2001

Uncertainty and Technological Change in Medicine

Annetine Gelijns, Columbia University
Joshua Graff Zivin, Columbia University
Richard Nelson, Columbia University

Available at: http://works.bepress.com/josh_graffzivin/7/
Uncertainty and Technological Change in Medicine

Annetine C. Gelijns, Joshua Graff Zivin, Richard R. Nelson
Columbia University

At the heart of Kenneth Arrow’s landmark article on the economics of medical care is the pervasive influence of uncertainty, both in regard to the occurrence of disease and to the efficacy of treatment. These uncertainties, as Arrow contends, have led to the following distortions in the operation of health care: (1) health insurance schemes that have insulated patients and physicians from the financial implications of their medical decisions (i.e., the moral hazard argument), and (2) delegation of medical care decisions from patients to physicians because of the extreme information asymmetry between the two parties (the principal agent theory). These arguments are made with little reference to technology or technological change, issues that Arrow explores in numerous other works (1962, 1969). Yet these issues of moral hazard and agency provide a significant thrust behind technological development in medicine. In the past forty years, physicians have faced strong clinical, economic, and social incentives to adopt and use new technologies in management of disease. The insulation of patients from true medical costs through insurance has compounded these effects. The growth of insurance has led to strong, positive feedback to the R&D sector, which fueled such rapid technological change that both the quality and costs of U.S. health care bear little resemblance to those prevailing at the time of Arrow’s writing.

This essay explores the dynamics of technological change in medicine

Authorship is alphabetical and does not indicate differential contribution.

and is divided into three parts.\(^1\) First, we briefly sketch the complex institutional interplay through which medical innovation emerges. Second, we propose that innovation must be understood as a process of “cultural” learning or evolution. That cultural evolutionary process, in turn, involves the coevolution of technique and knowledge. Third, we discuss several special features of the nature and process of technological change in medicine that set it apart from other sectors of the economy. In this respect, we highlight the persistence of uncertainty and expand on Arrow’s (1963: 951) observations that “uncertainty as to the quality of the product is perhaps more intense here than in any other important commodity. Recovery from disease is as unpredictable as its incidence.” We then draw some concluding observations.

**Institutional Interplay in Medical Innovation**

Since the 1960s, the technological contours of clinical practice have undergone considerable change. One useful index of the high degree of technological change is the plethora of new drugs and devices that have been introduced: Burton Weisbrod (1991), for example, reported that approximately 35 percent of the 200 largest-selling prescription drugs are new each year. Furthermore, in 1999, the Food and Drug Administration (FDA) approved some 5,000 new and modified devices. Over the same time period, physician-innovators were pioneering new clinical procedures, whose development did not necessarily center on a particular health care product. These procedures ranged from high-tech coronary artery bypass grafting to preventive measures for changing lifestyles of high-risk population groups.

This virtual explosion in medical technology raises a central question: How did all this innovation come about? Since World War II, powerful demand- and supply-side forces have encouraged medical innovation in most industrialized nations. On the demand side, we have witnessed an ongoing expansion of health insurance, and the existence of generous insurance schemes. Recall that the creation of large federal insurance plans, that is, Medicare and Medicaid, occurred after the writing of Arrow’s seminal work on medical care. On the supply side, government funds for medical research and education increased significantly during

---

\(^1\) Note that in this article we explicitly focus on technologies for the diagnosis and treatment of disease. A discussion of information technologies and its unique characteristics is beyond the scope of this article.
these years. This expansion, in part, arose out of the wartime successes of government-sponsored research and development efforts and the resulting report entitled, “Science the Endless Frontier,” which called for federal investment in basic biomedical research. In the United States, expenditures for medical research increased fortyfold in real terms between 1940 and 1987; the budget of the National Institutes of Health (NIH) in 2001 is now over $20 billion. Moreover, currently over 50 percent of the overall federal research budget is spent in the life sciences. These trends vastly strengthened the position of two major actors in the production of medical technology: academic health centers (AHCs) and the pharmaceutical, medical device, and biotechnology industries.

