatment of metastatic breast cancer that overexpress human epidermal growth factor receptor 2 protein (HER2) and for patients who have already received at least one chemotherapy regimen or, in the absence of a prior chemotherapy regimen, in conjunction with paclitaxel (FDA, 1998).

Rituximab (Rituxan): This Mab was approved in November 1997 for the treatment of CD20 positive relapsed or refractory low-grade or follicular, B-cell non-Hodgkin's lymphoma.

113EVIDENCE OF EFFECTIVENESS

Trastuzumab (Herceptin): Patients with metastatic breast cancer who are treated with herceptin and standard chemotherapy have increased survival time (25.4 months versus 20.9 months) compared to those receiving chemotherapy alone (NCI, 2000). Chemotherapy with herceptin has been shown to significantly slow tumor progression and increase one-year survival rates compared with chemotherapy alone (McGahan, 1998). The tumor response rate for the combined group was 45 percent versus 29 percent for the chemotherapy alone (McGahan, 1998). An additional clinical trial confirmed these results, reporting that herceptin had a tumor response rate of 15-21 percent for a median time of 8.4 months (Cobleigh et al, 1988; McGahan, 1998).

Rituximab (Rituxan): Rituxan is as effective as standard chemotherapy in the treatment of relapsed or refractory low-grade or follicular CD-20 positive B-cell non-Hodgkin's lymphoma (NYT; UHC, 1999a); half of the patients responded with a shrinking of their cancer (AHFMR, 2000; Leukemia and Lymphoma Society, 2000; UHC, 1999a). Research has found that 95 percent of patients treated with rituxan and the

CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vinicristine, and prednisone) showed improved results (Czuczman et al., 1999). Another study found that approximately one-third of patients with relapsing CD20 positive aggressive lymphoma responded to treatment with rituximab (Coiffier et al., 1998).

114COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

Trastuzumab (Herceptin): Herceptin for metastatic breast cancer is approved for use alone or in combination with taxol or other standard chemotherapy treatments (UHC, 1999b).

Rituximab (Rituxan): Some relapsing lymphoma patients may be treated with bone marrow transplants or additional chemotherapy regimens (such as CHOP) instead of rituxan. Rituxan may be used for relapsing patients who have already undergone bone marrow transplants (UHC, 1999a). In clinical practice, rituxan may be used alone, in combination with chemotherapy regimens, or as a substitute for chemotherapy options, but is commonly used in addition to standard therapies (Czuczman personal interview).

115RECENT PATTERNS OF USE

Trastuzumab (Herceptin): Anonymous industry source reports that approximately 25,000 patients, the majority in the U.S., have been treated since approval.

Rituximab (Rituxan): Anonymous industry source reports that more than 100,000 patients worldwide, most in the U.S., have been treated since approval.

116EXPECTED FUTURE DIFFUSION

Trastuzumab (Herceptin): This drug is currently being investigated for use as adjuvant therapy for HER-2 breast cancers. Use for the treatment of other cancer that overexpress HER-2 are also being investigated. Generally, such cancers must have confirmed evidence of overexpression of HER2 at 2 or, more often, 3+ (strongly positive). Current clinical trials for other cancers include colorectal, pancreatic, non-small cell lung, ovarian, salivary gland, prostate, osteosarcoma, and some adenocarcinomas that overexpress HER2 (NCI, 2000). It is estimated that 30 to 40 percent of these patients have cancers that overexpress HER2 and therefore may be appropriate candidates for Herceptin (NCI, 2000). A recent report estimated that about 50,000 patients with metastatic breast cancer meet the FDA guidelines for herceptin (UHC, 1999b). An estimated 10-30 percent of breast cancers have HER2 protein overexpression (UHC, 1999b), with about 10 percent of breast cancers estimated to be strongly – 3+ – positive and therefore candidates for herceptin. While use by patients in

other unapproved categories is possible, this off-label use is believed to be limited to adjuvant therapy for breast cancer and not common.

Herceptin sales increased from $188.4 million in 1999 to $275.9 in 2000 (Platt, 2001). Genentech revenues are growing at about 25 percent (with Mabs driving this growth) and the manufacturer anticipates similar growth in the next 5 years (Mantz, 2001a; Okimoto, 2001). This growth prediction may be optimistic (O'Brien, 2001), given that herceptin sales have recently slowed (Mantz, 2001b). Diffusion of herceptin for its approved use – to treat metastatic breast cancer – is high; future diffusion will likely be in use for adjuvant therapy for breast cancer (Moore personal communication). We have used 20 percent increase per year as the best estimate of growth. For the high estimates, we have assumed a 40 percent increase; for a low estimate, we have assumed a 10 percent increase over the next 5 years. Based on industry information and sales data, we have assumed that about 15,000 Americans used herceptin in the last year.

Rituximab (Rituxan): Rituximab is being investigated for use in other forms of non-Hodgkin's lymphoma including aggressive, relapsed or refractory diffuse large cell,

and AIDS-related. In addition, it is being evaluated to treat Hodgkin's lymphoma, chronic lymphocytic leukemia, and multiple myeloma (NCI, 2000). Findings presented at the American Society of Hematology meeting indicate that rituxan may be beneficial for the treatment of leukemias as well as non-Hodgkin's lymphoma (Platt, 2001). This Mab is also being investigated as a therapy for treatment of autoimmune diseases including rheumatoid arthritis, multiple sclerosis, and lupus.

Roughly 250,000 Americans are living with B cell non-Hodgkin's lymphoma (Leukemia and Lymphoma Society, 2000). Of all such lymphomas, roughly 90 percent are estimated to have the CD20 antigen (UHC, 1999a). Therefore, if rituximab use were to be extended to all B-cell lymphomas, approximately 225,000 additional patients may be treated. These types of lymphoma are about 43 percent of all cases (UHC, 1999a).

