### Halloween

#### This is my costume I just had to take it off for the round

A person wearing a white shirt

Description automatically generated with low confidence

### 1AC: Innovation

#### Advantage 1 is Innovation:

#### Most recent evidence concludes Aff – 78% of New Drugs aren’t innovative but rather repurposed.

PFAD 21 Patients for Affordable Drugs 2-3-2021 “BIG PHARMA’S BIG LIE: THE TRUTH ABOUT INNOVATION & DRUG PRICES” <https://patientsforaffordabledrugs.org/2021/02/03/innovation-report/> (a patient advocacy and lobbying organisation based in Washington, D.C. founded by David Mitchell who suffers from multiple myeloma. Ben Wakana is the executive director. It focuses on policies to lower drug prices.)//Elmer

The drug industry talks a lot about how reforms to lower prices threaten cutting-edge breakthroughs, but in reality, **only a fraction of new medications are truly innovative**. **Since 1975**, **only 10** to 15 **percent** of drugs entering the market **represented** **therapeutic advances**; **instead**, **drug companies prioritized the development of existing drugs with minor variations that lack clinical significance**.21 Drug patents offer a stark illustration of this point. Between 2005 and 2015, **78 percent of drug patents were related to drugs already on the market.**22 **Instead of investing in R&D that could lead to new** breakthrough **therapies**, **drug companies spend resources obtaining patents on old drugs** — not to improve user experience — but **to extend patent protection**, prolong monopoly pricing periods, and keep generic competitors off the market. So if we understand that new drugs are not the same as new cures, a small reduction in new drugs doesn’t pose a threat to innovation. Harvard economist Richard Frank summed it up this way: “If drug companies claim lowering drug prices means somewhat fewer new drug launches, remember that there are **numerous new products sold every year whose elimination would have little to no impact on the health of Americans**.”23 If our current system of drug development does not result primarily in truly innovative drugs, we can’t let the pharmaceutical industry use the threat of R&D cuts as a scapegoat to thwart reforms. We can create a system that incentivizes valuable innovation that delivers meaningful clinical benefit to patients — instead of repurposing old drugs.

#### The only major study confirms our Internal Link – Evergreening decimates competition by resulting in functional monopolies

Arnold Ventures 20 9-24-2020 "'Evergreening' Stunts Competition, Costs Consumers and Taxpayers" <https://www.arnoldventures.org/stories/evergreening-stunts-competition-costs-consumers-and-taxpayers/> (Arnold Ventures is focused on evidence-based giving in a wide range of categories including: criminal justice, education, health care, and public finance)//Elmer

In 2011, Elsa Dixler was diagnosed with multiple myeloma. That August, she was prescribed Revlimid, a drug that had come on the market six years earlier. By January 2012, she went into full remission, where she has remained since. So long as Revlimid retains its effectiveness, she will take it for the rest of her life. “I was able to go back to work, see my daughter receive her Ph.D, and have a pretty normal life,” said Dixler, a Brooklyn resident who is now 74. “So, on the one hand, I feel enormously grateful.” But Dixler’s normal life has come at a steep financial cost to her family and to taxpayers. Revlimid typically costs nearly $800 per capsule, and Dixler takes one capsule per day for 21 days, then seven days off, and then resumes her daily dose, requiring 273 capsules a year. Since retiring from The New York Times at the end of 2017, she has been on Medicare. Dixler entered the Part D coverage gap (known as the donut hole) “within minutes,” she said. She estimates that adding her deductible, her copayment of $12,000, and what her Part D insurance provider pays totals approximately $197,500 a year. Revlimid should have **been subject to competition** from generic drug makers starting in 2009, bringing down its cost by many orders of magnitude. But by obtaining **27 additional patents**, eight orphan drug exclusivities and 91 total additional protections from the U.S. Food and Drug Administration (FDA) since Revlimid’s introduction in 2005, its manufacturer, Celgene, has extended the drug’s **monopoly** **period** **by 18 years** — through March 8, 2028. “I cannot fathom the immorality of a business that relies on **squeezing people with cancer**,” Dixler said, noting her astonishment that Revlimid has obtained orphan drug protections when it treats a disease that is not rare and does not serve a very limited population. She also observed that Revlimid’s underlying drug is thalidomide, which has been around for decades. “They didn’t invent a new drug, rather, they found a new use for it,” she said. “The cost of Revlimid has imposed constraints on our retirement,” Dixler said, “but when I hear other people’s stories, I feel very lucky. A lot of people have been devastated financially.” Revlimid is a case study in a process known as “evergreening” — artificially sustaining a monopoly for years and even decades by manipulating intellectual property laws and regulations. Evergreening is most commonly used with blockbuster drugs generating the highest prices and profits. **Of the roughly 100 best-selling drugs, more than 70 percent have extended their protection** from competition at least once. More than half have extended the protection cliff multiple times. The true scope and cost of evergreening has been brought into sharper focus by a groundbreaking, publicly available, comprehensive database released Thursday by the Center for Innovation at the University of California Hastings College of Law and supported by Arnold Ventures. **The Evergreen Drug Patent Search is the first database to exhaustively track the patent protections filed by pharmaceutical companies**. Using data from 2005 to 2018 on brand-name drugs listed in the FDA’s Orange Book — a listing of relevant patents for brand name, small molecule drugs — it demonstrates the full extent of how evergreening has been used by Big Pharma to prolong patents and delay the entry of generic, lower-cost competition. “Competition is the backbone of the U.S. economy,” said Professor Robin Feldman, Director of the UC Hastings Center for Innovation, who spearheaded the database’s creation. “But it’s not what we’re seeing in the drug industry. “With evergreening, pharmaceutical companies repeatedly make slight, often trivial, modifications to drugs, dosage levels, delivery systems or other aspects to obtain new protections,” she said. “They pile these protections on over and over again — so often that 78 percent of the drugs associated with new patents were not new drugs coming on the market, but existing drugs.” Competition is the backbone of the U.S. economy. But it’s not what we’re **seeing in the drug industry**. Professor Robin Feldman Director of the UC Hastings Center for Innovation In recent decades, evergreening has systematically undermined the Drug Price Competition and Patent Term Restoration Act of 1984, which created the generic drug industry. Commonly known as the Hatch-Waxman Act, it established a new patent and market exclusivity regime in which new drugs are protected from competition for a specified period of time sufficient to allow manufacturers to recoup their investments and earn a reasonable profit. When that protection expires, generic drug makers are incentivized to enter the market through a streamlined regulatory and judicial process. Drug prices typically drop by as much as 20 percent when the first generic enters the market**, and with more than one generic manufacturer, prices can plummet by 80 to 85 percent**. “Hatch-Waxman created an innovation/reward/competition cycle, but it’s been distorted into an innovation/reward/more reward cycle,” Feldman said. “To paraphrase something a former FDA commissioner once said, the greatest creativity in Big Pharma should come from the research and development departments, not from the legal and marketing departments.” Feldman led the development of the Evergreen Drug Patent Search in response to repeated requests from Congressional committees, members of Congress, state regulators and journalists for information about specific drugs and companies. “We want to make it so anyone can have the question about drug protections at their fingertips whenever they want,” Feldman said. “It’s designed to be easy and user-friendly, and to enhance public understanding about how competition may be limited rather than enhanced through the drug patent system.” The **database** was **created through** a painstaking process of **combing** through **160,000 data points** **to examine every instance where a pharmaceutical company added a new drug patent or exclusivity**. “Most of it was done by hand,” Feldman said, “with multiple people reviewing it at every stage. And along the way we repeatedly made conservative choices. **We erred on the side of underrepresenting the evergreen gain** to be sure we were as fair and reasonable as possible.” Among the 2,065 drugs covered in Evergreen Drug Patent Search, there are many examples of the evergreening strategy used by pharma to delay the entry of competition, especially generics, often for widely prescribed drugs, including those used to treat heartburn, chronic pain, and opioid addiction. Nexium Before Nexium, there was Prilosec, a popular drug to treat gastroesophageal reflux disease (GERD). But its patent exclusivity was due to expire in April 2001. In the late 1990s, with a precipitous drop in revenue looming, Prilosec’s manufacturer, AstraZeneca, decided to develop a replacement drug. Using “one-half of the Prilosec molecule — an isomer of it,” the result was Nexium, which received approval in February 2001. Essentially an evergreened version of Prilosec, Nexium’s exclusivity was then extended by more than 15 years, as AstraZeneca received 97 protections stemming from 16 patents. These included revised dosages, compounds, and formulations. Feldman said that tinkering changes such as Nexium’s do not involve the substantial research and development required for a new drug, nor do they constitute true innovations, yet for a decade and a half, patients and taxpayers were forced to pay far more than was warranted for GERD relief. In fact, in 2016 — one year after patent exclusivity expired — Nexium still topped all drugs in Medicare Part D spending, totaling $1.06 billion. Suboxone Use of this combination of buprenorphine and naloxone for treating opioid addiction has exploded in the wake of the opioid epidemic. Since its approval, Suboxone’s manufacturer, Reckitt Benckiser (now operating as Indivior), extended its protection cliff eight times, gaining nearly two extra decades of exclusivity through early 2030. The drug maker gained six patents for creating a film version of the drug — notably around the time protection was expiring for its tablet version. (The therapeutic benefits of the film and tablet are identical.) An earlier version of Suboxone also obtained an orphan drug designation, despite an opioid epidemic that has expanded Suboxone’s customer base to millions of potential customers. Suboxone generates more than $1 billion in annual revenue and ranks among the 40 top-selling drugs in the U.S. Truvada When Truvada, commonly referred to as PrEP, was approved in 2004, this HIV-prevention drug was a breakthrough. But 16 years later — and 14 years after its original exclusivity was to expire — it retains its monopoly status. Truvada’s manufacturer, Gilead, has received 15 patents and 120 protections since it came on the market, extending its exclusivity for more than 17 years, until July 3, 2024. In countries where generic Truvada is available, PrEP costs $100 or less per month, compared to $1,600 to $2,000 in the U.S. As a result, Truvada is unaffordable to many people **who need protection from HIV**. Barred from access, they are left vulnerable to infection. “We’re establishing a precedent that a pharmaceutical company can charge whatever it wants even as it allows an epidemic to continue, and the government refuses to intervene,” said James Krellenstein, co-founder of the group PrEP4All. “That should scare every American. If it’s HIV today, it will be another disease tomorrow.” EpiPen First approved in 1987, the EpiPen has saved the lives of countless numbers of people with deadly allergies. But it is protected from competition until 2025 — 38 years after its introduction — because its owner, Mylan, has filed five patents, four since 2010, all involving tweaks to the automatic injector. The actual medication used, epinephrine, has existed for more than a century — the innovation here is in the delivery device. Because these small changes to the injector have maintained its monopoly for so long, the cost of an EpiPen package (containing two injectors) has risen from $94 when Mylan purchased the device to between $650 and $700 today. For many people, especially parents of children with severe reactions to common allergens like peanuts, EpiPen’s increasing price tag imposes an onerous financial burden. What Can Be Done As the Evergreen Drug Patent Search makes clear, the positive impact of Hatch-Waxman has been steadily and severely eroded by a regulatory system vulnerable to increasingly sophisticated forms of manipulation. “You might say that the patent and regulatory system has been weaponized,” Feldman said. “When billions of dollars are at stake, there’s a lot of money available to look for ways to exploit the legal system. And companies have become adept at this, as our work has found.” There are several key steps that Congress could take to restore the balance between innovation and competition that is the key to a successful prescription drug regulatory process. These may include: Imposing restrictions on the number of patents that prescription drug manufacturers can defend in court to discourage the use of anticompetitive patent thickets. Limiting the patentability of so-called secondary patents — which don’t improve the safety or efficacy of a drug — through patent and exclusivity reform. Reforming the 180-day generic exclusivity, which can currently be abused to block other competitive therapies. “**The Evergreen Drug Patent Search provides the publicly available, evidence-based foundation that defines the extent of the problem**, and it can be used to develop policies that solve the problem of anti-competitive patent abuses,” said Kristi Martin, VP of Drug Pricing at Arnold Ventures. “Our incentives have gotten out of whack,” Martin said. “The luxury of monopoly protection should only be provided to innovations that provide meaningful benefits in saving lives, curing illnesses, or improving the quality of people’s lives. It should not be provided to those gaming the system. If we can change that, we can save consumers, employers, and taxpayers many billions of dollars while increasing the incentives for pharmaceutical companies to achieve breakthroughs."

#### Reject Negative Turns – they’re pharmaceutical lies – the Plan isn’t anti-Patent, just pro-innovation – breaking down secondary patents is key.

* AT Advantage CPs to solve Drug Prices

Radhakrishnan 16 Priti Radhakrishnan 6-14-2016 "Pharma’s secret weapon to keep drug prices high" <https://www.statnews.com/2016/06/14/secondary-patent-gilead-sovaldi-harvoni/> (Priti Radhakrishnan is cofounder and director of the Initiative for Medicines, Access & Knowledge (I-MAK), a US-based nonprofit group of scientists and lawyers working globally to get people lifesaving medicines. Before founding I-MAK, she worked as a health attorney in the US, Switzerland, and India.)//Elmer

Skyrocketing drug prices are forcing states to take **unprecedented measures** to rein in health care spending. Vermont just became the nation’s first state to require prescription drug pricing transparency. The New York and Massachusetts attorneys general have launched investigations into major pharmaceutical companies’ and insurers’ drug pricing policies and strategies. These **are important steps**. **But** they **ignore a key driver of the problem: secondary patents**. Familiar to only a few people inside the insular world of intellectual property law, secondary patents work like this: Companies file for additional, defensive patents to thicken the protection around their original base patents. These additional patents **rarely represent anything new in terms of science**. Instead, their **purpose is to** **prolong** **a** company’s **monopoly** and, along with that, its ability to charge high prices for its drugs. Some drugs have dozens of secondary patents. Abbott Labs, for example, has over 108 patents on its HIV drug Kaletra. Take the case of Sovaldi, a treatment for hepatitis C developed by Gilead Sciences. In the United States, Gilead prices Sovaldi at up to $1,000 a pill, or about $84,000 for a complete course of treatment. This pricing strategy helped Gilead clear $18 billion in profits last year, while taxpayer-funded Medicaid programs, state health programs, and patients have trouble affording this astronomically priced drug. Sovaldi is comprised of a base compound — sofosbuvir — for which the pharma giant has filed three patents. On top of that, Gilead has pursued an additional 24 patents, with more likely to come. My organization, the Initiative for Medicines, Access & Knowledge (I-MAK), aims to ensure that people with hepatitis C and HIV around the world get the medicines they need to survive and lead healthy lives. We have evaluated Gilead’s patent portfolio and found that, based on US and international patent law, Gilead does not deserve any of its 27 patents for Sovaldi. Both the base and secondary patents for the drug are based on old science and commonly known techniques. Yet because of its defensive patenting strategy, Gilead will maintain an iron lock on its market share and charge exorbitantly high prices to Americans with hepatitis C until well into the 2030s. Harvoni, another medication that treats hepatitis C, combines sofosbuvir and a drug called ledipasvir. Currently, Harvoni has 27 secondary patents. If these were removed, people in the US could access far cheaper versions of the same drug as soon as 10 years earlier. Based on I-MAK’s conservative estimates, this could open access to treatment for millions of people in the US, saving patients and payers like Medicare and Medicaid $5 billion over an eight-year period. In the US, Harvoni is priced at $94,000 for a course of treatment. In middle-income, high-population countries like Argentina, Brazil, and China, people are forced to pay thousands of dollars for sofosbuvir. Stripping away unmerited patents would reduce drug costs and increase access for millions of people in the US and around the world. **Pharmaceutical companies love to claim that winnowing** their armada of **patents would be a disincentive to innovation** and would limit research into new drugs. **Don’t believe it**. **The industry devotes shockingly little funding to research and development**. Companies **spend** roughly **one-third** of their revenues **on marketing** **and only half as much on research** and development, while spending big on armies of lawyers to devise and defend secondary patents and other so-called “life cycle management” strategies. Drug **research funding** has been **declining for more than a decade**, **while** strategies of **secondary patenting have steadily increased.** We support patents — just not those that are unmerited and that unjustly prolong companies’ market power and prevent legitimate competition.

