

Enabling Schumpeterian Entrepreneurs in Medicine Can Speed Cures and Lengthen Lives

Arthur M. Diamond, Jr.

Department of Economics
University of Nebraska Omaha
Omaha, NE 68182-0048

(402) 554-3657

adiamond@unomaha.edu

Academic Web Site: <http://cba.unomaha.edu/faculty/adiamond/web/diahompg.htm>

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Abstract

Though some oppose longer lives, longevity is a primary good for the pursuit of credible life plans and is good for the economy by allowing more ambitious longer term plans. Demographers and economists have systematically under forecast achievable extensions of longevity. Past medical advances have been achieved by innovative medical entrepreneurs who were able to pursue their contrarian and often serendipitous insights. Centrally planned hierarchical medical institutions, and regulations based on the precautionary principle, raise substantial obstacles to these innovative entrepreneurs. By reducing these obstacles, we can achieve faster cures for diseases, and achieve faster and greater gains in longevity.

(100 words)

1. Introduction

Health care and education are two of the areas of the economy that are most important to human well-being, and yet have seen the least institutional changes over the past several decades (Bush and Baker 2014, pp. 61-62). Rigid hierarchies in both areas, restrict innovative entrepreneurship, limiting the pace and scope of innovations. In this paper, I argue that reducing the obstacles to innovative medical entrepreneurship will result in better health and longer lives.

The paper is related to a larger project in which I defend innovative entrepreneurship as making life better, providing an illustration of some of the points made in the broader project, and showing how important those points are. My method is to examine important examples of breakthrough innovations in medicine and ask what sort of people made those innovations, and what sort of conditions enabled or obstructed their innovations.

2. Longer Life Is Good

The Terminator famously said "Come with me, if you want to live!" (Terminator 2: Judgment Day, 1991). Life is a choice. You can choose death instead. Most people, most of the time, choose life. But there are examples of choosing death. Some intellectuals, such as Leon Kass (2001, p. 101 and passim) and Anthony Kronman (2007, p. 230), have argued that death is a good thing. E.g., oft-

quoted medical ethics "expert" Leon Kass is against current efforts to lengthen the human life span:

(p. D4) While an anti-aging pill may be the next big blockbuster, some ethicists believe that the all-out determination to extend life span is veined with arrogance. As appointments with death are postponed, says Dr. Leon R. Kass, former chairman of the President's Council on Bioethics, human lives may become less engaging, less meaningful, even less beautiful.

"Mortality makes life matter," Dr. Kass recently wrote. "Immortality is a kind of oblivion — like death itself."

That man's time on this planet is limited, and rightfully so, is a cultural belief deeply held by many. But whether an increasing life span affords greater opportunity to find meaning or distracts from the pursuit, the prospect has become too great a temptation to ignore — least of all, for scientists.

"It's a just big waste of talent and wisdom to have people die in their 60s and 70s," said Dr. Sinclair of Harvard. (^Mason 2006, p. D4)

In addition to philosophical concerns about the nature of the "good life," some social scientists and others worry that greater longevity will create negative externalities for society or the environment (e.g., several of the essays in ^Aaron and Schwartz 2004).

I believe that adequate answers can be given to all of these worries. But limited by space, I will only briefly give a couple of examples.

A first worry is that greater longevity will greatly increase the world population. This worry can be allayed on both empirical and theoretical grounds. Empirically, Ben Wattenberg and others have documented how increases in longevity have been

accompanied by declining birth rates (Wattenberg 2004). Theoretically, the economics of the family literature suggests that greater probability of child survival results in more investment in child quality and less investment in child quantity.

A second worry is that greater longevity will increase health care costs. Robert Fogel and others have shown that increases in longevity have come with decreases in costly disabilities (Fogel 2005a). And policy changes have been identified that can encourage cost-reducing innovations. For example, if credentialing rules were more flexible, increasingly routine medical technologies could be implemented by less-educated and lower-paid nurse practitioners and technicians, instead of by highly-educated and higher-paid physicians (Christensen, Grossman, and Hwang 2009; Bush and Baker 2014).

Against those who argue that longer life may be a problem rather than a boon, I argue that longer life, when accompanied by less disability, is good for individuals and good for the economy. Longer life is preferred by the vast majority of individuals and is good for the economy because it would permit more ambitious longer term plans.

