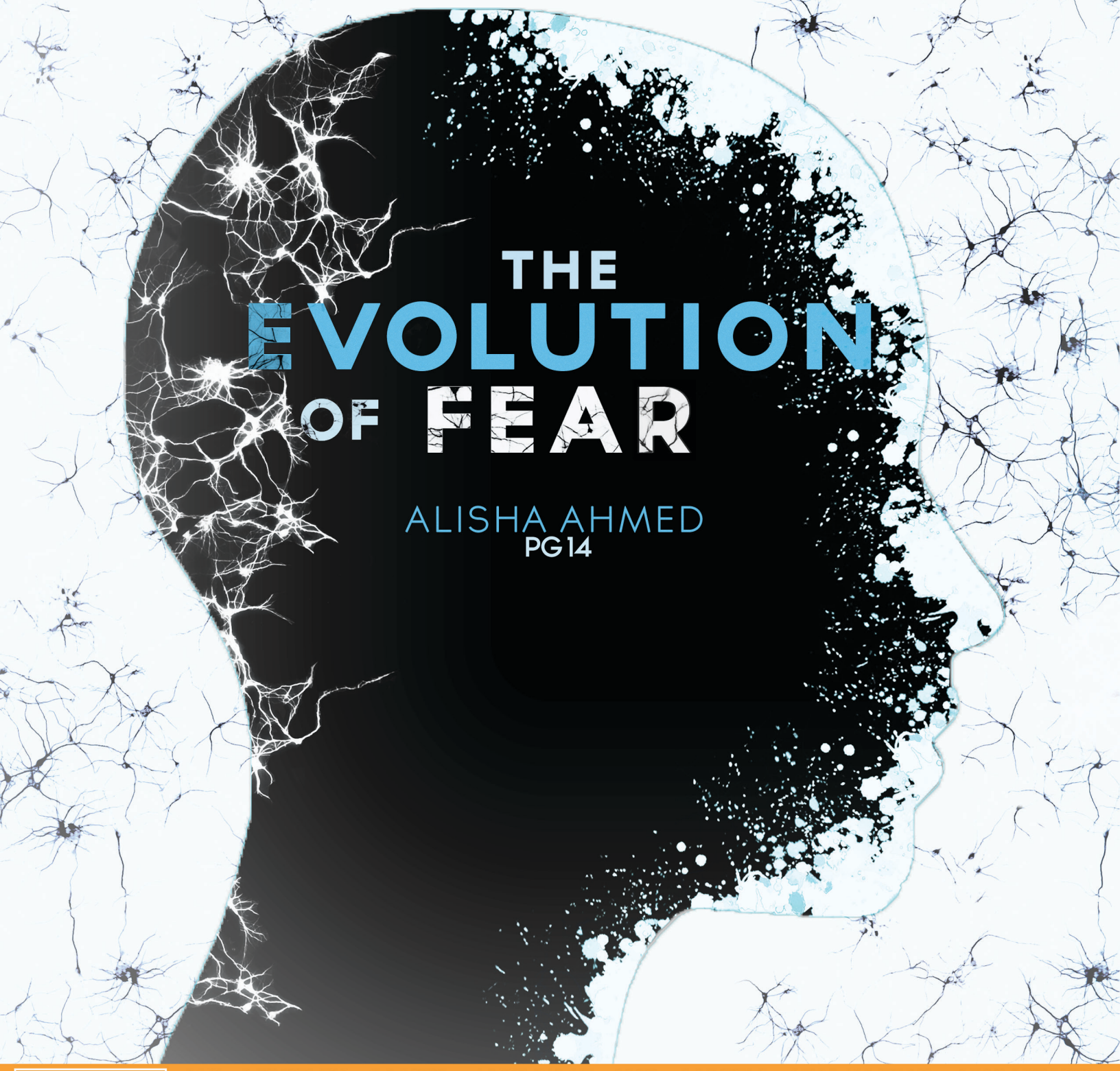
THE TRIPLE HELIX

FALL 2018



THE EVOLUTION OF FEAR

ALISHA AHMED
PG14

TEXAS

ASU • BERKELEY • BROWN • CAMBRIDGE • CMU • CORNELL • GEORGIA TECH • GEORGETOWN
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FROM THE EDITOR

Science & the Supernatural

As a child, I remember creeping downstairs in the middle of the night to get a glass of water. Turning around, I felt as if there was something in the dark behind me. I'd start walking faster and faster until my walk turned into a desperate sprint, sighing with relief when I reached my parent's room. As an adult, I know that my childhood fears of the dark were irrational and probably magnified due to my obsession with the Goosebumps series. Nowadays, my fears seem to be more rational like the fear of falling from great heights or of poisonous creatures. After all, the history of evolution has taught us that fear is a selective advantage that keeps us away from danger. But why is it that I still jump at something as harmless as clowns in a horror movie or the sound of my floorboards creaking?

Our cover story hopes to bring you some thoughtful discussion as to why humans fear unexplained phenomenon like ghosts and the paranormal. In "The Evolution of Fear" undergraduate Alisha Ahmed relates the physiological and neural basis of the fear response to broader implications like its role in anthropological and religious history. Although the study of such an abstract idea may attract skeptics, there are some significant implications that come with this, ranging from increased understanding of mental disorders to new fronts in national security. I hope you enjoy learning about this topic as much as I did. Turn to page 14.