Universities and their academic health centers are among the more complex institutions in modern societies. AHCs are multifunctional organizations that have a three-pronged mission: (1) they provide primary care as well as advanced specialty and tertiary care and are early adopters of the “latest” in technology; (2) they train biomedical researchers and clinicians, and, thereby, shape the distribution of skills and specialties; and (3) they conduct a wide range of biomedical research activities, ranging from laboratory-based fundamental research to population-based clinical studies. There is an inherent tension among the various missions of AHCs, but, at the same time, their high degree of research productivity may well be related to the fact that they house these three missions within one organization. In the language of economists, there may be “complementarities” between missions, where engaging in one mission makes the organization more effective in pursuing the other missions. For example, the experience derived from delivering specialty care may inspire new research directions as well as enhance physician training. These complementarities are likely to arise as a result of the AHC structure that allows for the close proximity of scientists and clinicians, which promotes mutual learning and collaborative efforts.

New medical technologies are manufactured by several industries with distinct and complex organizational characteristics. The oldest is the pharmaceutical industry, emerging in nineteenth-century Europe as an offspring of the dye and chemical industry. The pharmaceutical industry is multinational in scope and is undergoing significant consolidation. In the past few years, there have been more than a dozen major acquisitions or mergers involving world-class, research-based pharmaceutical firms, including Novartis, GlaxoSmithKline Wellcome, and Pfizer-Warner-Lambert. The pharmaceutical industry is highly competitive (not one of the companies holds more than an 8 percent share of the market) and
extremely research intensive (investing 18 percent of annual sales in R&D). The modern medical device industry is essentially a post–World War II phenomenon. In the United States, it comprises some 16,000 firms. The majority of firms are small (80 percent have less than 50 employees), but the medical device sector also contains some large multinational firms, such as Philips, Siemens, and General Electric. The device industry is also highly research intensive (investing over 12 percent of annual sales in R&D, with the most innovative firms investing up to 18 percent) (Lewin Group 2000). The biotechnology industry is the youngest addition, emerging in the past quarter century as a result of the revolution in genetics and molecular biology that began nearly half a century ago. Through continued innovation in the tools and techniques of genetic engineering, this sector has assumed an increasingly prominent role. In the United States alone, it involves numerous start-up firms, although most of the more than 2,000 firms are not currently producing products, but rather are investor-funded R&D ventures. It too is highly research intensive (investing $8 billion in R&D in 1999) and has strong university ties as well as many collaborative arrangements with pharmaceutical firms.

The common image of the university-industry interface assigns to universities the role of generating fundamental (basic) knowledge and to industry the conduct of applied research and the development of medical technology. A closer look at the ways in which medical innovation arises and spreads, however, suggests that both parties play much more complex, subtle, and wide-ranging roles than conventional wisdom maintains (Gelijns and Thier in review). If one were to be led, blindfolded, into one of the many R&D labs of the biotech industry, it would be hard to discern, upon removing the blindfold, whether one was in industry or academia. Industry performs basic research in part because the ability to learn about new scientific opportunities requires that industrial scientists be part of scientific networks and interact as peers with their academic colleagues. Moreover, universities play very important roles in the development, modification, and sometimes even in the manufacturing of technology, roles which have become more visible as a result of the Bayh-Dole Act in 1980, that gave universities strong incentives to patent federally funded research findings. Medical innovation thus thrives on extensive interactions between universities and industry, with knowledge and technology transfer occurring in both directions. In today’s knowledge-based economy, where the lines between science and technology
Technological Change as an Evolutionary Process

Scholars of technology from a wide variety of disciplines have argued that technological change proceeds through an evolutionary process (Nelson and Winter 1982). This process is evolutionary in the sense that the large advances that occur over time are not the result of a conscious process of planning and design. The uncertainty that is the focus of our discussion precludes this. Rather, it is the result of a process in which at any time a wide range of technological possibilities are being pursued to address a particular need or demand. In addition to competing with prevailing practice, these innovations are often in competition with one another as well. The technologies that ultimately prevail are determined by ex post evaluation and selection, rather than ex ante planning.