John Rawls (1971) famously argued that primary goods were those needed to fulfil a wide range of plausible life plans. Surely one such primary good would be longer life. (Abraham Maslow (1943 and 1954) and Gary Becker (Becker and Michael 1977) had very different accounts, that still share with the Rawls account the idea that there are certain goods that are foundational to the achievement of other goods.)

One of the great economic benefits of longevity (and of the greater certainty of longevity)--it not only allows *more* projects to be accomplished, it allows a different *kind* of project to be accomplished---more ambitious longer term projects.¹

3. Longer Life Is Achievable

Extrapolating current trends, Nobel-Prize winner Robert Fogel forecast that the median life span for the current college-aged cohort will be roughly 100 years (^Fogel 2005a). One might be excused for wondering if Fogel in his old age, yielded to some misty-eyed utopian wishful thinking. But arguments and evidence can be adduced to support the plausibility of Fogel's claims. For example, in a much cited paper in *Science*, demographers Oeppen and Vaupel (^2002) have shown that past researchers (demographers and public policy experts) have systematically under-estimated the maximum life-span that would be achievable in the future. But there is nothing inevitable in this; if institutions change to slow or quicken the rate of technophysio evolution, progress in increasing the lifespan will likewise slow or quicken.

Nobel-prize winner Robert Fogel has systematically summarized the improvements in longevity and health over the last three centuries, and forecast the possibilities for the century to come, in his 2004 monograph *The Escape from Hunger and Premature Death, 1700-2100*. He also has presented some of the main messages of the book in a briefer, more accessible, and more vivid form (^2005a). In his 2005 essay he compares the health experiences of three cohorts, those born between 1835-

1845, 1920-1930, and 1980-1990. The first cohort was roughly the cohort that fought the Civil War, the second cohort was roughly the cohort that fought World War II and the third cohort was roughly the cohort of today's college-aged students. Roughly 40% of the Civil War cohort died before the age of 15, compared with roughly 11% of the World War II cohort and roughly 1% of the college-aged cohort. Fogel describes life for the Civil War cohort as being not only short, but also nasty, as compared with the World War II cohort. Even when they survived, the cohort suffered from a variety of chronic and debilitating illnesses and conditions. Of those who survived to their late 30s, more than half were disabled. Large numbers suffered and died from malaria in the South and from tuberculosis in the cities. Chronic malnutrition was common.

Many more of the World War II cohort survived to old age, and of those, “the overwhelming majority have good to excellent health, live independent lives, and are socially active” (2005a, p. 7). Fogel attributes the improvements to what he (and Dora Costa) call “technophysio evolution,” which has resulted from “a synergism between technological advances and physiological improvements” (2005a, p. 7). Some examples he emphasizes include the chlorination of water, the pasteurization of milk, and the elimination in cities of diseases spread by pulverized horse manure.

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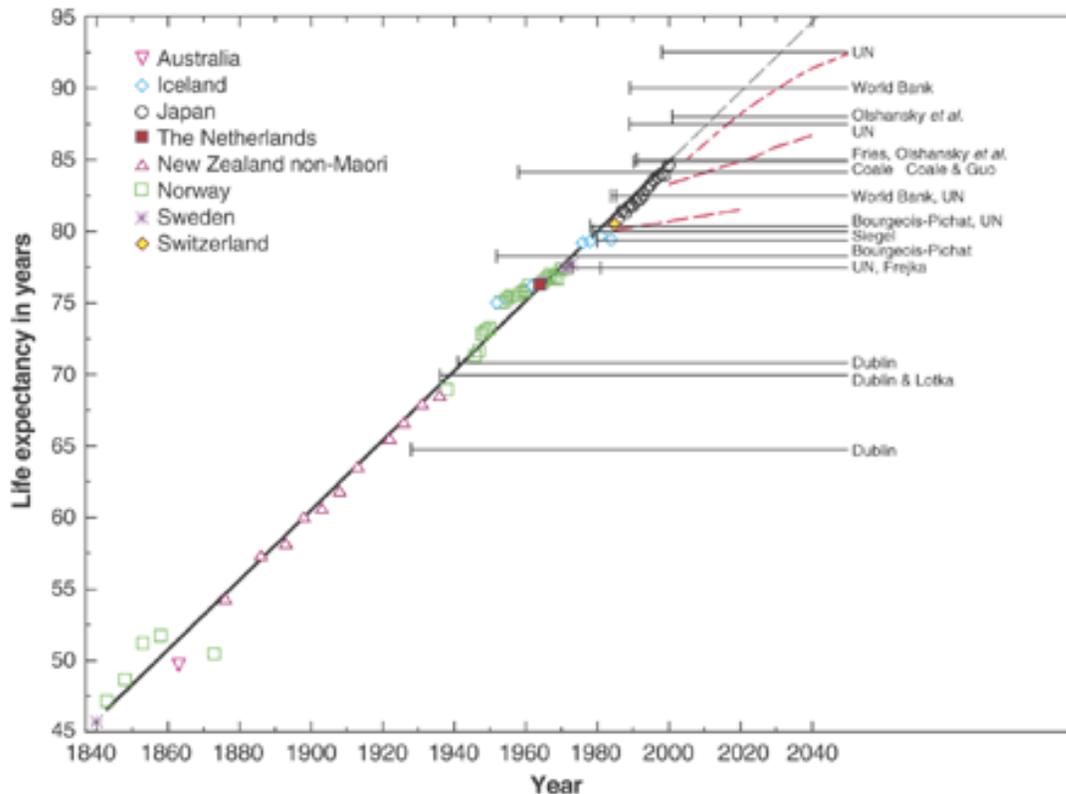