#### Biopharmaceutical innovation is key to prevent future pandemics and bioterror – turns case

Marjanovic and Feijao 20 [(Sonja Marjanovic, Ph.D., Judge Business School, University of Cambridge. Carolina Feijao, Ph.D. in biochemistry, University of Cambridge; M.Sc. in quantitative biology, Imperial College London; B.Sc. in biology, University of Lisbon.) "How to Best Enable Pharma Innovation Beyond the COVID-19 Crisis," RAND Corporation, 05-2020, https://www.rand.org/pubs/perspectives/PEA407-1.html] TDI

As key actors in the healthcare innovation landscape, pharmaceutical and life sciences companies have been called on to develop medicines, vaccines and diagnostics for pressing public health challenges. The COVID-19 crisis is one such challenge, but there are many others. For example, MERS, SARS, Ebola, Zika and avian and swine flu are also infectious diseases that represent public health threats. Infectious agents such as anthrax, smallpox and tularemia could present threats in a bioterrorism context.1 The general threat to public health that is posed by antimicrobial resistance is also well-recognised as an area in need of pharmaceutical innovation. Innovating in response to these challenges does not always align well with pharmaceutical industry commercial models, shareholder expectations and competition within the industry. However, the expertise, networks and infrastructure that industry has within its reach, as well as public expectations and the moral imperative, make pharmaceutical companies and the wider life sciences sector an indispensable partner in the search for solutions that save lives. This perspective argues for the need to establish more sustainable and scalable ways of incentivising pharmaceutical innovation in response to infectious disease threats to public health. It considers both past and current examples of efforts to mobilise pharmaceutical innovation in high commercial risk areas, including in the context of current efforts to respond to the COVID-19 pandemic. In global pandemic crises like COVID-19, the urgency and scale of the crisis – as well as the spotlight placed on pharmaceutical companies – mean that contributing to the search for effective medicines, vaccines or diagnostics is essential for socially responsible companies in the sector. 2 It is therefore unsurprising that we are seeing industry-wide efforts unfold at unprecedented scale and pace. Whereas there is always scope for more activity, industry is currently contributing in a variety of ways. Examples include pharmaceutical companies donating existing compounds to assess their utility in the fight against COVID19; screening existing compound libraries in-house or with partners to see if they can be repurposed; accelerating trials for potentially effective medicine or vaccine candidates; and in some cases rapidly accelerating in-house research and development to discover new treatments or vaccine agents and develop diagnostics tests.3,4 Pharmaceutical companies are collaborating with each other in some of these efforts and participating in global R&D partnerships (such as the Innovative Medicines Initiative effort to accelerate the development of potential therapies for COVID-19) and supporting national efforts to expand diagnosis and testing capacity and ensure affordable and ready access to potential solutions.3,5,6 The primary purpose of such innovation is to benefit patients and wider population health. Although there are also reputational benefits from involvement that can be realised across the industry, there are likely to be relatively few companies that are ‘commercial’ winners. Those who might gain substantial revenues will be under pressure not to be seen as profiting from the pandemic. In the United Kingdom for example, GSK has stated that it does not expect to profit from its COVID-19 related activities and that any gains will be invested in supporting research and long-term pandemic preparedness, as well as in developing products that would be affordable in the world’s poorest countries.7 Similarly, in the United States AbbVie has waived intellectual property rights for an existing combination product that is being tested for therapeutic potential against COVID-19, which would support affordability and allow for a supply of generics.8,9 Johnson & Johnson has stated that its potential vaccine – which is expected to begin trials – will be available on a not-for-profit basis during the pandemic.10 Pharma is mobilising substantial efforts to rise to the COVID-19 challenge at hand. However, we need to consider how pharmaceutical innovation for responding to emerging infectious diseases can best be enabled beyond the current crisis. Many public health threats (including those associated with other infectious diseases, bioterrorism agents and antimicrobial resistance) are urgently in need of pharmaceutical innovation, even if their impacts are not as visible to society as COVID-19 is in the immediate term. The pharmaceutical industry has responded to previous public health emergencies associated with infectious disease in recent times – for example those associated with Ebola and Zika outbreaks.11 However, it has done so to a lesser scale than for COVID-19 and with contributions from fewer companies. Similarly, levels of activity in response to the threat of antimicrobial resistance are still low.12 There are important policy questions as to whether – and how – industry could engage with such public health threats to an even greater extent under improved innovation conditions.

#### Patents incentivize Negative Innovation.

Feldman 21, Robin C., et al. "Negative innovation: when patents are bad for patients." <https://www.nature.com/articles/s41587-021-00999-0.pdf> (Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation)//Elmer

Patent law in the United States is historically premised on advancing the interests of society. From the store of productive activity available to all, the government restricts some activities for a limited time in hopes this will redound to the benefit of all by incentivizing innovation1 . The law thereby restricts competition, forgoing the concomitant advantages of the free market, but only during the patent period. After that time, the law expects that competition will enter, driving down prices and spurring new innovation. From this perspective, US patent law centers on the benefit to the public, with the inventor’s reward providing the vehicle for accomplishing this jurisprudential goal. In the health care space, these incentives have resulted in extraordinary success stories, but the **same incentives** can also **result in** a range of undesirable consequences, including excessive development of **similar (but not better) products** (‘me-too drugs’), the focus on drugs for diseases that affect wealthy people and wealthy countries rather than diseases that disproportionately affect the poor and developing nations, and a lack of innovation for types of medicines that may return fewer profits, such as antibiotics2–4 . Similarly, drug companies will **not research the utility of a known** (**and hence unpatentable) chemical**, since the ability to obtain patent protection is central to their business model5 . Past literature has highlighted these problems but has largely overlooked the problem of ‘**negative innovation’**, in which **patent** law **drives innovation into spaces that are affirmatively harmful to patients**. By this, we mean **scenarios** **whereby** **patents create incentives to bring a product to market in a way that is** relatively **harmful to consumers**, and the existence of a patent (and the associated rents) discourages the patentee from taking steps to improve the product so as to prevent the adverse health outcomes. Of course, there are other patent-driven situations of problematic utility, including scenarios that result in purely financial harms, such as drugs that are no better than existing options but are more expensive; scenarios where a small, heightened risk of direct physical harm is offset by lower prices for the drug in question6 ; and scenarios where there is no existing product on the market and inadequate incentives to develop such a product, so any physical harm is the result of the underlying disease or illness7 . Finally, there is a general concern that inadequate new information about existing products is generated in the current system8 . All of these scenarios are different in kind from negative innovation, which results in a harmful (but profitable) product. We focus on this dangerous but overlooked space of the patent landscape, wherein patents themselves lead fairly directly to patient harm. What does negative innovation look like? We highlight a particularly pernicious example, the case of Imbruvica (ibrutinib); suggest the likelihood of broader problems; and outline various strategies for preventing such outcomes going forward. The case of ibrutinib Ibrutinib, a small molecule drug discovered by Pharmacyclics (now a subsidiary of AbbVie), is an irreversible inhibitor of Bruton’s tyrosine kinase (BTK), a key regulator of B cell signaling and growth. It is approved by the US Food and Drug Administration for multiple indications and is most commonly used to treat B cell cancers, such as chronic lymphocytic leukemia. While ibrutinib is effective, it, like all anticancer agents, is toxic. It is all the more puzzling, then, that ibrutinib’s recommended dosage appears to be substantially higher than necessary to achieve the necessary therapeutic effect—or at least, what evidence is available points to that conclusion9 . Problematic incentives created by the patent system make this result unfortunately unsurprising. The basic story is disheartening but simple. Early studies published by Pharmacyclics showed efficacy at low doses (partial response at 1.25 milligrams per kilogram body weight, approximately 40% response at 2.5 mg kg–1, and no relationship of response to dose between 2.5 and 12.5 mg kg–1)10. These reports were shared by Pharmacyclics in a conference abstract in 200911,12 and a press release in 201013. An early patent application by Pharmacyclics (US 2012/0087915 A1) accordingly claimed a full range of doses. Trials to support approval by the US Food and Drug Administration (FDA) continued. In July 2013, ibrutinib received accelerated approval for mantle cell lymphoma based on a 66% response rate in 111 patients treated at 560 mg daily. Notably, the 2013 FDA review included an analysis of the relationship of ibrutinib dose and trough plasma concentration to both response and toxicity. This analysis demonstrated no relationship with response: “Dose-response relationship for BTK occupancy and clinical response in the phase 1 dose escalation trial showed that maximum BTK occupancy and maximum response were achieved at doses of ≥ 2.5 mg/kg (≥ 175 mg for average weight of 70 kg)”14—far below the approved dosage of 560 mg. Meanwhile, the FDA also granted accelerated approval for previously treated chronic lymphocytic leukemia on 12 February 2014 on the basis of a 58% response rate in 48 patients treated at a dose of 420 mg daily. Thus, there were now two different doses approved for ibrutinib, with the labeled dose based solely on the dose that was used in the single-arm studies supporting the accelerated approvals. Furthermore, in the context of that approval, the FDA reiterated its assessment that the labeled dose was higher than necessary and included the explicit suggestion to study lower doses: “However, the proposed dose is 2.4-fold higher than the lowest dose that resulted in maximum BTK occupancy and maximum clinical response. Dose-response relationship for ORR and BTK occupancy from phase 1 study suggested that maximum ORR and maximum occupancy was achieved at doses of ≥ 2.5 mg/kg (≥ 175 mg for average weight of 70 kg) [see Pharmacometrics review in DARRTS dated 11/01/2013]. The sponsor should thus consider exploring lower doses in future development programs.”15 Those lower doses have not, to our knowledge, been rigorously explored in clinical trials—an unfortunate outcome for patients, since if a lower dose is just as effective with lower side effects, treatment would be safer and better. However, if the lower dose were found to provide better patient outcomes and resulted in a change in the labeled dose, it is likely that the labeled dose would not be covered by the patent. Thus, generic competitors might be able to enter the market sooner, once the primary compound patent lost exclusivity. In fact, the process at the US Patent and Trademark Office (USPTO) and the limits of the granted patents encourage the patent holder to avoid such information entirely. The patent examiner evaluating Pharmacyclics’ method of treatment patents found lower doses obvious on the basis of the 2009 and 2010 conference and press release disclosures, which occurred more than a year before the relevant patent was filed. **Only the highest doses**—420 mg and higher—**were granted** in the issued method of **treatment patent16**. **Patent law thus created incentives to pursue a higher, more toxic dose rather than the lower doses the FDA suggested be explored**. And, adding insult to injury, **once the patent was issued** with narrower claims covering the high doses only, **the drug sponsor** not only lacked incentives to explore the possibility of lower doses, it **had an active incentive not to explore** those **doses** **because evidence that lower doses were safe** and effective **would** sharply **reduce the economic significance of the method of treatment patent** it had narrowly managed to obtain. The patent holder already knew it could not get protection on a lower dose––the USPTO had rejected lower doses as obvious–– so any evidence of the importance of lower doses would have undermined the value of the company’s patent-protected, higher-dose product. Broader possibilities Although ibrutinib is only one example, we are concerned that it may be an indicator of a broader problem, one that either lies ahead or is already lurking. More generally, consider combination products with two drugs at fixed dosages. Many treatment method patents exist in which an independent claim specifies a dose, nominally designed to increase patient adherence but often at a much higher cost17,18. The result is that a prescriber cannot adjust the dosage for only one of the two drugs or discontinue only one component. It is possible, perhaps likely, that some of these combination regimens mirror the dosage issue with ibrutinib, in which the incentives of the patent system have encouraged the development of a drug in a form that is suboptimal for patient health in certain circumstances. This would not be the first time in history that combination medications have proven problematic. More than 50 years ago, a US Senate investigation found that certain combination antibiotics products— developed in an effort to bring something ‘new’ to the market—were useless or dangerous19. Nor is ibrutinib the only time in history that medications have been sold at higher dosages than appropriate for safety and efficacy. Millions of women received the birth control pill Enovid (mestranol/ noretynodrel), containing ten times the necessary dose, before studies pointed to a concerning risk of blood clots19. In another sign of negative innovation, **Gilead** Sciences is alleged to have **intentionally delayed a less-toxic version of its HIV medicine** **until just a few years before the original version’s patent expiration20**. Unfortunately, the pernicious impact of patent incentives described above means that not only are these situations possible, but it is hard to know how frequent or how serious these situations are. Pharmacyclics did not follow the recommendation from the FDA and others to study lower doses. Because its method of treatment patents were tied to the higher dose, they had no economic incentive to do such research— any information on safer dosing outside the scope of the issued claims would undermine the value of their existing patent, and they would be unable to get a new patent for the safer dose on grounds of obviousness. The safety data are starting to emerge anyway, albeit from sources other than the company9.

#### Disease is a non-linear, existential risk - encompasses AND outweighs other threats

Pamlin and Armstrong 15 Dennis Pamlin and Stuart Armstrong February 2015 “Global Challenges: 12 Risks that threaten human civilization: The case for a new risk category” https://web.archive.org/web/20171006070112/https://api.globalchallenges.org/static/wp-content/uploads/12-Risks-with-infinite-impact.pdf (Dennis Pamlin, Executive Project Manager Global Risks, Global Challenges Foundation, and Stuart Armstrong, James Martin Research Fellow, Future of Humanity Institute, Oxford Martin School, University of Oxford)//Re-cut by Elmer

3.1 Current risks Pandemic 3.1.4 Global **A pandemic** (from Greek πᾶν, pan, “all”, and δῆμος demos, “people”) is an epidemic of infectious disease that has spread through human populations across a large region; for instance several continents, or even **worldwide**. Here only worldwide events are included. A widespread endemic disease that is stable in terms of how many people become sick from it is not a pandemic. 260 84 Global Challenges – Twelve risks that threaten human civilisation – The case for a new category of risks 3.1 Current risks 3.1.4.1 Expected impact disaggregation 3.1.4.2 Probability Influenza subtypes266 Infectious diseases have been one of the **greatest causes of mortality in history**. Unlike many other global challenges pandemics have happened recently, as we can see where reasonably good data exist. **Plotting** historic epidemic **fatalities** on a log scale **reveals** that these tend to follow **a power law with a small exponent**: many plagues have been found to follow a power law with exponent 0.26.261 These kinds of power laws are **heavy-tailed**262 **to a significant degree**.263 In consequence most of the fatalities are accounted for by the top few events.264 If this law holds for future pandemics as well,265 then **the majority** of people who **will die** from epidemics will likely die **from the single largest pandemic**. Most epidemic fatalities follow a power law, with some extreme events – such as the Black Death and Spanish Flu – being even more deadly.267 There are other grounds for suspecting that such a highimpact epidemic will have a **greater probability than usually assumed**. **All the features** of an extremely devastating disease **already exist** in nature: essentially **incurable** (Ebola268), nearly **always fatal** (rabies269), **extremely infectious** (common cold270), and **long incubation periods** (HIV271). **If a pathogen** were to emerge that somehow **combined these** features (and **influenza** has **demonstrated antigenic shift**, the **ability to combine features from different viruses272**), **its death toll would be extreme**. Many relevant features of **the world have** **changed** considerably, **making past comparisons problematic**. The modern world has better sanitation and medical research, as well as national and supra-national institutions dedicated to combating diseases. Private insurers are also interested in modelling pandemic risks.273 Set against this is the fact that **modern transport** and **dense** human **population** allow infections to spread much more rapidly274, and there is the potential for urban slums to serve as breeding grounds for disease.275 Unlike events such as nuclear wars, pandemics would not damage the world’s infrastructure, and initial survivors would likely be resistant to the infection. And there would probably be survivors, if only in isolated locations. Hence the risk of a civilisation collapse would come from the **ripple effect** of the fatalities and the policy responses. These would include **political and agricultural disruption** as well as economic dislocation and damage to the world’s trade network (including the food trade). Extinction risk is only possible if the aftermath of the **epidemic fragments** and diminishes **human society to the extent that recovery becomes impossible277 before humanity succumbs to other risks (such as** **climate** change **or further pandemics**). Five important factors in estimating the probabilities and impacts of the challenge: 1. What the true probability distribution for pandemics is, especially at the tail. 2. The capacity of modern international health systems to deal with an extreme pandemic. 3. How fast medical research can proceed in an emergency. 4. How mobility of goods and people, as well as population density, will affect pandemic transmission. 5. Whether humans can develop novel and effective anti-pandemic solutions.

