## Bioterror DA

#### Advances make bioweapon attacks increasingly probable

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In the fall of 2011, Dr. Ron Fouchier developed “[one of the most dangerous viruses you can make](https://www.nytimes.com/2012/06/22/health/h5n1-bird-flu-research-that-stoked-fears-is-published.html).” Fouchier, a Dutch virologist at the Erasmus Medical Center in Rotterdam, claimed that his team had “done something really, really stupid” and “mutated the hell out of H5N1.” At nearly the same time, Dr. Yoshihiro Kawaoka at the University of Wisconsin-Madison worked on grafting the H5N1 spike gene onto 2009 H1N1 swine flu, creating another transmissible, virulent strain. Despite only 600 human cases of the H5N1 (“bird flu”) virus in the previous two decades, the exceptionally high mortality rate — greater than 50 percent — pushed the National Science Advisory Board for Biosecurity to block the publication of both teams’ research. After a heated debate in the scientific community, the [World Health Organization deemed it safe](https://www.nytimes.com/2012/03/31/health/h5n1-bird-flu-research-is-safe-to-publish-panel-says.html) to publish the findings. While [Kawaoka’s paper](https://www.nature.com/articles/nature10831) appeared in the journal Nature, Fouchier’s original study appeared in [Science](https://science.sciencemag.org/content/336/6088/1534). Although both teams generated viruses that were not as lethal as their wild forms, critics worried that the papers would enable rogue scientists to replicate the manipulations and weaponize a more contagious virus. While some arms control experts like Graham Allison believe that “terrorists are [more likely to be able to obtain and use a biological weapon](https://preventwmd.org/report/) than a nuclear weapon,” others have dismissed bioweapons due to dissemination issues, exemplified in [failed biological attacks](https://s3.amazonaws.com/files.cnas.org/documents/CNAS_AumShinrikyo_SecondEdition_English.pdf?mtime=20160906080510).) with botulinum toxin and anthrax by the terrorist group Aum Shinrikyo. Furthermore, [studies from the U.S. Office of Technology Assessment](https://ota.fas.org/reports/9341.pdf) indicated that bioweapons could cause tens of thousands of deaths under ideal environmental conditions but would not severely undermine critical infrastructure. In 2012, Dr. Anthony Fauci, the longtime director of the National Institute of Allergy and Infectious Diseases, [argued that the benefits in vaccine advancement](https://www.newyorker.com/magazine/2012/03/12/the-deadliest-virus) from Fouchier’s research outweighed the risks of nefarious use. Today, however, Fauci is at the helm of America’s response to a global pandemic. Although the world has never experienced a mass-casualty bioweapons incident, COVID-19 has caused sustained, strategic-level harm. In the absence of a vaccine, it has [killed more than 60,000 Americans](https://news.google.com/covid19/map?hl=en-US&gl=US&ceid=US:en) and [forced over 30 million Americans into unemployment](https://www.usatoday.com/story/money/2020/04/30/unemployment-benefits-3-8-million-file-jobless-claims-amid-pandemic/3046759001/). The isolation of large segments of society has crippled the economy and traditional sources of American power: domestically, [cascading, second- and third-order effects](https://www.csfa.net/csfa/images/csfa/PDFs/The-Cascading-Effects-of-COVID-19-on-Critical-Infrastructure-Sectors-20-March-2020.pdf) plague critical national infrastructure; and internationally, power projection wanes, epitomized by the U.S. Navy’s [sidelining of the USS Theodore Roosevelt](https://breakingdefense.com/2020/03/covid-19-claims-aircraft-carrier-uss-roosevelt-as-latest-victim/). While the SARS-CoV-2 virus that causes COVID-19 is [not a bioweapon](https://www.defenseone.com/ideas/2020/03/how-counter-chinas-covid-19-disinformation-campaign/164188/), technological advances increase the possibility of a future bioweapon wreaking similar strategic havoc. Specifically, [advancements in genetic engineering](https://www.foreignaffairs.com/articles/2018-04-16/new-killer-pathogens) and delivery mechanisms may lead to the more lethal microorganisms and toxins and, consequently, the most dangerous pandemic yet. Therefore, the United States should develop a new strategy to deter and disrupt biological threats to the nation. Engineering the Next Pandemic Although a bioweapon-induced pandemic seems unlikely in the short term, preparedness for future attacks begins with understanding the possible threat. [According to the Centers for Disease Control](https://www.cdc.gov/anthrax/bioterrorism/index.html), bioweapons are intentionally released microorganisms — bacteria, viruses, fungi — or toxins, coupled with a delivery system, that cause disease or death in people, animals, or plants. In contrast to other chemical, biological, radiological, or nuclear weapons, they have distinctive dangerous characteristics: miniscule quantities — [even 10-8 milligrams per person](https://books.google.com/books?id=7ZnXZfwWwgcC&pg=PA81&lpg=PA81&dq=10-8+mg/person+bioweapons&source=bl&ots=NCw2vXqTTB&sig=ACfU3U2JiWQDEby7mIj5_XMyMfLPbNIwDw&hl=en&sa=X&ved=2ahUKEwjpgpbD9uDoAhXtGTQIHftFCU4Q6AEwAHoECA0QKQ#v=onepage&q=10-8%20mg%2Fperson%20bioweapons&f=false) — can be lethal; the symptoms can have a delayed onset; and [ensuing waves of infection](https://fas.org/biosecurity/resource/bioweapons.htm) can manifest beyond the original attack site. The Centers for Disease Control [grouped over 30 weaponizable microorganisms](https://emergency.cdc.gov/agent/agentlist-category.asp) and toxins into three threat categories based on lethality, transmissibility, and necessity for special public heath interventions. While Categories A and B cover existing high and moderate threats, respectively, Category C focuses on emerging pathogens, [like the Nipah virus and hantavirus](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC34064/), that could be engineered for mass dissemination. Historically, though, bioweapons were relatively unsophisticated and inexpensive when compared to chemical and nuclear production chains, which explains their protracted use. One of the earliest examples of biological warfare occurred over 2,000 years ago, when Assyrians [infected enemy wells](https://www.ncbi.nlm.nih.gov/pubmed/12849122) with rye ergot fungus. In 1763, the British army [presented smallpox-infested blankets](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1326439/) to Native American during the Siege of Fort Pitt. During World War II, the Japanese army [poisoned over 1,000 water wells](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1326439/) in Chinese villages to study typhus and cholera outbreaks. In 1984, the Rajneeshee cult [contaminated salad bars](https://www.cdc.gov/phlp/docs/forensic_epidemiology/Additional%20Materials/Articles/Torok%20et%20al.pdf) in Oregon restaurants with Salmonella typhimurium, causing 751 cases of enteritis. Most recently, Bacillus anthracis spores [sent in the U.S. postal system](https://warontherocks.com/2019/01/death-in-the-air-revisiting-the-2001-anthrax-mailings-and-the-amerithrax-investigation/) induced 22 cases of anthrax and five deaths in 2001, and three U.S. Senate office buildings shut down in February 2004 after the [discovery of ricin in a mailroom](https://www.emedicinehealth.com/biological_warfare/article_em.htm#facts_on_bioterrorism_and_biowarfare_today). Despite this history of usage, the challenge of disseminating the biological agent has, thus far, meant that bioweapons attacks have not produced high casualties. Bioweapons can be [delivered in numerous ways](https://www.medicalnewstoday.com/articles/321030#Bioterrorism:-Modern-concerns): direct absorption or injection into the skin, inhalation of aerosol sprays, or via consumption of food and water. The most vulnerable — and often most lethal — point of entry is the lungs, but particles must fall within a restrictive size range of [1 micrometer to 5](https://books.google.com/books?id=cA9rDwAAQBAJ&pg=PT408&dq=1%CE%BCm+5%CE%BCm+bioweapons+lungs&hl=en&newbks=1&newbks_redir=0&sa=X&ved=2ahUKEwiUxoTQ-ODoAhUEJzQIHQgsDnMQ6AEwAHoECAMQAg#v=onepage&q=1%CE%BCm%205%CE%BCm%20bioweapons%20lungs&f=false) micrometers to penetrate them. Fortunately, most biological agents [break down quickly in the environment](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2843949/) through exposure to heat, oxidation, and pollution, coupled with the roughly 50 percent loss of the microorganism during aerosol dissemination or 90 percent loss during explosive dissemination. The revolution in genetic engineering provides a path for overcoming delivery issues and escalating a biological attack into a pandemic. First, tools for analyzing and altering a microorganism’s DNA or RNA are available and affordable worldwide. The introduction of [clustered regularly interspersed short palindromic repeats](https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting) (CRISPR) — a technique that acts like scissors or a pencil to alter DNA sequences and gene functions — in 2013 [made biodefense more challenging](https://futureoflife.org/2018/10/12/genome-editing-and-the-future-of-biowarfare-a-conversation-with-dr-piers-millett/?cn-reloaded=1). Even as experienced researchers struggle to control clustered regularly interspersed short palindromic repeats and prevent unintended effects, malevolent actors with newfound access can [attempt to manipulate existing agents](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1326447/) to increase contagiousness; improve resistance to antibiotics, vaccines, and anti-virals; enhance survivability in the environment; and develop means of mass production. Infamously, Australian researchers in 2001 endeavored to induce infertility in mice by inserting the interleukin-4 gene into the mousepox virus. Instead, they [inadvertently altered the virus](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2816623/) to become more virulent and kill previously vaccinated mice, insinuating that the same could be done with smallpox for humans. Moving one step further, genetic engineering raises the possibility of creating completely new biological weapons from scratch via methods similar to the [test-tube synthesis of poliovirus](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1490301/) in 2002. It is, thankfully, hard to use this process to create agents that can kill humans. However, genetic engineering can be used to [create “non-lethal” weapons](https://www.ncbi.nlm.nih.gov/pubmed/10851144/) that, when coupled with [longer-range delivery devices](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1326447/), could kill crops and animals, and destroy materials — fuel, plastic, rubber, stealth paints, and constructional supplies — that are critical to the economy. Skeptics might question why a rational adversary would risk creating and employing bioweapons that are unpredictable and relatively hard to deliver to a target. First, some potential terrorists are “irrational” in the sense that death does not deter their service to a higher purpose; or, they may simply show a [willingness to carry out orders from a state sponsor](https://fas.org/irp/threat/an253stc.htm) or a lack of concern for public opinion. Second, future state aggressors might genetically engineer a vaccine to immunize their populations prior to unleashing a bioweapon so that the attack would only be indiscriminate within targeted nations. Third, the unprecedented harm done by COVID-19 demands a [transformation of 9/11-era priorities](https://warontherocks.com/2020/03/after-the-pandemic-america-and-national-security-in-a-changed-world/) to recognize that “preparing for domestic threats like pandemics will be far greater concerns for most Americans than threats from foreign adversaries.” Bioweapons combine the worst of these national and international threats. Ultimately, for a bioweapon attack to turn into a pandemic like the SARS-CoV-2 virus, [three initial conditions](https://www.newyorker.com/magazine/2012/03/12/the-deadliest-virus) must be met: first, the microorganism or toxin must not have an effective remedy available; second, it must be easily transmittable; and third, it must be fatal for some victims. Whereas a number of [natural-born microbes satisfied these conditions](https://www.mphonline.org/worst-pandemics-in-history/) in the past, it is possible for a genetically engineered bioweapon to have the same strategic impact in the future.