Figure 1: Oeppen and Vaupel Graph on Maximum Female Lifespan Ceilings Predicted and Achieved Lifespans. Horizontal lines indicate the ceiling predicted in a study; short vertical lines at left of each horizontal line is the year of publication of the prediction. Dashed curved lines are UN projections in 1986, 1999, and 2001 of how Japanese female life expectancies will rise over time. Source: ^Oeppen and Vaupel 2002, p. 1029.

In addition to the broad evidence of past progress, and the wrongness of past projections of ceilings to maximum lifespans, there are also several current research programs that credible scientific and health experts believe hold out the promise of significant advances in longevity and health.

The academically reputable Brookings Institute believes that substantial improvements in longevity are likely enough to be worth experts' attention to the problems that might arise from longer lifespans. In their *Coping with Methuselah* volume (^Aaron and Schwartz 2004) on the issue, the essay by Potts and Schwartz is a useful survey of many of the research programs currently underway that have the

potential to significantly lengthen life spans (^Potts and Schwartz 2004).

Two more recent research agendas that have received significant attention are those of David Sinclair and Aubrey de Grey. Sinclair is a researcher at the Harvard Medical School who has isolated a substance called resveratrol that has significantly extended the life of mice, and is believed to stimulate some of the chemical effects of near-starvation diets, which have been shown, again in mice, to significantly extend life spans (^Mason 2006; ^Pontin 2007; ^Stipp 2006). Aubrey de Grey's research has been taken seriously by reputable medical expert Sherwin Nuland (^2005). It aims to make progress in understanding the internal programming of key cells.

There is fundamental uncertainty about the probability of major longevity gains in the near future. It is a natural human characteristic (see ^Taleb's *The Black Swan* 2007) to extrapolate from our past experience. But in some areas, and medicine is one of them, extrapolating from past experience has not always turned out to be a very good predictor of the future.

4. Examples of Medical Entrepreneurship

Schumpeter saw the key role of the innovative entrepreneur as being the overcomer of resistance to innovations, which could come in a variety of forms, and from a variety of sources (^Schumpeter 1950, pp. 132-133). In this section I briefly examine a variety of cases in which major medical advances occurred, to see what obstacles were most binding on the medical innovators. The goal will be to see which

obstacles can be reduced, in order to enable medical innovators to bring us innovations more quickly and in greater number.

Histories of medical innovations in general (Meyers 2007) and medical innovations in fighting heart disease (Miller 2000) and cancer (Mukherjee 2010) in particular, show that the innovators frequently resemble Schumpeterian entrepreneurs. They are outsiders from the mainstream, who have the courage and persistence to continue to pursue their innovations in the face of sustained opposition from powerful incumbent medical institutions. Several examples will be briefly discussed.

At the start of the Boston smallpox epidemic of 1721, it is surprising that it was Cotton Mather, of Salem witch trial fame, who wrote a letter to all of the physicians of Boston, suggesting that they start the practice of inoculating the well by exposing them to smallpox matter from the infected. Mather had published a small report in the *Philosophical Transactions* of the Royal Society in London, which at the time was one of the world's most distinguished scientific associations (Coss 2016). In the same issue as his report had been an article by a Greek physician, of Italian descent, reporting his success at performing smallpox inoculations in Constantinople (Coss 2016). Mather also discovered that one of his slaves had been successfully inoculated in Africa, which led him to seek, and to find, several other slaves in Boston who had been successfully inoculated in Africa. With one exception, the entire medical community of the city rejected Mather's evidence and suggestion.

