

# The Foresight Chronicles

## Introduction

For more than twenty years the Institute for Alternative Futures (IAF) has organized Foresight Seminars to provide Congress, executive agencies and the private sector a forum for looking to the future of health and innovation. This paper chronicles the forecasts and insights developed through these Foresight Seminars from 1978 through 1998. The paper is also a guide to a larger body of information from the programs that is now available on the IAF website. Thanks to a grant from Merck & Co., IAF can now disseminate a large selection of summaries, transcripts and invitations from over 100 Foresight Seminars that were held for Congress. This paper provides electronic links that form a virtual table of contents to this information.

In retrospect, we believe the Foresight Seminars are proving successful beyond anyone's expectations. The record of the seminars provides a treasure trove of insights into leading edge developments in science and technology, business, the economy and society. Taken as a whole, this record is arguably the best source of foresight available to understand emerging innovations and opportunities in health care.

The Foresight Seminars deal with scores of topics from nanotechnology and cloning to demographics, new businesses and global markets in a transforming economy. On every topic IAF has sought to help policymakers improve their decisions by creating programs to explore forecasts, multiple points of view and visions of the best that can be created.

Over the years IAF has worked to integrate ideas from the hundreds of leading thinkers who have joined the Foresight Seminars to create a coherent view of possibilities for the future of health. What has emerged can be described as a "4<sup>th</sup> Wave Health System" that stands in sharp contrast to the traditional industrial model of illness care. Important elements of this emerging 4<sup>th</sup> Wave Health System include:

- ◆ The rise of a **Forecast, Prevent and Manage Paradigm** that involves forecasting potential health problems based on genetics, environment and disease history. These forecasts will be used to prevent problems through lifestyle change and biomedical interventions. Health management will include routine biomonitoring that detects deviations from normal functioning to identify problems and opportunities for improvement;
- ◆ A deep change in health care priorities to address preventable mortality caused by lifestyle, poverty and environmental insults;
- ◆ An emphasis on self-managed care, done in partnership with health care providers and other supportive organizations;
- ◆ A focus on creating healthy communities and workplaces, as well as healthy individuals;

- ◆ Development of the potential of biotechnology for genetic profiling and anticipatory prevention with improved diagnostics and a wide range of new treatments;
- ◆ The emergence of a new stage of medicine—customized care—with therapies tailored to genetically similar population groups and individual biochemical uniqueness;
- ◆ Development of the full potential of telehealth, not only within and between health care facilities, but reaching into homes to provide health information access, video housecalls, biomonitoring, expert system health coaching, support groups and other services;
- ◆ Widespread use of outcome measures and provider rating systems to accelerate medical progress and empower consumers;
- ◆ The use of a much wider range of tools from various alternative therapies integrated with allopathic medicine and using outcome measures to evaluate all approaches;
- ◆ A view of health as a wholeness and potential that goes beyond the absence of symptoms to an appreciation of the importance of love, tolerance, compassion and joy—qualities that bring measurable physiological benefits as well as mental health;
- ◆ An emphasis on caring in the fullest sense; a view of patients as multi-dimensional, with treatment addressed not just to the physical level but also to the level of emotions, understanding, and ultimate meaning and purpose;
- ◆ A long-term shift in focus—as biomedical advances cure or control major diseases and as prevention and genetic medicine “design disease out” of society—toward physiological and mental enhancements of our highest capabilities.

These and other themes have emerged in the Foresight Seminars, interweaving like the strands of a DNA helix. They have given rise to a larger realization. Converging knowledge revolutions in biomedical, technological and social fields are reaching a point of critical mass. Together they create a synergy which is larger than the effects of any single field. Together, they create an overarching **systems view** of the radical transition in which healthcare is now embroiled.

Why is this so significant? Problem-solving can be undertaken at a much higher level, its effects are more accurately anticipated and directed, when previously disjointed issues are seen in relation to a whole. ***In fact, only a systems approach to problem-solving truly works.*** Countless ineffective problem-solving efforts throughout history provide a lesson we ignore at our peril: trying to solve narrowly defined problems in isolation breeds new sets of problems no less daunting than those that policymakers first set out to solve.

Thus, the Foresight Seminars have taught us that a public conversation about creating health in the 21<sup>st</sup> century must adopt a systems approach if it hopes to be meaningful. The purpose of this report is to make the insights and information from the Foresight Seminars available to all health care stakeholders. We at IAF hope readers will see in this report that a new vision of health is waiting in the wings—a vision that encompasses innovation in policymaking as well as health care systems.

**Structure of the Paper and Links to More Information**

The Foresight Seminars are organized around three themes: **Innovation** (scientific and technical), **Governance** (federal government plus management generally) and **Socioeconomics**. Each has spawned important sub-themes over the years. As shown in the key below, throughout this report we color-code each theme plus three to five of its chief sub-themes. Readers who trace the color-coded strands through the pages can follow their interweaving over the years of Foresight discussions--spiralling up to a systems view of the future of health and health care.