#### Decrease in patent protection forces offshoring – risks proliferation of biological threats

Finlay 10 Finlay, Brian. The Bioterror Pipeline: Big Pharma, Patent Expirations, And New Challenges To Global Security. THE FLETCHER FORUM OF WORLD AFFAIRS, 2010. Web. 8 Sept. 2021. Brian Finlay is a senior associate at the Stimson Center in Washington, DC, where he directs the Managing Across Boundaries Program. He has worked at the Brookings Institution, the Century Foundation, and Canadas Laboratory Center for Disease Control/Health Canada.

Myriad private sector actors, ranging from single-employee enterprises to major multinational pharmaceutical giants dominate today's biopharmaceutical marketplace. Privately owned companies not only develop, produce, and operate the lion's share of biological industrial equipment, but carry out the greatest share of the scientific research and development for the relevant technologies, goods, and methods of application. University and other non-profit research is often commercially-funded, and many governments around the globe have built public-private partnerships, even in some of the most sensitive areas of biotechnology, to capitalize on cost reductions and innovation. According to a recent Ernest and Young study of the industry, today more than 80 percent of biotechnology firms-and, thus, the technologies they innovate-are in the hands of the private sector." In the United States, the industry's compound annual growth rate has historically hovered around 15 percent, yielding aggregate revenues of more than $70 billion in 2008.18 With fortunes to be made, unprecedented new applications to be discovered, and practically unlimited possibilities for growth, the biopharmaceutical industry has swelled dramatically over the past decade. It is estimated that the biotech sector supports about 3.2 million jobs across the U.S. economy-a little more than one job for every 100 Americans.' 9 In Europe, publicly traded biotech companies' revenues increased 17 percent in one year, from f9.6 billion in 2007 to £11.2 billion in 2008. And although the recent global financial crisis had a negative impact, the product pipelines of European industry are growing across all phases of clinical development.20 By virtually any measure, the United States and Europe remain unmatched global hubs for biotechnological investment and innovation. For national security analysts, this reality has long provided some measure of comfort. Although the system of security assurances mandated by technologically advanced (principally Western) governments is far from a panacea against biothreats, the absence of similarly robust legal barriers in many countries raises serious international security concerns. 2 ' For instance, although the United States, Canada, the United Kingdom, Germany, and Singapore have all introduced strict regulations on pathogenic agents that may be of interest to committed bioterrorists, most countries have not. Similarly, export controls and enforcement over many sensitive technologies are often extremely lax, particularly in countries of the Global South.22 And because terrorists and proliferant states may shop for pathogens and dual-use production technologies where controls are the weakest, this uneven patchwork of regulations leaves open a significant gap in global biosecurity standards.23 It was in this porous regulatory environment that President Obama released his National Strategy for Countering Biological Threats in November 2009. His plan cited both unparalleled innovations in the life sciences and imperfections in existing control regimes as the principle motivations for a new strategy that seeks to prevent biotechnology products from being used for harmful purposes.24 However, while the President's plan presented a more forward-leaning agenda to counter the rising risk of proliferation by explicitly leveraging public health in support of international security, at its root, the strategy extends the traditional state-centric approaches to a problem that is increasingly one of the private sector. A proper approach to the issue-and its solution set-must place industry at its epicenter. In short, the Obama strategy exemplifies the continued mismatch between governments' near singular focus on regulation of the industry on the one hand, and the elusive nature of privately-driven biotech innovation on the other. Beyond encouraging the industry to adopt more stringent security standards in the public interest, governments have generally proven bereft of innovative ideas that more directly link these measures to the private sector's enlightened self-interest. This mismatch is aggravated by the reality that the biotech and pharmaceutical community stands on the brink of yet another grand transformation that will render traditional control efforts, however effective they may have proven in the past, even more anachronistic. Over the course of the coming decade, the traditional drug development strategies employed so successfully by Western biopharmaceutical companies in the past will run headlong into two realities that will fundamentally alter biopharmaceuticals' business model: continued and rampant globalization of the life ciences and big pharma's patent expiration challenges. T hese forces w ill have profound implications on the future of drug development and the internationalization of intellectual property. Further, it threatens to open a new era of biological weapons proliferation by pushing bio-innovation into regions that are ill-prepared to manage the leakage of sensitive knowledge and equipment to those intent on developing biological weapons. As globalization began to take firm root in the 1980s, virtually every industrial sector across the Western world sought to capitalize upon its underlying forces to promote efficiency and financial gain. Conceptions of tightly integrated firms whose product development was bound by national borders gave way to an internationalization of R&D, production, and supply chains. Expedited global trade, hastened by advances in everything from information to transportation technologies, allowed profit and efficiency to be maximized through outsourcing, off-shoring, supply-chaining, and other activities that drove intellectual and manufacturing capacity far beyond Western shores. The corresponding transfer of information, processes, and technology generated new local enterprises, including subsidiary operations that collaborated with or competed for global market share. This dynamic, in turn, created a virtuous cycle that accelerated the biotechnological competencies of these new markets. Soon, states that were seen to have lacked the indigenous expertise to perform complex R&D and manufacturing operations began to develop advanced, competitive industrial sectors.25 By the late 1990s, the spread of biotechnological knowledge and equipment allowed even more companies, universities, and research institutes around the world to benefit from advances in the life sciences. Today, developing countries nurture competitive industrial sectors that challenge traditional suppliers in Western Europe. According to the United Nations, many developing countries, including Argentina, Brazil, China, Cuba, Egypt, India, Mexico, and South Africa are already approaching the leading edge of biotechnological applications and have "significant" research capacity in the biosciences.26 In aggregate, this can only be seen as a significant boon to global development. As in the North, the developing South is putting these biotech capacities to work for peaceful purposes. Recent technological breakthroughs are indicative of this new geographic diversity of biological talent: the first vaccine against meningitis B was developed in Cuba; South Africa was the first country involved in HIV-C strain preventive treatment; India is the world's largest producer of the hepatitis B vaccine; and China was the first country to license gene therapy.2 7 Meanwhile, biotechnology is providing an infusion of high-skilled, stable, and lucrative jobs, and endowing struggling economies with critical growth and diversification. For the security conscious, however, the globalization of biotechnology has also expanded the locus of the bioproliferation challenge from technologically advanced countries of the North into far-flung places around the globe.28 Thus, even as humankind reaps the benefits of the biotech revolution, governments around the world are increasingly challenged by the confluence of rapidly advancing science and technology and by globalization itself. High technical hurdles to isolation and weaponization of dangerous pathogens once confined fears about the development and use of biological weapons to advanced industrial states. But now, the spread of dual-use biotechnologies means that a growing number of countries-and even terrorist groups-may gain access to the capacities necessary to develop a bioweapon. As globalization continues to open new markets and develop the technical competencies of a greater share of global population, the like- lihood that dual-use technologies will fall into the wrong hands expands exponentially-especially as biotechnologies are developed in the legaland security-conscious vacuum that pervades much of the Global South. In short, the collision of the biotechnological revolution with globalization has the very real potential to create an unmanageable proliferation nightmare. The next decade will present a new challenge to beleaguered regulators around the globe that will redefine and dramatically accelerate the challenge of bio-proliferation, further complicating the issue for the national security community. Few industries are as high-risk as drug development. Its business model-and by extension, its competitive edge-is predicated on placing winning bets on uncertain science in the face of imperfect market data. Development of a single drug, from research and discovery to distribution and delivery, can take upwards of twenty years. 29 Extraordinarily high investment costs are routine up to the point of regulatory approval." A recent study looked at sixty-eight randomly selected new drugs from ten pharmaceutical firms to estimate the average pre-tax cost of new drug development up to the point of licensing. The study found an average estimated cost of $802 million (in constant 2000 dollars) per drug.31 One false bet can easily bankrupt a small-to medium-sized biotech or pharmaceutical firm seeking to bring a drug to market. Furthermore, the historical odds of placing a successful wager have not been in the industry's favor. For every ten candidate products that enter development, only one will achieve product registration and enter the drug market. Even fewer will become "blockbusters" that earn a significant return for the innovator company. In 2007, for instance, American pharmaceutical giant Pfizer abandoned development of a new medication that sought to offer diabetes patients an alternative to injected insulin. The decision would ultimately cost the company $2.8 billion in sunk costs-one of the drug industry's costliest failures in history2 Even when a drug has proven itself safe and effective, companies must surmount costly regulatory hurdles and cope with high costs of production, marketing, and distribution. Until recently, these investment risks were frequently mitigated by income generated from past drug development successes. In most markets, that income was guaranteed by strict patent protections that closed the window to outside competition for a set period of time. More recently, however, the uncertainty of R&D investments has been complicated not only by the global economic downturn, but more importantly by looming patent expirations that will open many of big pharma's patent-protected drugs to generic competition. Between 2007 and 2012, more than three dozen drugs will lose patent protection, removing an estimated $67 billion from big pharma's annual sales. 33 With existing drug development pipelines unable to fill the gaps, biopharmaceutical companies are under intense pressure not only to cut costs-which would provide only temporary relief to the bottom line-but also to rapidly replenish their development pipelines. Some industry analysts have described this "perfect storm" as an "existential" moment for big pharma31 Many pharmaceutical companies have approached this challenge by accelerating and widening the outsourcing and off-shoring of both R&D and manufacturing, and by aggressively buying promising assets from small biotech companies through acquisitions and strategic alliances. Interestingly, these partnerships are less frequently inked with American or even Western-owned and-operated companies than in the past. Many pharmaceutical giants like Indiana-based Eli Lilly are turning to alliances with firms in Asia and elsewhere around the world, outsourcing key technical operations. Instead of functioning as fully integrated firms, big pharma companies have found value in networked relationships with independent small to large firms, universities, and non-profit biotechnology laboratories around the globe. 35 The net result has accelerated technology proliferation-for both beneficial and nefarious uses-far beyond the traditional hubs for biotech innovation. Pharma's increasingly desperate search to seed and ultimately acquire innovative new biotechnologies means that foreign (non-Western) markets are pulling ahead in biotech innovation. Indeed, the quantity of biotech ompanies outside the United States has grown remarkably in recent years: in Israel, the number grew from 30 in 1990 to about 160 in 2000; in Brazil, from 76 in 1993 to 354 in 2001; and remarkably, in South Korea, from one in 2000 to 23 in 2003.36 More generally, the Asia-Pacific region has emerged as one of the world's fastest-growing biotechnology hubs, with the growth of publicly traded companies handily outpacing growth in the United States and Europe over recent years.37 As fruitful partnerships lead big pharma to increasingly generate resources, technologies, and knowledge, these capacities spin off new competitor firms in a self-executing multiplier effect. With the number of facilities and highly trained individuals increasing, the likelihood of a serious biological accident or nefarious incident will similarly rise, which will be particularly risky when dual-use technologies are introduced into insufficiently regulated markets.