The exception was a young surgeon named Zabdiel Boylston, whose father had been a physician who had observed the success of some American Indian therapies, and so may have been more open than most to possible cures arising from non-European

sources (^Coss 2016). On June 26, 1721, Boylston inoculated his first three patients. Among them was Thomas, his youngest son. Boylston was ridiculed and threatened with bodily harm and possible imprisonment. Mather's house was fire-bombed, though the wick from the bomb fortunately fell out before the bomb could ignite. Boylston proceeded to inoculate those who sought inoculation. All those who started the procedure in good health, and without previous exposure to the smallpox, survived, suffered mild cases of smallpox, and were immune to the current and future epidemics of the disease. The handful of those who died after inoculation from Boylston, either were already in the early stages of natural infection from smallpox, or were already frail or infirm from age or other diseases. It would have been easier for Boylston to have refused inoculation to these patients, since he knew that he, and inoculation, would be blamed for their death. But he allowed the patient to decide what risk was worth taking with their life. Boylston's most vitriolic opponent was Dr. William Douglass, who viewed himself as the only true "physician" in Boston, since he was the only one who at received his medical training at a European medical school, instead of through a then-more-common apprenticeship. To Douglas, his inferior colleagues were "practitioners," not "physicians."

When Ignaz Semmelweis suggested that doctors wash their hands more often, the medical establishment ridiculed to the point where he suffered a breakdown, was put in a mental asylum, beaten, and two weeks later was dead (^Ashton 2015, pp. 72-76). Australian Barry Marshall was ridiculed by the medical establishment for suggesting that ulcers were caused by bacteria, finally convincing some of them when he drank a vial of the bacteria, and developed an ulcer (^Meyers 2007, pp. 103-113;

Klein 2013, pp. 52-56). Min Chiu Li was fired by the U.S. National Cancer Institute (NCI) for continuing to administer chemotherapy after all tumors had disappeared, but before a key marker (the hcg level) had reached zero (^Mukherjee 2010, pp. 136-138). After several years, the NCI eventually noticed that another marker had also reached zero: the number of Li's patients who suffered relapses of their cancer. Stephen Rosenberg was slowed and discouraged by the continuous efforts of the U.S. Food and Drug Administration (FDA) to block his experiments to use the body's own immune system to fight cancer (^Rosenberg and Barr 1992). As part of a private start-up, the undercredentialed Craig Venter, used a sequencing technique rejected by the medical establishment, to greatly speed up the sequencing of the genome compared to the pace of the government sequencing effort led by James Watson (^Shreeve 2004; ^Venter 2007).

Judah Folkman's research on a submarine led to his insight on developing drugs to cut off blood vessels to tumors (^Cooke 2001; ^Kounios and Beeman 2015, pp. 20 and 135-136; ^Ashton 2015, pp. 60-65). For a long time many of Folkman's papers and grant applications were rejected by the medical establishment. Eventually his angiogenesis theory was recognized as important. And his entrepreneurial perseverance and independence may have contributed to his taking a chance on hiring the undercredentialed Robert Langer, who later established an M.I.T. lab, where he made major advances at his M.I.T. lab, including polymers to aid targeted drug delivery (^Wilkinson 2015, pp. 169-170). (Examples of advances from emergency/extreme medicine can be found in ^Fong 2014.)

Sidney Farber is credited with founding chemotherapy by showing that

aminopterin could produce temporary remission in childhood leukemia. His path was difficult. He had to scrounge clinic space in a back room near the bathrooms, with his staff assigned to back rooms and stairwell shafts (Mukherjee 2010, p. 34-35). The incumbent medical cancer establishment banned pediatric interns from assisting in Farber's unit (Mukherjee 2010, p. 34).