Rituxan sales were $444.1 million in 2000, up from $279.4 million in 1999 (Platt, 2001). Sales of Rituxan in the third quarter of 2000 increased 62 percent to $117.9 million from $72.6 million in the third quarter of 1999. This sales increase is due primarily to increased market penetration for the treatment of non-Hodgkin's lymphoma (Genentech press release). Rituxan is being used for more off-label uses than herceptin, especially for intermediate grade lymphomas (Czuczman personal interview; anonymous industry source). In addition, rituxan has the potential to treat more indications, including non-cancers. Therefore we have assumed a 50 percent increase for the high estimate. Based on Genentech's revenue growth predictions, we have assumed a 25 percent increase for each of 5 years as the best estimate and 20 percent as the low estimate. We assumed that current use levels are 40,000 patients in the past year.

Table A4-12. Incremental Cases

	2001	2002	2003	2004	2005
low	9,500	11,250	13,335	15,820	18,784
best	13,000	16,100	19,945	24,715	30,634

high	26,000	38,400	56,760	83,964	124,299

117FACTORS INFLUENCING THE COURSE OF DIFFUSION

Four factors are likely to affect diffusion of these two monoclonal antibodies: 1) cost; 2) their expanded use for other indications; 3) the identification of serious side effects with their use; and 4) the development of competing treatments.

1. Both of these treatments are expensive. Insurers may, therefore, be reluctant to cover their use for other than the approved uses or may impose restrictions on expanded use (though we have no evidence of such restrictions currently in use). For example, herceptin is useful against HER2 overexpressed tumors and rituxan is approved for use on CD-20 positive lymphoma. The level of HER2 overexpression can be measured using different tests including the HercepTest® and INFORM Her-2/neu® assays. The use of these tests, which would indicate the HER2 overexpression of tumors (and therefore potential patients), is a large factor affecting the diffusion of herceptin (McGahan, 1998). Recent evidence suggests that some tumors which test positive using the HercepTest® may not overexpress HER2 as measured by other tests. The patients with these tumors, therefore, would not be candidates for herceptin use.
2. Both of these Mabs are being investigated for expanded uses, both for the type of cancer for which they are approved, but for other forms of cancer and other conditions (such as auto-immune diseases). Limited off-label use is believed to be occurring currently, but may increase over the next five years. Additional approved indications for these drugs would substantially increase their use.
3. Mabs may be preferred by clinicians because they appear to have few side effects as compared with standard chemotherapy. However, herceptin has been associated with serious ventricular side effects. Identification of other serious side effects could limit the diffusion of these Mabs.
4. Research is on-going on potential competing therapies. Such therapies may include Mabs (such as bexxar for the treatment of lymphoma), angiogenesis products, vaccines, or other therapies. Zevalin and Bexxar are two potential competitors to rituxan; both await FDA approval (Mantz, 2001b). The availability of competing therapies will influence not only the diffusion of these Mabs but possibly their costs.

118COSTS

Trastuzumab (Herceptin): Herceptin is delivered by intravenous injection at a cost of about $2262.50 per 440 mg (1999 Red Book, McGahan, 1998). This drug is approved for an initial dose of 4 mg per kilogram and then weekly maintenance dose of 2 mg per kilogram. Herceptin may be delivered indefinitely, or until evidence of disease progression (suggesting the drug is no longer effective) is found (UHC, 1999b). The estimated annual cost depends on patient size, but may range from $16,125 to $25,628 for a patient weighing 70 kg for the drug alone (UHC, 1999b).

The initial dose of this drug is delivered over 90 minutes, subsequent dose over 30 minutes. Assuming infusion costs are approximately $50 for the first hour and $25 for subsequent hours, then the annual maximum costs for 52 treatments is $2,625 ($75 for the initial and $50 for each of the remaining 51 treatments). $15,000 is used as the low cost estimate, $20,000 as the best estimate, and $29,000 as the high estimate. Some serious cardiac side effects have been associated with herceptin use. Many patients undergo a baseline MUGA (multiple gated acquisition) scan before starting herceptin. Additional cardiac testing is done if patients complain of symptoms (Moore, personal communication). We have included the cost of a baseline MUGA scan – assumed to be $500 – for each incremental case.

Rituximab (Rituxan): This injectable drug is priced at $421.35 for 10 ml and $2106.75 for 50 ml at concentrations of 10 mg per ml (1999 Red Book). This drug is approved as a weekly dose of 375 mg per meters^2 for 4 weeks. Assuming the average person is 1.2 meters^2, then the annual dose would be 1800 mg at a cost of $7584.30 for the drug alone. One report estimates that a 4-weekly infusion will cost $11,130 (UHC, 1999a). The infusions and supply costs are assumed to be $50 per treatment for an annual maximum of $200.

Rituxan may be used in place of convention chemotherapy agents. One analysis compared the costs of rituxan compared with two common chemotherapy regimens. Annual costs for rituxan were $11,169.50, for CHOP $5,504.00, and fludarabine and mitoxantrone cost $13,904.00 (UHC, 1999a). Consequently, rituxan may double the treatment costs or save over therapy alternatives. In practice, rituxan seems to frequently be used in combination with other therapies, or after other therapies have not been effective (Czuczman personal interview). We have, therefore, assumed the costs for rituxan are additive to other regimens.

i) Table A4-13. Incremental Costs of Monoclonal Antibodies to the

ii) U.S. Health Care System (millions)

	2001	**2002**	**2003**	**2004**	**2005**
low	$83.3	$97.6	$114.5	$134.6	$158.5
best	$171.5	$211.3	$260.4	$321.1	$396.1
high	$457.0	$667.8	$976.9	$1430.7	$2097.5

119KEY ASSUMPTIONS

The cost for the drugs will not change over the 5-year time frame.

An adequate supply of the drugs will be available to support projected diffusion.

Only one four-week course of rituximab is assumed to be used per patient. Patients who responded to rituxan may have additional treatments if the lymphoma recurs, though repeat use within a year is not common (Czuczman personal interview).

One year of herceptin treatments is assumed.