This characterization does not deny purpose and direction to the technological enterprise or the existence of sophisticated bodies of scientific knowledge that guide efforts at advancing technology. Rather, it is to highlight that inevitably there remains a fundamental uncertainty regarding what will work and what will work best. Walter Vincenti 1990, for example, expands on this notion in an illuminating study of technological innovation in aviation. He shows how various bodies of complex knowledge help guide modern aeronautical engineers in discovering the optimal design characteristics of aircraft. However, he argues that these efforts at technological problem solving almost always reach beyond the range of options that are perfectly understood and therefore are to a considerable extent “blind.” Thus, technological change in aviation, as well as other high-tech industries, often involves a combination of sophisticated science and learning through trial-and-error processes. Indeed, Arrow 1962 explored this phenomenon in one of his other seminal works, “The Economic Implications of Learning by Doing.” The presence of sophisticated scientific knowledge and learning through experience is also very strong in medicine, as we elaborate later.

This evolutionary characterization is true for the work of the individual inventor, research groups, or at the level of firms. It is also true for the collection of individuals and organizations that is working on a particular problem. In every area where rapid technological advance has been
sustained, progress has been the fruit of the work of many parties, competing with one another and also building from one another’s work. Of course, some portions of new technologies are proprietary, and portions of what is learned are kept secret, at least for a while. However, over the long run progress is dependent on the ability of researchers and inventors to freely use and further develop one another’s work.

In the modern era, every field of technology that has experienced rapid, sustained technological advance has been closely connected to a field or collection of fields of science that is dedicated to illuminating solutions to shared problems. This is strikingly the case in medicine as well as in other high-tech sectors, such as aviation, electronics, and chemical products. Increasingly, advances in scientific understanding have stimulated technological change, enabling inventive efforts to be more focused and productive. In other cases, however, technological knowledge has come about initially with very little understanding, and the “science” has then been marshaled to try to understand what is going on (Rosenberg 1982). The development and introduction of the steam engine, for instance, which has been referred to as the technological innovation on which industrial society was founded, sparked interest in the mechanical effect of heat and helped spawn the science of thermodynamics. Similarly, the invention of the transistor resulted in a tremendous expansion of solid-state research in physics. When such understanding has been gained, it has generally facilitated rapid improvement and refinement of technological products or processes. Thus in a basic sense, understanding and technique coevolve. This is very much the case in medicine.

**Medical Innovation as an Evolutionary Process**

Remarkable advances have recently occurred in the understanding of the molecular and genetic bases of disease. In fact, many of the significant medical advances introduced in recent years have resulted from these insights. Indeed, some have argued that this knowledge will allow us to develop drugs tailored to the specific needs of population subgroups and perhaps even individuals sometime in the near future. Yet, despite the enormous increase in our understanding of disease pathways and the physiological models that belay them, tremendous uncertainty remains. The pervasiveness of these informational shortcomings in the face of huge technological advances is a result of several special characteristics that uniquely define medical innovation. These characteristics include:
(1) a high degree of uncertainty that persists long after the introduction of a new medical technology, (2) complex interplay between practice and understanding, and (3) an increasingly complex selection environment. Given this reality, it seems especially appropriate to view medical innovation as an evolutionary process.2

Uncertainty

Nathan Rosenberg (1996), a scholar of technical change, has argued that innovation is a learning process that takes place over time and that a fundamental meaning of learning is the reduction of uncertainty. Economists have long understood that a central and unavoidable feature of all research activities is that they are conducted under varying conditions of uncertainty. In considering the spectrum of activities incorporated in R&D—basic research, applied research, and development—it has become common practice to emphasize the high degree of uncertainty attached to the basic research end of the spectrum in contrast with much lower levels of uncertainty in the realms of applied research and development. Indeed, the development process in medicine typically involves a lengthy process of clinical testing, which is principally geared toward the reduction of uncertainty. However, in medicine, even after new technologies have been introduced, uncertainty over their eventual uses often remains extremely high.