Paul Carbone, correctly believing that chemotherapy could aid in treating breast cancer, was caught in a surreal catch-22 situation. The medical establishment would not let him practice his treatment without first conducting a substantial double-blind study. But at that time breast cancer patients were primarily the patients of surgeons, and very few surgeons were willing to enroll their patients in such a study, perhaps because the likely results of the study would be to reduce the role of surgery in breast cancer treatment (Mukherjee 2010, pp. 219-220). Such medical turf protection also occurred when Vincent DeVita, then head of the NCI, suggested that based on the evidence, post-operative radiation for breast cancer should be reduced, because it was not improving patient outcomes. A radiologist came up to him complaining that much of the radiologist's practice was post-operative breast cancer radiation, and if that was reduced, she would have to fire one of her radiotherapy technicians (DeVita and Devita-Raeburn 2015, pp. 182-183)³. Turf protection also occurred when Bernard Fisher wanted to test whether radical mastectomy actually had better outcomes than more modest lumpectomies. His research was substantially delayed because of the resistance of American surgeons to allowing their patients to participate (Mukherjee 2010, p. 200). After he finally completed his research, breast cancer surgeons almost succeeded in quashing publication of his article in which he presented evidence that

lumpectomies were just as effective as radical mastectomies (^DeVita and DeVita-Raeburn 2015, pp. 182-183; see also pp. 222-223).

Emil Freireich was so aggressive in fighting cancer that he was threatened with firing, but he proceeded anyway. He said that he wouldn't want to work at a place that wouldn't let him do all he could do to save lives (^DeVita and Devita-Raeburn 2015, pp. 55-56). Week-by-week his team (that one medical intern affectionately called the "Society of Jabbering Idiots") adjusted the dose and composition of the chemical mixture they were developing to fight childhood leukemia (^DeVita and Devita-Raeburn 2015, pp. 63-64). Most advances in the treatment of cancer have been in terms of months or a few years of longer life. But their work resulted in a rare instance where a type of cancer can frequently and routinely be cured.

Vincent DeVita was a young member of Emil Freireich's team, who soon went on to use the same approach to develop a cure for the cancer known as Hodgkin's lymphoma. DeVita later tried to change institutions to increase the pace of cancer innovation, first as head of the NCI, and eventually as physician in chief of the Memorial Sloan Kettering Cancer Center. He left the NCI in part out of frustration of fighting the bureaucracy and special interests within the government (^DeVita and Devita-Raeburn 2015, pp. 188-189). But he also experienced frustration in the quasi-governmental, non-profit hospital, where entrenched medical incumbents defended their turf against innovations that would save lives. When he was fired from that position, his boss told the hospital board: "the problem with Vince is that he wants to cure cancer" (^DeVita and DeVita-Raeburn 2015, pp. 227-228).

DeVita offers an extended critique of current medical institutions in the United

States. He points out that incentives and regulations strongly constrain physicians to follow established protocols. But the kind of entrepreneurial advance achieved by Freireich and his Society of Jabbering Idiots, was achieved through alert, extended trial and error, and could not have been achieved by following the then-mandated protocols. Freireich in part survived long enough to cure leukemia through the “umbrella” protection of the administrator Tom Frei, who had the courage and skill to sufficiently protect Freireich from the incumbent interests that want to rein him in (DeVita and DeVita-Raeburn 2015, p. 94).

Today DeVita blames a dominant research methodology that says that research proposals need to be carried out as originally approved, even when (as should and does happen) the research process leads the researcher to conclude that the procedures need to be modified (DeVita and DeVita-Raeburn 2015, pp. 196-197). This slows progress and loses lives. He also blames the FDA for restricting cancer researchers’ ability to experiment with different drug and dose combinations, in the way that led Freireich and his Society to cure leukemia (DeVita and DeVita-Raeburn 2015, pp. 8, 192 and 254). The FDA slows progress in another way, by refusing to approve drugs that slow aging, on the grounds that aging is not a disease, and that the only drugs that should be approved are those that are effective against disease (Anton 2013).

5. How to Cure Cancer

Nixon predicted in the 1960s that cancer could be eliminated within a

generation. He and others declared a "war" on cancer. The "war" analogy may be useful in arguing for a high intensity of effort and funding. But often it is taken further to suggest that the effort to cure a disease should be commanded by a centrally planned hierarchy, based on the common assumption that real war is best fought by hierarchies that centrally plan. (This common assumption has actually been disputed, in different ways, by books such as *Corps Business* (^Freedman 2000), *Start-up Nation* (^Senor and Singer 2011), and *The Generals* (^Ricks 2012).)

Using the war analogy as a guide to medical policy for curing diseases is based on the idea that a centralized hierarchy can predict the right approach, and marshal resources to achieve it, like a conquering army. But a centralized approach will only work when there is clarity on how to solve the problem, and all that remains is to marshal resources to execute the solution. But with cancer there have been a variety of approaches with varying degrees of success. I briefly discuss several of them.