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POSITRON EMISSION TOMOGRAPHY AND ITS USE IN THE DIAGNOSIS AND STAGING OF CANCER

Description and Indications for Use

Positron emission tomography (PET) is a diagnostic procedure that is used to quantify metabolic disease processes through multi-slice, whole-body imaging. An image is produced through coincidence detection when the collision of positron-emitting radioisotopes and electrons results in two photons traveling in opposite directions from the point of impact. In oncology, PET is commonly used in combination with a glucose–bound radioisotope, F-18 fluorodeoxyglucose (FDG), which is more quickly metabolized by malignant than nonmalignant cells. The use of PET may allow for more accurate cancer staging and help to better predict patient response to therapy, thus, lead to more appropriate treatment planning.

Until recently, the use of PET for cancer detection has been primarily limited to research centers with dedicated PET systems. This is largely due to the fact that the radioisotopes used for PET have a short half life (110 minutes) and had been mainly produced on site, usually with expensive cyclotrons. However, the advent of regional suppliers of FDG is eliminating the need for an on-site cyclotron.

PET has been used to:

- better define a primary cancer;
- detect metastatic cancer;
- stage cancer to more appropriately direct treatment;
- monitor the response to therapy; and
- distinguish recurrence from scarring..

Although used for a variety of cancers, the available data show the use of PET for lung, colorectal, head and neck and melanomas account for 70-80 percent of oncology use (Adams et al., 1999; unpublished data from the VHA PET Registry).

Technological advances in recent years have made PET scanning faster, more reliable, and more accurate. The development of alternatives to the expensive dedicated full-ring systems, such as dual-use gamma cameras, partial-ring PET systems, and mobile PET, have also made the technology more accessible to US hospitals. Although some suggest the image resolution of converted (dual-use) gamma cameras is not as high as dedicated systems (Lewellen, 1999), industry sources say the quality of these alternatives is improving rapidly. Within the next decade, tumor-specific marker molecules are also anticipated to provide more specificity for whole-body PET scanning (Institute for the Future, 2000).

121EVIDENCE ABOUT EFFECTIVENESS

Clinical studies have shown PET can have high diagnostic accuracy for some metastatic and recurrent cancers. Partly because of its expense, PET has been the focus of several technology assessments. These include assessments conducted by the Blue Cross Blue Shield Association Technology Evaluation Center (BCBSA TEC), the Veterans Affairs, ECRI, and Hayes, Inc. in the United States. Assessments have been completed by other countries, such as the UK and Australia and a joint collaboration among members of the International Network of Agencies for Health Technology Assessment that summarized what had been done by member agencies was recently completed (Adams et al., 1999).

Most of these assessments concurred the quality of the research to date on PET has been lacking. Although the data suggest PET may add value to conventional imaging strategies, the studies have been small case series conducted by single research centers. Nevertheless, the BCBSA TEC concluded the quality of the evidence was sufficient to show PET appeared to improve net health outcome for patients with melanoma, head and neck cancer, and colorectal cancer. A recent coverage decision made by the Health Care Financing Administration used both the BCBSA TEC assessments (BCBSA TEC, 2000 (a-d)) and more recent evidence to conclude there was sufficient evidence to expand Medicare coverage to six indications (see below). There is some evidence that image resolution is poorer among converted than among dedicated systems (Tunis et al., 2000), which has led Medicare to cover PET performed only with dedicated full-ring and some partial ring systems (see below).

The hope, although it has not yet been well documented, is that earlier detection may save patient lives and better staging of the disease and monitoring the response to therapy may avert unnecessary surgery and chemotherapy. Among assessment agencies and HCFA, there are still concerns that the use of PET may not change patient management. (Tunis et al., 2000).

122COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

a) Although PET could supplant other imaging techniques in the diagnosis and staging of cancer, such as CT or MRI, it is most likely to be used in a sequence after other diagnostic procedures. PET will likely substitute for gallium studies in the diagnosis of metastatic melanoma and lymphomas. Pretreatment of patients with antibiotics or steroids may improve the positive predictive results. Some have suggested PET may avert histologic sampling (BCBSA TEC, 2000 (b)), but clinicians suggest PET is not a substitute for laboratory results.

123RECENT PATTERNS OF USE

The number of facilities with PET scanning capabilities has grown rapidly in recent years. Industry sources say there are 300 dedicated PET systems in the United States, which represents a six-fold increase over the installed base in 1992 (Project HOPE, 1992). In the last year alone, the number of dedicated PET scanners doubled, and industry sources expect a further doubling in 2001. There are an estimated 30 mobile PET systems in the United States and another 300 camera-based systems, a number which has increased four and a half fold since 1997 (Robert and Milne, 1999).

Data from selected centers also suggest growth in the volume of PET studies has been explosive in recent years. Clinical oncology studies performed in Veterans Affairs Hospitals (which maintains a registry of its 10 dedicated PET centers) increased more than eight-fold from around 400 in 1997 to 3,630 in 2000. Oncology uses account for more than 70 percent of PET scans, and this proportion has been growing in recent years (Adams et al., 1999; unpublished data from the VHA PET Registry).

Dedicated PET systems average 6 patients per day, suggesting an annual volume of 284,000 oncology PET scans were performed in the United States in 2000. An efficiently operated dedicated system can scan as many as 10 to 15 patients per day, and this number is expected to increase as machine throughput increases. Throughput in converted gamma camera systems are much lower (4-5), although many hospitals are acquiring these just for the possibility of using the PET capability. Based on an estimate provided from a hospital with such a system, the average use is probably in the neighborhood of .15 scans per day.

124EXPECTED FUTURE DIFFUSION

According to industry sources, the number of dedicated PET systems is expected to double next year, and to level off at about 200 new systems per year. Camera-based systems are expected to grow at a similar rate. A best case scenario assumes the average use for a dedicated system is 6 per day and this grows slightly to 8 per day over a five-year period, in existing and new dedicated PET systems. Camera-based systems will

average .15 persons per day. The low scenario uses data from the current average daily volume shown in the VA system. A high scenario assumes existing and future systems will dramatically increase the patient throughput to 10 patients per day.

Although the growth of dual-use gamma cameras is expected to continue, their growth is expected to level off at 150 new systems per year. Industry sources say hospitals feel they have the potential volume to support dedicated systems, and with their price expected to decrease in the future, and regional production of radiopharmaceuticals to grow, the biggest increase is expected in dedicated PET systems. Mobile PET systems, which represent a small proportion of the volume, have not been included in making the forecast, although their use is expected to grow the most rapidly.