Elsewhere we have argued that the sources of this uncertainty are twofold: (1) the complexity of the human body and (2) the heterogeneity of the human population (Gelijns, Rosenberg, and Moskowitz 1998). For example, alpha-blockers were first tested for hypertension. At the time of their introduction, it was not known that alpha-receptors existed in the urological tract as well as in the arterial system and that, therefore, their blockade could constitute a symptomatic treatment for benign prostate disease. Initial trials, which focused on hemodynamics, did not notice its urological value. In fact, it took another twenty years to establish this. Generally speaking, the full range of information on a technology’s effectiveness cannot be expected to emerge in clinical trials that are designed to test a narrowly defined set of clinical benefits. Further, much of the additional focus in these trials is placed on identifying and eliminating complications. While the considerable testing conducted during

2. This section draws heavily on insights developed in Gelijns, Rosenberg, and Moskowitz 1998.
the development process provides invaluable information, there are inherent limits to how much can be known about a technology prior to its widespread use. It is often the case that the detection of delayed or rare adverse events requires exposure of hundreds of thousands of people and/or prolonged observation periods.

A second factor generating high uncertainty in medical innovation is the heterogeneity of the human population, which may be due to genetic, environmental, or behavioral differences. Because of it, the same technology may have wide-ranging eventual effects in treating different individuals with observationally equivalent medical conditions. Randomized controlled trials do little to minimize this uncertainty because the selection criteria often exclude, by design, many patients who might benefit from and eventually receive the intervention. A case in point is bypass surgery—only 4 to 13 percent of patients who now undergo this surgery would have qualified for the initial randomized controlled trials that established its efficacy.

The history of medical innovation, therefore, is replete with instances in which new indications have been discovered only after drugs and devices have been introduced into clinical practice. Recently, we examined the top twenty blockbuster drugs from 1993 and discovered that by 1995, 40 percent of revenues came from secondary indications (ibid.). A similar pattern exists for medical devices. Identification of these new uses is often possible only after these new technologies have spent numerous years in the hands of physicians and patients. Medical innovation involves great uncertainties that require especially heavy reliance upon information that can only be generated by extensive clinical experience.

Interplay between Practice and Understanding

The resolution or reduction of uncertainty through “applied” learning in clinical practice occurs by means of trial, error, and seeming serendipity. As such, learning-by-using experiences generate different types of knowledge. At one end of the spectrum, these experiences may generate information about shortcomings or potential new applications of a technology that require significant modifications. The evolution of technology, in this case, requires lines of communication that allow information to freely flow from practitioners back to the research enterprise. For example, the laparoscope, which was commonly used in gynecological procedures, could only be extended to orthopedic procedures after the equipment was appropriately modified with a connection to a television
camera. Complex knee surgery requires the participation of several physicians who must all be able to view the intricacies of the operation simultaneously. Only through feedback about the special needs of the orthopedic community could this technological advance take place. In other cases, information generated through clinical practice may influence future directions for basic science research.

At the other end of the spectrum, the knowledge generated in clinical practice leads to alterations in technological use that require no modifications in design. In this case, the change is simply one of indications, and the feedback between practitioners and researchers plays a less central role. A case in point is the treatment of peptic ulcer disease. The clinical observation in 1983 that some peptic ulcers were caused by a bacterium, *H. Pylori*, led to the use of antibiotics in the treatment of this disease. Similarly, bupropion, which was introduced as an antidepressant drug, was found to be quite successful as an aid in smoking-cessation programs. In general, the unexpected and anomalous findings of clinical experience often pose new questions and applications for both translational and basic biomedical research. This feedback, in turn, promotes future technological development, thus enriching the eventual payoff from the initial research.

**Selection Environment**

The number of potential technological innovations is very large in comparison with the number of those that actually “survive” the development process. These figures are even more dramatic in comparison to those that survive in the health care system. The central question of interest here is, Why do some survive while others fail? The answer is complex because various user groups have different views about what aspects of a technology are problematic or successful. These views are often derived from unique experiences and preferences and are articulated according to differential abilities to marshal power and expertise to influence the process.