Surgical excision. As surgical technologies failed to achieve their predicted success, surgeons were did not abandon their predictions, but instead practiced more and more "radical" surgeries, cutting away more and more of the cancer patient's body.

Radiation therapy. Radiation therapy achieved some short term successes, but often itself caused other cancers, and serious side effects, later in life. (Scars from radiation therapy for breast cancer, have blocked some of my mother's blood vessels, possibly contributing to her recent strokes.)

Chemotherapy. Chemotherapy often has very serious short-term side-effects, and often results in eventual relapses. Many cancers have seemed able to evolve resistance to particular chemotherapy cocktails.

Angiogenesis. A plausible approach, once predicted to cure cancer, is angiogenesis, which attempted to cut off the development of blood vessels to cancer tumors, starving them (^Ashton 2015, pp. 63-65; Kounios and Beeman 2015, pp. 135-136). It had limited success at extending the lives of some cancer patients by a few months, but has not become a widespread cure (^DeVita and DeVita-Raeburn 2015, pp. 277-280).

Immunotherapy. Immunotherapy stimulates the patient's own immune cells to fight their cancer, either by drugs such as interferon that enhance the immune system, or by increasing the number of the patient's own cancer-fighting immune cells. Successes have been limited and have been very expensive and time-consuming.

Some have predicted that cancer would not be cured by a particular medical technology, but by restricting cancer-causing agents, such as tar in cigarettes, or certain viruses. This has had some success, but many cancers have no known external agents causing them.

One assumption of all of these approaches has been that cancer is one disease that can be cured by the successful pursuit of one common best technology, although there have been major differences on just what that one common best technology is. In contrast, a current approach, one that had not been predicted by the experts from decades past, is that what we call "cancer" may turn out to be several different diseases, with different medical technologies curing different variants.

Those advances against cancer, and other diseases, that have occurred have often been the result of serendipitous events observed by alert medical outsiders (^Meyers 2007). If the path of technical progress in medicine is in fact predictable,

then centralized policies, such as President Richard Nixon's past declaration of a "war on cancer" or President Barack Obama's current establishment of a "Cancer Moonshot" are plausible (^Kolata and Harris 2016, p. A17). If, on the other hand, technical progress is not predictable, and depends on alertness to serendipitous events, then it might be wiser to follow the policy attributed to Mao to 'let a thousand flowers bloom' (^Meyers 2007, p. 173).

6. Generalizations and Implications for Policy

From prominent cases of medical breakthroughs, I highlight four generalizations, and policy implications that are suggested by these generalizations.

Breakthrough innovators are outsiders. George Gilder observes that most innovative entrepreneurs are not successful credentialed insiders, but are the unproven, uncredentialed outsiders (^1990, pp. 113-114). (E.g., Cohendet et al. 2016, where the authors describe the "underground" of innovators in Montreal.) Gilder's point is re-affirmed in the history of advances of medicine, where breakthrough medical innovations are frequently achieved by outsiders to the incumbent medical establishment. Examples of outsiders in medical innovation include Zabdiel Boylston, Emil Freireich, Jonas Salk, Barry Marshall, Vincent DeVita. These outsiders have fewer and less prestigious past credentials, and have lower funded and less prestigious current positions. Sometimes they are not even in the incumbent disciplines the experts have assigned to the problem.

These claims can be illustrated by many examples. Emil Freireich had been a street kid (^Gladwell 2013). Vincent DeVita had not attended a prestigious medical school (^DeVita and DeVita-Raeburn 2015). In the cancer realm, there are many other examples (^Mukherjee 2010). Ditto for Jonas Salk, and his first independent lab, where he did most of his research to develop the polio vaccine, was not prestigious (^Jacobs 2010). John Hill, who documented that tobacco use increases the chances of cancer, was viewed as a “buffoon” by the medical establishment (^Mukherjee 2010, pp. 239-240). Zabdiel Boylston was ridiculed by Dr. William Douglas for being a "practitioner" instead of a physician, since Boylston had received his medical knowledge through the apprenticeship method rather than by attending a European medical school, as Douglas had (^Coss 2016). Australian Barry Marshall was ridiculed by the medical establishment for pointing out evidence that ulcers were caused by bacteria; the ridicule ceased when he swallowed a vial of the bacteria, and developed an ulcer (^Meyers 2007).