Table A4-14. Incremental Cases

	2001	2002	2003	2004	2005
low	145,000	98,000	98,000	98,000	98,000
best	287,000	256,000	289,000	319,000	350,000
high	382,000	350,000	413,000	476,000	476,000

125FACTORS INFLUENCING THE COURSE OF DIFFUSION

Federal regulatory and coverage decisions have been a major factor influencing the diffusion of PET in recent years. Until 1997, the Food and Drug Administration regulated drug manufacturing processes in PET facilities, and the use of FDG was approved only for a single site and single use (BCBSA TEC, 2000 (a)). In Spring of 2000, the FDA concluded FDG is safe and effective for oncologic and cardiac indications. The agency is still working on manufacturing regulation guidelines.

Medicare coverage of PET has also been expanding in recent years. In 1998, Medicare offered provisional coverage for FDG PET using either dedicated or camera-based systems for characterizing solitary pulmonary nodules and initial staging of suspected metastatic non-small cell lung cancer. In 1999, Medicare expanded coverage to include detecting and localizing recurrent colorectal cancer, staging and characterizing both Hodgkin's and non-Hodgkins lymphoma, and identifying metastases in melanoma recurrence in place of gallium studies. In December 2000, HCFA announced a decision to cover PET for six cancer indications: lung, colorectal, lymphoma, melanoma, esophageal, and head and neck (but not brain or thyroid) cancer (Tunis et al., 2000). PET coverage will be allowed for dedicated full circular ring PET scanners and some partial ring systems .

Private insurance coverage has generally followed Medicare rulings, and until recently has mainly covered lung cancer indications (Adams et al., 1999).

126COSTS

A dedicated PET system costs from under $1 million to $2.9 million and a cyclotron costs from $1.2 million to $1.7 million. Installation and construction costs can add a further $1.2 to $2.0 million to this price, and annual operating costs are in the same magnitude (ECRI, 1999). The price of the radiopharmaceutical varies by region and

depends on whether or not the agent needs to be flown in by special shipment from a regional supplier. According to industry sources, although the list price is around $650, its price can reach $2000 for some more remote hospitals. The cost per scan will vary depending on the volume of patients, and the nature of its arrangements to acquire the radiopharmaceutical. Assuming an 8-year life for the PET system and a 30-year life for the construction at interest rates approaching the prime and treasury bills, respectively (9 percent and 6.5 percent), total annual costs for a PET system may average $2.3 million. With an annual volume of 2,190 patients, costs per scan would approach $1,700, excluding professional fees. The national average Medicare payment for a PET scan is $2,429, including professional, technical and radiopharmaceuticals. (ICPET, 2000). Hospitals that can attain, or exceed, this average volume are likely to find PET scans profitable.

Camera-based PET systems sell for $800,000. (Adams et al., 1998) The cost of upgrading dual-headed gamma cameras is approximately $250,000. Dual-headed gamma cameras without the upgrade sell for about $600,000 (ECRI, 1996).

Although PET has the potential of replacing other diagnostic imaging techniques, some radiologists suggest it is more likely to supplement the current diagnostic work up. Historically, diagnostic technologies have been additive – new technologies do not replace old ones, but rather supplement their use (Eisenberg et al., 1989). It is very likely that other radiologic procedures, such as gallium scans for melanomas and lymphomas, will be replaced by PET (an estimated $172 per scan). Among the larger PET centers with dedicated systems, gallium scans are done only when there is a long queue for a PET scan. Among smaller centers, gallium scans are often done

now for lymphomas, but will likely be replaced in the near future.

Some studies have suggested that PET's use for cancer staging and the diagnosis of recurrent and metastatic cancer may be cost-effective, depending on how it is ultimately used. For example, in lung cancer, if restricted to those patients with proven lung cancer and no involvement of the lymph nodes, rather than earlier in the diagnostic algorithm, PET may be cost saving (Mitchell et al, 1998). PET's use could potentially avoid surgery for nonresectable tumors and for benign tumors (diagnosed by CT alone), in addition, PET may help to avoid prolonged chemotherapy for patients who are not responding to treatment. The cost-effectiveness of PET will likely be influenced by its diffusion to non-tertiary care centers where more benign cases are found and false-positive readings are expected to increase (an idea derived partly from Adams et al., 1998). Others have shown PET is unlikely to be cost reducing (Kosuda et al. 2000)

It is difficult to forecast an incremental cost for PET, as the impact of PET on patient management and health outcomes is not well documented. Assuming PET will

avert contraindicated surgery in 12-18 percent of cases (Valk et al., 1996; Lewis et al., 1994; BCBSA TEC, 2000 (d)), and the cost of contraindicated surgery exceeds a PET scan cost by 2 to 6 times (Project HOPE analyses of MEDPAR 1998 data; Valk et al., 1996), the incremental cost of a PET scan could range from saving $180 per scan to costing an additional $1,750. A best case estimate assumes the mid-range of $780 per PET scan. These estimates may overstate the cost of PET, because other cost-reducing improvements in patient management, such as averted chemotherapy or no surgical intervention for benign tumors, are not included. They may also be low because the costs of inappropriately treating false positives or using PET for contraindicated purposes have not been factored in.

The incremental cases above suggest an incremental cost for treating cancer patients attributable to PET will be:

i) Table A4-15. Incremental Costs of PET to the

ii) US Health Care System (millions)

	2001	**2002**	**2003**	**2004**	**2005**
low	($28)	($19)	($19)	($19)	($19)
best	$224	$199	$225	$248	$273
high	$668	$612	$723	$833	$833

127KEY ASSUMPTIONS

Oncology uses will continue to account for 70% of all cases

PET will avert surgery and result in better planning in 18 percent of cases.

PET will substitute for gallium scans in 5 percent of cases, but will not replace histologic analyses.

Private reimbursement reflects Medicare reimbursement. Private coverage will continue to expand.

Payment rates for PET do not decline, even though the cost of a PET scan is expected to fall.