Innovation	Governance	Socioeconomics
<p>Information technology (computers &amp; communications)</p> <p>The knowledge revolution</p> <p>Customization, facilitated by biotechnology/genomics</p> <p>A prevention paradigm in health care</p> <p>Complementary and alternative approaches in mainstream medicine</p>	<p>Regulation &amp; regulatory reform</p> <p>Turning government agencies into "learning organizations"</p> <p>Facilitating innovation</p> <p>Vision</p>	<p>The 4<sup>th</sup> Wave Economy (values-based; networked; knowledge-driven; customized; global)</p> <p>Consumer empowerment</p> <p>Ethical issues</p> <p>Outcome measures</p> <p>Aging</p>
<p><i>Health Systems Perspective</i></p>		

## The 4<sup>th</sup> Wave Economy

Alvin Toffler, in his 1981 foreword [\[link to Toffler foreword\]](#) to *The Future of Pharmaceuticals*--IAF's report on the first year of the Foresight Seminars [\[link to publication and ordering info\]](#)--noted that the future of pharmaceuticals opens a window into the future of Congress and, indeed, of governing bodies everywhere. "Designed for a late agrarian or early industrial age," Toffler wrote, "the US Congress today is ... drenched and deluged with data it can neither digest properly nor apply intelligently."

The "Information Age" Toffler was referring to (which he terms the Third Wave, succeeding a 1<sup>st</sup> Wave/Agricultural Age and 2<sup>nd</sup> Wave/Industrial Age) will be brief. We are already entering a "4<sup>th</sup> Wave" economy, characterized by all of the elements of the Information Age--ubiquitous communications via computers and networks, knowledge-driven, global, placing individuals over institutions, etc.--but adding the crucial element of **values**. Consumers increasingly will base their choices of health care--and everything else--on values, abetted by **outcome measures** and **expert knowledge** accessible over **communications networks**.

Portents of this shift were identified as long ago as 1982, at a two-day Foresight conference on "Pharmaceuticals in the Year 2000." [\[link to publication and ordering info for Pharmaceuticals in the Year 2000\]](#) One speaker predicted that by 2000, sophisticated consumers will be using home computers, two-way television and other products of the "telematics revolution" to receive health care information and submit their own health data for inclusion in large consumer databases. A system linking thousands of consumers could provide "**prospective epidemiology**"--cataloguing the reactions of various population subgroups' to drugs.

**Globalization**, has another dimension in 4<sup>th</sup> Wave economics, which was first examined in an April 1983 Foresight Seminar. [\[link to 4/11/83 summary\]](#) Pharmaceutical R&D--like its market--is globalizing rapidly. As a result nations need to harmonize their regulations for drug development. Globalization was reexamined in a June 1996 discussion. The US pharmaceutical industry was characterized as robust and capable of leading towards a better functioning global market based on **international collaboration and harmonized regulations**. Globalization could also affect the ongoing conversation about **outcome measures**. Consumers everywhere will benefit, to the extent outcomes can be internationally defined to include quality of life and other psycho-socioeconomic measures.

**Genomics/customization** are also tied to globalization, since ethnic diversity between one country and another presents a spectrum of genetic pools from which to study differences in drug reaction. The seminars on globalization also touched on **socioeconomics**: most of the pharmaceutical marketplace is in the wealthiest countries, but most of the growth is in developing nations (a trend that has since accelerated).

By September 1989 **consumer activism** had earned a decisive voice in **regulatory reform**, leveraged by AIDS issues. Foresight speakers anticipated consumer activists will continue to press for minimal regulatory delay in new-drug approvals, but also will seek information about the drugs' clinical trials and success in the marketplace. Patients with life-threatening diseases will continue to challenge a regulatory and development philosophy that pursues greater evidence of efficacy at the expense of potentially life-saving effects. Speakers predicted **patients will become increasingly involved in the research process and scientists will be encouraged to participate in activism**. In 1990, these views were echoed by a panel of former FDA commissioners who predicted **patient activism will alter the FDA's mission**.

Such harbingers of the **4<sup>th</sup> Wave economy** will accelerate as the Baby Boomers come to dominate the nation's political and health care systems. Panelists at a November 1995 Foresight Seminar saw that the decentralization of health care to states increases the likelihood that **social values and individual preferences** will create "**smart markets**". In health care, these values will transform the power relationship between patient and provider--in many cases, reversing it. **Patient rights** will become the newest chapter in a long history of empowerment movements.

Patient empowerment will increase health, one panelist observed at the 1989 session. Studies show that empowered consumers tend to emphasize **prevention** and to seek the information they need to choose among modalities, providers and therapeutics. (One 1982 Foresight speaker argued that consumers in a "smart market" will replace the government's guarantee of a *minimum* standard of safety and efficacy with their own *optimum* standards.)

All these developments require a powerful **information technology infrastructure**, speakers noted. This infrastructure is advancing every day, of course--with profound effects on innovation and governance, as detailed below. The weakest link right now is **wiring consumers to information, health care systems, providers and each other**. In 1982 a Foresight speaker predicted the market for electronic tools for consumer health monitoring, promotion and care would be half a billion dollars per year by the late 1980s. Yet it was not until a July 1996

Foresight Seminar that it became evident that the Internet had hit a take-off point and was emerging as a major tool for patient empowerment. Strengthening this link between homes and health systems is critical since consumers are society's primary "caregivers": self-care is the dominant mode of care and will be even more so as behavior-based prevention strategies take center stage.

The role of patients and consumers is a central focus because:

- Managed care is reaching the limits of its cost-effectiveness in many ways.

Continuing health gains will have to come from another revolution--namely, a consumer-oriented system.

- The government can facilitate patient empowerment by helping ensure that "good" (valid) health information is not driven out by "bad" (inaccurate or misleading) information on the Internet or other public venues.

The government has other crucial roles to play in a networked economy--for example, guaranteeing the privacy, confidentiality and security of patient information and preventing discrimination based on health information. This point was reemphasized in a June 1997 seminar: until privacy, confidentiality and security can be ensured, the Information Age won't make its fullest contribution to health.