This contributions of outsiders are often prominent, not just for practical therapies, but also for fundamental advances in biological knowledge. One of the most fundamental advances in our genetic understanding, was first established by the modest monk Gregor Mendel, publishing in a modest regional publication, and long ignored by the biology establishment (^Wagner 2014). Antoine van Leeuwenhoek who first identified microbes, was a cloth merchant and minor city official, not an academic (Snyder 2015, p. 1). Galileo was supported by Medici bankers, not by incumbent academics (Westfall 1985). Craig Venter was viewed as an under-credentialed

eccentric, as compared to his government-sponsored rival, the Nobel-Prize-winner James Watson (^Shreeve 2004).

Peter Thiel observes that the most important ingredient for successful entrepreneurship is not intelligence, but courage (^Thiel and Masters 2014, p. 5). Since the medical establishment protects its own turf (^Bush and Baker 2014; ^DeVita and DeVita-Raeburn 2015; ^Topol 2012), the success of the less-credentialed has frequently required persistence and courage.

Implications: we should not give too much power to the prestigiously credentialed gate-keepers. We should not marshal resources in a centrally organized plan.

Breakthrough innovations are often achieved by ‘seeing what others don’t.’

You might say that it was serendipitous that Robin Warren saw the bacteria that cause ulcers. But it is his co-author Barry Marshall who is perhaps better remembered for the discovery. It was he who drank the cocktail of the bacteria, and developed an ulcer. But if “serendipity” implies the good luck to experience a rare event, then that is not quite right for the ulcer case. The bacteria were there for others to see too, and there are published pre-Warren-and-Marshall photographs where we now can identify them, but they were not “seen” by the photographers (Marshall 2001). Daniel Kahneman has noted that we see what we expect to see. One example is what he calls “theory-induced blindness” (^2011, pp. 10, 277, 280, 286-287, and 290). “Serendipity” involves seeing the unexpected. But it involves more. It involves seeing and remembering and having the resources and courage to stick with it, while others are denying it.

When Galileo argued for his views of the heavens with the clerical and academic incumbents of his day, he invited some of them to look through his telescope to see for themselves. Some did not look (^Bucciantini et al. 2015, pp. 101-102). What was radical about Galilean science was not the individual assertions about the heavens, but that they were to be judged by one's own eyes rather than by the authority of the credentialed. The Royal Society's motto "Nullius in Verba" embraces this method: belief should be based on evidence, not on the words of authorities (^Rosen 2010, p. 68).

In the United States, the economic crisis of 2008 came as a surprise to most, including those who were credentialed as authorities in finance and economics. Since 2008, the conscientious have gone through a soul-searching quest to discover what went wrong, and why it had not been more widely expected. *The Big Short* suggests that much of the evidence was out in the open, but that the credentialed and uncredentialed refused to look; in some cases they were bullied and obfuscated not to look, by the reassurances and confusing constructs of those who were trusted to know (^Lewis 2011, p. 56).

Breakthrough medical entrepreneurs are frequently in a similar situation. They have the courage and persistence to look, sometimes in straightforward ways, sometimes in non-mainstream ways.

Implications: opportunities for longer-term projects, and multiple funding sources and self-funding, are desirable. (E.g., see: Wang, Veugelers and Stephan 2016.) We should tolerate and maybe even value, cognitive diversity. (In *The Big*

Short those who saw what was happening with the mortgage crisis, tended to be what is derogatorily called Aspergers symptoms.)

Breakthrough innovations often come from nimble trial and error. Outside of medicine, Isaacson's book on *Steve Jobs* documents (^2011) the importance of nimble trial and error in the development of his signature innovations such as the iPhone. The frequent procedure would be for him to have his team present him with four or five versions of a particular product. He would evaluate them and pick the best for further development. When he was dying of cancer, he was having trouble breathing and the medical staff tried to put an oxygen mask over his face. He stopped them, gasping that he did not like the design of the mask. He then went on to gasp that they should bring him four or five versions of the mask, and he would pick the best. In the area of cancer research, Min Chiu Li was fired from the National Cancer Institute, because he believed that elevated levels of something called hCG, indicated that cancer was still lurking at low levels not evidenced by cancer symptoms. His patients did not suffer relapses of their cancers, and he is now viewed as the first to have shown that chemotherapy can cure cancer. Vincent DeVita feels guilty that he had learned that the chemotherapy needed to be applied longer, to save his friend. But he stuck with the protocol, and his friend died. Is that good science? Is that how to treat our fellow human beings?