State CON will continue to loosen restrictions on construction of PET centers now that there is a clear statement from Medicare about the efficacy of PET.

128WILD CARDS

Medicare agrees to cover PET for breast, ovarian and cervical cancer indications.

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SCREENING FOR COLORECTAL CANCER

Description and Indications for Use

Colorectal cancer is the third most commonly diagnosed cancer among Americans, with more than 130,000 new cases diagnosed in 2000 (American Cancer Society, 2000; AHCPR, 1998). The five-year relative survival rate for cancers found early is 90 percent, but survival falls to 8 percent for those diagnosed after distant metastases have occurred (American Cancer Society, 2000). This difference in survival based on stage at diagnosis highlights the importance of effective screening for colorectal cancer.

Almost 90 percent of colorectal cancer cases are found in those aged 50 and older (American Cancer Society, 2000). The average 50-year old has a 6 percent lifetime risk for colorectal cancer (Lieberman, 2000). Screening recommendations for average risk Americans beginning at age 50 include annual fecal occult blood tests (FOBT) and periodic sigmoidoscopies (Podolsky, 2000). FOBT is most effective for larger polyps (since they are more likely to bleed). Other recommendations include flexible sigmoidoscopy at 50 and every 5 years, in combination with annual FOBT, and an examination of the whole colon every 5 to 10 years with double-contrast barium enema (DCBE) or every 10 years with colonoscopy (Smith et al., 2000). It is estimated that fewer than one-third of Americans comply with these recommendations (Podolsky, 2000).

The cost-effectiveness of annual FOBT screening with flexible sigmoidoscopy every 5 years has been established (AHCPR, 1998). However, sigmoidoscopy does not detect a substantial number of cancers because they are in the proximal colon (Podolsky, 2000). Recent reports, however, have suggested that screening colonoscopy every 10 years beginning at age 50 may be effective. Many clinicians and researchers believe that screening colonoscopy is the preferred surveillance method (Winawer et al., 2000).

130EVIDENCE OF EFFECTIVENESS

Recent analysis has suggested that colonoscopy screening is more cost effective than FOBT alone (Lewis, 2000). Colonoscopy's cost advantage over flexible sigmoidoscopy depends on the assumed costs of each procedure, but it is proven to be cost-effective (Lewis, 2000). Some are calling for guidelines to recommend screening colonoscopies every 10 years starting at age 50 for average risk individuals (Sonnenberg et al., 2000).

Evidence of the impact of screening with colonoscopy on mortality has not been studied, though the inference from recent published reports is that mortality from colorectal cancer will be reduced (Podolsky, 2000; Lieberman et al., 2000). One study found that about 30 percent of cancers detected with a colonoscopy would not have been

detected with a sigmoidoscopy (Lieberman et al., 2000). Two studies found that half of patients with proximal colorectal neoplasms did not have lesions in the distal colon (Imperiale et al., 2000; Lieberman et al., 2000). Consequently, sigmoidoscopy would not detect these cancers.

A recent study comparing the use of colonoscopy to DCBE for patients with previously identified polyps, colonoscopy was found to detect more polyps than DCBE (Winawer et al., 2000). DCBE found only 20 percent of adenomatous polyps found by colonoscopy (Winawer et al., 2000). About 3 percent of screening colonoscopies detect polyps greater than 1.0 cm. It is believed that polyps take 10 to 20 years to become cancerous (Winawer et al., 2000). Winawer et al. (2000) did not find convincing evidence that the use of both screening tests would be beneficial, though a small number of additional adenomas would be identified. Colonoscopy is estimated to miss about 20 percent of polyps, almost all smaller than 1.0 cm (Winawer et al., 2000).

The incremental cost-effectiveness ratio of colonoscopy over traditional colorectal cancer screening methods is low (Lewis, 2000).[13] Screening colonoscopies would initially have large costs, with reduced costs in the future, perhaps reducing colorectal cancer costs by 75 percent. Given the proportion of colorectal cancer cases that occur in persons aged 65 or older, screening colonoscopies appears to be a good buy for Medicare (Lewis, 2000).

While complications from colonoscopy are more common than other screening procedures, the rate is still low. Perforation of the colon and complications from anesthesia occur in only 0.2 to 0.3 percent of colonoscopies performed by gastroenterologists (Podolsky, 2000; Lieberman et al., 2000).

131COMPLEMENTARY AND SUBSTITUTE TECHNOLOGY

As discussed above, other established screening tests for colorectal cancer are available. These include FOBT, flexible sigmoidoscopy, and DCBE. Each of these screening tests are less expensive than colonoscopy, and they may be more widely accepted by physicians and patients. The combination of annual FOBT and periodic flexible sigmoidoscopy have been shown to be effective screening tests. However, compliance with this regimen is low and these tests are less sensitive than colonoscopy (Lewis, 2000; CDC, 1999).

Research is currently being conducted on virtual colonoscopy which would provide many of the advantages of colonoscopy but at a lower cost, risk of complications,

[13] Two points are relevant. First, the cost-effectiveness of screening colonoscopy considering societal costs has been established. Sonnenberg and colleagues' recent analysis considered only third-party payer's costs and found colonoscopies cost-effective, but used the lifetime of the patient as their time frame (Lewis, 2000). Our shorter time frame – 5 years – means that most benefits will not be realized in that time.

and invasiveness to the patient. While virtual colonoscopy is promising, it is still in development and not yet approved (Johnson, personal communication; Miller, personal communication; Wyatt, personal communication).

132RECENT PATTERNS OF USE

In the last 10 years, the number of colonoscopies performed has increased (ECRI, 2000). According to National Center for Health Statistics (NCHS), approximately 1.5 million screening and diagnostic colonoscopies were performed in 1997. Colonoscopies have been increasing at a rate of about 10 percent per year.