### **How Government Is Helping--and Hindering--Innovation**

A March 1983 seminar on brain research, one of the fastest-moving areas of research, highlighted important weaknesses in federal biomedical funding policy. [\[link to 3/15/83 summary\]](#) Federal funding typically is disbursed in three-year cycles--encouraging short-horizon studies rather than the long-term programs many scientists believe are needed. Congressional involvement introduces another concern: the tendency to "overfeed, then starve, a field of research" depending on public attention to it.

Yet government has often been crucial to jumpstarting biomedical innovation. For example, federal funding of NIH's psychopharmacology research branch helped foment the current revolution in understanding the brain. Clinical psychopharmacology, which aims to reduce drugs' side effects by determining scientifically which drugs work on whom, developed through this collaboration; it also augured the broader trends to customization and to

neuroscience's revelations about of the **mind's influence on bodily responses**, which will transform health care in the 21<sup>st</sup> century.

A seminar in November 1983 on **cost containment and biomedical research** argued more explicitly for a **systems view of biomedical innovation**. [[link to 11/10/83 summary](#)] Since **policy, economics** and **innovation** are all subsystems of the health picture, looking at any of them in the context of another precipitates deeper understanding. For example, speakers predicted that the advent of diagnostic related groups (DRGs) would spur hospitals to develop cost-reducing technologies--including **home health care technologies** that will allow hospitals to move patients out quicker. (A year and a half later this had occurred, as highlighted in a March 1985 panel discussing the ripple effects of new IV technologies for home use.)

In November 1984 one speaker brought a **systems perspective to federal funding for biomedical innovation**, eliciting a crucial insight. Policy makers need to know that new medical technologies often evolve in a **"cycle of innovation."** Early technological solutions to significant diseases tend to be expensive and partial--like the iron lung used to treat polio. But later they often turn out to be the "halfway" technologies that are replaced by a more "fully decisive" prevention or cure that drives costs back down -- viz., the polio vaccine.

Many experts now agree that the rapid rise in health care costs in the 1980s and '90s has occurred partly because technical innovations in many fields are still at an expensive "halfway" point. Technologies that now are cost drivers could be precursors of breakthrough technologies that will allow stunning savings later. In order to gather the benefits that our current biological **knowledge revolution** offers, policymakers need to understand how systems of innovation can achieve long-term health outcomes.

An enthralling session in June 1994 addressed **reforming the health system to foster innovation**. [[link to 6/9/94 transcript](#)] Knowledge revolutions are underway in numerous fields affecting health and health care, but reaping their fruits will require reorganizing within and between institutions to promote creativity and collaboration. Speakers laid out the key principles for turning any organization--academic lab, company, business, health care system--into an innovation-rich **"learning organization."** The best environment for innovation is one in which divisional boundaries are permeable to information flow, allowing **fluid exchange of ideas and information** among diverse participants. **Information technology** is a crucial facilitator.

Health care reform therefore should be premised on "innovating the system"--starting with a system-wide view that identifies and minimizes the boundaries that retard learning. These boundaries are everywhere: in Congress' committee structure, between Congress and the federal agencies, between NIH and industry, between research and development, between intellectual disciplines generally. Congress should act as the catalyst, using policy to dissolve boundaries and nourish innovation within this framework.

One important early opportunity that could be enabled by a system-level reform is for industry and the FDA to work together to speed medical innovations into the marketplace, while certifying their safety.

This vital theme was revisited in November 1995, and again in November 1997, in Foresight sessions assessing Medicare and Medicaid as "learning systems." Perhaps unsurprisingly, neither Medicare nor Medicaid received a passing grade. How can these programs, upon which so many Americans' lives depend, expect to save money, achieve health gains or improve quality without being able to learn? speakers asked in 1995. Health care, along with every other aspect of American society, is entering a "4<sup>th</sup> Wave" economy characterized in part by near-instantaneous information and knowledge exchange. Success for any element of the system--consumers, clinicians, practitioners, researchers, health care systems, payers or policy makers--will depend on constant learning. Although this ability is becoming evident in some parts of the system, Medicare and Medicaid lag woefully behind.

### **"Bio-informatics" and the Future of Pharmaceutical R&D**

IAF's first Foresight Seminar in 1978 quoted Lewis Thomas' assertion that the major human diseases "have become approachable biological puzzles, ultimately solvable." Twenty years later pharmaceutical research is on the brink of filling in large pieces of the puzzle. Information technology tools powerful enough to process the massive amounts of data in a gene sequence, or to register more than 5 million compounds in a global medical-chemistry "library," are enabling a knowledge revolution in pharmaceutical innovation. Synergies are burgeoning between formerly segregated disciplines including mathematics, the cognitive sciences, biochemistry, biophysics and bio- and chemical engineering.

This application of IT to biotechnology has been dubbed "bio-informatics." A December 1995 seminar [[link to 12/1/95 transcript](#)] presented a spellbinding snapshot of this revolution-in-

progress. The [Human Genome Project](#), which was the basis for a December, 1994 session [\[link to 12/2/94 transcript\]](#), "opens a window into a whole new paradigm [of] medical treatment," as one speaker put it. The new paradigm will mean treatments are [customized](#) to an individual's unique genetic profile rather than based on statistical norms as they have been for decades. "We have the ability to now go in at the very finest possible level and determine the exact molecular different between people," he added.