Traditionally, physicians acting as agents for their patients have been considered the principal users by the developers of new technology. The experience and preferences of physicians heavily determined which technologies would be selected and accepted into practice. Judgments by the relevant medical specialty about a technology’s clinical performance also predominated in determining the direction in which improvements were sought. Over time, however, other actors—such as regulatory agencies
Food and Drug Administration. Since the thalidomide tragedy of the early 1960s and the subsequent amendments to the Food, Drug and Cosmetic Act in 1962, the role of regulatory agencies—to approve a drug before it can be marketed—has been strengthened. Regulatory schemes generally allow considerable latitude for subjective interpretation of the terms safety and effectiveness in determining the acceptable risk-benefit ratio for approval. Under social and political pressures to reduce pharmaceutical risks and owing to growing sophistication in animal toxicology and clinical research techniques, premarketing requirements for drugs have become increasingly detailed over time. In the 1970s, the U.S. government extended the mandate of the FDA to incorporate certain classes of medical devices.

Payers. There has been a rapid growth in managed care organizations and, in turn, in the use of cost containment mechanisms designed to limit the utilization of certain costly medical services. In addition, insurers are taking a more critical stance regarding the technologies that they will cover as part of a standard benefit package. Either explicitly or implicitly, cost-effectiveness criteria are taking on an increasingly important role in the technological selection process.

Patients. Patients are making a stronger independent contribution to the choice of particular technologies. Direct-to-consumer advertising and the explosion of medical information on the Internet has led to dramatic changes in the knowledge base of the general public. Further, the rapid pace of technological change has, in many cases, led to multiple treatment options for a single condition. In this context where patients are better informed and face genuine choices, patient preferences about treatment risks, costs, and benefits associated with each technology have taken on an increasingly important role in the selection process.

The interaction of these actors and their subsequent influence on technological change is itself an evolutionary process. Very little is known about the precise manner in which these feedback signals are incorporated in the activities of the research enterprise. Of course, each actor wants effective, quality-enhancing, safe, and affordable technology, but in practice these are not all achievable. The design of technology requires trade-offs across these characteristics, and agents differ in their attitudes...
regarding these trade-offs. If the preferences of payers become more prominent, an emphasis will be placed on the search for cost-reducing innovations. If, on the other hand, patient preferences become more influential, considerations regarding quality of life may become more important. Irrespective of these differences in focus across actors, concerns about uncertainty unite them. The recent renewed emphasis on clinical evaluative research can be thought of as a means to address these unified concerns.

**Concluding Observations**

At the time of Arrow’s writing it would have been impossible to predict the incredible growth of the technology sector in health care. Yet his astute focus on the interplay of uncertainty with insurance, patients, and caregivers lies at the heart of this technological evolution. Arrow writes of two major players in health care, the patient and the physician, attributing a relatively minor role to a third player, insurance. Today, we note that insurance has become a more prominent player, and a major fourth player has emerged: the medical research enterprise. These four players interact and coevolve with each other in complex ways, but uncertainty remains at the centerpiece of them all.

This essay highlights a neglected source of uncertainty, whose reduction is heavily dependent on the interplay between practice and the research enterprise. From this interplay, wide ranges of new and unexpected indications of use for existing technologies arise. However, the dynamics of clinical practice have undergone significant changes; new players have emerged that help shape utilization patterns for medical technology. In particular, payers have taken on a more prominent role in response to the spiraling costs of health care and seemingly unexplainable variations in treatment practices. Payers obviously have an important role in ensuring that health care resources are used effectively and efficiently. Yet, we must be careful not to allow payers to supplant the physician in medical decision making, and current payer policy trends, such as highly detailed coverage decisions and utilization reviews, appear to be moving in that direction. Some clinical variation is desirable when patients are heterogeneous in their preferences. Moreover, this variation, as we have argued, leads to important downstream benefits in research. In the important quest to reduce unnecessary health care costs, we should beware of inadvertently eliminating an exploratory and evaluative process that often leads to important medical advances. Of course, prac-
tice diversity should not proceed unchecked and will require a stronger emphasis on medical professionalism. Again, we find ourselves returning to the insights developed some forty years ago by Ken Arrow.

References