#### The next pandemic will be worse---action now is key.

Andy Plump 21. President for research and development at Takeda Pharmaceuticals and a cofounder of the Covid R&D Alliance. “Luck is not a strategy: The world needs to start preparing now for the next pandemic” 05-18-21. https://www.statnews.com/2021/05/18/luck-is-not-a-strategy-the-world-needs-to-start-preparing-now-for-the-next-pandemic/

As countries grapple with the worst global pandemic in a century, it’s hard to think about preparing for the next one. But if we don’t, it could be worse than Covid-19. Over the last 30 years, infectious disease outbreaks have emerged with alarming regularity. The World Health Organization lists an influenza pandemic and other high-threat viral diseases such as Ebola and dengue among the top 10 biggest threats to public health. The rate of animal-to-human transmission of viruses has been increasing, with the U.S. Centers for Disease Control and Prevention estimating that 75% of new infectious diseases in humans come from animals. These zoonotic infections can have profound effects on human life. The overall infection fatality rate is around 10% for severe acute respiratory syndrome (SARS), between 40% and 75% for Nipah virus, and as high as 88% for Ebola. While the infection fatality rate for Covid-19 is lower — likely less than 1% — the overall burden of death has been significantly higher since it has affected so many people, more than 160 million people as I write this. Luck is not a pandemic strategy Although the Covid-19 pandemic has been a human and health care disaster, by scientific measures the world was lucky this time. Covid-19 was far less lethal than its predecessors, less contagious than previous pandemic viruses, and we were able to quickly develop a cadre of effective vaccines. But luck is not a strategy. The same way the U.S. invests in and prepares for national defense, it must also prepare for another pandemic. Though the next viral outbreak cannot be prevented, the next pandemic can — but only with better preparation.

#### Extinction – defense is wrong

Piers Millett 17, Consultant for the World Health Organization, PhD in International Relations and Affairs, University of Bradford, Andrew Snyder-Beattie, “Existential Risk and Cost-Effective Biosecurity”, Health Security, Vol 15(4), http://online.liebertpub.com/doi/pdfplus/10.1089/hs.2017.0028

Historically, disease events have been responsible for the greatest death tolls on humanity. The 1918 flu was responsible for more than 50 million deaths,1 while smallpox killed perhaps 10 times that many in the 20th century alone.2 The Black Death was responsible for killing over 25% of the European population,3 while other pandemics, such as the plague of Justinian, are thought to have killed 25 million in the 6th century—constituting over 10% of the world’s population at the time.4 It is an open question whether a future pandemic could result in outright human extinction or the irreversible collapse of civilization.

A skeptic would have many good reasons to think that existential risk from disease is unlikely. Such a disease would need to spread worldwide to remote populations, overcome rare genetic resistances, and evade detection, cures, and countermeasures. Even evolution itself may work in humanity’s favor: Virulence and transmission is often a trade-off, and so evolutionary pressures could push against maximally lethal wild-type pathogens.5,6

While these arguments point to a very small risk of human extinction, they do not rule the possibility out entirely. Although rare, there are recorded instances of species going extinct due to disease—primarily in amphibians, but also in 1 mammalian species of rat on Christmas Island.7,8 There are also historical examples of large human populations being almost entirely wiped out by disease, especially when multiple diseases were simultaneously introduced into a population without immunity. The most striking examples of total population collapse include native American tribes exposed to European diseases, such as the Massachusett (86% loss of population), Quiripi-Unquachog (95% loss of population), and theWestern Abenaki (which suffered a staggering 98% loss of population).

In the modern context, no single disease currently exists that combines the worst-case levels of transmissibility, lethality, resistance to countermeasures, and global reach. But many diseases are proof of principle that each worst-case attribute can be realized independently. For example, some diseases exhibit nearly a 100% case fatality ratio in the absence of treatment, such as rabies or septicemic plague. Other diseases have a track record of spreading to virtually every human community worldwide, such as the 1918 flu,10 and seroprevalence studies indicate that other pathogens, such as chickenpox and HSV-1, can successfully reach over 95% of a population.11,12 Under optimal virulence theory, natural evolution would be an unlikely source for pathogens with the highest possible levels of transmissibility, virulence, and global reach. But advances in biotechnology might allow the creation of diseases that combine such traits. Recent controversy has already emerged over a number of scientific experiments that resulted in viruses with enhanced transmissibility, lethality, and/or the ability to overcome therapeutics.13-17 Other experiments demonstrated that mousepox could be modified to have a 100% case fatality rate and render a vaccine ineffective.18 In addition to transmissibility and lethality, studies have shown that other disease traits, such as incubation time, environmental survival, and available vectors, could be modified as well.19-2

#### Expanding breadth of Pharma Innovation into neglected diseases results in global linkages that revitalizes global health diplomacy.

Hotez 16, Peter J. Blue marble health: an innovative plan to fight diseases of the poor amid wealth. JHU Press, 2016. (Sabin Vaccine Institute and Texas Children’s Hospital Center for Vaccine Development, Departments of Pediatrics and Molecular Virology and Microbiology)//Elmer