#### Bioweapons cause extinction – overcomes natural barriers

Barratt et al. ‘17 — Owen Cotton-Barratt et al- PhD in Pure Mathematics, Oxford, Lecturer in Mathematics at Oxford, Research Associate at the Future of Humanity Institute; (“Existential Risk: Diplomacy and Governance;” pg. 9; <https://www.fhi.ox.ac.uk/wp-content/uploads/Existential-Risks-2017-01-23.pdf>)

1.1.3 Engineered pandemics For most of human history, natural pandemics have posed the greatest risk of mass global fatalities.37 However, there are some reasons to believe that natural pandemics are very unlikely to cause human extinction. Analysis of the International Union for Conservation of Nature (IUCN) red list database has shown that of the 833 recorded plant and animal species extinctions known to have occurred since 1500, less than 4% (31 species) were ascribed to infectious disease.38 None of the mammals and amphibians on this list were globally dispersed, and other factors aside from infectious disease also contributed to their extinction. It therefore seems that our own species, which is very numerous, globally dispersed, and capable of a rational response to problems, is very unlikely to be killed off by a natural pandemic. One underlying explanation for this is that highly lethal pathogens can kill their hosts before they have a chance to spread, so there is a selective pressure for pathogens not to be highly lethal. Therefore, pathogens are likely to co-evolve with their hosts rather than kill all possible hosts.39 Recent developments in biotechnology may, however, give people the capability to design pathogens which overcome this trade-off. Some gain-of-function research has demonstrated the feasibility of altering pathogens to create strains with dangerous new features, such as vaccine-resistant smallpox40 and human-transmissible avian flu,41 with the potential to kill millions or even billions of people. For an engineered pathogen to derail humanity’s long-term future, it would probably have to have extremely high fatality rates or destroy reproductive capability (so that it killed or prevented reproduction by all or nearly all of its victims), be extremely infectious (so that it had global reach), and have delayed onset of symptoms (so that we would fail to notice the problem and mount a response in time).42 Making such a pathogen would be close to impossible at present. However, the cost of the technology is falling rapidly,43 and adequate expertise and modern laboratories are becoming more available. Consequently, states and perhaps even terrorist groups could eventually gain the capacity to create pathogens which could deliberately or accidentally cause an existential catastrophe.

## AMR DA

#### AMR research hanging by a thread – reliant on a few companies

Al Jazeera 20 "Pharma Firms Not Making Enough Progress Against Superbugs: Report." Aljazeera.com. N.p., 2020. Web. 27 Aug. 2021.

Drug companies are not making progress against the spread of antibiotic resistance at a scale and speed great enough to tackle the global health threat posed by superbugs, a key benchmark analysis found on Tuesday. The findings of a second [Antimicrobial Resistance (AMR) Benchmark report](https://accesstomedicinefoundation.org/amr-benchmark) by the Access to Medicine Foundation showed that while a few pharmaceutical companies are expanding their efforts, change is not happening at the scale needed to radically impact the problem. Antibiotic and antifungal resistance is estimated to kill 35,900 people in the [United States](https://www.aljazeera.com/topics/country/united-states.html) alone each year. In the European Union and European Economic Area, data show that antimicrobial resistance accounts for at least 17 percent of infections and leads to 33,000 deaths each year. In India, drug resistance exceeds 70 percent for many widespread bacteria, the AMF report said. Compared with 2018, the pipeline of new drugs in development to combat bacterial and fungal infections remains small, with only 51 potential treatments in late-stage clinical trials, the 2020 report found. And only a handful more clinical-stage antibiotics are being developed with integral plans to make them available to those who need them most. “This second benchmark provides a reality check,” said Jayasree Iyer, executive director of AMF. “The progress we see is being overshadowed by our increasing reliance on just a handful of companies.” Drug resistance is driven by the misuse and overuse of antibiotics and other antimicrobials, which encourages bacteria to evolve to survive by finding new ways to beat the medicines. But the low profitability of antibiotics means that only a dwindling number of pharmaceutical companies still invest in developing and manufacturing them. The 2020 AMR Benchmark report said that since 2018, two more companies – Novartis International AG and Sanofi SA – have retreated from new antibiotics research and development, while two more have filed for bankruptcy. Tim Jinks, a specialist in drug resistance at the Wellcome Trust global [health](https://www.aljazeera.com/topics/subjects/healthcare.html) foundation, said the findings pointed to a “tipping point in the manufacturing of new antibiotics – with progress hanging by a thread”. “Drug-resistant infections are one of the greatest global public health threats of our time,” he said. “The pace of change does not match the scale of the challenge.” The report identified three drug companies – GlaxoSmithKline, Entasis Therapeutics and Cipla – as leaders in antimicrobial research and development. It also said they were “followed closely by a few strong performers”, including Pfizer and Johnson & Johnson. Iyer warned, however, that the world should not take these firms’ commitment for granted. The AMR Benchmark measures 30 companies with interests in the anti-infectives market, including multinational pharma companies, biotechnology firms, and generics makers.

#### AMR research on the brink – any reduction in IP forces less research

Plackett 20 Plackett, Benjamin. "Why Big Pharma Has Abandoned Antibiotics." Nature.com. N.p., 2020. Web. 26 Aug. 2021. Benjamin Plackett is a freelance writer in London.

When scientists, public-health bodies and governments around the world warn that antimicrobial resistance is the next great health crisis, they have good reason. Since the 1960s, bacteria and other microorganisms have become increasingly resistant to antimicrobial drugs, leading to more and more people dying. Drug-resistant diseases kill around 700,000 people each year, but a United Nations interagency group on antimicrobial resistance estimates that this could swell to 10 million a year by 2050 if no action is taken. This is more than the number of people who currently die from cancer worldwide every year. Despite the clear need for more antimicrobial agents, such drugs have not been forthcoming. Fewer new antibiotics are reaching the market; the last entirely original class of antibiotic was discovered in the late 1980s. One reason is that discovering and bringing antibiotics to market is often not profitable for pharmaceutical companies. A 2017 estimate puts the cost of developing an antibiotic at around US$1.5 billion[1](https://www.nature.com/articles/d41586-020-02884-3#ref-CR1). Meanwhile, industry analysts estimate that the average revenue generated from an antibiotic’s sale is roughly $46 million per year. “That’s tiny and nowhere near the amount needed to justify the investment,” says Kasim Kutay, chief executive of Novo Holdings, an investment firm in Hellerup, Denmark, focused on the life sciences. As a result, many large pharmaceutical firms have dropped out of the market in favour of pursuing profitable lines of drug development, such as cancer treatments (see ‘Low approval ratings’). In their place, smaller companies and funding bodies are striving to fill the gap. But fixing the economics of drug development might take a radical approach. Deaths caused by infectious diseases have fallen by 70% since antibiotics were introduced on a large scale in the 1940s, according to the UK biomedical funding charity Wellcome. This could be in jeopardy unless the economics of the market can be re-imagined. A 2017 review found that in one strain of bacteria, the prevalence of resistance to levofloxacin, an antibiotic used to treat a wide variety of infections, grew from roughly 2% before 2000 to 27% between 2011 and 2015 in the Asia Pacific region[2](https://www.nature.com/articles/d41586-020-02884-3#ref-CR2). “The problem is terrible and not too far away,” warns Asad Khan, a microbiologist at the Aligarh Muslim University in Aligarh, northern India. “I think many governments and funding bodies haven’t yet understood the scale of what we’re facing.” Many economists have also been slow to act. One review found that only 55 of more than 1 million peer-reviewed economics articles in the EconLit database were related to antimicrobial resistance[3](https://www.nature.com/articles/d41586-020-02884-3#ref-CR3). Papers on climate change, by comparison, totalled around 16,000. Yet economics has a significant role in the lack of antibiotics coming to market. Any type of pharmaceutical development is an expensive process, but for antibiotics it is especially hard. One issue is that the cost–benefit ratio — how much profit will result from an investment — is much less favourable than for other drugs. “Profit is basically volume multiplied by price,” says Richard Smith, a health economist at the University of Exeter, UK. For antibiotics, neither element is high enough to offset the cost of development. Prices are low because in many countries government agencies have a role in assessing the price, not the manufacturer alone. In the United Kingdom, for instance, the National Institute for Health and Care Excellence (NICE) assesses the clinical strength and cost-effectiveness of new medicines. “The point of NICE is to try and keep drug prices low,” says Smith. Other countries have a similar set-up. For a new drug to be included in the Australian government’s Pharmaceutical Benefits Scheme, which subsidizes the cost of medication, it has to be approved by a committee of health professionals and economists, who evaluate whether the drug offers value for money. Canada also regulates the price of patented medicines to keep prices low. At the same time, physicians avoid prescribing new antibiotics to help delay the development of bacterial resistance. This means that governments and health agencies are even less likely to accept a premium for new antibiotics, says Smith. “Antibiotics used to be profitable back in the 1960s when you didn’t have to consider resistance as an issue,” he says. Typically, a drug is granted a 5–10 year exclusivity period, during which the manufacturer is shielded from competition from any generic versions that might be developed. But even this isn’t enough to recoup the vast development costs. Once the exclusivity period expires, other drug makers can enter the market — and, without the need to account for large research expenditures, they can drop the price. According to a policy review[4](https://www.nature.com/articles/d41586-020-02884-3#ref-CR4) by the UK Office of Health Economics, the relatively short treatment cycle for a course of antibiotics reduces the volume that can be sold. Antibiotics are typically prescribed for a couple of weeks, whereas therapies for chronic diseases are taken for months or even years. In a 2003 study, researchers found that an injectable antibiotic is roughly three times less profitable than are drugs used for the treatment of cancer[5](https://www.nature.com/articles/d41586-020-02884-3#ref-CR5). Drugs for musculoskeletal conditions, meanwhile, are around 11 times more lucrative.