Implications of bio-informatics are broad and deep: genetically customized treatments will save enormous costs, reduce clinical failures, improve health and save lives. Treatment will move closer and closer to diagnosis itself; in fact, the distinction between treatment and diagnosis will dissolve in many cases as tools combine diagnostic and therapeutic effects (more in "The Genetics Revolution," below).

For drug development, too, the implications are profound. When animal testing was first addressed in 1982--before the advent of bio-informatics--diverse speakers from a top NIH toxicologist to a Humane Society executive found surprising agreement in a discussion about the FDA's ["LD50" toxicology standard](#). LD50, which identifies what dose of a substance will kill 50% of a population of test animals, is needlessly destructive and costly, they concurred. New models of non-animal testing would soon allow efficient and effective results without such morally troubling expenditure of life. [\[link to 11/16/82 summary\]](#)

By December 1995 scenarios for practically replacing most animal testing had become plausible. Bio-informatics is replacing in vivo (live animal) testing with [in vitro testing at the cellular/molecular levels](#)--and heralds future ["in silico" testing](#) conducted via computer simulation.

Cellular/molecular-level testing using human gene materials holds numerous advantages over animal assays; besides being more humane, cellular/molecular assays "tend to be more rapid, require small amounts of compound, and be more suitable for automation," one panelist pointed out. It's also much more efficient: until recently, pharmaceutical companies typically expected to screen 5,000 compounds to produce a viable therapeutic; today, they can "talk about doing 5 million compounds in a six-month period," said one participant, potentially producing thousands of new drugs. Animal testing eventually may be limited to cloned, genetically enhanced organisms tailor-made for a particular set of studies (see "The Genetics Revolution," below).

Thus, for the pharmaceutical industry bio-informatics betokens an era of innovation that “will surpass the golden era of the industry in the late 1940s-1950s,” as one December 1995 speaker put it. **Drug discovery and development will become integrated**, stimulating many times more innovations as well as new efficiencies. “Companies have discovered ... this process needs to be seamless, involving good communication between discovery scientists, pre-clinical development scientists and clinical scientists,” said one expert.

For policy makers, bio-informatics yields at least three important new foci that have been discussed in the Foresight Seminars:

- Questions of **government investment into bio-informatics research**;
- Balancing **protection of intellectual property rights** with appropriate **public access** to genomic and bio-informatics information; and
- Protecting the public’s rights to **privacy, confidentiality** and **freedom from genetics-based discrimination**.

Impacts of information technology on clinical trials were examined in 1989, in a look at the potential for **telemetry** (24-hour monitoring, which had just been introduced in clinical trials) and **automated data collection**. Information systems were identified as the main catalyst for change in clinical trial methodologies in the 1990s, allowing more physicians to enroll their patients and new methodologies to be considered. Speakers anticipated that the increasing availability of population data could speed the development of a cohort design for very large controlled trials at reasonable cost. Information technology would also allow **routine participation by community physicians in clinical trials**. Policy makers were encouraged to support these trends, and to support clinicians trying new models for improving clinical trials.

But by July 1997 it was clear that progress had been slow. [\[link to 7/18/97 summary\]](#) Speakers at this juncture criticized clinical trials' outdated emphasis on acute care. Most people are chronically, not acutely, ill, one speaker pointed out. Beyond FDA reform, a radical overhaul of clinical research is needed--refocusing it away from expensive randomized, controlled trials towards practice itself. **Patient self-reporting** and **practitioner involvement** can make clinical research more truly relevant to clinical practice. An infrastructure of **patient-questionnaire databases** was foreseen to be a priceless resource, speeding the arrival of **customization** and providing a clearer picture of the population as a whole (more on this in "Beyond the Medical Paradigm," below).

## Regulatory Reform

FDA regulation, of course, is a part of the system for pharmaceutical R&D. The **future of the FDA** has been addressed repeatedly by Foresight over the years. Do we really need FDA regulation, asked a 1981 panel? In “a no-FDA scenario,” consumers could rely on brands and company names for assurance of quality, safety and efficacy.

Yet other early Foresight speakers credited regulation with saving the US pharmaceutical industry from extinction. [\[link to "Highlights of the Discussion," FoP, p. 7\]](#) The thalidomide tragedy and other high-profile scandals shook public trust in the late 1950s and early 1960s; a disenchanted public was turning to **non-drug therapies such as nutritional therapy, chiropractic and homeopathy**, which had few or no side effects. The 1962 amendments to the Food, Drug and Cosmetic Act of 1938 (still in force today) gave the public a "government seal of approval" that commercial drugs met minimum standards of safety and efficacy. Without the 1962 amendments, said one panelist, there might no longer be a pharmaceutical industry in the United States. Advocates of deregulation, however well-intended, were warned to keep in mind that regulation is often a reaction to market failure.

Nonetheless, regulation's costs--financial and otherwise--were undeniably rising. As one early Foresight speaker pointed out, before 1962 an average of 50-60 new chemical entities (NCEs) were introduced each year. From 1962-1978 this number dropped precipitously to only 17 NCEs per year. By 1978 the cost of introducing a new drug had increased from an average \$1 million to \$24 million. And the average development time increased from two years in 1962 to between seven and ten years by 1978. When the cost of capital and expense of failed compounds were factored in, an NDA approved in 1978 came at an average cost of \$54 million [*Future of Pharmaceuticals*, p. 63]. A speaker at the December 11, 1989 Foresight Seminar on the Cost of Developing Medicines estimated the average cost had risen as high as \$300 million.