Implication: we should not fund or regulate on the basis of rigid adherence to pre-established protocols.

Breakthrough innovations are often achieved at great risk, sometimes even of injury and death. (A few died from Boylston's smallpox inoculations, and even from

the later and safer smallpox vaccinations. But many more lives were saved than lost. And, at least with the inoculation cases, the risks mainly were taken voluntarily.)

A growing obstacle to medical innovation has been the growing advocacy and implementation of the “Precautionary Principle,” which states that new innovations should not be allowed to proceed until it has been shown that they cause no harm (^Sunstein 2005). Perhaps one reason that medical advances have sometimes arisen in war theaters or emergency medicine, is that the Precautionary Principle is **not** implemented in those settings. For instance, Nobel-Prize winner Alexis Carrel honed his technique for re-attaching small blood vessels in the crucible of WW I⁴ (^Friedman 2007). Examples of advances from emergency/extreme medicine can be found in Fong (^2014).

Such cases show that exemption from the Precautionary Principle allows for quick and substantial experimental trial-and-error that can speed innovation. They do not provide a justification for war, but they do suggest the pursuit of other ways to counter the Precautionary Principle. These might include patients voluntarily signing waivers to accept experimental treatments, either because they know that no other treatment is available to them, or because they have made a conscious decision to accept risk for the goal of advancing medicine (^DeVita and DeVita-Raeburn 2015). If we allow extreme athletes to accept risks for the sake of “flow” or the adrenaline rush (^Kotler 2014), should we not also allow thoughtful patients to accept risks for the sake of advancing medical knowledge?

Implication: we must reject the Precautionary Principle that is increasingly behind regulation of innovations.

Other important issues, such as how to fund longevity research, should be addressed. Patents could be one source of funds (^Diamond 2015). Aubrey de Grey's suggestion of the establishment of prizes, is also worth serious consideration (^de Grey and Rae 2007). Entrepreneur Peter Thiel, co-founder of PayPal, has donated up to \$3 million in matching funds for one of de Grey's prizes to be awarded for the substantial extension of mouse lifespans (^Critser 2007). Other innovative entrepreneurs, such as John Sperling, the founder of the University of Phoenix, also provided substantial funding for longevity research (^Alexander 2004).

Substantially longer life is achievable in the short to mid-term if our policies free Schumpeterian entrepreneurs to undertake bold medical innovations (Topol ^2012, ^2015).

7. Conclusions

If we take these steps, how much will we speed up cures for cancer, and the extension of longevity? That is impossible to predict because we do not know what breakthrough innovations, innovative medical entrepreneurs will achieve. We do know, based on past experience, that the pace and number of breakthrough innovations will increase. And we do know that Vincent DeVita, who himself is in a position to know, says that if we allowed practicing physicians to act more entrepreneurially, the immediate effect would be that thousands of those who will otherwise die of cancer in the next year, will live.

Prometheus was punished for bringing fire to humanity. In reality, as in myth, the medical benefactors of humanity often have been punished. They have been ridiculed, defunded, fired, and ignored. If we reduce the obstacles to innovative entrepreneurship we will be treating our benefactors more justly. We may expect that our benefactors will respond by bringing us better health and longer lives.

Footnotes

* A distant ancestor of this paper was presented at the meetings of the Association of Private Enterprise Education (APEE) in Nassau on April 12, 2011. A much closer ancestor of this paper was presented on July 6, 2016 at the 16th Biennial Conference of the International Schumpeter Society in Montréal, Canada.

¹ This point is in the spirit of Eugen von Böhm-Bawerk's emphasis that the importance and value of capital is that it permits longer (more "roundabout"), and more productive methods and processes of production (^Böhm-Bawerk 1890).

² Fogel (^2005b) has also found that economists at the end of WW II, uniformly had overly pessimistic expectations of the prospects for economic growth. Schumpeter in his *History of Economic Analysis*, had much earlier provided a possible motive for systematic academic pessimism: the public perceives pessimism as more erudite than optimism (see ^McCraw 2007, p. 457). Matt Ridley (^2010) also has a good discussion of this issue.

³ DeVita does not specify the gender of the radiologist.

⁴ Gerhard Domagk who discovered one of the first antibiotics, became convinced of the importance of antibiotics through observing infections kill those operated on during WW I. (But the war's contribution to his eventual innovation was more due to the building of motivation than from the building of relevant experiences.) [^Hager 2007, pp. 18-20]

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