#### Increase use of generics leads to increase resistance of microbes

Eban 19 [Katherine Eban, an investigative journalist and the author of the New York Times bestseller Bottle of Lies: The Inside Story of the Generic Drug Boom, May 17 2019, “How Some Generic Drugs Could Do More Harm Than Good,” Time Magazine, <https://time.com/5590602/generic-drugs-quality-risk/> ]

For the 16 years that Dr. Brian Westerberg, a Canadian surgeon, worked volunteer missions at the Mulago National Referral Hospital in Kampala, Uganda, scarcity was the norm. The patients usually exceeded the 1,500 allotted beds. Running water was once cut off when the debt-ridden hospital was unable to pay its bills. On some of his early trips, Westerberg even brought over drugs from Canada in order to treat patients. But as low-cost generics made in India and China became widely available through Uganda’s government and international aid agencies in the early 2000s, it seemed at first like the supply issue had been solved. Then on February 7, 2013, Westerberg examined a feverish 13-year-old boy who had fluid oozing from an ear infection. He suspected bacterial meningitis, though he couldn’t confirm his diagnosis because the CT scanner had broken down. The boy was given intravenous ceftriaxone, a broad-spectrum antibiotic that Westerberg believed would cure him. But after four days of treatment, the ear had only gotten worse. As Westerberg prepared to operate, the boy had a seizure. With the CT scanner working again, Westerberg ordered an urgent scan, which revealed small abscesses in the boy’s skull, likely caused by the infection. When a hospital neurosurgeon looked at the images and confidently declared that surgery was unnecessary and the swelling and abscesses would abate with effective antibiotic treatment, Westerberg was confused. They had already treated the boy with intravenous ceftriaxone, which hadn’t worked. His confusion deepened when his colleague suggested that they switch the boy to a more expensive version of the drug. Why swap one ceftriaxone for another? Most people assume that a drug is a drug — that Lipitor, for example, or a generic version, is the same anywhere in the world, so long as it’s made by a reputable drug company that has been inspected and approved by regulators. That, at least, is the logic that has driven the global generic-drug revolution: that drug companies in countries like India and China can make low-cost, high-quality drugs for markets around the world. These companies have been hailed as public-health heroes and global equalizers, by making the same cures available to the wealthy and impoverished. PAID PARTNER CONTENT 6 Prepaid Funeral Plan Myths: Learn More BY DIGNITY MEMORIAL But many of the generic drug companies that Americans and Africans alike depend on, which I spent a decade investigating, hold a dark secret: they routinely adjust their manufacturing standards depending on the country buying their drugs, a practice that could endanger not just those who take the lower-quality medicine but the population at large. These companies send their highest-quality drugs to markets with the most vigilant regulators, such as the U.S. and the European Union. They send their worst drugs — made with lower-quality ingredients and less scrupulous testing — to countries with the weakest review. The U.S. drug supply is not immune to quality crises — over the last ten months, dozens of versions of the generic blood pressure drugs valsartan, losartan and irbesartan have been subject to sweeping recalls. The active ingredients in some, manufactured in China, contained a probable carcinogen once used in the production of liquid rocket fuel. But the patients who suffer most are those in so-called “R.O.W. markets” — the generic-drug industry’s shorthand for “Rest of World.” In swaths of Africa, Southeast Asia and other areas with developing markets, some generic drug companies have made a cold calculation: they can sell their cheapest drugs where they will be least likely to get caught. In Africa, for instance, pharmaceuticals used to come from more developed countries, through donations and small purchases. So when Indian drug reps offering cheap generics started arriving, the initial feeling was positive. But Africa soon became an avenue “to send anything at all,” said Kwabena Ofori-Kwakye, associate professor in the pharmaceutics department at the Kwame Nkrumah University of Science and Technology in Kumasi, Ghana. The poor quality has affected every type of medication, and the adverse impact on health has been “astronomical,” he told me. Multiple doctors I spoke to throughout the continent said they have adjusted their medical treatment in response, sometimes tripling recommended doses to produce a therapeutic effect. Dr. Gordon Donnir, former head of the psychiatry department at the Komfo Anokye teaching hospital in Kumasi, treats middle-class Ghanaians in his private practice and says that almost all the drugs his patients take are substandard, leading him to increase his patients’ doses significantly. While his European colleagues typically prescribe 2.5 milligrams of haloperidol (a generic form of Haldol) several times a day to treat psychosis, he’ll prescribe 10 milligrams, also several times a day, because he knows the 2.5 milligrams “won’t do anything.” Donnir once gave ten times the typical dose of generic Diazepam, an anti-anxiety drug, to a 15-year-old boy, an amount that should have knocked him out. The patient was “still smiling,” Donnir said. Many hospitals also keep a stash of what they call “fancy” drugs — either brand-name drugs or higher-quality generics — to treat patients who should have recovered after a round of treatment but didn’t. Confronted with the ailing boy at the Mulago hospital, Westerberg’s colleagues swapped in the more expensive version of ceftriaxone and added more drugs to the treatment plan. But it was too late. In the second week of his treatment, the boy was declared brain dead. Westerberg’s Ugandan colleagues were not surprised. Their patients frequently died when treated with drugs that should have saved them. And there were not enough “fancy” drugs to go around, making every day an exercise in pharmaceutical triage. It was also hard to keep track of which generics were safe and which were not to be trusted, said one doctor in Western Uganda: “It’s anesthesia today, ceftriaxone tomorrow, amoxicillin the next day.” Westerberg, shaken by his newfound knowledge, flew back to Canada and teamed up with a Canadian respiratory therapist, Jason Nickerson, who’d had similar experiences with bad medicine in Ghana. They decided to test the chemical properties of the generic ceftriaxone that had been implicated in the Ugandan boy’s death. Another of Westerberg’s colleagues brought him a vial from the Mulago hospital pharmacy. The drug had been made by a manufacturer in northern China, which also exported to the U.S. and other developed markets. But when they tested the ceftriaxone at Nickerson’s lab, it contained less than half the active drug ingredient stated on the label. At such low concentration, the drug was basically useless, Nickerson said. He and Westerberg published a case report in the CDC’s Morbidity and Mortality Weekly Report. Although they couldn’t say with certainty that the boy had died due to substandard ceftriaxone, their report offered compelling evidence that he had. Some companies claim that, while their drugs are all high-quality, there may be some variance in how they are produced because regulations differ from market to market. But Patrick H. Lukulay, former vice president of global health impact programs for USP (formerly U.S. Pharmacopeia), one of the world’s top pharmaceutical standard-setting organizations, calls that argument “totally garbage.” For any given drug, he says, “There’s only one standard, and that standard was set by the originator,” meaning the brand-name company that developed the product. It’s not just those in developing markets who should be alarmed. Often, substandard drugs do not contain enough active ingredient to effectively cure sick patients. But they do contain enough to kill off the weakest microbes while leaving the strongest intact. These surviving microbes go on to reproduce, creating a new generation of pathogens capable of resisting even fully potent, properly made medicine. In 2011, during an outbreak of drug-resistant malaria on the Thailand-Cambodia border, USP’s chief of party in Indonesia Christopher Raymond strongly suspected substandard drugs as a culprit. Treating patients with drugs that contain a little bit of active ingredient, as he put it, is like “putting out fire with gasoline.” USP is so concerned about this issue that in 2017 it launched a center called the Quality Institute, which funds research into the link between drug quality and resistance. In late 2018, Boston University biomedical engineering professor Muhammad Zaman studied a commonly used antibiotic called rifampicin that, if not manufactured properly, yields a chemical substance called rifampicin quinone when it degrades. When Zaman subjected bacteria to this substance, it developed mutations that helped it resist rifampicin and other similar drugs. Zaman concluded from his work that substandard drugs are an “independent pillar” in the global menace of drug resistance. The low cost of generic drugs makes them essential to global public health. But if those bargain drugs are of low quality, they do more harm than good. For years, politicians, regulators and aid workers have focused on ensuring access to these drugs. Going forward, they must place equal value on quality, through an exacting program of unannounced inspections, routine testing of drugs already on the market and strict legal enforcement against companies manufacturing subpar medicine. One model is the airline industry, which through international laws and treaties, has established clear global standards for aviation safety. Without something similar for safe and effective drugs, the twin forces of subpar medicine and growing drug resistance will be so destructive that developed countries won’t be able to ignore them. As Elizabeth Pisani, an epidemiologist who has studied drug quality in Indonesia, put it, “The fact is, pathogens know no borders.”An increase in poverty increases likelihood of civil war, terrorism, and instability that destabilizes on a global scale

#### AMR increases poverty substantially in developing countries

Dadgostar 19 Dadgostar, Porooshat. “Antimicrobial Resistance: Implications and Costs.” Infection and drug resistance vol. 12 3903-3910. 20 Dec. 2019, doi:10.2147/IDR.S234610 Porooshat Dadgostar is a Ph.D. student in Health Services Research and Policy at University of Rochester

The literature review findings indicate that the cost of AMR across the globe is extremely high and different in each country.[66](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0066),[72](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0072) The CDC estimated that the cost of antimicrobial resistance is $55 billion every year in the United States, $20 billion for health care and about $35 billion for loss of productivity.[3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0003),[8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0008) Recent research by the World Bank indicates that antimicrobial resistance would elevate the rate of poverty and impact low-income countries compared to the rest of the world.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Studies show that annual global GDP could decrease by approximately 1% and there would be a 5–7% loss in developing countries by 2050.[71](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0071),[72](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0072) This percentage ultimately translates into $100-210 trillion.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028),[66](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0066) Multidrug- resistant TB alone could cost the world $16.7 trillion by 2050.[73](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0073),[74](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0074) Furthermore, due to AMR, the gap between the developing countries and the developed countries will become more pronounced; as a result, inequity will substantially increase.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Most of the people who are pushed into extreme poverty as a result of AMR will be specifically from low-income countries.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) This highlights the fact that the underprivileged population of the world will eventually be affected the most because these countries are more contingent on labor income which will be reduced if there is a high prevalence of infectious diseases.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) In addition to the direct impact on GDP, antimicrobial resistance has a major influence on labor through the loss of productivity caused by sickness and premature death.[68](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0068) Deaths because of antimicrobial resistance decrease the workforce, which in turn negatively impacts the size of the population as well as the quality of the country’s human capital.[68](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0068),[75](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0075) Taylor et al have created a theoretical model in order to estimate the economic impacts of AMR on the labor force in the future. In their work, they have compared a baseline (absence of AMR) with the current trend in AMR as well as worse alternatives that might happen if appropriate measures are not taken. According to their results, if there is no change in the current pattern of AMR, in ten years, the world working-age population will decrease by two years. This change will be more pronounced in Eurasia compared to the rest of the world.[75](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0075) In addition, in terms of annual GDP loss, if there is no change in the trends of AMR, the world will lose about $28 billion in ten years. According to this model, with a $20 billion loss in GDP, the European Union and The Organization for Economic Co-operation and Development (OECD) countries stand to lose more than the rest of the world.[75](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0075) The global trade will also be heavily affected by antimicrobial resistance if the continuous trends in AMR still persist.[32](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0032) The World Bank report demonstrates that global exports might decrease significantly by 2050 due to the effects of antimicrobial resistance on labor-intensive sectors.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Thus, it can be concluded that the undesirable outcomes of AMR on the global economy are projected to be even more severe than the global financial recession due to its long-term impacts on the economy.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Impacts of AMR on livestock output will also be significant.[30](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0030) Just like humans, the effect of AMR on animals will be due to mortality and morbidity. The increase in resistance to antimicrobials will make treatments on animals ineffective and cause the infections to become more severe.[26](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0026) Ultimately, this will lead to decreased production and trade of livestock, resulting in elevated prices of protein due to the decrease in protein sources such as milk, egg, and meat.[26](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0026),[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Shortage of protein will be a major concern, considering that the demand for animal proteins is on the rise worldwide.[36](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0036) According to the World Bank, AMR will have drastic impacts on livestock production in low-middle income countries.[32](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0032) Estimates have indicated that if the persistent trends in AMR do not slow down, there will be an 11% loss in livestock production by 2050.[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0028) Such a substantial loss in animal production will lead to a decline in income generation which will exacerbate the economic situation.[26](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6929930/#CIT0026)

AMR

#### Increase in poverty threatens global stability – terrorism, civil war, and disease

Patrick 09 Patrick, Stewart. Too Poor For Peace? Global Poverty, Conflict, And Security In The 21St Century Reviewed By Stewart Patrick. 2009. Web. 28 Aug. 2021 tewart Patrick is a senior fellow and director of the Program on International Institutions and Global Governance at the Council on Foreign Relations (CFR). Prior to joining CFR, he directed the Center for Global Development’s project on Weak States and U.S. National Security. His most recent book is The Best Laid Plans: The Origins of American Multilateralism and the Dawn of the Cold War (Rowman & Littlefield, 2008).