We also need to better understand how these NTDs are actually transmitted within US borders, and I think it is extremely important to learn more about the links between these diseases and poverty. As I noted earlier, a drive through Houston’s Fifth Ward provides some insights, as one can quickly identify predisposing risk factors, including stray animals, dilapidated houses without window screens, standing water and discarded tires, and other evi- dence of environmental degradation, but we need to conduct careful epidemiological studies to really understand the links between poverty and NTDs, as well as animal reservoirs for illnesses such as Chagas disease and others. All of this presents an important research and development agenda for the **NTDs** in the United States. There are no point-of-care diagnostic tests available for most of the NTDs endemic to the nation, so blood from pa- tients must be sent to the CD С or other specialty research laboratories in order to establish a diagnosis for these conditions. As I sometimes point out to general audiences, when you go to your physician and get blood work done, there is no box to check off for toxocariasis or Chagas disease as there is for blood chemistries or other routine tests. We need diagnostic tests that are easily accessible to physicians and nurses. We also need new and improved treatments and vaccines. Because the NTDs are poverty-related diseases, they often fly below the radar screen of the major pharmaceutical companies and are not prioritized. Thus, the drugs used to treat these illnesses are not widely available, so typically the CDC has to be contacted in order to access them. In addition, many of these medicines were developed decades ago and produce a lot of side effects. For instance, the two medicines for Chagas disease—benznidazole and nifurtimox—cause skin rashes, diarrhea, and other unpleasant or even dangerous symptoms and illnesses. Patients using these medications have to interrupt their treatments up to 20% of the time. Moreover, these drugs cannot be used by pregnant women. Currently, new innovations for NTDs like Chagas dis- multinational ease still rely on nonprofit PDPs. The Geneva-based Drugs pharmaceutical for Neglected Diseases Initiative is leading efforts to de- companies have velop new and safer Chagas disease medicines [60], while shown little or modest at our National School of Tropical Medicine the Sab in interest in American Vaccine Institute and Texas Childrens Hospital Center for NTDs. As a result, new Vaccine Development (Sabin PDP) is working to develop products are being a therapeutic vaccine that could be used alongside exist- developed in the ing treatments [61]. These efforts rely on major philan- nonprofit sector. thropic donors. In our case at the Sabin PDP, they include the Kleberg Foundation, the Carlos Slim Foundation, the Southwest Electronic Energy Medical Research Institute, and Texas Childrens Hospital. Summary Points 1. In the United States, 45.3 million people live below the poverty line, roughly the same number of impoverished Americans alive during the early 1960s when Michael Harrington wrote The Other America. Approximately 20 million Americans now live in extreme poverty at one-half the US poverty level, and approximately 5 million are living on less than $2 per day 2. American poverty concentrates in specific areas, especially in southern states, with Texas having the largest numbers who live in poverty Important areas in the South include the Gulf Coast, border areas with Mexico, the Mississippi Delta, and Appalachia. 3. Approximately 12 million Americans are infected with NTDs, led by toxocariasis and trichomoniasis—which disproportionately affect African Americans—and Chagas disease (American trypanosomiasis) and cysticercosis—which disproportionately affect people of Hispanic origin. Toxoplasmosis is another important NTD. Toxocariasis, cysticercosis, and toxocariasis exert important mental health effects on impoverished Americans. Many of these NTDs are transmitted within US borders (autochthonous infections). 4. Arboviral infections are also important NTDs, led by dengue fever in Gulf Coastal areas and West Nile virus infection. WNV can cause chronic, persistent viral infections linked to chronic neurologic and renal disease. 5. There is an urgent need to promote awareness about the NTDs, especially for physicians and other health-care providers. 6. New policies are needed to expand surveillance for the NTDs affecting the United States. New legislation has been adopted in Texas, while additional bills are being introduced in the US Congress. Epidemiological studies are also needed to better understand how these diseases are transmitted and how they are linked to extreme poverty in the American South and elsewhere. 7. There is an urgent need for new “control tools” for American NTDs, including point-of-care diagnostics, antiparasitic and antiviral drugs, and vaccines. Many of these products are being developed by nonprofit PDPs rather than pharmaceutical companies. he G20 "A Theory of Justice" In his landmark 1971 book A Theory of Justice, the Harvard political philosopher John Rawls articulates two overriding principles of a just and fair society, namely, (1) “equality in the assignment of basic rights and duties” and (2) allowance of some social and economic inequalities, but only if they ultimately benefit “the least advantaged members of society” [1]. In terms of Rawls’s worldview, I believe that finding widespread NTDs among the extreme poor (and least-advantaged) who live amidst wealth—the central tenet of blue marble health—might represent one of the most jarring affronts to what he terms “justice as fairness” Because NTDs are now widespread among the leastadvantaged members of the worlds wealthiest economies, and they represent a major basis for thwarting their future growth, it is urgent for these nations, especially the G20 countries, to adopt strong internal policies to combat these diseases. I envision a three-pronged strategy to best address the G20 s (and Nigeria’s) poorest citizens afflicted by NTDs: 1. Each of the G20 nations and Nigeria has the capacity to fully understand the extent of these diseases within their own borders and then provide their own impoverished populations access to essential medicines used in mass drug administration to target helminth infections, in addition to trachoma, leprosy, yaws and scabies, and to provide treatments for other high-disease burden NTDs, including leishmaniasis and Chagas disease. The G20 countries and Nigeria Three major steps are required to effectively address blue marble health. 141 142 Blue Marble Health need to allocate resources and implement programs to achieve universal coverage for these diseases. 2. Each of the G20 nations and Nigeria has the capacity to conduct research and development for new NTD biotechnologies; they need to allocate resources toward this goal. 3. Both activities should be conducted within an overall framework of health system strengthening. Mass Drug Administration in the G20 A good place to revisit MDA among the G20 countries is to more closely examine the six G20 countries with positive worm indices—Brazil, China, India, Indonesia, Mexico, and South Africa—in addition to Nigeria. Together these countries account for one-half of the worlds helminth infections [2]. An analysis of WHO s PCT database reveals that most of these nations are severely underachieving when it comes to providing MDA for people who require regular and periodic treatment for their intestinal helminth infections, schistosomiasis, and LF. Shown in table 11.1 is WHO’s estimate of the percentage that received treatment in 2013 [3-5]. Overall, the G20 nations affected by helminth infections and Nigeria perform poorly when it comes to treating their affected populations through MDA. In terms of specific countries in Latin America, Brazil is reaching only approximately one-third of its children and population at risk. And although Mexico provides complete coverage for intestinal worms, it—as previously mentioned—neither diagnoses nor treats hundreds of thousands (and possibly millions) of people with Chagas disease. In Africa, Nigeria’s MDA reaches less than 25% of its children at risk for helminth infections, and there is no information about schistosomiasis coverage in South Africa forthcoming from WHO. However, as Dr. Eyrun Kjetland (who works extensively in South Africa) has pointed out, female genital schistosomiasis remains widespread there, in part because praziquantel has been mostly unavailable in the country, owing to its drug importation laws. Schistosomiasis and other NTDs are still found among the poor in the Kingdom of Saudi Arabia. The entire MENA region severely underdiagnoses most of its NTDs, including leishmaniasis. In Asia, Indonesia largely does not promote widespread deworming for its children, and only a small percentage of its population receives treatment for LF, while India does only marginally better. Indonesia also suffers from high rates of yaws, which can also be targeted by MDA using the antibiotic azithromycin. Similarly in India, the vast majority of its children do not have access to regular and periodic deworming, and only about one-half of the population receives MDA for LF. India also has the worlds largest numbers of leprosy cases. This disease can also be attacked through MDA using a multidrug therapy regimen. WHO does not present information on China, either because it has not been determined or is unavailable. However, China has made great strides in reducing its schistosomiasis prevalence since 1949, and it has eliminated LF. Similarly, Japan and South Korea have achieved significant success both in economic development and in reducing or eliminating its NTDs. 144 Blue Marble Health Key common factors for poor performance in meeting MDA targets are vast geographies, decentralization of health care, inadequate resource allocation, and lack of political will. Overall, the six G20 countries with positive worm indices, together with Nigeria, have the means and capacity to eliminate LF within their own borders, while greatly reducing the disease burdens of their intestinal helminth infections and schistosomiasis through MDA. Some of the key common factors for poor performance in meeting MDA targets are vast geographies, decentralization of health care that results in fragmentation of drug delivery, inadequate resource allocation, and lack of political will and commitment. What about G20 countries affected by NTDs but without a positive worm index? In the United States, the 12 million Americans infected and living with NTDs are largely unrecognized, undiagnosed, and untreated. The United States also does very little in terms of conducting active surveillance for Chagas disease (and other major NTDs), and only a tiny percentage of its population receives access to diagnosis and treatment—the same is true for Argentina. In both North America and Europe, toxocariasis and other parasitic zoonotic infections are seldom diagnosed and treated. Minimal information is available on eastern ------------------- Europeans, Turks, and Russians with intestinal worms or zoonotic NTDs or their access to diagnosis and treatment. NTDs remain widespread among Aboriginal Australians, including intestinal helminth infections and scabies—both of which can be targeted through MDA. Thus, the current status of access to essential medicines for people living in poverty and with NTDs among the G20 countries and Nigeria can be summarized as abysmal. The fact that so few are being treated through MDA programs is especially sad, given its low costs. As previ- ------------------- ously mentioned, there are approximately 1.07 billion treatments required among the populations at greatest risk in the G20 countries and Nigeria. At a cost of 50 cents per person per year, approximately $500 million would be required—that is, a dollar amount representing a tiny percentage (<0.001%) of the $65 trillion combined economy of these countries. The bottom line is that each of these nations has the internal capacity to provide these low-cost treatments to its impoverished populations. WHO has now launched a Universal Health Coverage (UHC) initiative that builds on its 1978 “Health for All” Alma-Ata declaration and the MillenThe current status of access to essential medicines for people living in poverty and with NTDs among the G20 countries and Nigeria can be summarized as abysmal. The G20 145 nium Development Goals, with a focus on protecting the health of the worlds most economically vulnerable populations. The activities highlighted here clearly fall within WHO s UHC mandate. Research and Development for New Control Tools and Biotechnologies For many of the leading NTDs—including vector-borne diseases such as dengue, leishmaniasis, Chagas disease, African sleeping sickness, and malaria, and also some helminth infections such as hookworm, schistosomiasis, onchocerciasis, and foodborne trematodiases—there are equally urgent needs to develop new drugs, diagnostics, and vaccines. Each year, the Australian policy group known as Policy Cures publishes an annual G-FINDER Report that measures the global investment in new technologies for neglected diseases, defining them broadly to include both the NTDs and the “big three” diseases: HIV/ AIDS, ТВ, and malaria [6]. For the year 2014, G-FINDER determined that approximately $3.37 billion was invested globally in neglected disease R&D technology, with most of that support going toward the big three diseases [6]. A look at total government support for neglected disease R&D, almost all of it from G20 countries, is also interesting. The public sector provided 64% of the total funding, and the United States provided two-thirds of that funding, mostly from the US National Institutes of Health [6]. In all, 71% of the total government funding for neglected diseases comes from the United States, European Commission, and United Kingdom. However, as the G-FINDER Report points out, these absolute numbers do not consider the GDPs of these nations. In terms of public funding relative to GDP ratios, countries such as Ireland, Denmark, Norway, and Argentina do particularly well in this regard [6]. Shown in table 11.2 are selected estimates from G-FINDER of the percentage of their GDP that various governments have devoted to R&D on Of government funding for neglected diseases R&D, a whopping 71% comes from the United States, European Commission, and United Kingdom. We need greater involvement and support from the remainder of the G20 countries, including positive worm index G20 countries— Brazil, China, India, Indonesia, Mexico, and South Africa, in addition to Nigeria. 146 Blue Marble Health Although NTDs and other poverty-related diseases account for almost 14% of the global disease burden, they receive only a bit more than 1% of the global health-related R&D funds. neglected diseases. Using data from the G-FINDER Report combined with GDP information, I calculate that the world spends approximately 0.0028% of its GDP on neglected diseases R&D. Only three G20 countries—United States, United Kingdom, and Australia—match or exceed that percentage, ------------------- although India and France come close to it. The worstperforming countries were China and Japan. However, in 2013 the Japanese government, together with Japans major pharmaceutical companies and the Bill & Melinda Gates Foundation, formed a partnership known as the Global Health Innovative Technology (GHIT) Fund for supporting PDPs and other entities to develop and shape new biotechnologies for neglected diseases, with an emphasis on NTDs [7, 8]. China is a different matter. The New York Times has reported that China paid out $86.3 billion in foreign investments in the year 2013 [9], with much of that spent in fragile nations where health systems are broken and NTDs are widespread. Clearly, China needs to allocate some of those funds to neglected diseases, either for MDA or new technologies. In addition, the nation of Brazil could easily increase its global contribution to NTD technologies by ю -fold in order to match higher-performing nations in this regard. Germany is now looking at supporting NTD technologies as part of an overarching G7 initiative on NTDs. In 2011, the German government launched a policy roadmap for neglected and poverty-related diseases [10]. Indeed, a recent analysis conducted by German investigators has found although NTDs ------------------- and other poverty-related diseases account for almost 14% of the global disease burden, they receive only a bit more than 1% of the global health-related R&D funds [11]. As shown in figure 11.1, by presenting R&D expenditures for a particular disease divided by the disability adjusted life years (DALYs) it is possible to get a sense of ------------------- diseases that are especially underfunded—even compared with other NTDS—such as the intestinal helminth infections and other neglected enteric diseases, as well as rheumatic fever [11]. Such data argue for the great urgency needed in addressing these health disparities by increasing R&D funding and support. Recently, the Dutch and German governments and the European Union (EU) have established important initiatives to support NTD R&D. The Dutch Ministry of Foreign Affairs, for instance, has been a major partner in our human hookworm vaccine initiative, while the EU has an important Frameworks Program 7 (FP7) for supporting new technologies [12], including a HOOKVAC Consortium of partners organized through the Amster dam Institute of Global Health and Development [13]. Most recently, the EU has established an ambitious Horizon 2020 program for expanding R&D in Europe, including NTD R&D activities [14], on top of a European and Developing Countries Clinical Trials Partnership (EDCTP) for clinically evaluating new NTD technologies [15]. New German government funding for NTD R&D funding was just announced. These Dutch, German, and EU initiatives represent an important advance for shaping the next generation of products to treat and prevent NTDs. Yet another aspect of blue marble health is the rise in comorbid conditions between the NTDs, the big three diseases, and the noncommunicable diseases. Impoverished and neglected populations in the G20 countries and Nigeria are facing a double hit resulting from the convergence of NTDs and NCDs. For instance, in Texas, Mexico, and India (but presumably elsewhere) they include both ТВ and diabetes interactions and, lately, dengue and diabetes interactions. In South Africa, HIV/AIDS now flourishes amidst the high prevalence of female genital schistosomiasis. Studying the pathogenesis and epidemiology of these comorbid interactions will also be an important theme in the coming years. Shaping a Policy for the G20 The G20 began meeting in 2008 in response to that years global recession and have since convened in a summit each year to discuss the major policy issues of the day [16]. At the 2015 G20 Summit held in Turkey, the major areas of broad emphasis included strengthening the global recovery and enhancing resilience, while ensuring sustainability [17]. Clearly, lifting the bottom segments of their populations out of poverty through NTD control and elimination could fall within the G20 remit. It is imperative that the six member nations with positive worm indices commit to providing total MDA coverage for their populations affected by the major helminth infections, and also that the four Western Hemispheric countries step up surveillance, diagnosis, and treatment for Chagas disease. Leishmaniasis, both kala-azar and the cutaneous form, also represent major NTDs affecting the G20, and these diseases need to be targeted for control and elimination. The US, Dutch, German, and Japanese governments, along with the EU, stand out for their contributions toward supporting product development to counter NTDs, 150 Blue Marble Health Equally important is the R&D agenda. There are some obvious underachievers among the G20 countries that must step up and contribute to R&D for new drug, diagnostic, and vaccine products to fight the neglected diseases [18]. Toward that aim, several investigators have proposed the establishment of R&D funds to support neglected disease research. They include a global vaccine development fund [19] and a general biomedical R&D fund focused on antimicrobial resistance, emerging infectious diseases, and neglected diseases [20]. Both proposals are thoughtful, have a lot of merit, and need to be considered, but I offer an alternative or complementary solution. In 2013, the World Health Assembly passed a resolution (66.22) that proposes a “strategic work plan” to achieve sustainable funding for health R&D that could emphasize NTDs. The plan commits the director-general of the World Health Organization to establish a global “observatory” in order to identify gaps and opportunities for health R&D related to neglected diseases [21]. Through a pooled fund managed by WHO-TDR (a special program on tropical disease research and training), several pilot projects are now being supported [22]. Given that todays neglected disease R&D support comes mostly from the United States—and indeed mostly from a single agency, the National Institutes of Health—it is difficult to envision how such a fund would be created without calling on the NIH yet again. Realistically, it is unlikely the NIH leadership or the well-established community of US scientists would be willing to cede control of NIH budgets to an international body. Instead, I think it is worth considering the possibility of having each of the G20 countries establish its own version of the Japanese GHIT Fund, which builds on indigenous scientists and academic institutions and their own pharmaceutical industries. A Chinese or South Korean version of GHIT for example could become a vital and important institution. Creating twenty separate innovation funds could achieve the same goals as a global fund, while simultaneously ensuring national ownership and capacity building for indigenous academic and industrial institutions. Many of them could develop and shape new biotechnologies in collaboration with the 16 international PDPs. This approach would be especially useful for the less developed G20 countries, including Brazil, Global funds for R&D are an option. An attractive alternative is to create national funds for product development R&D in each of the G20 countries and Nigeria—ones that resemble those put forward by the Dutch and Japanese governments. The G20 151 India, Indonesia, and Mexico. These nations have indigenous vaccine manufacturers, which are represented by the Developing Country Vaccine Manufacturers Network, and therefore have a level of sophistication for producing next-generation NTD vaccines. Still another option is for smaller groups of G20 countries to come together to support R&D investments. The EU’s programs for new NTD technologies highlighted above represent important examples. In addition, if institutions from China and India (both rivals and neighbors) collaborated in the area of neglected diseases [23], some important NTD problems affecting Asia could be solved in the coming years. The United States has potential to extend its outreach on NTDs by collaborating with other G20 nations in the Americas or other countries [24]. As a UN agency, WHO could certainly partner with one or more of these G20 NTD R&D investment funds, especially through its global health R&D observatory mechanism. Another key United Nations agency might include WIPO—the World Intellectual Property Organization. Through the Patent Cooperation Treaty mechanism, the Geneva-based WIPO represents one of the few revenue-generating UN agencies. In 2011, in collaboration with BIO Ventures for Global Health, it established WIPO Re:Search to facilitate the development of products to combat NTDs by bringing together major pharmaceutical companies and academic investigators working on these diseases [25]. As a revenue-generating UN agency under the charismatic leadership of Francis Gurry, WIPO has the potential to expand this remit to support NTD product R&D. Looking beyond the G20 The major NTDs linked to wealthy countries and blue marble health could also be addressed by nongovernmental organizations, including faith-based groups. For example, in 2011 the Pew Research Centers Forum on Religion and Public Life reported that the center of the worlds Christian-majority countries has shifted from Europe and North America to the Global South, meaning Africa, Asia, and Central and South America [26]. Thus, countries such as Brazil, Philippines, Angola, Democratic Republic of Congo, and Papua New Guinea now have some of the highest percentages of Christian populations. As shown in table 11.3, from an analysis published in PLOS NTDs I found that almost all of the world s Chagas disease cases and African trypanosomiasis (sleeping sickness) can be found in Christian-majority countries, in addition to almost one-half of the schistosomiasis cases [26]. These findings suggest the possibility of bringing in new actors to combat NTDs. They could include the Vatican and Pope Francis, especially given the new popes renewed commitment to impoverished populations [19]. The Orthodox Christian Church also has opportunities to highlight NTDs in countries such as Ethiopia or those in the Middle East, as do many Christian faith-based organizations and universities. The G20 153 Summary Points 1. The six G20 countries with positive worm indices—Brazil, China, India, Indonesia, Mexico, and South Africa, together with Nigeria, have the means and capacity to eliminate LF within their own borders, while greatly reducing the disease burdens of their intestinal helminth infections and schistosomiasis through MDA. 2. G20 countries without classical worm indices, including the United States, also need to find mechanisms for promoting surveillance and access to essential medicine options for the poor living with NTDs within their own borders. 3. The G20 countries also have important biotechnology capabilities, which have yet to be adequately tapped for producing new NTD diagnostics, drugs, and vaccines. Beyond the United States, European nations, Australia, and Japan, they also include Brazil, China, India, Indonesia, Mexico, Russian Federation, Saudi Arabia, South Africa, and South Korea. 4. Yet another aspect of blue marble health is the rise in comorbid conditions between the NTDs, the big three diseases, and the NCDs. 5. The EU and the Dutch and German governments have launched important NTD technology initiatives, as has the Japanese government and its partners through a new GHIT Fund. These activities support PDPs committed to NTDs as well as indigenous academic institutions and industrial organizations. 6. Large G20 economies such as Brazil and China must increase their global commitment to support new NTD technologies and R&D. 7. There are opportunities to link these new investments with parallel activities ongoing at two UN agencies, namely, WHO and WIPO. 8. These topics should be highlighted at future G20 summits. 9. Faith-based organizations could have a future role. For instance, the Vatican and related entities have opportunities to expand commitments to control those NTDs that are found to be prevalent among Christian-majority countries. Central to the blue marble health concept is that each of the G20 nations and Nigeria need to take greater responsibility for their own neglected diseases and neglected populations. Doing so could result in the control or elimination of one-half or more of the planets NTDs, with substantial gains made against HIV/AIDS, ТВ, and malaria. Thus, while programs of overseas development assistance devoted to health, such as PEPFAR, GFATM, PMI, and USAID’s NTD Program, in which the worlds richest countries provide support to the poorest nations for their neglected diseases, must continue and should even expand, we need increasingly to recognize the hidden burden of neglected diseases among the poor living in wealthy countries. As a first step, we must expand initiatives that raise awareness about the problem of NTDs within each of the G20 countries and Nigeria. The Global Network for NTDs linked to the Sabin Vaccine Institute has been working closely with the governments of India and Nigeria, respectively, in order to explain the opportunity for mass drug administration and its potential impact on health and economic development. MDA coverage rates are disappointingly low in these nations, especially for intestinal helminth infections and LF, as well as for schistosomiasis in the case of Nigeria. An extraordinary finding is that at least three nations with positive worm indices—India, Pakistan, and China—also maintain nuclear stockpiles [1]. Could the scientific horsepower of these nuclear states be partly redirected toward reducing endemic NTDs at home? 154 A Framework for Science and Vaccine Diplomacy 155 Outside of India and Nigeria, there is a need to promote NTD awareness in each of the G20 countries. For example, in the United States, our National School of Tropical Medicine has been highlighting the plight of some 12 million Americans living with NTDs. We have now worked with the Texas Legislature to enact a bill for NTD surveillance in suspected high-prevalence areas. However, similar initiatives need to be enacted across the G20 nations, including the European Union. In addition, international cooperation between the different G20 nations and Nigeria could be critical in achieving higher population coverage for MDA. For instance, China, despite its billions of dollars of business investments in sub-Saharan Africa, has not yet promoted NTD control efforts there. Yet China has tre- mendous expertise in MDA for NTDs and could provide Africa with valuable advice in this area. China was the first country to eliminate LF and has achieved successes in re- ducing its burden of schistosomiasis more than ю -fold since the 1949 revolution. China could also share its best practices with neighboring India, where NTDs remain practically ubiquitous [ 2]. Similarly, Japan and South Korea have made great gains toward eliminating intestinal helminth infections, while the former has also successfully eliminated LF and schistosomiasis. International cooperation between these three East Asian nations and Nigeria, or with the G20 countries with positive worm indices, especially India, Indonesia, and Brazil (where they are the highest), could result in important, positive health and economic gains. Each of these activities represents examples of what some refer to as global health diplomacy. Global Health Diplomacy My former colleague at Yale University, Ilona Kickbusch, currently the director of the Global Health Programme at the Graduate Institute of International and Development Studies in Geneva, has provided several working definitions of global health diplomacy, including efforts to “position health in foreign policy negotiations,” together with the establishment of global health governance initiatives [3]. Indeed, the creation of the GAVI Alliance, GFATM, UN AIDS, and other Geneva-based organizations might be considered vital examples of organizations created under the auspices of global health diplomacy, with the first two created following the 2000 Millennial Development Goals. The MDGs themselves represent an important framework for global health diplomacy, and arguably the most successful. Since 2005, several global health diplomacy initiatives have been enacted that could facilitate NTD activities among the G20 and Nigeria, although most of these actions are more focused on emerging viral infections of pandemic potential rather than the widespread chronic and debilitating NTDs. The International Health Regulations (IHR) were enacted in 2005 as a binding legal mechanism for all member states of WHO and focused on responses to acute public health emergencies [4]. IHR demands that countries report outbreaks and other public health events, while WHO responds with measures to uphold and enforce global health security [4]. IHR also establishes an emergency committee that advises the WHO director-general on whether an unexpected event should be considered a public health emergency. It also provides recommendations on initial steps for travel restrictions, surveillance, and infection control. With the possible exception of dengue fever, it is not clear how IHR will substantively address the NTDs or other blue marble health conditions. Moreover, even with IHR in place, the global response to the 2014 emergence of Ebola in West Africa was slow and inadequate and led to a catastrophic outbreak in the fall of that year [5]. This failure may require future revisions in the IHR, as recently recommended in a 2015 Lancet article by Lawrence Gostin and his colleagues at Georgetown University [6]. The Global Health Security Agenda (GHSA) is an interagency initiative of the US government conducted in partnership with other nations and international organizations, including WHO [7]. GHSA is also focused on preventing or reducing the impact of epidemics and outbreaks of pandemic potential, such as H7N9 influenza virus or MERS coronavirus, as well as detecting emerging threats and implementing rapid and effective responses. In some respects, GHSA represents the US component or response to IHR. It also covers intentional or accidental releases of dangerous infectious disease pathogens. Global Health 203s and The Lancet Commission were launched in 2013, coinciding with the twentieth anniversary of a landmark 1993 World Development Report that helped to ignite international efforts to link investments in health with economic development [8]. The Lancet Commission identifies four key messages and actions: (1) the substantial economic return on investing in health, which can be as much as 24% in low- and middle-income countries; (2) implementation of a “grand convergence” in global health through scale-up of health technologies and strengthening health systems by the year 2035; (3) fiscal policies such as taxation of tobacco and reduction of subsidies for fossil fuels, which represent powerful forces or “levers” for elected leaders; and (4) universal health coverage as an efficient mechanism to improve health as well as to provide “financial protection” [8]. The Addis Ababa Action Agenda (AAAA) is the product of the first of three international meetings for implementing the UN s 2015 Sustainable Development Goals. However, health is at present only a minor component of the AAAA. Indeed, the SDGs have been criticized because health is now only 1 of the 17 goals, whereas it was front and center among the 2000 MDGs. So far, the AAAAs recommendations have included the promotion of the health systems strengthening component of the GFATM and GAVI Alliance and the establishment of a Global Financing Facility (GFF) for womens and childrens health that would go hand-inhand with the UN secretary generals new Global Strategy for Every Woman Every Child [9]. The emphasis of these initiatives is to reduce preventable maternal, child, and adolescent deaths by 2030. Despite the evidence that hookworm infection and Chagas disease rank among the leading complications of pregnancy among women living in poverty in low- and middle-income countries, while female genital schistosomiasis is among sub-Saharan Africa’s most common gynecologic condition, there is not yet a specific mention of NTDs in the AAAA or GFF. Ultimately, the G20 nations can identify ways to address blue marble health disparities under the auspices of the SDGs or the global health diplomacy initiatives highlighted above. However, at present there is no specific mandate for them to do so. Vaccine Science Diplomacy Concurrently, the G20 nations have opportunities to collaborate in scientific activities leading to the development of new drugs, diagnostics, and vaccines. I have used the term “vaccine science diplomacy” to refer to inter- national scientific codevelopment of lifesaving vaccines between scientists of different nations, but particularly from nations with strained or evenly openly contentious international relations. The best historical example of vaccine science diplomacy is the codevelopment of the oral polio vaccine, led on the American side by Dr. Albert B. Sabin, and his Soviet virologist counterparts, including Dr. Mikhail Petrovich Chumakov [3]. In modern times there is potential interest in explor ing vaccine science diplomacy opportunities between the United States and some of the worlds Muslim-majority nations belonging to the Organisation of Islamic Cooperation [10,11]. OIC countries include most of the Middle East and North Africa, as well as some highly populated Southeast Asian nations, including Bangladesh, Indonesia, and Malaysia, as well as most of central Asia. New estimates that we published in PLOS NTDs in 2015 indicate that the 30 most-populated OIC countries account for 35% of the worlds helminth infections comprising the global Worm Index, including 50% of the worlds children who require MDA for schistosomiasis [11]. Given that approximately 1.5 billion people live in OIC countries, or about 20% of the global population, helminth infections appear to disproportionately affect the health and economic development of Muslim-majority countries, as does leishmaniasis, trachoma, and possibly other NTDs [11]. As shown in figure 12.1, there is also tight inverse association between the worm index and human development index in the Muslim world [11]. OIC nations with strong infrastructures in science and biotechnology are potentially attractive candidates to pursue joint vaccine science diplomacy initiatives with the United States. Here the idea would be to promote scientific collaborations between US scientists and scientists from selected OIC countries in order to create new NTD technologies for some of the worst-off Muslim-majority countries. The “worst-off” might include OIC countries at the high end of the worm index, including Mali, Cote d’Ivoire, Mozambique, Cameroon, Burkina Faso, and Niger, as well as Nigeria [11].