133EXPECTED FUTURE DIFFUSION

The recent growth of 10 percent per year is used as our low estimate. Recent studies demonstrating the effectiveness of screening colonoscopy and media coverage of the benefits such screening may lead to a greater increase in the coming years, so a 15 percent growth rate has been used as our best estimate. Increased media coverage, additional evidence of effectiveness, or changes in screening guidelines may lead to even greater growth, so we have used a 25 percent annual increase as our high estimate. There are about 80 million Americans 50 or older; assuming a colonoscopy every 10 years, there is the potential for about 8 million screening colonoscopies per year.[14] As mentioned above, compliance with current screening guidelines is low, and since colonoscopies require more preparation than other screening methods, compliance may not be improved for screening colonoscopies.

Table A4-16. Incremental Cases

	2001	2002	2003	2004	2005
low	150,000	165,000	181,500	199,650	219,615
best	225,000	258,750	297,563	342,197	393,526
high	375,000	468,750	585,938	732,422	915,527

[14] In practice, this number would be slightly lower. Some people are not appropriate candidates for screening colonoscopies due to frailty or comorbidities. In addition, some people over 50 have already had colorectal cancer or are at increased risk and therefore are not part of the average-risk population. The rate of full examinations ranges from 80 to 99 percent (Winawer et al., 2000).

134FACTORS INFLUENCING THE COURSE OF DIFFUSION

Several factors will affect the increased use of screening colonoscopies for average-risk adults over the next 5 years. First, the acceptance by physicians is crucial. The preferred use of colonoscopy screening is debated among physicians, with some division according to specialty (i.e., radiologists vs. gastroenterologists). Some physicians believe that screening colonoscopies are preferred (ECRI, 2000). In addition, colonoscopy may be considered a lucrative procedure (ECRI, 2000), which may encourage their use. Patient awareness of the importance of colorectal cancer screening – and the benefits of colonoscopy in particular – will play a critical role in future diffusion of colonoscopies. Patient levels of compliance with current guidelines are low; in 1992 less than 20 percent of people 50 and older complied with the current screening recommendations (AHCPR, 1998). Since the patient time and preparation for colonoscopies for sigmoidoscopy is more extensive, it might be reasonable to conclude that only those willing to undergo sigmoidoscopy would be willing to undergo screening colonoscopy. However, recently some well-known personalities have been advocating screening colonoscopies for average-risk adults. If the public responds to these campaigns, then screening colonoscopy could grow extensively in the next 5 years. A third important factor is insurance coverage for colonoscopy screening. Currently, many insurers cover colonoscopies only if patients are at high risk (e.g., have a family history of colorectal cancer). The Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 requires that Medicare cover dicennial screening colonoscopies for average risk beneficiaries (BIPA, 2000). If major societies or associations, such as the American Cancer Society, were to change their recommendations to include screening colonoscopy, then diffusion would be increased.

135COSTS

While there is evidence that screening colonoscopies may be cost-neutral relative to other screening strategies over a ten-year period (Lieberman, 2000), the development of cancer from a polyp is slow, estimated from 10 to 20 years. Thus, most of the benefits (averted cancer care) are unlikely to be realized in the next 5 years. In our time frame, therefore, this is a cost increasing technology.

Our estimates assume screening colonoscopy conducted every 10 years would replace a strategy of annual fecal occult blood tests (FOBT) and a sigmoidoscopy every five years. The cost of a screening colonoscopy is $1,012, the cost of a screening sigmoidoscopy is assumed to be $280, and the cost of annual fecal occult blood tests are assumed to be $38 (Frazier et al., 2000). The major cost difference in the short term between these two strategies is the relative costs of the tests. Thus the incremental cost of screening colonoscopy for a given cohort would be:

Table A4-17. Additional Costs of 10-year Colonoscopy Over 5-Year Sigmoidoscopy and Annual FOBT

	Year 1	Year 2	Year 3	Year 4	Year 5
Colonoscopy	1012				
Less FOBT	38	38	38	38	38
Less sigmoidoscopy	280				280
Net cost	694	-38	-38	-38	-318

These assumptions lead to the following incremental costs for all new cases of colorectal cancer screens:

Table A4-18. Incremental Costs of Colorectal Cancer to the U.S. Health Care System (millions)

	2001	2002	2003	2004	2005
low	$104	$109	$114	$120	$84
best	$156	$171	$188	$208	$239
high	$260	$311	$375	$454	$448

136KEY ASSUMPTIONS

New screening tools, such as virtual colonoscopy, which could substitute for screening colonoscopies are currently under investigation. We have assumed that such technologies will not be in wide use in the next 5 years.

Most private insurer will only cover colonoscopies for the high risk population.

We have assumed that the cost of colonoscopies will remain constant over the next 5 years.

Costs per screened person of polyp care and averted cancer care are small in the five year period and can be ignored in this time frame.

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THIN-LAYER CYTOLOGY (THINPREP) FOR
CERVICAL CANCER SCREENING

i) Description and Indication for Use

A sharp increase in litigation against pathologists and pathology laboratories involving false negative Papanicolaou (Pap) smear results in the late 1980's and the 1990's spurred the development of new technologies to improve the efficacy of cervical cancer screening (Gilbert, 1997, Yeoh et al,1999). The ThinPrep system, one such technology, is aimed at reducing the false negative rate due to cytologic sampling error, which is responsible for about two thirds of false negative readings (McCrory et al., 1999).

Most sampling errors in conventional screening result from preparation problems. Diagnostic cells are collected but are not transferred to the microscope slide or are transferred to the slide but are unreadable. Liquid-based thin-layer preparations like ThinPrep, approved by the Food and Drug Administration (FDA) in May 1996 as a "significantly more effective" method than conventional Pap smear testing for preparing cervical cytology samples, are designed to enhance random sampling and cell clarity for screening on the slide (Cytyc, 2000).