Five years ago, the World Bank published Breaking the Conflict Trap, a groundbreaking book identifying intrastate war as a critical barrier to poverty eradication in a large cohort of developing countries (Collier et al., 2003). Too Poor for Peace? Global Poverty, Conflict, and Security in the 21st Century picks up where Paul Collier and his colleagues left off, this time focusing on the impact of poverty on violent conflict. The book’s broad thesis is that alleviating poverty in the 21st century is not only a moral but also a security imperative. “Extreme poverty literally kills,” write editors Lael Brainard and Derek Chollet (p. 3). This claim is true both directly—through hunger, malnutrition, and disease—and indirectly, by leaving poor countries vulnerable to domestic upheaval and war and by generating transnational threats that endanger regional and international security. At the same time, the poverty-insecurity nexus constitutes a “tangled web,” with overlapping threads of intervening variables and strands of reverse causality. Poverty and violence reinforce one another, but their specific relationship is mediated by context-specific drivers ranging from resource scarcity to weak institutions to malignant political leadership to demographic trends. Like spiders’ webs, each country is unique; there is no single route to prosperity (or penury), no single pathway to peace (or war). Drawn from an August 2006 conference sponsored by the Aspen Institute, “The Tangled Web: The Poverty-Insecurity Nexus,” this slim volume is divided into two parts.The first chapters usefully distill recent findings (including some published elsewhere by the same authors) on specific links between poverty and conflict. The later chapters review, more unevenly, the practical dilemmas confronting external actors seeking to engage poor, conflict-prone states. Throughout, the authors use refreshingly clear, jargon-free prose aimed at an educated policy audience. Among the most interesting—if controversial—chapters is Susan Rice’s examination of the negative implications of developing-country poverty for global (as opposed to human) security. (Full disclosure: Rice and I are frequent collaborators.) She makes an impassioned case that poverty breeds insecurity by undermining the capacity of states to deliver four sets of critical goods: basic physical security, legitimate governance, economic growth, and social welfare. Beyond bringing misery to their inhabitants, such poverty-induced capacity gaps produce negative “spillovers” for regional and global security, in the form of cross-border terrorism, crime, disease, and environmental degradation. She contends that in an age of global threats—from terrorists in Mali to Ebola in the Democratic Republic of the Congo—the United States cannot afford to be indifferent to poverty that weakens state capacity. Rice’s chapter raises as many questions as it answers. The world is full of weak states, of course, and not all generate negative spillovers, much less those of the same type or magnitude, which suggests that intervening mechanisms and situational variables are involved. Are states that suffer from particular types of weakness more susceptible to particular types of threats? And does a state’s vulnerability depend on whether its weak performance is a function of the political will of its governing regime, a low level of state capacity, or some combination of the two? Rice is more persuasive in showing the linkage between weak states and transnational spillovers than in demonstrating how poverty is linked to state weakness. Although she qualifies her argument by noting that “though poverty underlies state weakness” the latter is “also a consequence of other capacity deficits,” her use of the bloodless term “capacity” gives too short shrift to the role of human agency (and particularly the role of corrupt, misgoverning elites) in generating poor state performance (p. 34). The role of intervening variables is front and center in Colin Kahl’s chapter addressing the links between demography, environment, and civil strife in the developing world, based on his similarly titled book (Kahl, 2006). In recent years, the environmental security literature has been dominated by two diametrically opposed perspectives. The “neo-Malthusian” view attributes civil strife to deprivation brought about by population growth, environmental degradation, and natural resource scarcity. The alternative “resource abundance” thesis contends that an embarrassment of resource riches fuels violence, whether by creating a tempting “honey pot” for factions to fight over or by subsidizing institutional pathologies (the wellknown “resource curse”). Kahl considers this dichotomy a false one, noting that scarcity and abundance can occur simultaneously at different levels of analysis. For instance, abundance in one resource can create scarcity in another; different sorts of resources present different risks for developing countries; and the pathologies of scarcity and abundance can occur and interact with one another in the same country over time. Kahl’s distinctive contribution is to recognize that resource “scarcity” is not only a natural but also a social phenomenon, reflecting political and economic competition, and that the relationship between demographic and environmental pressures and conflict is mediated by (among other factors) the strength of the state, the nature and quality of its governing institutions, and the identity, solidarity, and power of societal groups. According to Berkeley economist Edward Miguel, “the poverty-violence link is arguably the most robust finding in the growing research literature investigating the causes of civil wars” (p. 51). But is poverty breeding violence, or vice versa? To answer this question, Miguel and two colleagues employ an intriguing natural experiment: They analyze the impact of drought—a purely exogenous economic shock that increases poverty—on state propensity for conflict in Africa. Their findings are startling: “The size of the estimated impact of lagged economic growth on conflict is huge,” Miguel writes, with a one percent decline in GDP “increasing the likelihood of civil conflict by more than two percentage points” (pp. 54-56). In contrast, they find little correlation between violent conflict and variables like political repression, democratic freedom, ethnic fragmentation, colonial history, or population density. In sum, “economic factors trump all others in causing African civil conflicts” (p. 55). Miguel suggests that this robust finding has clear policy implications: Very little foreign aid, he observes, addresses the immediate triggers of civil conflict. Donors could change this by directing a significant proportion of external assistance toward helping countries cope with the sharp income fluctuations created by exogenous shocks, such as poor weather or collapsing commodity prices. By extending such insurance, the international community could help remove support for rebel movements. The past decade and a half has seen a surge in policy attention to the possible security implications of demographic change—some of it thoughtful (e.g., Cincotta et al., 2003; Urdal & Brunborg, 2005), some of it sensationalized (e.g., Kaplan, 1994). Henrik Urdal’s chapter provides a judicious assessment of the potential risks and rewards of “youth bulges” in developing countries. He finds a robust correlation between a country’s youth cohort and its propensity for low-intensity conflict. “For each percentage point increase of youth in the adult population,” he writes, “the risk of conflict increases by more than four percent” (p. 96). And yet large youth cohorts have the potential to be a blessing rather than a curse, particularly if they precede significantly smaller cohorts. As fertility rates continue to decline (sometimes dramatically) in the coming years, much of the developing world stands to gain a “demographic dividend,” in the form of increased economic growth and lower vulnerability to violence. The second portion of the book is devoted to several policy challenges confronting external actors in violence-prone poor countries. These chapters address working with youth in war-torn countries (Marc Somers); bolstering responsible political leadership where corruption is the norm (Robert Rotberg); operating as private actors in insecure environments (Jane Nelson); and promoting democracy as well as security and basic needs (Jennifer Windsor). Somers observes that young people—and particularly young males—are typically demonized as a national liability, rather than as a potential asset in building a more peaceful future. Ironically, he notes, “it often seems that nations do not know what to do with their own young people while armed groups keep discovering new ways to make use of them” (p. 102). Somers calls for carefully targeted programs that harness the energy and vision of youth and provide young men, in particular, with the opportunity to gain both employment and dignity. Rotberg looks at the other end of the status hierarchy, highlighting the critical role of leadership in overcoming poverty in Africa. Throwing a bucket of cold water on those who still attribute poverty in developing countries primarily to a lack of foreign aid, he argues that the divergent trajectories of African countries can be explained overwhelmingly by their quality of governance, and specifically the personal leadership qualities of heads of state or government. He pointedly juxtaposes the authoritarian Robert Mugabe, the former independence hero who has managed to drive once-prosperous Zimbabwe into the ground, with visionary leaders like South Africa’s Nelson Mandela, Botswana’s Festus Mogae, and Senegal’s Abdolaye Wade. Rotberg documents a rising demand for good governance in Africa, but what of the supply? Here the answers are less clear. Rotberg claims that sub-Saharan Africa appears to lack “a practical ethic of public service,” but he offers few ideas on how outside actors might work with internal reformers to help instill such an ethos. The book’s one shortcoming might be the modesty of its aims and claims. The editors could have been bolder in seeking to break new conceptual ground, to offer more definitive conclusions on the basis of current research, and to address the policy implications of the book’s overall findings. Like many conference volumes, it lacks an overarching theoretical framework or conceptual model to lend coherence to its disparate chapters and to explain how the various drivers and intervening variables can and do fit together.Theintroduction, for instance, includes no trend lines or maps of current levels of poverty or conflict, leaving the reader to wonder if the situation is as dire as described—and which states, precisely, areentwined in the “nexus.” And although the editors review some prominent debates, they generally abstain from evaluating purported causal linkages or proposing steps to cut them. The absence of a conclusion reinforces the depressing sense that the filaments of “the tangled web” will remain tightly knotted.

#### Instability leads to nuclear war

Ramberg 16 Ramberg, Bennett. "Nuclear Weapons In Civil War Zones | By Bennett Ramberg - Project Syndicate." Project Syndicate. N.p., 2016. Web. 7 Sept. 2021. Bennett Ramberg, a policy analyst in the US State Department’s Bureau of Politico-Military Affairs under President George H.W. Bush, is the author of Destruction of Nuclear Energy Facilities in War and [Nuclear Power Plants as Weapons for the Enemy](https://www.ucpress.edu/op/9780520049697/nuclear-power-plants-as-weapons-for-the-enemy).