#### Solves hotspot escalation

Nang and Martin 17, Roberto N., and Keith Martin. "Global health diplomacy: A new strategic defense pillar." Military medicine 182.1-2 (2017): 1456-1460. (MC, Global Health Division, Uniformed Services University of the Health Sciences)//Elmer

INTRODUCTION: FORCE IF NECESSARY BUT NOT NECESSARILY FORCE The world appears unhinged. Instability from the Middle East, Caucasus, Africa, and Central America to Asia abound. The Study of Terrorism and Response to Terrorism database identified fewer than 300 major terrorist incidents between 1998 and 2004 in the Middle East and North Africa. In 2013, they listed 4,650 such incidents.1 Quieter cracks tear at the fabric of South America and parts of Asia. Although geographically distinct, many of these areas of instability share underlying causes that give rise to threats to the United States and the global community. Human-generated causes include corruption, poor governance, absence of the rule of law, violence, gross human rights abuses, climate change, environmental degradation, a weak civil society, and a lack of professional capabilities across skill sets within the government departments needed to effectively manage the operations of a well-run state.2 Natural causes include disasters, disease, demographic changes, and limited access to the resources essential for life. When these human or natural causes create conditions that result in poor provision of, or unequal access to essential services, such as water, food, shelter, health services, education, and economic opportunity, people lose confidence in government and hope for their children and their future. They become restless, demonstrate, can become violent and overthrow their governments (such as the self-immolation of Mohamed Bouazizi, the Tunisian cart vendor, which sparked 35 more selfimmolations by extralegal businessmen and started the Arab Spring), or can result in mass migrations.3 Desperate human security, conditions create desperate people undermining stability and creating even more demands from host nation governments and governments in neighboring states. Although force and counter terrorism programs are sometimes needed to address security threats, enormous opportunities are available to use nonkinetic capabilities within the Department of Defense (DoD), Department of State, U.S. Agency for International Development, other U.S. Government agencies, and civilian organizations to address the underlying causes of instability. Global health diplomacy is an underutilized strategic asset to do this. At a far lower cost, it will save lives, decrease economic losses, reduce the need for kinetic military operations, increase security cooperation, improve diplomatic relations, encourage trade, and create the foundations for longterm stability. HEALTH IS A NATIONAL SECURITY IMPERATIVE—DISTANT HEALTH THREATS ARE GLOBAL THREATS Health is a national security imperative. The second- and thirdorder effects of a strategic health or global health issue that severely impacts and overwhelms the stability of a far-distant nation can have broad and multiplying effects that transcend boundaries and can become regional and global security threats. When human immunodeficiency virus/acquired immunodeficiency syndrome first started to be seen in the United States, there were U.S. leaders that were not too concerned about its impact on the general public, alluding to the fact that it was a disease that mostly affected the four H’s: homosexuals, heroin addicts, hemophiliacs, and Haitians.4 From its first known cases in 1981 up to 2013, human immunodeficiency virus has infected almost 78 million people and killed about 39 million.5 The Chernobyl power plant accident that occurred on October 26, 1986, was a catastrophic nuclear accident. Several studies have been done to estimate the increase in health effects and cancer-related morbidity and mortality in Europe.6 Communicable diseases can be easily carried from a distant area of the world to a teeming metropolis within 24 hours because of the ease and affordability of plane travel. The interconnectedness of countries as a result of trade has its drawbacks— biological or chemical contamination of food or products commonly occur across oceans and continents.7 Noncommunicable diseases are also affecting not just high income countries but also low-to-middle income countries. Ubiquitous exports of fast-food meals, high-fructose drinks, and salty, fried foods have contributed to a tremendous increase in obesity and hypertension.8 Obese and sedentary populations negatively impact the workforce of a nation and its productivity. The offices of military personnel and readiness cite obesity as the number one disqualifying reason for new recruits.9 Twenty seven percent of the U.S. young adults are not fit to serve in the military.10 Addiction to illegal drugs is an important global health threat. The problems created by the manufacture of opium in Afghanistan, methamphetamine in Mexico, and cocaine in Peru and Columbia create tremendous and devastating health effects, loss of productivity, social disruptions, breed corruption in a nation’s military and police forces, and create turbulent violence all along its wake, both in the countries manufacturing the drugs and the countries importing them. Weather forecasters often discuss the multiplying effects that the fluttering of a butterfly’s wings in one country may have on the regional weather of another distant country. Global health professionals and more and more of our military and political leaders are now concerned that the disease that we see in a child in Africa or a pig in Asia may have tremendous impacts on the public health, economic productivity, military readiness, and strategic security interests of their nation. In addition, a weak health and political system anywhere can be a threat everywhere. LINKAGES: GLOBAL HEALTH, SECURITY, AND STRATEGIC CHALLENGES Global health encompasses the basic needs required for human security: respect for people’s universal rights, personal protection, the rule of law, access to food, water, health care, education, basic infrastructure, and shelter.11 Their absence leaves populations vulnerable to the depredations of insurgent groups and corrupt, venal cabals that can hijack a region or state for the benefit of themselves and a select group of people. This creates an environment of the privileged and abused, the included and excluded, and an environment ripe for insecurity and conflict.12 For a nation to provide the environment where people’s basic needs can be met requires capabilities within their governing infrastructure and communities. This includes management, finance, education, social sciences, law,medicine, public health, engineering, veterinary medicine, agronomy, and more. Their absence [undermines] ~~cripples~~ a nation’s ability to support a foundation for human security and stability, inhibits its ability to thrive in good times, and respond effectively to natural and man-made threats in bad times. It **breeds corruption**, poverty, poor health outcomes, spread of lethal diseases, gross **human rights abuses and conflict. This we have seen played out with grim efficiency in Afghanistan, Pakistan, Iraq, Syria, Sudan, Democratic Republic of the Congo, Central African Republic, Libya, Yemen, Somalia, Nigeria, Honduras, and beyond**. All have had disastrous regional effects, many have created direct threats to U.S. interests. Islamic State in Iraq and Syria was borne out of the brutal kleptocracy of Assad’s Syria and a destructive government in Iraq. Al-Shabaab was created in the failed state of Somalia. Boko Haram grew in the destitute and neglected regions of northern Nigeria. Al Qaeda and the Taliban secured a haven in the lawless western regions of Pakistan. Weak governments in Central America created a fertile ground for organized criminal gangs to terrorize the populace and profiteer off the illegal drug trade that destroys lives, and drives people to desperately flee northward into the United States. Insurgencies, terrorist organizations, and other nonstate actors thrive in the presence of an incompetent or abusive state government that violates segments of its citizenry and fails to provide an environment where peoples’ rights are protected and their basic needs met. These groups divine counter narratives that take advantage of people’s lack of hope and fears. They create a refuge and an outlet for people’s rage. Such messages and place of belonging can be a powerfulmagnet for youths, the poor, and the disenfranchised,who see little hope in the future. Security threats are not only manmade but also can come from nature. The international community’s failure to dramatically reduce our carbon footprint leaves us vulnerable to an increasing number of extreme weather events that threaten everything from coastal communities to food and water security. This will amplify existing tensions over natural resources and could result in the forced migrations of massive numbers of vulnerable people. The world’s population is expected to reach 9 billion by 2030. The growth will primarily occur in cities in the developing world most of which already have fractured or nonexistent infrastructure. Climate change will have a dramatic effect on densely populated poor urban areas, especially those in arid zones and in littoral areas. This is a recipe for disaster. Environmental degradation is also increasing the spread of infectious diseases and facilitating zoonoses to jump the species barrier and infect humans. The Ebola outbreak, like severe acute respiratory syndrome and H1N1 before it, is part of a long list of diseases that have infected humans from an animal reservoir with devastating impact. Many zoonoses exist and more will come. Using history’s guide, the next pandemic will likely be a zoonotic agent. Recognizing this, the United States last year led the creation of the Global Health Security Agenda to prevent, detect, and respond to deadly disease outbreaks.13 Though accepted by many countries, it has been implemented by few. No amount of force can resolve these challenges. However, global health diplomacy, exercised through civil-military and military-military programs, is a promising strategic tool that should be employed to address these wicked strategic or global health problems and improve domestic and international security. AN OPPORTUNITY TO ACT Despite a growing level of interest in academia and government agencies, there is little agreement on how to define “global health diplomacy.”14 Michaud defined it as “international diplomatic activities that (directly or indirectly) address issues of global health importance, and is concerned with how and why global health issues play out in a foreign policy context.”14 The World Health Organization (WHO) states that it “brings together the disciplines of public health, international affairs, management, law, and economics, and focuses on negotiations that shape and manage the global policy environment for health.”15 We summarize global health diplomacy as the application of a broad range of skill sets to cooperatively improve human security throughout the world. A vital area of focus must be to strengthen public service, governance capabilities, and civil society in unstable regions. Doing so will enable nations to create an environment where their citizens’ basic needs can be met, universal rights respected, and the ability to hold a government to account, secure. This includes building and retaining capabilities to manage effective, noncorrupt, justice, finance, health, education, defense, public works, and environmental departments. The absence of these structures cripples a country’s ability to govern itself and leaves it vulnerable to the causes of instability, both human and natural. The United States, by virtue of its strengths across diplomacy, defense, development, trade, and its inherent domestic civilian capabilities, has an opportunity to exercise its leadership and mobilize these assets. Using global health diplomacy to comprehensively strengthen public service and governance capabilities has been chronically neglected by the international development community. It needs a leader to start this process and the United States has the ability and authority to do so in the national and international interest.

### 1AC: Drug Prices

#### Advantage 2 is Drug Prices:

#### Evergreening is the root cause of high drug prices by delaying generics – that’s a critical internal link to healthcare costs.

Vanni 21 Amaka Vanni 3-23-2021 “On Intellectual Property Rights, Access to Medicines and Vaccine Imperialism” <https://twailr.com/on-intellectual-property-rights-access-to-medicines-and-vaccine-imperialism/> (PhD and LLM degrees in International Economic Law from the University of Warwick)//re-cut by Elmer

Third, **patent practices** in recent decades have **seen** **pharmaceutical companies engaging in trivial** and cosmetic **tweaking of a drug** **whilst** still **reaping the benefit of 20 years of patent protection**. This tweaking sometimes involves making minor changes to patented drugs, such as changes in mode of administration, new dosages, extended release, or change in color of the drug. These changes normally **do not offer** **any** significant **therapeutic advantage** even though pharmaceutical companies argue they provide improved health outcomes to patients. These additional patents on small changes to existing drugs, known as **evergreening** or patent thickets, **block** the early **entry of** competitive, **generic medicines** **that drive medicine prices down**. For example, while not mandated by TRIPS, many US led TRIPS-plus free trade agreements have expanded the scope for evergreening. These include the US-Jordan FTA (2000), US-Australia FTA (2004) as well as the US-Korea FTA (2007), which allow for the patenting of new forms, uses, or methods of using existing products. The cancer drug Gleevec®, owned by Novartis, is another example of how pharmaceutical companies often secure patents on new, more convenient versions with marginal therapeutic benefit to patients whilst blocking the entry of generic medicines. In 2013, Novartis’ patent application for Gleevec®– the β crystalline form of the salt imatinib mesylate – was rejected by the Indian Supreme Court because it lacked novelty. However, the company has secured patents for this product in other jurisdictions such as the US and has maintained a high price of Gleevec there. But in India the price of Gleevec® was reduced from approximately USD 2,200 to USD 88 for one month’s treatment in the generic drugs market as a result of the 2013 Indian Supreme Court judgement. Novartis is not the only culprit. The depression drug Effexor® by Pfizer was granted an evergreen patent when the company introduced an extended-release version, Efexor-XR®, even though there was no additional benefit to patients. Eventually, the patent was declared invalid, but by then it had already cost an estimated USD 209 million to Australian taxpayers and kept generic competition off the market for two and a half years. In another instance, Pfizer went on to secure an additional patent for the Pristiq®, which contained identical chemical compound as Efexor-XR®,and again with no added therapeutic benefit. These evergreening practices, of course, have material effects. Apart from delaying the entry of generic versions, they give brand-name pharmaceutical companies **free reign in the market**, which allows them to set the market price. Recent years have seen **monopoly prices rise** exorbitantly **causing** significant **financial strain to patients**, domestic **healthcare services and** even **insurance companies** in developed countries. A notorious example is Martin Shkreli, who in 2015 bought the rights to an anti-malarial drug, then raised the price by 5,000 per cent from a cost of USD 13.50 to USD 750. Similarly, a white paper by I-MAK shows how excessive patenting and related strategies are driving families to overspend on lifesaving medicines. Celgene, the makers of Revlimid® raised the price of the drug by more than 50 per cent since 2012 to over USD 125,000 per year of treatment. Using the example of Solvadi® by Gilead, which costs USD 84,000 per treatment, Feldman notes the drug would cost the US Department of Defense more than USD 12 billion to treat all hepatitis-infected patients in US Veterans Affairs. But the US is not alone. In Europe, expensive drugs have prompted a growing backlash against pharmaceutical corporations. Reacting to these price hikes, Dutch pharmacies are bypassing these exorbitant prices by preparing medicines in-house for individual patients. The broken IP system ranging from an extraordinarily low standard for granting patents to permissions of patent thickets around a single molecule has not only severely distorted the system of innovation, but they have also skewed access to life-saving drugs. As a result, prices for new and existing medicines are constantly rising, making essential medicines inaccessible for millions of people around the world.