In the standard Pap smear procedure, collected cells are smeared directly from the collecting implement onto a slide. In the ThinPrep method, cells are collected from the cervix using a conventional Pap test broom-type device or plastic spatula and endocervical brush combination and immediately suspended in a fixative solution. At the laboratory, the specimen is dispersed and filtered and then is transferred to a microscope slide for examination. The specimen in solution can be maintained for up to three weeks for additional study. Virtually all collected cells are immediately preserved in a suspension that is filtered and subsequently used to deposit a monolayer of cells on a slide. (ECRI, 1996; ECRI, 1999)

Thin-layer cytology is preferred to conventional Pap smears because it provides a more representative sample of cells, reduces rescreening, has greater sensitivity using a cytological or histological reference standard (McCrory et al., 1999), and can be used to test for a variety of cervical conditions. In addition to its use in detecting atypical and abnormal cervical cytology, ThinPrep has FDA approval for testing for human papillomavirus (HPV) DNA using Digene Corporation's Hybrid Capture II system. ThinPrep may potentially be used for chlamydia, improved detection of glandular (adenoid) lesions, and molecular testing (Cytyc, personal communication; Lin et al., 2000).

The primary population for cervical cancer screening using thin-layer cytology is women who are candidates for conventional Pap smear screening, i.e., women from the age of onset of sexual activity. No upper age limit for screening has been established.

Annually, over 56 million women have Pap smears. (Associated Press, 2000, National Health Interview Survey, 1998) Each year there are about 15,000 new cases of cervical cancer and 4,900 cervical cancer deaths. (National Cancer Institute, 1998)

The number of deaths from cervical cancer declined by 74 percent between 1955 and 1992. The decline is attributed to the success of mass screening using the 50 year old Pap test to diagnose premalignant, early-stage cases. (American Cancer Society, 2000) The majority of new cases and deaths from cervical cancer are a result of failure to screen rather than deficiencies in the screening process. (Brown and Garber, 1998).

138EVIDENCE OF EFFECTIVENESS

There have been a number of technology assessments of the ThinPrep process including studies by ECRI, Blue Cross Blue Shield Association, Hayes, Inc, and AHRQ, in the United States. Technology review groups in countries including Australia, New Zealand, Canada, and the United Kingdom have also studied ThinPrep. Most agree that the quality of data makes estimation of sensitivity and specificity difficult, but conclude ThinPrep improves sensitivity compared with traditional Pap smear screening, at an increase in cost. However, especially when part of a strategy with screening intervals of 3 years, the cost-effectiveness ratio for ThinPrep may be within

the range of accepted health care practices. (McCrory et al., 1999).

Brown and Garber (1998), based on a synthesis of the clinical literature, concludes that ThinPrep compared with conventional slide preparation has a significantly higher sensitivity (91 percent versus 80 percent) and roughly equivalent specificity. A more recent meta-analysis estimated conventional Pap smears had a much lower sensitivity than generally believed (51 percent) (McCrory et al., 1999). Both assessments state that, because of limits in the data, although the weight of evidence suggests ThinPrep has a better sensitivity, its specificity is unknown, making it difficult to draw conclusions about the relative costs and effectiveness of the two strategies.

The levels of sensitivity and specificity assumed for conventional versus ThinPrep Pap smear, which vary widely across studies, are important determinants of findings regarding ThinPrep's incremental performance; how well a laboratory currently

performs conventional Pap smear screens will also affect the relative advantage of a ThinPrep system. Part of the difficulty of measuring the performance of Pap smear screening technologies is that there is no clear gold standard for comparison, and the ultimate test of their performance (improved survival) requires long term follow up under usual laboratory conditions.

Recent evidence has shown presence of the human papillovirus (HPV), particularly chronic infections, can accurately identify precancerous changes in the cervix (Schiffman et al., 2000). HPV is a sexually transmitted disease that is usually transient. The ten to twenty percent of cases that persist may provide evidence of cervical neoplasia. Women with low grade or borderline cytological tests who test negative for oncogenic HPV are at low risk of developing high grade cervical intraepithelial neoplasia (CIN) within three years (Cuzick et al, 1999).

One advantage of a ThinPrep Pap test is that the same sample captured with liquid-

based technology can also be used for HPV DNA testing. Recently, Cytyc and Diogene, the manufacturer of the DNA-based Hybrid Capture II for detecting HPV, reached an agreement for Cytec to market DNA HPV testing in conjunction with ThinPrep (Chea, January 19, 2001). A combined screening test offers the opportunity for earlier detection and/or longer screening intervals that could reduce cost.

Studies are currently ongoing to evaluate the utility of ThinPrep specimens for detecting Chlamydia, which causes pelvic inflammatory disease (PID). Women with Chlamydia often do not display outward symptoms, although it is a major cause of infertility among young women. Joint Pap and Chlamydia screening could be highly beneficial, particularly among young, sexually active women (Hutchinson, personal communication).

The ThinPrep Pap test is used as a substitute for the conventional Pap smear screening. Two automated screening technologies may be used as complements to either the Pap or ThinPrep tests. Each of these automated techniques is designed to deal with the second major source of false negative tests, cytologic detection error, responsible for about one third of false negative readings. (McCrory et al, 1999) Detection errors are due to screening errors in which abnormal cells present on the slide are not located or interpretation errors in which cells are located but incorrectly classified. The algorithmic classifier AutoPap300 QC and the computerized rescreening device Papnet combine automated microscopy and computerized analysis to find abnormal cells missed on initial examination to reduce screening errors. Both of these technologies have received regulatory approval from the FDA for rescreening. AutoPap 300 QC is also approved for primary screening. Brown and Garber (1998) estimated the inclusion of AutoPap or Papnet in a screening strategy

increases both sensitivity and incremental cost.

There are some new technologies that could replace Pap screening or conventional techniques to help clarify atypical squamous cells of undetermined significance (ASCUS) readings (which account for about 7 percent of Pap results). A technology suggested as a potential replacement for Pap screening include in vivo biophotonic scanning which identifies suspicious lesions by analyzing light shined on the cervix and detecting biochemical and morphological changes at the cellular level. This is expected to reach the market after 2002 (MedPro Month, 2000). The NMP 179 test, causes pre-cancerous cells in a cervical cytology specimen to glow making them easier to detect (MedPro Month, May, 2000). The NMP 179 test might also come into use as an adjunct to traditional cytology screening to help clarify ASCUS readings and reduce unnecessary colposcopies. This technology is in an early phase of study. Vaccines are also being

developed to prevent HPV (MedPro Month, 2000).