LOS ANGELES – The [recent failed military coup in Turkey](https://www.project-syndicate.org/commentary/turkey-coup-erosion-of-law-by-dani-rodrik-2016-07) has produced instability, paranoia, and a crackdown on the regime’s perceived opponents, including many journalists. Luckily, it did not end with rebel forces seizing some of the dozens of US nuclear weapons stored at Turkey’s Incirlik Air Base, from which rebel aircraft departed. But what about next time? The world’s nine nuclear powers claim that there is little to worry about. They argue that the combination of physical protection and, in most cases, electronic safeguards (permissive action links, or PALs) means that their arsenals would remain secure, even if countries where they are stored or deployed were engulfed by violence. Robert Peurifoy, a former senior weapons engineer at Sandia National Laboratories, disagrees. He recently [told the Los Angeles Times](http://www.latimes.com/world/asia/la-na-turkey-nukes-20160721-snap-story.html) that such safeguards – earlier versions of which he helped to design – may only delay terrorists in using seized nuclear weapons. “Either you keep custody or you should expect a mushroom cloud.” Peurifoy’s statements have rightly raised concerns about the security of nuclear weapons stockpiled in [insecure regions](https://www.project-syndicate.org/commentary/bennett-ramberg-highlights-the-vulnerability-of-nuclear-assets-in-volatile-countries). Consider Pakistan, which has the world’s fastest-growing nuclear arsenal and suffers relentless jihadi terrorism and separatist violence. Attacks have already been carried out on Pakistani military installations reportedly housing nuclear components. The country’s new mobile “battlefield nuclear weapons” – easier to purloin – augment current fears. North Korea, with its volatile and mercurial regime, is another [source of concern](https://www.project-syndicate.org/commentary/north-korea-kim-collapse-by-kent-harrington-and-bennett-ramberg-2015-01). Suspicious of the military, Kim Jong-un’s government has repeatedly purged senior officers, which has surely stoked opposition that someday could spark serious civil strife. Adding nuclear weapons to that mix would be highly dangerous. While other nuclear powers appear stable, countries like China and Russia, which rely increasingly on authoritarianism, could face their own risks, should political cohesion fray. Of course, there are plenty of examples of security enduring strife. The 1961 revolt of the generals in French Algeria, which placed a nuclear test device in the Sahara at risk, produced no dangerous incidents. In China, the government effectively protected nuclear weapons sites threatened by Revolutionary Guards during the Cultural Revolution. And neither the attempted coup against Mikhail Gorbachev nor the Soviet collapse resulted in a loss of control over the country’s nuclear arsenal. But it is a leap to presume that these precedents mean that nuclear weapons will remain safe, especially in unstable countries like Pakistan and North Korea. Nuclear bombs or materials risk being controlled by rebels, terrorist groups, or even failing and desperate governments. And, in those cases, the international community has few options for mitigating the threat. External powers can, for example, launch a targeted attack, like the one that Israel carried out on suspected reactors under construction in Iraq and Syria. Those strikes would not have succeeded had Israel not been able to identify the targets accurately. Indeed, though the existence of Iraq’s Osirak plant was public knowledge, uncovering Syria’s Al Kibar plant was an intelligence coup. Carrying out such a strike on North Korean or Pakistani nuclear sites in a time of crisis would require a similar breakthrough – one that may be even more difficult to achieve, given extensive concealment efforts. Stealthy movement of bombs or materials amid the unrest would further complicate targeting. Another option – invasion and occupation – avoids the challenge of identifying nuclear sites. The defeat of Nazi Germany permitted the Allies to find and destroy the country’s nascent nuclear program. The 2003 invasion of Iraq granted the US unfettered access to all possible sites where weapons of mass destruction could be stored. But the costs were huge. Likewise, invasion and occupation of either North Korea or Pakistan would require massive armies risking a bitter conventional war and possible use of the weapons against the invaders. A third option is nuclear containment, which relies on several measures. First, in order to prevent nuclear migration, all land, sea, and air routes out of the country in question would have to be controlled, and homeland security near and far would have to be strengthened. While the [Proliferation Security Initiative](http://www.state.gov/t/isn/c10390.htm) (PSI) is already in place to stop the smuggling of nuclear contraband worldwide, the International Atomic Energy Agency [reports](https://www-ns.iaea.org/downloads/security/itdb-fact-sheet.pdf) continued trafficking of small amounts of nuclear material. An increase in monitoring may reduce, but still not eliminate the problem. Containment also requires nuclear custodians be persuaded to risk their lives to defend nuclear sites against terrorists or rebels. And it demands that states neighboring the country in question put ballistic missile defenses on alert. While India, South Korea, and Japan continue to modernize [such systems](https://www.project-syndicate.org/commentary/thaad-south-korea-nuclear-weapons-by-richard-weitz-2016-08), no missile defense is perfect. In a time of crisis, when the facts on the ground change fast and fear clouds thinking, mitigating the nuclear threat is no easy feat. While concerned governments do have confidential contingency planning in place, such planning has a mixed record when it comes to responding to recent international upsets in the Middle East. And simply hoping that things will go according to plan, and nuclear command and control will stick, remains a gamble. The time has come to discuss new ideas, with the United States – still the global leader in combating proliferation – taking the lead. A public discussion with input from the executive branch, Congress, think tanks, investigative journalists, and scholars should lay a foundation for policy. We cannot allow ourselves to stand on the precipice of catastrophe without a well-considered and broadly supported plan in place. The lesson from Turkey is not that the bombs of Incirlik – not to mention other nuclear weapons in unstable regions – are safe. Rather, it is that our most deadly weapons could be compromised in an instant. It ought to be a wake-up call for all of us.

## Single Payer CP

#### CP: The US Federal Government ought to establish a single payer healthcare system

#### Single Payer encourages innovation and covers costs

Lemley et al. 20 [MARK A. LEMLEY, William H. Neukom Professor of Law, Stanford Law School, LISA LARRIMORE OUELLETTE, Associate Professor of Law and Justin M. Roach, Jr. Faculty Scholar, Stanford Law School, and RACHEL E. SACHS, Associate Professor of Law, Washington University, 04-2020, “THE MEDICARE INNOVATION SUBSIDY,” NYU Law Review, https://www.nyulawreview.org/wp-content/uploads/2020/04/NYULAWREVIEW-95-1-LemleyOuelletteSachs.pdf]