#### Pharma’s the largest drive of healthcare costs.

Brennan 16, Hannah, et al. "A prescription for excessive drug pricing: leveraging government patent use for health." Yale JL & Tech. 18 (2016): 275. (Law Clerk to the Honorable Theodore McKee, Chief Judge, Third Circuit)//re-cut by Elmer

The **soaring cost of pharmaceuticals is one of the most pressing domestic policy issues** in the United States today. Nearly **one-fifth of** the U.S. Gross Domestic Product (**GDP) is spent on healthcare**, and **pharmaceuticals are a key expenditure**.1 In 2014, the **U**nited **S**tates **spent a record $297.7 billion** on pharmaceuticals, over 12% more than the previous 2 year. The 2014 increase in prescription drug spending can be attributed almost entirely to recently approved drugs that treat the Hepatitis C virus (HCV). 3 With list prices that approach $100,000 for a twelve-week regimen, 4 these new medicines have brought the issue of drug pricing roaring to the fore in policy debates. **High drug prices are of enormous concern** to voters, 5 policymakers, and politicians across the political 6 spectrum. High drug prices also have a significant impact on health. The new HCV drugs offer an excellent example. Potentially deadly if untreated, HCV is one of the most pressing health problems facing the United States. 7 The new drugs are far superior to previous treatments and could potentially enable elimination of the disease.8 But treating all of the approximately 5.2 million people who currently have HCV in the United States at the best reported prices offered by Gilead, the sole supplier of the most important new drugs, would cost at least $234 billion.9 Given the budget impact of these new medicines, most payors have sharply restricted their availability-covering them only for the very sickest, or refusing to cover them at all 0-instead of rapidly rolling them out. Medicaid, for example, treated only 2.4% of enrollees estimated to have HCV in 2014, despite spending more than a billion dollars on the new medicines1.1 Even with the small number treated, Gilead's earnings have been stratospheric: the company earned $36 billion from its new HCV medicines in their first twenty-seven months on the market. 12

#### That hurts the Economy

Sood et Al 7, Neeraj, Arkadipta Ghosh, and J. Escarse. "The effect of health care cost growth on the US economy." Office of the Assistant Secretary for Planning and Evaluation, US Department of Health and Human Services (September). Available at (http://aspe. hhs. gov/health/reports/08/healthcarecost/report. html (HHS) (2007). (PhD, is professor and vice dean for research at the USC Price School of Public Policy and a founding member the USC Schaeffer Center)//Elmer

2. CONCEPTUAL OVERVEIW OF POTENTIAL MECHNISMS THROUGH WHICH HEALTH CARE INFLATION COULD AFFECT THE US ECONOMY Not surprisingly, the dramatic increases in health care spending and the share of GDP devoted to health care have raised concerns about the **negative impact of health care cost inflation on the U.S. economy**. In an era of global economic markets, these concerns are reinforced by the status of the U.S. as a spending outlier among competing nations. The major concern is that **rapid increases in health care spending** **can affect** **major economic indicators such** per capita **GDP, employment and inflation**. The effects are likely to occur **across all sectors** of the economy – governments, businesses and households – as all these interrelated sectors play an important role in the provision, financing and consumption of health care in the US. For example, Federal, state and local governments collect taxes from businesses and households to finance public health insurance programs and to directly provide health care to households. Businesses provide employment to US households and also provide health insurance to their employees. Households are the final consumers of health care and also bear some incidence of health care costs. In this report we separately identify the effects of health care costs on the aggregate economy and on each one of these interrelated sectors. However, it is important to note that the **effects** of health care costs **on one sector** are **likely to affect** outcomes in **other sectors**. For example, **faced with rising health care costs** **governments** might **attempt to reduce health spending by reducing eligibility for public health insurance**, consequently **increasing** **uninsurance rates** among households. The increase in health care costs might also prompt governments **to raise taxes**, increase borrowing or **reduce investments in** other **critical sectors such as education and infrastructure,** **suppressing economic growth** and affecting both businesses and households. Similarly, **US companies** faced with rapidly growing health care costs **might reduce employment** and investments in the US economy. Rising health care costs could also **fuel inflation** in the U.S. and make U.S. goods and services less competitive in international markets over time, because increasing health care costs might eventually be reflected in higher product prices. Since most other nations do not have employer-sponsored health insurance, companies in thosenations may be better able to keep prices low.2 Finally, high health care costs could reduce access to health care, bankrupt consumers and deplete retirement savings.

#### Economic decline results in multilateral breakdown that causes state collapse, conflict, climate change, and Arctic and Space War.

McLennan 21 – Strategic Partners Marsh McLennan SK Group Zurich Insurance Group, Academic Advisers National University of Singapore Oxford Martin School, University of Oxford Wharton Risk Management and Decision Processes Center, University of Pennsylvania, “The Global Risks Report 2021 16th Edition” “http://www3.weforum.org/docs/WEF\_The\_Global\_Risks\_Report\_2021.pdf //Re-cut by Elmer

Forced to choose sides, governments may face **economic** or diplomatic **consequences**, as proxy disputes play out in control over economic or geographic resources. The deepening of geopolitical fault lines and the lack of viable middle power alternatives make it harder for countries to cultivate connective tissue with a diverse set of partner countries based on mutual values and maximizing efficiencies. Instead, networks will become thick in some directions and non-existent in others. The COVID-19 crisis has amplified this dynamic, as digital interactions represent a “huge loss in efficiency for diplomacy” compared with face-to-face discussions.23 With some **alliances weakening**, diplomatic relationships will become more unstable at points where superpower tectonic plates meet or withdraw. At the same time, without superpower referees or middle power enforcement, global **norms** may **no longer govern** state **behaviour**. Some governments will thus see the solidification of rival blocs as an opportunity to engage in regional posturing, which will have destabilizing effects.24 Across societies, domestic discord and **economic crises will** **increase** the risk of **autocracy**, **with corresponding** **censorship, surveillance**, restriction of movement and abrogation of rights.25 Economic crises will also amplify the **challenges for middle power**s as they navigate geopolitical competition. **ASEAN countries, for example, had offered a potential new manufacturing base as the United States and China decouple, but the pandemic has left these countries strapped for cash to invest in the necessary infrastructure and productive capacity.26** Economic fallout is pushing many countries to debt distress (see Chapter 1, Global Risks 2021). While G20 countries are supporting debt restructure for poorer nations,27 larger economies too may be at **risk of default** in the longer term;28 this would **leave them further stranded**—**and unable to exercise leadership—on the global stage**. Multilateral meltdown **Middle power weaknesses** will be **reinforced** in weakened institutions, which may translate to **more uncertainty and lagging progress on shared global challenges such as climate change**, **health, poverty reduction and technology governance**. In the absence of strong regulating institutions, **the Arctic and space represent new realms for** potential **conflict** as the superpowers and middle powers alike compete to extract resources and secure strategic advantage.29 If the global superpowers continue to accumulate economic, military and technological power in a zero-sum playing field, some middle powers could increasingly fall behind. Without cooperation nor access to important innovations, middle powers will struggle to define solutions to the world’s problems. In the long term, GRPS **respondents forecasted “w**eapons of **m**ass **d**estruction” **and “state collapse**” as the two top critical threats: in the absence of strong institutions or clear rules, clashes— such as those in **Nagorno-Karabakh or the Galwan Valley**—**may more frequently flare into** full-fledged **interstate conflicts**,30 which is particularly worrisome where unresolved tensions among nuclear powers are concerned. These conflicts may lead to state collapse, with weakened middle powers less willing or less able to step in to find a peaceful solution.

#### COVID creates an economic brink---recovery is strong now because of effective monetary policy, but we’ve hit the zero-lower bound.

Christopher Rugaber 21. Associated Press. “Federal Reserve keeps key interest rate near zero, signals COVID-19 economic risks receding.” https://www.chicagotribune.com/business/ct-biz-fed-interest-rates-economy-20210428-bumyc3ynpza6ri4ygsntmdsmya-story.html.

WASHINGTON — The Federal Reserve is keeping its ultra-low interest rate policies in place, a sign that it wants to see more evidence of a strengthening economic recovery before it would consider easing its support.

In a statement Wednesday, the Fed expressed a brighter outlook, saying the economy has improved along with the job market. And while the policymakers noted that inflation has risen, they ascribed the increase to temporary factors.

The Fed also signaled its belief that the pandemic’s threat to the economy has diminished, a significant point given Chair Jerome Powell’s long-stated view that the recovery depends on the virus being brought under control. Last month, the Fed had cautioned that the virus posed “considerable risks to the economic outlook.” On Wednesday, it said only that “risks to the economic outlook remain” because of the pandemic.

The central bank left its benchmark short-term rate near zero, where it’s been since the pandemic erupted nearly a year ago, to help keep loan rates down to encourage borrowing and spending. It also said in a statement after its latest policy meeting that it would keep buying $120 billion in bonds each month to try to keep longer-term borrowing rates low.

The U.S. economy has been posting unexpectedly strong gains in recent weeks, with barometers of hiring, spending and manufacturing all surging. Most economists say they detect the early stages of what could be a robust and sustained recovery, with coronavirus case counts declining, vaccinations rising and Americans spending their stimulus-boosted savings.

#### Eroding financial resilience causes global war---that overcomes traditional barriers to conflict.

Jomo Kwame Sundaram & Vladimir Popov 19. Former economics professor, was United Nations Assistant Secretary-General for Economic Development, and received the Wassily Leontief Prize for Advancing the Frontiers of Economic Thought in 2007. Former senior economics researcher in the Soviet Union, Russia and the United Nations Secretariat, is now Research Director at the Dialogue of Civilizations Research Institute in Berlin “Economic Crisis Can Trigger World War.” <http://www.ipsnews.net/2019/02/economic-crisis-can-trigger-world-war/>.

Economic recovery efforts since the 2008-2009 global financial crisis have mainly depended on unconventional monetary policies. As fears rise of yet another international financial crisis, there are growing concerns about the increased possibility of large-scale military conflict.

More worryingly, in the current political landscape, prolonged economic crisis, combined with rising economic inequality, chauvinistic ethno-populism as well as aggressive jingoist rhetoric, including threats, could easily spin out of control and ‘morph’ into military conflict, and worse, world war.

Crisis responses limited

The 2008-2009 global financial crisis almost ‘bankrupted’ governments and caused systemic collapse. Policymakers managed to pull the world economy from the brink, but soon switched from counter-cyclical fiscal efforts to unconventional monetary measures, primarily ‘quantitative easing’ and very low, if not negative real interest rates.

But while these monetary interventions averted realization of the worst fears at the time by turning the US economy around, they did little to address underlying economic weaknesses, largely due to the ascendance of finance in recent decades at the expense of the real economy. Since then, despite promising to do so, policymakers have not seriously pursued, let alone achieved, such needed reforms.

Instead, ostensible structural reformers have taken advantage of the crisis to pursue largely irrelevant efforts to further ‘casualize’ labour markets. This lack of structural reform has meant that the unprecedented liquidity central banks injected into economies has not been well allocated to stimulate resurgence of the real economy.

From bust to bubble

Instead, easy credit raised asset prices to levels even higher than those prevailing before 2008. US house prices are now 8% more than at the peak of the property bubble in 2006, while its price-to-earnings ratio in late 2018 was even higher than in 2008 and in 1929, when the Wall Street Crash precipitated the Great Depression.

As monetary tightening checks asset price bubbles, another economic crisis — possibly more severe than the last, as the economy has become less responsive to such blunt monetary interventions — is considered likely. A decade of such unconventional monetary policies, with very low interest rates, has greatly depleted their ability to revive the economy.

The implications beyond the economy of such developments and policy responses are already being seen. Prolonged economic distress has worsened public antipathy towards the culturally alien — not only abroad, but also within. Thus, another round of economic stress is deemed likely to foment unrest, conflict, even war as it is blamed on the foreign.

International trade shrank by two-thirds within half a decade after the US passed the Smoot-Hawley Tariff Act in 1930, at the start of the Great Depression, ostensibly to protect American workers and farmers from foreign competition!

Liberalization’s discontents

Rising economic insecurity, inequalities and deprivation are expected to strengthen ethno-populist and jingoistic nationalist sentiments, and increase social tensions and turmoil, especially among the growing precariat and others who feel vulnerable or threatened.

Thus, ethno-populist inspired chauvinistic nationalism may exacerbate tensions, leading to conflicts and tensions among countries, as in the 1930s. Opportunistic leaders have been blaming such misfortunes on outsiders and may seek to reverse policies associated with the perceived causes, such as ‘globalist’ economic liberalization.

Policies which successfully check such problems may reduce social tensions, as well as the likelihood of social turmoil and conflict, including among countries. However, these may also inadvertently exacerbate problems. The recent spread of anti-globalization sentiment appears correlated to slow, if not negative per capita income growth and increased economic inequality.

To be sure, globalization and liberalization are statistically associated with growing economic inequality and rising ethno-populism. Declining real incomes and growing economic insecurity have apparently strengthened ethno-populism and nationalistic chauvinism, threatening economic liberalization itself, both within and among countries.

Insecurity, populism, conflict

Thomas Piketty has argued that a sudden increase in income inequality is often followed by a great crisis. Although causality is difficult to prove, with wealth and income inequality now at historical highs, this should give cause for concern.

Of course, other factors also contribute to or exacerbate civil and international tensions, with some due to policies intended for other purposes. Nevertheless, even if unintended, such developments could inadvertently catalyse future crises and conflicts.

Publics often have good reason to be restless, if not angry, but the emotional appeals of ethno-populism and jingoistic nationalism are leading to chauvinistic policy measures which only make things worse.

At the international level, despite the world’s unprecedented and still growing interconnectedness, multilateralism is increasingly being eschewed as the US increasingly resorts to unilateral, sovereigntist policies without bothering to even build coalitions with its usual allies.

Avoiding Thucydides’ iceberg

Thus, protracted economic distress, economic conflicts or another financial crisis could lead to military confrontation by the protagonists, even if unintended. Less than a decade after the Great Depression started, the Second World War had begun as the Axis powers challenged the earlier entrenched colonial powers.

They patently ignored Thucydides’ warning, in chronicling the Peloponnesian wars over two millennia before, when the rise of Athens threatened the established dominance of Sparta!

Anticipating and addressing such possibilities may well serve to help avoid otherwise imminent disasters by undertaking pre-emptive collective action, as difficult as that may be.

#### Growth is sustainable, physical limits aren’t absolute, AND resource use is declining now---degrowth unleashes global disaster

Bailey 18 [Ronald; February 16; B.A. in Economics from the University of Virginia, member of the Society of Environmental Journalists and the American Society for Bioethics and Humanities, citing a compilation of interdisciplinary research; Reason, “Is Degrowth the Only Way to Save the World?” https://reason.com/2018/02/16/is-degrowth-the-only-way-to-save-the-wor; RP]

Unless us folks in rich countries drastically reduce our material living standards and distribute most of what we have to people living in poor countries, the world will come to an end. Or at least that's the stark conclusion of a study published earlier this month in the journal Nature Sustainability. The researchers who wrote it, led by the Leeds University ecological economist Dan O'Neill, think the way to prevent the apocalypse is "degrowth."

Vice, pestilence, war, and "gigantic inevitable famine" were the planetary boundaries set on human population by the 18th-century economist Robert Thomas Malthus. The new study gussies up old-fashioned Malthusianism by devising a set of seven biophysical indicators of national environmental pressure, which they then link to 11 indicators of social outcomes. The aim of the exercise is to concoct a "safe and just space" for humanity.

Using data from 2011, the researchers calculate that the annual per capita boundaries for the world's 7 billion people consist of the emission of 1.6 tons of carbon dioxide per year and the annual consumption of 0.9 kilograms of phosphorus, 8.9 kilograms of nitrogen, 574 cubic meters of water, 2.6 tons of biomass (crops and wood), plus the ecological services of 1.7 hectares of land and 7.2 tons of material per person.

On the social side, meanwhile, the researchers say that life satisfaction in each country should exceed 6.5 on the 10-point Cantril scale, that healthy life expectancy should average at least 65 years, and that nutrition should be over 2,700 calories per day. At least 95 percent of each country's citizens must have access to good sanitation, earn more than $1.90 per day, and pass through secondary school. Ninety percent of citizens must have friends and family they can depend on. The threshold for democratic quality must exceed 0.8 on an index scale stretching from -1 to +1, while the threshold for equality is set at no higher than 70 on a Gini Index where 0 represents perfect equality and 100 implies perfect inequality. They set the threshold for percent of labor force employed at 94 percent.