In addition to aggressive competition to find a better screening technology than conventional Pap smears, treatments for cervical cancer are becoming more effective. Combined chemotherapy and radiation therapy could dramatically extend patient survival and may change the relative cost of screening techniques (MedPro Month, February 2000).

- Recent Patterns of Use

Roughly 2.8 to 4.5 million Pap smear screenings used ThinPrep in 1998. (*New York Times,* December 1, 1998) Cytyc sources report in 2000 they had attained a 30 percent market share, which would suggest 17.2 million Pap tests used ThinPrep. The proportion of U.S. doctors using ThinPrep has increased from about one percent in 1996 to 25 percent in the first quarter of 2000. (*MedPro Month*, October, 2000) The ThinPrep technology is available in over 800 U.S. laboratories that collectively provide 80 percent of Pap testing analysis (Cytyc personal communication).

An estimated 3.5 million Pap smear tests do not provide conclusive results. HPV capture is being used for about 15 percent of these and is expected to experience a slow upward climb in its use in the next few years (Chea, January 18, 2001).

- Expected Future Diffusion and Factors Influencing Diffusion

Reimbursement has been an important factor constraining the diffusion of ThinPrep technology. Beginning in January 2000, the Health Care Finance Administration (HCFA) increased its payment to cover the cost of the ThinPrep procedure. Most major insurers now cover ThinPrep including private payers and, in many states, Medicaid. Industry sources state that reimbursement is still a major barrier to diffusion in western states.

In addition to improved reimbursement, the versatility of liquid-based cytology may serve to speed ThinPrep's diffusion in the future. Mono-layer technology has applications beyond the traditional

examination of cervical cytology. As noted previously, the ThinPrep system has FDA approval for HPV testing. Currently, ThinPrep is also being studied for Chlamydia trachomatis, glandular lesion, and molecular testing.

A factor that could decrease the rate of growth of ThinPrep cases would be clinicians' adoption of triennial, rather than annual, Pap smear screenings for women with a history of normal results. Annual testing has been common and is preferred by many physicians. A survey of recently trained gynecologists in the mid-1980's indicated that 97 percent recommended a Pap test at least once a year. Advocates of annual testing cite concerns about aggressive, rapidly growing cancers escaping early detection; women having low compliance, the importance of encouraging visits to receive other preventive interventions (Woolf, 2000). However, The American Cancer Society, the National Cancer Institute, the American College of Obstetricians and Gynecologists (ACOG), the American Medical Association, and the American Academy of Family Physicians (AAFP) among others have adopted a consensus recommendation that permits less frequent testing at the discretion of the physician after three or more annual tests have been normal. Of course, the frequency of testing has important economic consequences. (Woolf, 2000)

Industry sources expect the use of ThinPrep technology for cervical cancer screening will increase in the next five years; with HCFA's recent reimbursement increase for ThinPrep Pap smears and evidence about the effectiveness of adjunct HPV testing, diffusion may increase significantly. Based on information provided by the company, ThinPrep was used in approximately 30 percent of Pap screenings in 2000, and is expected to reach 50 percent of the market by 2001. Our best case scenario assumes steady, but slower growth for the years 2002 to 2005, with ThinPrep attaining a market share of 80 percent by 2005. Our high estimates assume more aggressive, and earlier growth, with the product attaining a market share of 90 percent in 2005. Under our low growth assumptions, ThinPrep reaches 70 percent of the market by 2005.

Table A4-19. Incremental Cases of ThinPrep Pap Smears (millions)

	2001	2002	2003	2004	2005
High	***18***	***11***	***11***	***11***	***11***
Best	***12***	***5***	***5***	***5***	***5***
Low	***9***	***4***	***4***	***4***	***4***

- Costs

Cytyc sources report conventional Pap smears currently cost approximately $14.60 per test. ThinPrep technology adds $12.00 to $16.00 to that price depending on laboratory efficiency. Medicare reimburses for Pap smear samples collected using the ThinPrep method at $28 per test and for those collected using conventional screening at $10 per test (Keene, personal communication; McCrory et al., 1999). HPV capture tests cost around $45 (Chea, January 18, 2001). Industry calculations suggest the use of this technique could result in $15 savings per individual screened with ASCUS results. Savings arise from a reduction in repeat Pap smears and colposcopy procedures performed (*MedPro Month, May 2000).*

Several cost-effectiveness analyses have been done comparing ThinPrep with alternative screening methods, such as conventional Pap smears, and ThinPrep or conventional Pap smear technology combined with the AutoPap rescreening device or (e.g., Hutchinson et al., 2000; Brown and Garber, 1998; McCrory et al., 1999). The results of these studies vary widely and depend on the choice of test sensitivity and incremental costs of a ThinPrep system over alternative screening methods. McCrory et al. (1999) and Brown and Garber (1998) estimate the incremental cost per test of ThinPrep over conventional Pap screening is approximately $10.

Because cervical cancer is a slowly developing process, the major clinical benefits (reduction in cancers and associated mortality) will not be realized in the short term. Short-term benefits are more accurate testing and fewer repeat Pap tests and colposcopies for ACSUS (Hutchinson, personal communication). Assuming a $10 increase of ThinPrep over conventional Pap smear screening and HPV capture tests are used in 7 percent of cases saving $15 per case, our best case estimate for an incremental cost of the ThinPrep system is $8. Our low incremental cost estimate is $3 (Martha Hutchinson, personal communication); our high incremental cost estimate is $14. Multiplying these times the incremental cases shown above, the aggregate incremental cost for the ThinPrep procedure is shown below.

Table A4-20. Incremental Costs of ThinPrep Pap Smears to the U.S. Health Care System (millions)

	2001	2002	2003	2004	2005
low	$27	$12	$12	$12	$12
best	$96	$40	$40	$40	$40
high	$252	$154	$154	$154	$154

140KEY ASSUMPTIONS

New developments in competing technologies will not significantly alter the

growth of the ThinPrep market in the next five years.

Insurance coverage and reimbursement will continue to improve.

Many of the potential benefits will not be realized in the short term.

Major changes in the periodicity of Pap screenings among American women will not occur in the next five years.

The potential benefits of a joint chlamydia/Pap smear test are not included.

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