II PHARMACEUTICAL SUBSIDIES AS INNOVATION INCENTIVES Governments have created the complex array of prescription drug allocation mechanisms described in Part I because those drugs are costly and public payers face tradeoffs about how to allocate scarce resources. As noted above, the ability of drug manufacturers to set prices well above the cost of production stems from the IP used to protect R&D investments.168 This ex post, market-set incentive is provided not only through patent law, but also through other forms of IP, including trade secrets, trademarks, and regulatory exclusivity.169 It is hard to disentangle the effects of these different forms of IP, but companies generally report that the pharmaceutical industry is the sector in which patents are most effective,170 and scholars often agree.171 But patents and other forms of IP come with significant drawbacks. They raise prices, impose administrative costs, and can discourage follow-on innovation. As discussed below, market-based IP rewards are misaligned from social value for a variety of biomedical innovations, including for goods that generate positive externalities or for which the social value exceeds consumers’ ability to pay. Governments can offset these IP-related biases with other innovation policies, including R&D tax incentives, direct funding through grants and research at national labs, and prizes.172 Here, we focus on one such policy tool—one that policymakers have rarely seemed to think of as implementing innovation policy at all: government subsidies for particular drugs through health insurance programs like Medicare and Medicaid. From an incentive perspective, reimbursement programs can function as market-based prizes, in which the reward incorporates both a government assessment of social value and market information based on consumer choices.173 For example, suppose policymakers decide that the expected IP-based market reward is insufficient for incentivizing a vaccine for a particular disease.174 The government could offer an additional fixed prize—say, $1 billion for the first firm to develop a cure. But to encourage distribution of the vaccine and to tie the reward to some measure of patient preference, policymakers could also offer a market-based prize—say, $100 per patient vaccinated. Particularly for interventions with positive externalities or high disparities between patients’ ability and willingness to pay, administering this kind of additional incentive through government health insurance programs improves the alignment between the returns to innovation and social value. The incentive effect of demand-side healthcare subsidies depends critically on details of institutional design. Section II.A shows how Medicare-like programs can provide a significant subsidy to drug manufacturers beyond expected profits in an unsubsidized market. Section II.B discusses the effect of this kind of subsidy on overall pharmaceutical innovation. Finally, Section II.C examines how subsidies from government insurance can bias innovation incentives in favor of particular biomedical technologies. But those details should not obscure the larger point, to which we turn in Part III: Healthcare reimbursements are innovation incentives. Indeed, they may be among the largest innovation incentives in the pharmaceutical sector. A. The Medicare Innovation Subsidy To illustrate how pharmaceutical profits under Medicare reflect more than the “market value” of a drug, we begin with an ordinary, unsubsidized market in which a seller has monopoly power, as illustrated in Figure 1. The demand curve (D) represents how much quantity of the drug (Q) consumers will purchase at a given price (P); an ordinary market has a downward-sloping demand curve because more consumers are typically able to purchase a good at lower prices.175 The supply curve (S) represents the quantity of drug that will be sold at a given price. Monopoly pricing involves reducing sales in order to increase the price. Why do monopolists reduce output while increasing prices? The key to this “normal” monopoly is the absence of price discrimination. The patentee would like to sell to everyone who is willing and able to pay more than it costs to sell them a drug: that is, everyone for whom the demand curve is higher than the supply curve. But if they lower the price to reach those who can afford to pay less, they also lower the price for all the other buyers, too, reducing the marginal revenue from adding a new sale. Monopolists, then, price not where the supply curve meets the demand curve (the competitive market price),176 but instead where the supply curve meets the marginal revenue curve (MR), resulting in a higher price (Pmonop) and lower quantity (Qmonop) than in a competitive market. If they cut the price any further, the money they would lose from existing customers would counteract the additional sales, making the additional sale unprofitable. If this monopoly price is used to allocate access to the drug, consumers who value the drug above the cost of production but below the monopoly price are unable to access the drug. The social loss due to these lost transactions is known as deadweight loss (DWL), represented by the striped triangle in Figure 1. In the context of essential medicines, this represents patients who will be unable to access the treatments they need. IP policy tolerates this allocative inefficiency on the theory that it will be exceeded by gains in dynamic efficiency: The prospect of monopoly profits will incentivize a producer to create this drug in the first place. In other words, the development of the drug is necessary to provide any access at all. IP policy is thus typically described as representing a tradeoff between short-term access and longer-term innovation.177 The full interaction between IP and pharmaceutical access is more complicated than this simple model suggests. One of us has recently questioned the conventional view that the fundamental tradeoff in IP is between dynamic and allocative efficiency: IPfacilitated market power does create incentives to restrict quantity and thus decrease consumption, but it also has consumptionexpanding effects.178 But for our purposes, the standard monopolypricing model suffices to illustrate the basic effect of insurance and demand-side subsidies. In Figure 2 we add the effect of coinsurance, in which an insurer covers a fixed percentage of medical costs. Compared to a market without insurance, a coinsurance system expands demand, moving the demand curve to the right. The curve pivots rather than simply shifting because coinsurance pays a percentage of the total cost, so it magnifies the effect of a consumer’s existing willingness and ability to pay. If insurance pays 80% of the cost, a consumer who can pay $100 out of pocket can buy a $500 drug. But a consumer who can pay $1000 ($900 more than her neighbor) can buy a $5000 drug.179 The effect of adding insurance is to expand the patent owner’s profits beyond the monopoly profit without insurance. Because consumers effectively can pay more (with the help of their insurers), a monopolist can charge each consumer more and can also sell to more consumers. Note that as patients’ share of costs decreases, the demand curve pivots further to the right, and more consumers gain access to the drug. This effect is generally framed in the health economics literature in terms of the resulting moral hazard problem in which patients may choose treatments that are more expensive than the value they actually receive.180 But there has been less attention to the way insurance greatly increases prices and profits for a seller with market power. If patients’ share of costs declines to zero (such as through insurance that requires only a flat copayment), then there would be no upper bound on price. That’s why, as a practical matter, public or private insurance systems providing free or low-cost care must have some other mechanism to contain costs. For example, as described in Part I, Medicaid links prices to private markets, the VA and UK systems can exclude drugs from coverage, and the German system will only reimburse up to a reference price. Coinsurance systems in which insurers cover a large percentage of costs typically also have some cost-control mechanism, including copayments, deductibles, and formulary management tools. But even if there is some mechanism for limiting price, the patentee may still receive additional profits in a market in which all patients have coinsurance as compared with the “normal” monopoly market, as we illustrate in Figure 3.181 A mechanism for limiting prices is particularly necessary if the model moves from one in which all consumers have coinsurance (requiring them to pay some percentage of the price) to one in which all consumers have generous access to drugs with no cost-sharing, as suggested by some Medicare for All proposals.182 As we illustrate in Figure 4, even if prices are limited to the original monopoly price, providing coverage for all patients with no cost-sharing leads to a substantial additional profit for the patentee.183 Real-world pharmaceutical markets are substantially more complex than any of the simplified models shown in Figures 1–4. The important conceptual point, however, is that when insurance-related policies effectively shift demand upward or to the right, the seller of a drug with market power can receive higher profits for that drug. These added profits grow as patients’ share of pharmaceutical costs shrinks, particularly in the absence of robust cost-containment mechanisms. To some degree, this is what Medicare’s prescription drug benefits do. Medicare beneficiaries generally are responsible for only twenty to twenty-five percent of brand-name drug costs under Parts B and D,184 and millions of patients receive government subsidies lowering these amounts.185 Many of these are people who didn’t have private insurance or who had insurance that was less generous,186 who can now effectively pay much more for drugs than they used to. Medicare also increases overall demand for drugs by causing beneficiaries to live longer.187 These factors tend to push the demand curve upward to the right, artificially adding to the number of people who can pay the monopoly price. And unlike private insurers, who have greater legal authority to negotiate prices freely and to refuse to cover drugs that cost too much, Medicare Parts B and D often impose coverage requirements with little ability for the government to negotiate prices beyond the price set in the private market, giving drug manufacturers significant leverage in setting prices.188 Expanding the demand curve in this way increases the patentee’s profits even further beyond what they would make without government insurance. The patentee no longer has to worry about cutting prices to match demand for customers who can pay less; some combination of the government and supplemental private insurance will pay the monopoly price for almost everyone. Medicare does expand access to consumers who value the drug more than its cost of production but less than the unsubsidized monopoly price (the striped DWL triangle in Figure 1). But it also transfers a great deal of additional profit to the patent owner. The scope and duration of the patent hasn’t changed, but it is generating a lot more profit for the simple reason that, thanks to the government subsidy, there are many more customers who can pay and they all pay the monopoly price or close to it, even if they value the drug at less than that price. We call this added profit the Medicare innovation subsidy. The real world has more complications than this stylized model, of course. Here are four important ones: First, not all pharmaceutical patents confer market power, though they are more likely to than patents in other fields.189 Even where drugs face quite a lot of competition, as with antidepressants, patentees may not face effective price competition if doctors don’t view the drugs as substitutes for any given patient or if Medicare must cover all FDA-approved drugs for certain illnesses.190 Second, Medicare plans and the PBMs that negotiate on their behalf do have some bargaining leverage, including threatening to cover only certain drugs for non-protected classes, using prior authorization or step therapy, and threatening to move drugs to less desirable formulary tiers.191 This leverage has allowed them to lower prices for drugs with competition in a particular therapeutic class, although their bargaining power is limited by the government’s inability to directly negotiate and by the plans’ inability to walk away from the table in most cases.192 As Figure 3 illustrates, however, patentees still receive substantial additional profits even with tools for limiting price. Third, Medicare Part D covers primarily Americans aged over sixty-five. For drugs that affect only the elderly, the model just described is accurate. But it doesn’t apply to drugs for diseases that only affect children, and it applies only partially to drugs taken by patients of all ages. We discuss the biases this may cause in more detail in Section II.C. Finally, the above graphs assume that Part D was created against a baseline in which seniors did not have prescription drug insurance. This was true for twenty-seven percent of seniors,193 creating a demand expansion effect among this population. Before Part D implementation, sixty-six percent of Medicare-eligible seniors already had some prescription drug insurance plan.194 However, at least some of those patients also increased pharmaceutical returns when substituting into Medicare—nine million patients moved from lowerreimbursement Medicaid coverage to higher-reimbursement Part D coverage.195 Effects may be more variable for the beneficiaries substituting from private insurance into Medicare. Despite these complications, the Medicare innovation subsidy is real. It has significantly increased the returns to pharmaceutical patent owners. Medicare now accounts for thirty percent of U.S. retail prescription drug spending,196 even though it applies primarily to people over sixty-five, who make up just thirteen percent of the population,197 and not all of whom even opt-in to Medicare. Medicare, then, is a big source of additional money for drug companies, both because it increases the number of people who can afford drugs and because it may increase the price companies can charge for those drugs. B. Effect on Innovation Above-baseline-monopoly profits aren’t necessarily bad. Few dispute that higher profits for certain innovations increase incentives to produce those knowledge goods,198 and a number of empirical studies have found increases in private-sector R&D investment following legal changes that increased market size in the contexts of vaccines and orphan drugs.199 Based on analysis of time-series data of drugs entering clinical development, Margaret Blume-Kohout and Neeraj Sood conclude that “passage and implementation of Medicare Part D is associated with significant increases in pharmaceutical R&D for therapeutic classes with higher Medicare market share.”200 They found that this was largely new investment, not substitution away from other drugs, and that the effect was smaller for drugs that had been previously covered under Part B and larger for drugs in protected Part D classes.201 (In contrast, the original introduction of Medicare in 1965—without the prescription drug benefit—didn’t increase drug use among the elderly or induce significant pharmaceutical innovation,202 though it did increase medical-equipment patenting.)203 True, increases in R&D alone do not necessarily enhance patient welfare. Subsequent work focused on biologics found a similar incentive effect from Part D implementation, but also concluded that “most of this effect is concentrated among products aimed at diseases that already have multiple existing treatments,”204 and the net welfare impact of such drugs is ambiguous. Even though the size of the Medicare subsidy is large, its net innovation benefit might be relatively modest. The United States offers a huge array of innovation incentives in the pharmaceutical industry already, including not just patents but also direct research funding through grants and national laboratories, prizes, tax incentives, regulatory exclusivities, data exclusivities, and special incentives for orphan drugs and pediatric research.205 Pharmaceutical “lifecycle management” through secondary patents and regulatory gaming mean that companies keep market power for years and even decades after initial patent expiration.206 For at least some drugs, patent-owner returns for pharmaceuticals seem to far exceed the risk-adjusted R&D costs.207 Greatly increasing this innovation subsidy through expansion of government insurance may thus lead to limited innovation gains— although, as discussed in the following Section, existing incentives appear to be insufficient for at least some kinds of socially valuable innovation. Even so, perhaps we should celebrate the expansion of patent owner profits above the baseline monopoly level, since it seems to spur at least some additional R&D investment. If Medicare Part D is justified solely for the access benefits it provides for the elderly, the fact that there is also an innovation subsidy that leads to the production of even some new drugs is an extra benefit for the world. It is found money. And more drugs to treat diseases for no extra cost seems like an unambiguously good thing.

### AT Evergreening

#### Challenges solve evergreening in the status quo

Hemphill and Sampat 12 Hemphill, C. S., & Sampat, B. N. (2012). Evergreening, patent challenges, and effective market life in pharmaceuticals. Journal of Health Economics, 31(2), 327–339. doi:10.1016/j.jhealeco.2012.01.00 Scott Hemphill is a JD from Columbia University. Bhaven Sampat is the head of the Department of Health Management and Policy, Mailman School of Public Health, Columbia University.

The average nominal patent term is 16 years for drugs with first generic entry between 2001 and 2010. By comparison, average effective market life for these drugs is 12 years, not much different than in the previous decade, and greater than in the decade before Hatch–Waxman(Grabowski andVernon, 1996). Patent challenges are the key driver of the gap between nominal patent term and effective market life. Our research confirms predictions that challenges are more prominent for large sales drugs. We also find a rise in early challenges, suggesting growing sophistication by generic firms in a race to secure first-to-file status, and thus eligibility for exclusivity. Thesefindingsmay provide some justification for those concerned aboutincreasingly aggressive generic challengers. However, the conventional prospecting account is too simple. After all, as our descriptive data show, the average market life for new molecular entities is essentially stable over time. And the largest sales drugs do not have very different effective market life compared to drugs in other categories, even though they are more likely to be challenged, and challenged early. The full story is more complicated. Generic challenges disproportionately target drugs with weak, late-expiring patents. While it is possible that these drug-level models reflect unobserved heterogeneity, the fixed effects models also show that within drugs, challenges reflect the extent of evergreening. There is only limited evidence for the prospecting story, which would predict that challenges to “basic” patents are more common for higher sales drugs. Moreover, challenges to AI patents are not associated with significant reductions in market term. Taken together, our results show that challenges are playing a restorative role, ratcheting back the effective market life of drugs with large nominal patent terms to about 12 years. They are particularly likely for large sales drugs, as critics of these challenges warn. However, this appears to reflect that evergreening is also particularly likely for these drugs. In drugs, and in other industries, resource-constrained patent examiners at the U.S. Patent and Trademark Office may lack the incentive or capacity to thoroughly assess each of the hundreds of thousands of patent applications they process annually (Jaffe and Lerner, 2004). And the FDA does not independently assess the merits of patents (confining their role to an evaluation of safety and efficacy), instead deferring to PTO decisions. In this context, generic patent challenges may reflect society’s strongest defense against non-meritorious patents that would harm payers and patients. To be sure, challenges reduce market life. But compared to what? Our analyses underscore the importance of choosing the right baseline in answering this question. Consider the case of Fosamax (alendronate), a blockbuster osteoporosis drug made by Merck. Higgins and Graham (2009) offer this drug as their leading example of a troubling drug patent challenge. As the authors note, after Merck lost its patent challenge, the generic drug entered the market in February 2008—“∼4 years before the Fosamax patents were due to expire”—which produced a sharp drop in Fosamax sales. Fig. 5 shows how the choice of baseline affects our understanding of the Fosamax example. Higgins and Graham appear to focus on patents due to expire in 2013. A successful generic challenge permitted entry in 2008 (when another patent expired). That account is incomplete, however, in two respects. First, the drug was approved in 1995, meaning that Fosamax enjoyed 12.5 years of exclusivity before generic entry. More important, 2013 was not the end of Merck’s patent protection. Merck had also acquired 9 other patents on the drug, the last of which is due to expire in 2019. Had the generic firm not challenged these later expiring patents, the total market life for the drug would have been almost a quarter century. Even if generics are now more aggressive than they once were, it does not follow that strong, basic patents are routinely being invalidated or invented around, thereby leading to early generic entry. On average, current exclusivity is already about 12 years, even for the most lucrative quintile of drugs. If firms make R&D choices based on expectations of marketlife, itis unlikely that a rise in challenges has blunted R&D incentives or otherwise contributed to the current pipeline problem in pharmaceuticals. Of course, there is variation across drugs, and a longer data exclusivity term would provide certainty, itself a useful policy goal.28 But if the argument is that 12 years is the “right” amount of protection, perhaps it should serve as an upper as well as lower bound.Aplausible quid pro quo would be to trade longer data exclusivity for restrictions on evergreening. One means to accomplish the latter would be to subject all Orange Book-listed patents to immediate re-examination by the PTO, where they would get a strong second look.29 Branstetter et al. (2011) find the short run welfare gains from patent challenges to be large, $93 billion between 1997 and 2008 for the hypertension market alone. Like their analysis, this paper focuses on static rather than dynamic effects of patent challenges, so we can only speculate on the latter.30 If “low quality” patents are on innovations that do not require costly R&D (e.g., obvious changes to the drug) their elimination may not meaningfully affect R&D incentives. Under this scenario, Paragraph IVchallenges would appear to be a net social benefit, even considering dynamic effects. On the other hand, it is possible that the increment to market life from “bad” patents is needed to stimulate “good” innovation. We can imagine two possible stories along these lines. A first is that non-AI patents do in fact represent costly and socially valuable innovation, but patent standards are misaligned with the social value of inventions (Roin, 2009), making these patents legally vulnerable. A second is that these non-AI patents themselves are not innovative, but the additional market life they generate for the underlying basic inventions supports important R&D: that is, the optimal patent term for NCEs is greater than 12 years on average, and “weak” patents help sustain this. We do not attempt to answer these questions there, but raise them as important ones for future work on patent challenges.