Actually, numerous factors besides regulation were jacking up the cost and time of development, as Foresight panelists recognized. One speaker in 1978 maintained the decline in NCEs had little to do with regulation; that it began well before the 1962 amendments and began rising again after the amendments restored public confidence in pharmaceuticals.

Nevertheless, the FDA became a lightning rod for criticism of pharmaceutical R&D--with

some justification. Demonstrably, regulation was inhibiting market entry and stifling innovation. Drug development became increasingly concentrated in large companies and within therapeutic lines that had good track records. Alternative models for reform were reviewed in November 1994. [\[link to 11/10/94 transcript\]](#) In an intriguing presentation about the options for [industry self-regulation](#), a speaker noted that self-regulation has almost overwhelming advantages when the entities being regulated have more technical expertise than their regulatory overseers. They also have greater incentive to comply with self-enforced rules, since self-regulation allows more flexible implementation and other benefits. This is even truer in [highly decentralized decision-making environments](#)--such as is likely to prevail when case-by-case [customization of therapies](#) becomes the norm. The obvious disadvantage of self-regulation is the "fox in the henhouse" problem. But speakers maintained that where self-regulation occurs, an agency typically is still needed to review the regulations but not to enforce them.

By 1995, a [systems perspective on regulatory reform](#) had spontaneously emerged among many stakeholders--among other results, casting the FDA in quite a different light. At a two-day Foresight workshop in August 1995 on "[Vision and FDA Reform](#)," it became strikingly clear that not just regulators, but all stakeholders determine how the regulatory process functions--including its high cost. [\[link to workshop report\]](#) Pharmaceutical companies were conducting an average of 64 clinical trials per new drug application, according to a contemporary study cited. Consumers meanwhile hold pharmaceutical companies to an "absolute expectation" of safety and efficacy. Congress tends to pay attention to regulatory issues only when things go wrong. And scientific innovation is spawning expensive new technologies. Clearly, "FDA-bashing" was far from a solution. All behaviors in the system need to be modified for reform to be meaningful.

A May 1996 session on the [future of regulation](#) reinforced this insight. While the time from drug discovery to market entry had lengthened overall, the interval for FDA review had shrunk. Government was becoming more efficient; industry less so. Why? According to panelists, while the pharmaceutical industry is in many ways at the leading edge of knowledge, [clinical development still relies on an old-style model of quality-safety-efficacy](#) that was specified in the 1960s but is outmoded for a 4<sup>th</sup> Wave, [bio-informatics](#) era. As one speaker put it, "the current drug development process is in many respects primitive...it's really inadequate for the development of multi-drug disease management strategies" which increasingly will define therapeutics.

The prospects for change were evident in the 1995 workshop, which revealed that diverse stakeholders, including industry representatives, consumers, patient advocates and regulators themselves, were remarkably harmonious in their goals. There was potential for partnering throughout the system: between legislators, the FDA, sponsor companies, provider organizations and patients. The desire to ensure that medical innovation makes its maximum contribution to health, and to reinvent drug regulation to enable this contribution, was widely shared.

Crucially, many leaders at the FDA also had realized by this time that the agency needs to **change its role from "gatekeeper" to "odds-maker"**. As a gatekeeper, the FDA protects the public health by stopping hazardous products, even though many people might benefit by accepting the risk from the product. As an odds-maker, the agency will expand its focus to help "risk-takers"--patients and consumers—gain information about the risk of hazard and the hope for benefit. An "FDA as odds-maker" model means the public may need to **accept higher levels of risk in new medications that can reach consumers faster** (as the 1990 panel of former commissioners had predicted--see "4<sup>th</sup> Wave Economy," above). Equally important, **the FDA then acts as an information arbiter**, helping **empower health care providers and consumers** with information so they can assess risks themselves and make informed decisions. [[link to \*Pharmaceuticals in the Year 2000\*, appendix, "Risk Taking vs. Risk Placing," p. 138](#)]

### **The Promise of Outcome Measures**

Another seminal trend set in motion by **information technology** is the move to **outcome measures**. Early in the 21<sup>st</sup> century these will become the major driver of the health care marketplace. Modalities, delivery systems, payment schemes and even individual providers will "win" in the market based on their outcomes.

Foresight speakers first addressed outcome measures' importance in March 1980, but because personal computers had not been introduced it was hard to see the centrality of this research. By 1984 a Foresight Seminar could make clear that the combination of **information technology** and **cost containment** measures would take a quantum leap into outcomes measures. A panel in July 1984 could see that data gathering and statistical analysis techniques from the social sciences could be applied to **large longitudinal databases** of patient information. This will replace crude, "broad-stroke" outcomes like morbidity and death with fine-grained measures like disability, comparative costs and iatrogenic effects. [[link to 7/30/84](#)]

## summary]

An important spinoff will be a new respect for **the predictive power of “soft” data** such as patients’ self-assessments. Indeed, when the three 1984 panelists representing widely divergent research approaches were given a thought experiment--which would yield the most accurate prognosis: blood tests and other hard measures, doctors’ evaluations or a patient’s own responses to a questionnaire?--all three selected the patient-response option. “Soft” data measuring subjective beliefs, impressions or feelings will optimally be combined with the “hard” objective measures that have been the central concern in medical research. This combination holds the best predictive power for health status.