So how does the U.S. do with regard to their biophysical boundaries and social outcomes measures? We Americans transgress all seven of the biophysical boundaries. Carbon dioxide emissions stand at 21.2 tons per person; we each use an average of 7 kilograms of phosphorus, 59.1 kilograms of nitrogen, 611 cubic meters of water, and 3.7 tons of biomass; we rely on the ecological services of 6.8 hectares of land and 27.2 tons of material. Although the researchers urge us to move "beyond the pursuit of GDP growth to embrace new measures of progress," it is worth noting that U.S. GDP is $59,609 per capita.

On the other hand, those transgressions have provided a pretty good life for Americans. For example, life satisfaction is 7.1; healthy life expectancy is 69.7 years; and democratic quality stands at 0.8 points. The only two social indicators we just missed on were employment (91 percent) and secondary education (94.7 percent).

On the other hand, our hemisphere is home to one paragon of sustainability—Haiti. Haitians breach none of the researchers' biophysical boundaries. But the Caribbean country performs abysmally on all 11 social indicators. Life satisfaction scores at 4.8; healthy life expectancy is 52.3 years; and Haitians average 2,105 calories per day. The country tallies -0.9 on the democratic quality index. Haiti's GDP is $719 per capita.

Other near-sustainability champions include Malawi, Nepal, Myanmar, and Nicaragua. All of them score dismally on the social indicators, and their GDPs per capita are $322, $799, $1,375, and $2,208, respectively.

The country that currently comes closest to the researchers' ideal of remaining within its biophysical boundaries while sufficient social indicators is…Vietnam. For the record, Vietnam's per capita GDP is $2,306.

"Countries with higher levels of life satisfaction and healthy life expectancy also tend to transgress more biophysical boundaries," the researchers note. A better way to put this relationship is that more wealth and technology tend to make people happier, healthier, and freer.

O'Neill and his unhappy team fail drastically to understand how human ingenuity unleashed in markets is already well on the way toward making their supposed planetary boundaries irrelevant. Take carbon dioxide emissions: Supporters of renewable energy technologies say that their costs are already or will soon be lower than those of fossil fuels. Boosters of advanced nuclear reactors similarly argue that they can supply all of the carbon-free energy the world will need. There's a good chance that fleets of battery-powered self-driving vehicles will largely replace private cars and mass transit later in this century.

Are we about to run out of phosphorous to fertilize our crops? Peak phosphorus is not at hand. The U.S. Geological Survey (USGS) reports that at current rates of mining, the world's known reserves will last 266 years. The estimated total resources of phosphate rock would last over 1,140 years. "There are no imminent shortages of phosphate rock," notes the USGS. With respect to the deleterious effects that using phosphorus to fertilize crops might have outside of farm fields, researchers are working on ways to endow crops with traits that enable them to use less while maintaining yields.

O'Neill and his colleagues are also concerned that farmers are using too much nitrogen fertilizer, which runs off fields into the natural environment and contributes to deoxygenated dead zones in the oceans, among other ill effects. This is a problem, but one that plant breeders are already working to solve. For example, researchers at Arcadia Biosciences have used biotechnology to create nitrogen-efficient varieties of staples like rice and wheat that enable farmers to increase yields while significantly reducing fertilizer use. Meanwhile, other researchers are moving on projects to engineer the nitrogen fixation trait from legumes into cereal crops. In other words, the crops would make their own fertilizer from air.

Water? Most water is devoted to the irrigation of crops; the ongoing development of drought-resistant and saline-tolerant crops will help with that. Hectares per capita? Humanity has probably already reached peak farmland, and nearly 400 million hectares will be restored to nature by 2060—an area almost double the size of the United States east of the Mississippi River. In fact, it is entirely possible that most animal farming will be replaced by resource-sparing lab-grown steaks, chops, and milk. Such developments in food production undermine the researchers' worries about overconsumption of biomass.

And humanity's material footprint is likely to get smaller too as trends toward further dematerialization take hold. The price system is a superb mechanism for encouraging innovators to find ways to wring ever more value out less and less stuff. Rockefeller University researcher Jesse Ausubel has shown that this process of absolute dematerialization has already taken off for many commodities.

After cranking their way through their models of doom, O'Neill and his colleagues lugubriously conclude: "If all people are to lead a good life within planetary boundaries, then the level of resource use associated with meeting basic needs must be dramatically reduced." They are right, but they are entirely backward with regard to how to achieve those goals. Economic growth provides the wealth and technologies needed to lift people from poverty while simultaneously lightening humanity's footprint on the natural world. Rather than degrowth, the planet—and especially its poor people—need more and faster economic growth.

#### The Alternative to the Aff isn’t no medicine but exploitive medicine – the Plan’s orientation is a sequencing strategy to resistance.

Ahmed 20 A Kavum Ahmed 6-24-2020 "Decolonizing the vaccine" <https://africasacountry.com/2020/06/decolonizing-the-vaccine> (A. Kayum Ahmed is Division Director for Access and Accountability at the Open Society Public Health Program in New York and teaches at Columbia University Law School.)//Duong+Elmer

Reflecting on a potential COVID-19 vaccine trial during a television interview in April, a French doctor stated, “If I can be provocative, shouldn’t we be doing this study in Africa, where there are no masks, no treatments, no resuscitation?” These remarks reflect a colonial view of Africa, reinforcing the idea that Africans are non-humans whose black bodies can be experimented on. This colonial perspective is also clearly articulated in the alliance between France, The Netherlands, Germany and Italy to negotiate priority access to the COVID-19 vaccine for themselves and the rest of Europe. In the Dutch government’s announcement of the European vaccine coalition, they indicate that, “… the alliance is also working to make a portion of vaccines available to low-income countries, including in Africa.” In the collective imagination of these European nations, Africa is portrayed as a site of redemption—a place where you can absolve yourself from the sins of “vaccine sovereignty,” by offering a “portion of the vaccines” to the continent. Vaccine sovereignty reflects how European and American governments use public funding, supported by the pharmaceutical industry and research universities, to obtain priority access to potential COVID-19 vaccines. The concept symbolizes the COVID-19 **vaccine** (when it eventually becomes available) as **an instrument of power deployed to exercise control** **over who will live and who must die**. In order to counter vaccine sovereignty, we must decolonize the vaccine. Africans have a particular role to play in leading this decolonization process as subjects of colonialism and as objects of domination through coloniality. Colonialism, as an expansion of territorial dominance, and coloniality, as the continued expression of Western imperialism after colonization, play out in the vaccine development space, most notably on the African continent. So what does decolonizing the vaccine look like? And how do we decolonize something that does not yet exist? For Frantz Fanon, “**Decolonization**, which sets out to change the order of the world, **is**, obviously, a program of **complete disorder**.” **Acknowledging** **that the** COVID-19 **vaccine has been weaponized** **as an instrument of power** by wealthy nations, **decolonization** **requires** a Fanonian program of **radical re-ordering.** In the context of vaccine sovereignty, this re-ordering **necessitates** the **dismantling** of the **profit-driven biomedical system**. This program starts with **de-linking from** **Euro-American constructions of knowledge and power** that reinforce vaccine sovereignty through the profit-driven biomedical system. Advocacy campaigns such as the “People’s Vaccine”, which calls for guaranteed free access to COVID-19 vaccines, diagnostics and treatments to everyone, everywhere, are a good start. Other mechanisms, such as the World Health Organization’s COVID-19 Technology Access Pool, similarly supports universal access to COVID-19 health technologies as global public goods. Since less than 1% of vaccines consumed in Africa are manufactured on the continent, regional efforts to develop vaccine manufacturing capacity such as those led by the Africa Center for Disease Control and Prevention, as well as the Alliance of African Research Universities, must be supported. These efforts collectively advance delinking and move us closer toward the re-ordering of systems of power. The opportunity for disorder is paradoxically enabled by the COVID-19 pandemic, which has permitted moments of existential reflection in the midst of the crisis. A few months ago, a press release announcing the distribution of “a portion of the vaccines” to Africans, may have been lauded as European benevolence. But in the context of a pandemic that is more likely to kill black people, Africa’s reliance on Europe for vaccine handouts is untenable, necessitating a re-examination of the systems of power that hold this colonial relationship in place. The Black African body appears to be good enough to be experimented on, but not worthy of receiving simultaneous access to the COVID-19 vaccine as Europeans. Consequently, Africans continue to feel the effects of colonialism and white supremacy, and understand the pernicious nature of European altruism. By reinforcing the current system of vaccine research, development and manufacturing, it has become apparent that European governments want to retain their colonial power over life and death in Africa through the COVID-19 vaccine. Resistance to this colonial power requires the decolonization of the vaccine.

#### This is a form of pharmaceutical capitalism – exploiting marginalized groups in the third world.

Lift Mode 17 3-10-2017 "Pharmaceutical Colonialism” <https://medium.com/@liftmode/pharmaceutical-colonialism-3-ways-that-western-medicine-takes-from-indigenous-communities-3a9339b4f24f> (We at Liftmode.com are a team of professionals from a variety of backgrounds, dedicated to the mission of providing the highest quality and highest purity nutritional health supplements on the market. We look specifically for the latest and most promising research in the fields of cognition enhancement, neuroscience and alternative health supplements, and develop commercial strategies to bring these technologies to the marketplace.)//Elmer

3. **Cost of medicine as a form of debt** **One of the biggest methods of extracting money from rural and indigenous communities is through increased costs of medication**. Pharmaceutical colonialism often uses the premise of providing cheap medication for the world’s neediest to acquire local knowledge and natural resources. This premise is pushed into society through advertising campaigns and processes like lobbying. However, those who benefit most are often the shareholders, and not the people who need help. An example was the 2009 Reuters report which found that nearly **a million people** were **dying from malaria** dying every year **due to overly expensive medication**. According to the report, Artemisinin combination therapies (ACTs) can cost up to 65 times the daily minimum wage in countries that are most affected by malaria. These high prices **come after the government subsidies** which push them down as low as possible.[19] Another famous and recent example was the businessman Martin Shkreli, who pushed the cost of an AIDS drug up from $13.50 to over $700 per pill. This created an outrage on social media and it highlighted the underlying mindset behind most pharmaceutical companies — profit above all. An interesting and disturbing source of information about this is the film Fire in the Blood, which documents how **western pharmaceutical companies** **blocked the sale of cheap antiretroviral drugs to AIDS patients** **in Sub-Saharan Africa**.[20] “There is indeed a sense in which all modern **medicine** is **engaged in a colonizing process**… It can be seen in **the** increasing **professionalization of medicine and the exclusion of ‘folk’ practitioners**, in the close and often symbiotic relationship between medicine and the modern state, in the far-reaching claims made by medical science for its ability to prevent, control, and even eradicate human diseases.”[21] — D Arnold, Colonizing the Body, 1993 Pharmaceutical companies have been responsible for saving millions of lives due to their advances in medicine. However, the number of lives that have been lost due to the lack of affordability of medicine and the lack of equity and sharing of profits is estimated to be extremely high. **Western capitalism** has the **potential to act as a new form of colonialism**, and the modern medical method is one great way to extend the branches of capitalism into developing countries. The slums in Brazil highlight the blatant inequality between nations and people.

### 1AC: Plan

#### Plan – The member nations of the World Trade Organization ought to reduce intellectual property protections for medicines by implementing a one-and-done approach for patent and exclusivity protection for patent originators.

#### The Plan solves Evergreening.

Feldman 3 Robin Feldman 2-11-2019 "‘One-and-done’ for new drugs could cut patent thickets and boost generic competition" <https://www.statnews.com/2019/02/11/drug-patent-protection-one-done/> (Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation)//SidK + Elmer

I believe that one period of protection **should be enough**. We should make the legal changes necessary to prevent companies **from building patent walls** and piling up mountains of rights. This could be accomplished **by a “one-and-done” approach** for patent protection. Under it, a drug would receive just one period of exclusivity, and no more. The choice of which “one” could be left entirely in the hands of the pharmaceutical company, with the election made when the FDA approves the drug. Perhaps development of the drug went swiftly and smoothly, so the remaining life of one of the drug’s patents is of greatest value. Perhaps development languished, so designation as an orphan drug or some other benefit would bring greater reward. The choice would be up to the company itself, based on its own calculation of the maximum benefit. The result, however, is that a pharmaceutical company chooses whether its period of exclusivity would be a patent, an orphan drug designation, a period of data exclusivity (in which no generic is allowed to use the original drug’s safety and effectiveness data), or something else — but **not all of the above** and more. Consider Suboxone, a combination of buprenorphine and naloxone for treating opioid addiction. The drug’s maker has extended its protection cliff eight times, including obtaining an orphan drug designation, which is intended for drugs that serve only a small number of patients. The drug’s first period of exclusivity ended in 2005, but with the additions its protection now lasts until 2024. That makes almost two additional decades in which the public has borne the burden of monopoly pricing, and access to the medicine may have been constrained. Implementing a one-and-done approach in conjunction with FDA approval underscores the fact that these problems and solutions are designed for pharmaceuticals, not for all types of technologies. That way, one-and-done could be implemented through **legislative changes to the FDA’s drug approval system**, and would apply to patents granted going forward. One-and-done would apply to both patents and exclusivities. A more limited approach, a baby step if you will, would be to invigorate the existing patent obviousness doctrine as a way to cut back on patent tinkering. Obviousness, one of the five standards for patent eligibility, says that inventions that are obvious to an expert or the general public can’t be patented. Either by congressional clarification or judicial interpretation, many pile-on patents could be eliminated with a ruling that the core concept of the additional patent is nothing more than the original formulation. Anything else is merely an obvious adaptation of the core invention, modified with existing technology. As such, the patent would fail for being perfectly obvious. Even without congressional action, a more vigorous and robust application of the existing obviousness doctrine could significantly improve the problem of piled-up patents and patent walls. Pharmaceutical companies have become adept at maneuvering through the system of patent and non-patent rights to create mountains of rights that can be applied, one after another. This behavior lets drug companies keep competitors out of the market and beat them back when they get there. We shouldn’t be surprised at this. Pharmaceutical companies are profit-making entities, after all, that face pressure from their shareholders to produce ever-better results. If we want to change the system, we must change the incentives driving the system. And right now, the incentives for creating patent walls are just too great.

#### Reforming the Patent Process would lower Drug Prices and incentivize Pharma Innovation by revitalizing the Market.

Stanbrook 13, Matthew B. "Limiting “evergreening” for a better balance of drug innovation incentives." (2013): 939-939. (MD (University of Toronto) PhD (University of Toronto))//Elmer

At issue in the Indian case was “evergreening,” a now widespread practice by the pharmaceutical industry designed to extend the monopoly on an existing drug by modifying it and seeking new patents.2 Currently, half of all drugs patented in Canada have multiple subsequent patents, extending the lifetime of the original patent by about 8 years.3 Manufacturers, in defence of these practices, predictably tout the advantages of new versions of their products, which often represent more potent isomers or salts of the original drugs, longer-lasting formulations or improved delivery systems that make adherence easier or more convenient. But the new versions are by definition “**me too” drugs**, and demonstration that the resulting **incremental benefits** in efficacy and safety are clinically meaningful **is often lacking**. Moreover, the original drugs have often been “blockbusters” used for years to improve the health of millions of patients. It seems hard to argue convincingly why such beneficial drugs require an upgrade, often just before their patents expire. Rather than the marginal benefits accrued from tinkering with already effective agents, patients worldwide are in desperate need of new classes of pharmaceuticals for the great many health conditions for which treatments are presently inadequate or entirely lacking. But developing truly innovative drugs is undeniably a high-risk venture. It is important and necessary that pharmaceutical companies continue to take these risks, because they are usually the only entities with sufficient resources to do so. Therefore, companies must continue to perceive **sufficient incentives** to continue investing in innovation. Indeed, there is evidence that the prospect of future evergreening has become part of the incentive calculation for innovative drug development.4 But surely it is perverse to extend unpredictably a period of patent protection that the government intended to be clearly defined and predictable, and to maintain incentives that drive companies to divert their **drug-development resources away from innovation**. **Current patent legislation may not be optimal** for striking the right balance between encouraging innovation and facilitating profiteering. Given the broad societal importance of patent legislation, ongoing research to enable active governance of this issue should be a national priority. In the last decade, Canada’s laws have been among the friendliest toward evergreening in the world.5 We should now reflect on whether this is really in our national interest. Governments, including Canada’s, would do well to take inspiration from India’s example and tighten regulations that currently facilitate evergreening. This might involve **denying future patents for modifications** that currently would receive one. An overall reduction in the duration of all secondary patents on a therapy might also be considered. Globally, a more flexible and individualized approach to the length of drug patents might be a more effective strategy to align corporate incentives with population health needs. Limits on evergreening would likely reduce the **extensive patent litigation** that contributes to the **high prices of generic drugs** in Canada.3 Reducing economic pressure on generic drug companies may facilitate current provincial initiatives to lower generic drug prices. As opportunities to generate revenue from evergreening are eliminated, research-based pharmaceutical companies would be left with no choice but to invest more in innovative drug development to maintain their profits.