#### Criticism of evergreening flawed – follow-on creates value and doesn’t prevent use of original

Holman 20 Holman, Christopher. "Why Pharmaceutical Follow-On Innovation Should Be Eligible For Patent Protection - Geneva Network - Secondary Patents - Evergreening Patents." Geneva Network. N.p., 2020. Web. 24 Aug. 2021. Professor of Law, University of Missouri-Kansas City School of Law; J.D., University of California, Berkeley; Ph.D., University of California, Davis.

Despite the important role of intellectual property rights in incentivizing innovation, the patenting of pharmaceutical innovation is frequently accused of impeding access to medicine. Criticism of the prevailing patent regime has focused in particular on patents directed towards follow-on innovation, i.e., innovation that seeks to improve upon existing pharmaceuticals and their use in treating patients. Patents on follow-on innovation are often derided as “secondary” patents, with the implication that the underlying inventions are somehow lesser in nature than the subject matter claimed in “primary” patents, i.e., the drug active ingredient per se. While implicitly acknowledging the legitimacy of primary patents, critics of so-called secondary patents contend that patents on follow-on innovation allow drug innovators to “evergreen” their products, i.e., to extend the period of patent exclusivity beyond the expiration of any original patent on the drug active ingredient, and in doing so contribute to the high cost of drugs, thereby limiting the ability of patients to access the drugs upon which they have come to rely. In 2015, the United Nations Development Programme (UNDP) issued a document entitled [Guidelines for Pharmaceutical Patent Examination: Examining Pharmaceutical Patents from a Public Health Perspective](http://www.undp.org/content/dam/undp/library/HIV-AIDS/UNDP_patents_final_web_2.pdf) (the “Guidelines”), which, in an effort to promote access to medicines, recommends that courts and patent offices implement newly heightened patentability requirements for follow-on pharmaceutical innovation that would be uniquely stringent and largely unprecedented. [1](https://geneva-network.com/article/follow-on-innovation/#note-3156-1) In 2017, I challenged many of the assertions made in the Guidelines in an article entitled [In Defense of Secondary Pharmaceutical Patents: A Response to the UN’s Guidelines for Pharmaceutical Patent Examination (“Defense of Secondary Patents”)](https://mckinneylaw.iu.edu/ilr/pdf/vol50p759.pdf), which provides numerous examples of so-called secondary patents that have withstood validity challenges in the courts and patent offices throughout the world and which were directed towards follow-on pharmaceutical innovation clearly meriting patent protection. [2](https://geneva-network.com/article/follow-on-innovation/#note-3156-2) More recently, I teamed up with legal scholars Timo Minssen and Eric Solovy in authoring [Patentability Standards for Follow-on Pharmaceutical Innovation (“Patentability Standards”)](https://www.liebertpub.com/doi/abs/10.1089/blr.2018.29073.cmh), an article that reiterates the important role of follow-on pharmaceutical innovation in addressing compelling human health concerns, and which proposes what we consider to be the appropriate standards and criteria to be applied in assessing the patentability of this sometimes underappreciated aspect of medical innovation. [3](https://geneva-network.com/article/follow-on-innovation/#note-3156-3) Why Protect Follow-On Innovation? The attack on secondary pharmaceutical patents is based in part on the flawed premise that follow-on innovation is of marginal value at best, and thus less deserving of protection than the primary inventive act of identifying and validating a new drug active ingredient. In fact, follow-on innovation can play a critical role in transforming an interesting drug candidate into a safe and effective treatment option for patients. A good example can be seen in the case of AZT (zidovudine), a drug ironically described in the Guidelines as the “first breakthrough in AIDS therapy.” AZT began its life as a failed attempt at a cancer drug, and it was only years later that its potential application in the fight against AIDS was realized. Follow-on research resulted in a method-of-use patent directed towards the use of AZT in the treatment of AIDS, and it was this patent that incentivized the investment necessary to bridge the gap between a promising drug candidate and a safe, effective, and FDA-approved pharmaceutical. Significantly, because of the long lag time between the first public disclosure of AZT and the discovery of its use in the treatment of AIDS, patent protection for the molecule per se was unavailable. In a world where follow-on innovation is unpatentable, there would have been no patent incentive to invest in the development of the drug, and without that incentive AZT might have languished on the shelf as simply one more failed drug candidate. Other examples of important drugs that likely never would have been made available to patients without the availability of a “secondary” patent include Evista (raloxifene, used in the treatment of osteoporosis and to reduce the risk of invasive breast cancer), Zyprexa (olanzapine, used in the treatment of schizophrenia), and an orally-administrable formulation of the antibiotic cefuroxime. Pharmaceutical development is prolonged and unpredictable, and frequently a safe and effective drug occurs only as a result of follow-on innovation occurring long after the initial synthesis and characterization of a pharmaceutically interesting chemical compound. The inventions protected by secondary patents can be just as critical to the development of drugs as a patent on the active ingredient itself. The Benefits of Follow-On Innovation The criticism of patents on follow-on pharmaceutical innovation rests on an assumption that follow-on innovation provides little if any benefit to patients, and merely serves as a pretense for extending patent protection on an existing drug. In fact, there are many examples of follow-on products that represent significant improvements in the safety-efficacy profile. For example, the original formulation of Lumigan (used to treat glaucoma) had an unfortunate tendency to cause severe hyperemia (i.e., redeye), and this adverse event often lead patients to stop using the drug, at times resulting in blindness. Subsequent research led to a new formulation which largely alleviated the problem of hyperemia, an example of the type of follow-on innovation that significantly benefits patients but that which would be discouraged by a patent regime that does not reward follow-on innovation. Follow-on pharmaceutical innovation can come in the form of an extended-release formulation that permits the drug to be administered at less frequent intervals than the original formulation. Critics of secondary patents downplay the significance of extended-release formulations, claiming that they represent nothing more than a ploy to extend patent protection without providing any real benefit to patients. In fact, the availability of a drug that can be taken once a day has been shown to improve patient compliance, a significant issue with many drugs, particularly in the case of drugs taken by patients with dementia or other cognitive impairments. Extended-release formulations can also provide a more consistent dosing throughout the day, avoiding the peaks and valleys in blood levels experienced by patients forced to take an immediate-release drug multiple times a day. Other examples of improved formulations that provide real benefits to patients are orally administrable formulations of drugs that could previously only be administered by more invasive intravenous or intramuscular injection, combination products that combine two or more active pharmaceutical agents in a single formulation (resulting in improved patient compliance), and a heat-stable formulation of a lifesaving drug used to treat HIV infection and AIDS (an important characteristic for use in developing countries with a hot climate). “Evergreening” – an Incoherent Concept Drug innovators are often accused of using secondary patents to “evergreen” the patent protection of existing drugs, based on an assumption that a secondary patent somehow extends the patent protection of a drug after the primary patent on the active ingredient is expired. As a general matter, this is a false assumption — a patent on an improved formulation, for example, is limited to that improvement and does not extend patent protection for the original formulation. Once the patents covering the original formulation have expired, generic companies are free to market a generic version of the original product, and patients willing to forgo the benefits of the improved formulation can choose to purchase the generic product, free of any constraints imposed by the patent on the improvement. Of course, drug innovators hope that doctors and their patients will see the benefits of the improved formulation and be willing to pay a premium for it, but it is important to bear in mind that ultimately it is patients, doctors, and third-party payers who determine whether the value of the improvement justifies the costs. Of course, this assumes a reasonably well-functioning pharmaceutical market. If that market breaks down in a manner that forces patients to pay higher prices for a patented new version of a drug that provides little real improvement over the original formulation, then it is the deficiency in the market which should be addressed, rather than the patent system itself. For example, if a drug company is found to have engaged in some anticompetitive activity to block generic competition in the market for the original product once it has gone off patent, then antitrust and competition laws should be invoked to address that problem. If doctors are prescribing an expensive new formulation of a drug that provides little benefit compared to a cheaper, unpatented original product, then that is a deficiency in the market that should be addressed directly, rather than through a broadside attack on follow-on innovation. In short, if is found that secondary patents are being used in a manner that creates an unwarranted extension of patent protection, it is that misuse of the patent system which should be addressed directly, rather than through what amounts to an attack on the patent system itself. Compatibility with TRIPS The heightened requirements of patentability proposed in the Guidelines not only pose a threat to important follow-on pharmaceutical innovation, but if they were to be adopted could constitute noncompliance with certain international treaties, including in particular the Agreement on Trade-Related Aspects of Intellectual Property Rights (“TRIPS Agreement”), which the 164 Members of the World Trade Organization (WTO) have agreed to abide by. The TRIPS Agreement requires WTO Members to provide certain minimum levels of protection for patentable inventions, thus placing substantive limitations on the ability of WTO Members to raise the bar for patentability. The TRIPS Agreement in no way sanctions subject matter-specific heightened requirements of patentability; to the contrary, the antidiscrimination provision in the TRIPS Agreement affirmatively precludes such measures. Unfortunately, this point is all too often lost in discussions of international and domestic patent policy.