In a subsequent look at outcomes in April 1991, speakers forecast that outcomes research will support treatment protocols that will improve quality and eliminate unnecessary costs in health care. [\[link to 4/22/91 summary\]](#) But they identified a potential “dark side”: if protocols are overly rigid, they could harm patient subpopulations and stifle **innovation** by reducing openness to new therapeutics. Health care systems will need to **balance patient rights and preferences with cost considerations and the moral dictates of society**. As an expert in technology assessment noted in a 1993 Foresight Seminar, whenever an assertion is made that an outcome is cost effective, the question always should be “from who’s point of view?” [\[link to 12/10/93 invitation\]](#). Also, as speakers on a October 1997 panel stressed, **quality is a moving target** and has to be recognized as such. It should always be linked to health outcomes, not to processes (which can become very political).

Aside from isolated trials, outcome measures remain elusive. Consumer information is not collected and processed routinely either in clinics or homes; clinical trials would need to be restructured to yield outcome measures. But although the timeframe is in question, outcomes research is likely to **radically reconfigure physician and patient behavior in the 21<sup>st</sup> century**, “doing for health care what Freud did for psychiatry,” as one 1984 panelist put it. They could, for example, make **integrative medicine** --the melding of conventional and holistic approaches-- the core of health care by demonstrating its superior outcomes. **Payment schemes would be fundamentally reshaped, too**, to capitalize on the knowledge imparted by outcome measures. To accomplish these gains, however, will require **vision and leadership**, admonished the October 1997 speakers. Absence of leadership could mean losing one of the most important health care innovations of all time: the ability to extend healthy years of life.

## The Genetics Revolution

Carl Sagan observed that about 350 million years ago animal brains first surpassed DNA in their information-processing capacity. Since that point, "much of history can be described as the gradual ... dominance of brains over genes," Sagan wrote in 1977. Today that trend is reaching a historic culmination as we learn to manipulate genes themselves.

In a June 1979 Foresight meeting addressing recombinant DNA, speakers could already see that both large pharmaceutical companies and small start-ups were entering a new scientific era that would see rapid growth. In retrospect, the "Human Genome Project" that began a decade later was beginning to take shape in these early discussions of the "conscious control of evolution" through gene replacement therapy. But these early speakers did not anticipate what are emerging as the most important health benefits of genomics: the potentials for customization, cloning and pharming.

By March 1987 genetics was on the threshold of enormous change. Although there were only seven commercialized products, hundreds of compounds, devices and technologies were in the pipeline. Foresight speakers projected a \$60 billion biotechnology marketplace by the year 2000. Genetics would transform disciplines including immunology, neurochemistry and neurobiology. The Foresight Seminar's ongoing conversation about customization gathered speed here, with a discussion of genetics' promise for creating individually tailored pharmaceuticals--although speakers acknowledged that neither the business nor the regulatory models of the day would support customization. Panelists spoke of a Human Genome Project, which technology (e.g., automated DNA sequencing using robotics) was now capable of supporting. For regulators, they predicted, this could mean learning to evaluate product safety at the molecular level. [\[link to 3/18/87 summary\]](#)

Ethical issues in genetic testing were addressed in June 1988. [\[link to 6/21/88 summary\]](#) Speakers looked forward to a time when genetic tests will identify predispositions in individuals. But it was already clear the technology was developing faster than the epidemiologic knowledge base that would ensure its wise use--that is, by helping us understand the predictive validity of tests by gauging the proportion of the population carrying specific mutations.

Genetic information (like all new information) creates new uncertainties with no easy answers. Foresight speakers in 1988 were already pointing out that continued progress in genetics threatens to significantly widen the gap in understanding between science and lay

**culture**, potentially leading to polarization over the best use of genetic discoveries. Troubling social issues, such as insurance discrimination and workplace conflicts over rights, will proliferate when genomics' effects reach the mainstream. As never before, panelists warned in 1997, **socially concerned citizens will have to monitor and grasp sophisticated technical information** if they hope to influence discussions of its use. (See more under "Cloning," below.)

By December 1994 the **Human Genome Project** was well underway. [[link to 12/2/94 transcript](#)] Genomics had already had wide-ranging effects. Since 1978, when the Foresight Seminars began, about 5,000 human genes had been identified--5% of the total human genome. This small library had spawned the world's entire **biotechnology sector**, with hundreds of companies staking their futures on translating these few genes into important therapeutics. Genetically produced insulin and human growth hormone were among the early successes.

Meanwhile the same 5,000 genes had **revolutionized traditional pharmaceutical R&D**. Drug discovery historically was accomplished by medical chemists and pharmacologists who used animal tissues for testing. By 1994, research was using more human gene materials. "It's changed the entire way we do R&D in the industry," said one scientist. (Also see "Bio-informatics and the Future of Pharmaceutical R&D," above.)

Now the paradigm is about to shift again. Soon, all 100,000 human genes will be identified. This information will yield far better understanding of diseases, and myriad new targets for therapies. Cancer, for example, will be identified as "a plethora of various genes going wrong at different stages," said one panelist in 1994.

This will have at least three profound effects for pharmaceutical R&D:

- **Research will be far more finely tailored** to the conditions under study, and far more efficient. **"Array" technologies**, for example, will embed thousands of genes on a chip and allow researchers to test an individual's tissues to see which genes are present
- Diseases result from a complex interplay of genetic, environmental and other factors; genomics will allow medicines to be **customized** to an individual's unique status.
- Treatments will move steadily upstream, from addressing late-stage problems to treating **root causes**. Diagnostics and therapeutics will gradually align in what one industry expert called the **"diagnostic-therapeutic tandem,"** catching disease much earlier--even before it manifests--when **prevention** or decisive cures can be most effective. Diagnostics will become

an armamentarium unto itself--beginning with "diagnostic monitoring" that tracks an entire constellation of markers (not single markers like today) pointing to various effects.