### 1AC: Framing

#### The standard is maximizing expected wellbeing or act hedonistic util.

#### Prefer:

#### 1] Pleasure and pain *are* intrinsic value and disvalue – everything else *regresses* – robust neuroscience.

Blum et al. 18

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**Pleasure** is not only one of the three primary reward functions but it also **defines reward.** As homeostasis explains the functions of only a limited number of rewards, the principal reason why particular stimuli, objects, events, situations, and activities are rewarding may be due to pleasure. This applies first of all to sex and to the primary homeostatic rewards of food and liquid and extends to money, taste, beauty, social encounters and nonmaterial, internally set, and intrinsic rewards. Pleasure, as the primary effect of rewards, drives the prime reward functions of learning, approach behavior, and decision making and provides the **basis for hedonic theories** of reward function. We are attracted by most rewards and exert intense efforts to obtain them, just because they are enjoyable [10].

Pleasure is a passive reaction that derives from the experience or prediction of reward and may lead to a long-lasting state of happiness. The word happiness is difficult to define. In fact, just obtaining physical pleasure may not be enough. One key to happiness involves a network of good friends. However, it is not obvious how the higher forms of satisfaction and pleasure are related to an ice cream cone, or to your team winning a sporting event. Recent multidisciplinary research, using both humans and detailed invasive brain analysis of animals has discovered some critical ways that the brain processes pleasure [14].

Pleasure as a hallmark of reward is sufficient for defining a reward, but it may not be necessary. A reward may generate positive learning and approach behavior simply because it contains substances that are essential for body function. When we are hungry, we may eat bad and unpleasant meals. A monkey who receives hundreds of small drops of water every morning in the laboratory is unlikely to feel a rush of pleasure every time it gets the 0.1 ml. Nevertheless, with these precautions in mind, we may define any stimulus, object, event, activity, or situation that has the potential to produce pleasure as a reward. In the context of reward deficiency or for disorders of addiction, homeostasis pursues pharmacological treatments: drugs to treat drug addiction, obesity, and other compulsive behaviors. The theory of allostasis suggests broader approaches - such as re-expanding the range of possible pleasures and providing opportunities to expend effort in their pursuit. [15]. It is noteworthy, the first animal studies eliciting approach behavior by electrical brain stimulation interpreted their findings as a discovery of the brain’s pleasure centers [16] which were later partly associated with midbrain dopamine neurons [17–19] despite the notorious difficulties of identifying emotions in animals.

Evolutionary theories of pleasure: The love connection BO:D

Charles Darwin and other biological scientists that have examined the biological evolution and its basic principles found various mechanisms that steer behavior and biological development. Besides their theory on natural selection, it was particularly the sexual selection process that gained significance in the latter context over the last century, especially when it comes to the question of what makes us “what we are,” i.e., human. However, the capacity to sexually select and evolve is not at all a human accomplishment alone or a sign of our uniqueness; yet, we humans, as it seems, are ingenious in fooling ourselves and others–when we are in love or desperately search for it.

It is well established that modern biological theory conjectures that **organisms are** the **result of evolutionary competition.** In fact, Richard Dawkins stresses gene survival and propagation as the basic mechanism of life [20]. Only genes that lead to the fittest phenotype will make it. It is noteworthy that the phenotype is selected based on behavior that maximizes gene propagation. To do so, the phenotype must survive and generate offspring, and be better at it than its competitors. Thus, the ultimate, distal function of rewards is to increase evolutionary fitness by ensuring the survival of the organism and reproduction. It is agreed that learning, approach, economic decisions, and positive emotions are the proximal functions through which phenotypes obtain other necessary nutrients for survival, mating, and care for offspring.

Behavioral reward functions have evolved to help individuals to survive and propagate their genes. Apparently, people need to live well and long enough to reproduce. Most would agree that homo-sapiens do so by ingesting the substances that make their bodies function properly. For this reason, foods and drinks are rewards. Additional rewards, including those used for economic exchanges, ensure sufficient palatable food and drink supply. Mating and gene propagation is supported by powerful sexual attraction. Additional properties, like body form, augment the chance to mate and nourish and defend offspring and are therefore also rewards. Care for offspring until they can reproduce themselves helps gene propagation and is rewarding; otherwise, many believe mating is useless. According to David E Comings, as any small edge will ultimately result in evolutionary advantage [21], additional reward mechanisms like novelty seeking and exploration widen the spectrum of available rewards and thus enhance the chance for survival, reproduction, and ultimate gene propagation. These functions may help us to obtain the benefits of distant rewards that are determined by our own interests and not immediately available in the environment. Thus the distal reward function in gene propagation and evolutionary fitness defines the proximal reward functions that we see in everyday behavior. That is why foods, drinks, mates, and offspring are rewarding.

There have been theories linking pleasure as a required component of health benefits salutogenesis, (salugenesis). In essence, under these terms, pleasure is described as a state or feeling of happiness and satisfaction resulting from an experience that one enjoys. Regarding pleasure, it is a double-edged sword, on the one hand, it promotes positive feelings (like mindfulness) and even better cognition, possibly through the release of dopamine [22]. But on the other hand, pleasure simultaneously encourages addiction and other negative behaviors, i.e., motivational toxicity. It is a complex neurobiological phenomenon, relying on reward circuitry or limbic activity. It is important to realize that through the “Brain Reward Cascade” (BRC) endorphin and endogenous morphinergic mechanisms may play a role [23]. While natural rewards are essential for survival and appetitive motivation leading to beneficial biological behaviors like eating, sex, and reproduction, crucial social interactions seem to further facilitate the positive effects exerted by pleasurable experiences. Indeed, experimentation with addictive drugs is capable of directly acting on reward pathways and causing deterioration of these systems promoting hypodopaminergia [24]. Most would agree that pleasurable activities can stimulate personal growth and may help to induce healthy behavioral changes, including stress management [25]. The work of Esch and Stefano [26] concerning the link between compassion and love implicate the brain reward system, and pleasure induction suggests that social contact in general, i.e., love, attachment, and compassion, can be highly effective in stress reduction, survival, and overall health.

Understanding the role of neurotransmission and pleasurable states both positive and negative have been adequately studied over many decades [26–37], but comparative anatomical and neurobiological function between animals and homo sapiens appear to be required and seem to be in an infancy stage.

Finding happiness is different between apes and humans

As stated earlier in this expert opinion one key to happiness involves a network of good friends [38]. However, it is not entirely clear exactly how the higher forms of satisfaction and pleasure are related to a sugar rush, winning a sports event or even sky diving, all of which augment dopamine release at the reward brain site. Recent multidisciplinary research, using both humans and detailed invasive brain analysis of animals has discovered some critical ways that the brain processes pleasure.

Remarkably, there are pathways for ordinary liking and pleasure, which are limited in scope as described above in this commentary. However, there are **many brain regions**, often termed hot and cold spots, that significantly **modulate** (increase or decrease) our **pleasure or** even produce **the opposite** of pleasure— that is disgust and fear [39]. One specific region of the nucleus accumbens is organized like a computer keyboard, with particular stimulus triggers in rows— producing an increase and decrease of pleasure and disgust. Moreover, the cortex has unique roles in the cognitive evaluation of our feelings of pleasure [40]. Importantly, the interplay of these multiple triggers and the higher brain centers in the prefrontal cortex are very intricate and are just being uncovered.

Desire and reward centers

It is surprising that many different sources of pleasure activate the same circuits between the mesocorticolimbic regions (Figure 1). Reward and desire are two aspects pleasure induction and have a very widespread, large circuit. Some part of this circuit distinguishes between desire and dread. The so-called pleasure circuitry called “REWARD” involves a well-known dopamine pathway in the mesolimbic system that can influence both pleasure and motivation.

In simplest terms, the well-established mesolimbic system is a dopamine circuit for reward. It starts in the ventral tegmental area (VTA) of the midbrain and travels to the nucleus accumbens (Figure 2). It is the cornerstone target to all addictions. The VTA is encompassed with neurons using glutamate, GABA, and dopamine. The nucleus accumbens (NAc) is located within the ventral striatum and is divided into two sub-regions—the motor and limbic regions associated with its core and shell, respectively. The NAc has spiny neurons that receive dopamine from the VTA and glutamate (a dopamine driver) from the hippocampus, amygdala and medial prefrontal cortex. Subsequently, the NAc projects GABA signals to an area termed the ventral pallidum (VP). The region is a relay station in the limbic loop of the basal ganglia, critical for motivation, behavior, emotions and the “Feel Good” response. This defined system of the brain is involved in all addictions –substance, and non –substance related. In 1995, our laboratory coined the term “Reward Deficiency Syndrome” (RDS) to describe genetic and epigenetic induced hypodopaminergia in the “Brain Reward Cascade” that contribute to addiction and compulsive behaviors [3,6,41].

Furthermore, ordinary “liking” of something, or pure pleasure, is represented by small regions mainly in the limbic system (old reptilian part of the brain). These may be part of larger neural circuits. In Latin, hedus is the term for “sweet”; and in Greek, hodone is the term for “pleasure.” Thus, the word Hedonic is now referring to various subcomponents of pleasure: some associated with purely sensory and others with more complex emotions involving morals, aesthetics, and social interactions. The capacity to have pleasure is part of being healthy and may even extend life, especially if linked to optimism as a dopaminergic response [42].

Psychiatric illness often includes symptoms of an abnormal inability to experience pleasure, referred to as anhedonia. A negative feeling state is called dysphoria, which can consist of many emotions such as pain, depression, anxiety, fear, and disgust. Previously many scientists used animal research to uncover the complex mechanisms of pleasure, liking, motivation and even emotions like panic and fear, as discussed above [43]. However, as a significant amount of related research about the specific brain regions of pleasure/reward circuitry has been derived from invasive studies of animals, these cannot be directly compared with subjective states experienced by humans.

In an attempt to resolve the controversy regarding the causal contributions of mesolimbic dopamine systems to reward, we have previously evaluated the three-main competing explanatory categories: “liking,” “learning,” and “wanting” [3]. That is, dopamine may mediate (a) liking: the hedonic impact of reward, (b) learning: learned predictions about rewarding effects, or (c) wanting: the pursuit of rewards by attributing incentive salience to reward-related stimuli [44]. We have evaluated these hypotheses, especially as they relate to the RDS, and we find that the incentive salience or “wanting” hypothesis of dopaminergic functioning is supported by a majority of the scientific evidence. Various neuroimaging studies have shown that anticipated behaviors such as sex and gaming, delicious foods and drugs of abuse all affect brain regions associated with reward networks, and may not be unidirectional. Drugs of abuse enhance dopamine signaling which sensitizes mesolimbic brain mechanisms that apparently evolved explicitly to attribute incentive salience to various rewards [45].

Addictive substances are voluntarily self-administered, and they enhance (directly or indirectly) dopaminergic synaptic function in the NAc. This activation of the brain reward networks (producing the ecstatic “high” that users seek). Although these circuits were initially thought to encode a set point of hedonic tone, it is now being considered to be far more complicated in function, also encoding attention, reward expectancy, disconfirmation of reward expectancy, and incentive motivation [46]. The argument about addiction as a disease may be confused with a predisposition to substance and nonsubstance rewards relative to the extreme effect of drugs of abuse on brain neurochemistry. The former sets up an individual to be at high risk through both genetic polymorphisms in reward genes as well as harmful epigenetic insult. Some Psychologists, even with all the data, still infer that addiction is not a disease [47]. Elevated stress levels, together with polymorphisms (genetic variations) of various dopaminergic genes and the genes related to other neurotransmitters (and their genetic variants), and may have an additive effect on vulnerability to various addictions [48]. In this regard, Vanyukov, et al. [48] suggested based on review that whereas the gateway hypothesis does not specify mechanistic connections between “stages,” and does not extend to the risks for addictions the concept of common liability to addictions may be more parsimonious. The latter theory is grounded in genetic theory and supported by data identifying common sources of variation in the risk for specific addictions (e.g., RDS). This commonality has identifiable neurobiological substrate and plausible evolutionary explanations.

Over many years the controversy of dopamine involvement in especially “pleasure” has led to confusion concerning separating motivation from actual pleasure (wanting versus liking) [49]. We take the position that animal studies cannot provide real clinical information as described by self-reports in humans. As mentioned earlier and in the abstract, on November 23rd, 2017, evidence for our concerns was discovered [50]

In essence, although nonhuman primate brains are similar to our own, the disparity between other primates and those of human cognitive abilities tells us that surface similarity is not the whole story. Sousa et al. [50] small case found various differentially expressed genes, to associate with pleasure related systems. Furthermore, the dopaminergic interneurons located in the human neocortex were absent from the neocortex of nonhuman African apes. Such differences in neuronal transcriptional programs may underlie a variety of neurodevelopmental disorders.

In simpler terms, the system controls the production of dopamine, a chemical messenger that plays a significant role in pleasure and rewards. The senior author, Dr. Nenad Sestan from Yale, stated: “Humans have evolved a dopamine system that is different than the one in chimpanzees.” This may explain why the behavior of humans is so unique from that of non-human primates, even though our brains are so surprisingly similar, Sestan said: “It might also shed light on why people are vulnerable to mental disorders such as autism (possibly even addiction).” Remarkably, this research finding emerged from an extensive, multicenter collaboration to compare the brains across several species. These researchers examined 247 specimens of neural tissue from six humans, five chimpanzees, and five macaque monkeys. Moreover, these investigators analyzed which genes were turned on or off in 16 regions of the brain. While the differences among species were subtle, **there was** a **remarkable contrast in** the **neocortices**, specifically in an area of the brain that is much more developed in humans than in chimpanzees. In fact, these researchers found that a gene called tyrosine hydroxylase (TH) for the enzyme, responsible for the production of dopamine, was expressed in the neocortex of humans, but not chimpanzees. As discussed earlier, dopamine is best known for its essential role within the brain’s reward system; the very system that responds to everything from sex, to gambling, to food, and to addictive drugs. However, dopamine also assists in regulating emotional responses, memory, and movement. Notably, abnormal dopamine levels have been linked to disorders including Parkinson’s, schizophrenia and spectrum disorders such as autism and addiction or RDS.

Nora Volkow, the director of NIDA, pointed out that one alluring possibility is that the neurotransmitter dopamine plays a substantial role in humans’ ability to pursue various rewards that are perhaps months or even years away in the future. This same idea has been suggested by Dr. Robert Sapolsky, a professor of biology and neurology at Stanford University. Dr. Sapolsky cited evidence that dopamine levels rise dramatically in humans when we anticipate potential rewards that are uncertain and even far off in our futures, such as retirement or even the possible alterlife. This may explain what often motivates people to work for things that have no apparent short-term benefit [51]. In similar work, Volkow and Bale [52] proposed a model in which dopamine can favor NOW processes through phasic signaling in reward circuits or LATER processes through tonic signaling in control circuits. Specifically, they suggest that through its modulation of the orbitofrontal cortex, which processes salience attribution, dopamine also enables shilting from NOW to LATER, while its modulation of the insula, which processes interoceptive information, influences the probability of selecting NOW versus LATER actions based on an individual’s physiological state. This hypothesis further supports the concept that disruptions along these circuits contribute to diverse pathologies, including obesity and addiction or RDS.