All of this can radically improve health and reduce health care costs. The earlier an intervention is made, the greater the likelihood of prevention or cure, the fewer the drugs that are needed, the shorter any hospital stay and the lower the chances of recurrence.

## Biotechnology's Other Offspring

Genomics' spectacular advances are the result of what some Foresight speakers have called **bio-informatics** and others term **bionic convergence**--by either name, the synergistic creation of knowledge when advanced computing technologies are applied to biotechnology. Other important spinoffs of bionic convergence include:

- **Nanotechnology**, identified by the Foresight Seminars as a vital track of innovation in December 1982 (long before most of the world had heard the term). [\[link to 12/15/82 summary\]](#) Nanotechnology is still a dream--but a powerful one. As illustrated in this session, applications will include manipulating molecules to create materials "outside the range found in nature's catalogue." In medicine, nanotechnology will enable both new therapeutics and new delivery systems. Self-assembling, molecular-scale machines might be used to repair cells, for example. Nanotechnology will be a "decisive technology" for health care--like penicillin or the smallpox vaccine--but with broader abilities. By 1997, nanotechnology was recognized as so promising that the Department of Defense had IAF forecast its potential for military medicine. [\[link to IAF web site\]](#)

- **Cloning** was a topic for a seminar in May 1997. [\[link to 5/9/97 "What's New with Ewe?" summary\]](#) One of the most urgent problems highlighted by the arrival of Dolly, the world's first cloned sheep, is not scientific but cultural: the **growing divide in understanding between the science and lay communities**. Cloning and other genetics breakthroughs will affect us all; establishing mutually useful debate about how to apply and/or control the capabilities they impart is imperative. According to one speaker, "We have a scientific culture and a humanistic culture which scarcely speak the same language.... If there is to be sound public policy in this area, it will have to be bi-cultural." For a start, policy makers and industry should support **public education** so decisions can be informed by understanding, not fear.

The most important result of cloning described in the Foresight Seminar is not the publicized questions about applying the technology to humans. Instead the application to research promises far-reaching benefits that promise both new health and wealth. **Cloned herds** bearing specific genetic traits will help us uncover the genetic basis of many human health problems. The animals can be used to test new treatments and to manufacture highly specific medicines. This may make possible huge reductions in manufacturing cost and time. Ultimately pharmaceutical development and production could migrate from today's \$100 million chemical factories to \$100,000 sheep herds. These herds may make the fast-disappearing family farm viable again.

This new form of medical agriculture, called "**pharming**", will make bioengineered animal products (such as cow's milk containing therapeutic medications) commercially viable. Plants will be genetically altered into health-enhancing "**nutraceuticals**," such as bananas that vaccinate the person who eats them. **Policies should support using such products to improve health in poorer areas of the world.** In fact, both health and wealth could be created in economies failing in the transition from an agrarian base to industrial production.

The government's role vis-à-vis genetics was another question addressed in May 1997. In the United States, federal oversight has been limited to voluntary guidelines (made less stringent in 1980). But panelists felt that, given the huge potentials for both genetic health enhancement and social ramifications, the **government should adopt explicit policies and collaborate with industry to set research priorities and assure equitable access** to these technologies and their products.

Business, meanwhile, needs to strategize about how to collaborate with the government and the public to help channel genomics' ripple effects in health and medical research, development, manufacturing and distribution.

- **Neuroscience**, another important strand of biotechnology, was addressed by Foresight in October 1996. [\[link to summary\]](#) While genetics teaches us about individuals' predispositions to disease, whether or when a predisposition is "switched on" often depends on environmental influences--something beyond genetics' power to predict. Neuroscience reveals how and when a gene's potential is triggered by internal and external influences, including not only the central nervous system but the endocrine, immune and metabolic systems as well as social and other environmental factors.

Neuroscience will lead to profound changes in health, society and the future. It will change humans' very self-conception, as well as our conception of community.

➤ Medically, neuroscience will catalyze new generations of medicines as well as **advanced diagnostic technologies** like the PET scanner, which reveals patterns of neurological firing in the brain in response to mental stimuli and could someday be applied clinically. Such discoveries could fundamentally change **the aims of health and mental health policy**. The seminar raised the question: If we realize that medicines that slow down Alzheimer's or dementia can also make healthy people smarter, does that not change the goals of mental health?

➤ Socially, psychologically and philosophically, neuroscience promises to dissolve the polarizing "nature/nurture" controversy forever. It has taught that **"human nature" comprises an extraordinarily complex, uniquely individual interplay of nature and nurture**--culminating in each of us in a brain whose potential is awesomely elastic. Learning to understand this interplay will enable new, more effective interventions for improving physical and mental health. For example, if an infant has a genetic predisposition to violence, then altering the environment may be a vital strategy. If the infant has been born into a household that is likely to "switch on" that disposition with violent punishments, we may discover there is a certain window in such an infant's life when intensive social work intervention could be uniquely helpful in preventing that outcome. Likewise, we could learn how best to stimulate people's genetic potential for learning.

Thus, the neurosciences point to a learning agenda that is not limited by nature or nurture, instead illuminating both in their intimately complementary roles in health. The "self" will no longer be as great a mystery, as enigmatic effects of the brain like learning, insanity, depression and creativity are brought into the light.

### **Beyond the Medical Paradigm**

Every policy is underpinned by implicit assumptions--usually a reflection of the larger paradigm shaping the thinking of the day, and usually invisible. [[link to \*Future of Pharmaceuticals\*, Chap 2: "Alternatives to Drug Therapy" \(but not to chap 2 appendices or summary, which are linked below\)](#)] In 1979 the Foresight Seminars explored important dimensions which the allopathic paradigm of medicine was missing. The rational, industrial,

reductionist paradigm was a legacy of Descartes that had split body and mind to approach learning only through empirical data. Consumers had started to turn away from this reductionist medical model towards alternative solutions, especially ones that incorporated nutritional and environmental factors. A “holistic health” movement was growing--presaging a new paradigm for health, one focused on prevention and wellness and incorporating behavioral, social and environmental factors.

The advent of [complementary and alternative approaches to health care](#) raised questions about the government's role as a promoter and regulator of new therapies. In February 1979, Foresight speakers suggested policy options for regulating new drugs in light of the growing popularity of holistic health. [\[link to Future of Pharmaceuticals, Chapter 2, Appendix A: Policy Options... \(p. 27\)\]](#) More important, speakers stressed that medical systems change only when society changes. Thus, [the future of health care depends on the future and values of society as a whole](#), more than on policy.

A 1998 IAF study on the future of complementary and alternative approaches in U.S. health care describes the trend of growing interest in the holistic perspective in more detail. [\[link to Ex. Summary on IAF web site\]](#)

In September 1983, a Foresight Seminar panel on coronary heart disease was one of the early public forums to address holistic approaches in a medical context. [\[link to 9/26/83 summary\]](#) Speakers argued for shifting the focus of research and funding from curing acute disease, as exemplified by NIH, to promoting health through “wellness programs.” Recommendations for a “mixed approach” to health care, combining the best of allopathic and holistic modalities, foreshadowed today’s cutting-edge concept of [integrative medicine](#).

A 1983 session on [aging](#) [\[link to 6/13/83 summary\]](#) likewise highlighted the merits of [holism](#). The notion that “standard” aging markers, like osteoarthritis or diabetes, can be postponed until the last months of life by controlling behavioral factors like diet, smoking and social relationships was embraced in one speaker's concept of “[compressing morbidity](#).” Applying a [psychosocial model of health to aging](#), he predicted, would go far to reduce society's illness burden--which is, after all, [the ultimate goal of health policy](#). At the time, this hypothesis was medical heresy. (Indeed, a leading gerontologist refused to join the panel on the grounds that it was "irresponsible" to expose Congress to such a misguided argument .) A decade later "compressing morbidity" had become conventional wisdom.

Aging was revisited in a 1984 session on the future of **drugs and the elderly**. [\[link to 10/16/84 summary\]](#) Elderly patients' drug reactions differ from those of younger people, making an early argument for greater **customization**. The session also pointed to the powerful benefits that could accrue if physicians begin using **information technology** on a wide scale to track their patients' responses--over time, yielding a priceless **longitudinal database on population variation**. (In fact, one panelist optimistically stated that no group practice physician would practice medicine without a computer within five years--a sunny prediction which, 14 years later, has yet to come true.)

By December 1997 a Foresight Seminar could describe how health gains were creating a **revolution in aging**, with far-reaching social and economic effects. Foresight speakers made three key points:

- **Demography has to learn more from biology**, since longer lives mean new patterns of health, illness and lifestyle.
- Americans of all ages face **new socioeconomic choices** as a consequence of living longer--e.g., in long-term investing, careers, insurance and lifelong learning.
- Policy makers need to see that today's **paradigm-straddling elderly** are in a difficult position--healthy, but living in a society that gives them few options either for contributing their energy and talent or for acquiring wealth.

Clearly, government programs need to adapt to changing times. Medicare and Social Security were designed for a different era and are no longer "fair." Today it might make more sense to bring taxpayers and retirees together in the same economic boat, encouraging everyone to row together; and/or to find new ways to tap the energy and wisdom of America's zesty elders.

**Prevention** earned its own seminar in December 1993, as the core of an **emerging new paradigm for health and health care reform**. Speakers pointed out that the **growth in medical knowledge** enables far more effective prevention technologies, supported by policy and paid for by health care systems. But the panel recognized that **behavior change** is the central concern of prevention. The pharmaceutical industry has already employed some of the most advanced behavior-changing methodologies as they encourage physicians to shift from less effective older drugs to more effective new ones. Such resources could also be conscientiously applied to changing consumer behavior.

## A Common Vision

IAF sought to initiate a public conversation about [shared vision for America's health care system](#) in December 1996. [\[link to 12/10/96 summary\]](#) The major trends identified herein--dramatic advances in research, deepening understanding of the factors affecting health, the rise of holistic approaches, ubiquitous networking and knowledge exchange, expansion of care into enhancing human capabilities--are converging. [A new paradigm for health and health care is emerging, predicated on prevention and health management in a global context of social and economic equity.](#)

But huge barriers are stalling these historic shifts. These include fear of change, mutual lack of trust and competing political/ideological agendas. Perhaps the absence of [a shared vision](#) stands as an even greater hurdle. Government leaders have yet to articulate a vision that can forge unity across ideological boundaries.

IAF concludes that the will and the tools do exist to define a vision for health care in the United States. The time is coming when Americans will see the need to put their fears aside and forge ahead to realize the potential for unprecedented gains in health that have become increasingly evident over the past decades.

-- End --