We are incredibly happy to share the tremendous amount of work put into each of the features of our inaugural issue by our writers, editors, designers, and managerial staff. The late night writer-editor meetings, designer sessions, email correspondences, and long hours put into making the content were well worth the effort to bring you this issue. As the roots of The Triple Helix spread through the Austin community, we hope the ideas in these articles inspire you to develop opinions of your own and to share your stories with the world.

Vishal Patel is editor in chief of The Triple Helix, connect with him at TexasTTH@gmail.com.

About Us

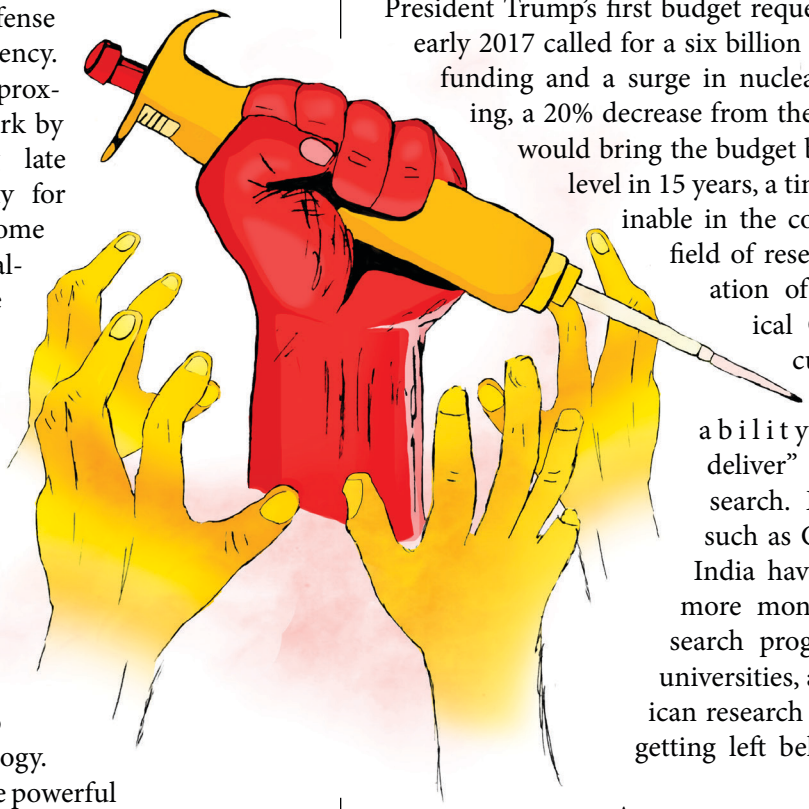
The Triple Helix at UT Austin is an interdisciplinary journal committed to bridging the gap between science, ethics, and society. We aim to explore the intricate moral, socioeconomic, and environmental ramifications of an increasingly science-driven world while highlighting the ways that science affects our ideas of humanity. Covering subject matter ranging from technology to law and business to biology, we provide a forum to discuss issues in society from multiple perspectives. Staffed by a diverse group of writers, editors, and graphic designers, the Triple Helix strives to promote an interdisciplinary mindset for people of all backgrounds, with the hope of encouraging readers to ask questions and gain new perspectives. We are proud to showcase our Fall 2018 publication, a collection of articles and ideas designed, written, and edited by students here, at The University of Texas at Austin. We hope you enjoy!

CONTENTS

Politics of Grant Writing

Article by **Kavya Rajesh**
Graphic Design by **Josh Goh**

Scientists and researchers are at the mercy of the personal opinions of those in political power, as they hold the ultimate key to success: money. Funding permeates every aspect of a researcher's life, from hiring graduate students to attending conferences and buying chemicals. The vast majority of scientific research is funded by governmental institutions such as the National Science Foundation, National Institutes of Health, and the Defense Advanced Research Projects Agency. Grant writing accounts for approximately 40% of time spent at work by tenured faculty, encompassing late nights and weekends, especially for younger professors. In fact, some grants even have a net negative value- they take away valuable time that applicants and peer reviewers could use to teach, attend conferences, and do research. The already labyrinthine system of scientific funding and grant writing is exacerbated by the political nature of governmental organizations and the impact of the personal views of those in power. Even more so, the nature of the governmental landscape can be detrimental to the progress of science and technology.



Research topics can often induce powerful and polarizing opinions, especially in biological and genetic engineering disciplines. For example, "fetal tissue research" is a term thrown around in Congress and a topic of great controversy. A handful of Planned Parenthood clinics in two states supply fetal tissue for medical research and came under fire in 2015 when covertly filmed videos of physicians discussing fetal organs for research were released. Most of the NIH projects utilizing fetal tissue study infectious diseases, specifically HIV/AIDS, and developmental biology. Researchers who oppose these methods claim that other model systems and techniques can be used, while those involved champion the idea that fetal tissue cannot be replaced as an experimental model. Regardless of the claims posed by either side, the real question remains how much power our modern-day scientific patrons have over the men and women who pursue scientific discovery. The patrons who control the allocation of fiscal resources to research institutions inevitably impact the scientifics topics pursued.

While controversial topics receive more public attention and captivate the desks of lawmakers for longer periods of time, day to day research is also at the mercy of the government. Transitions of power and policy modifications can sway scientific research in a myriad of ways. President Trump's first budget request to Congress in early 2017 called for a six billion dollar cut to NIH funding and a surge in nuclear weapons funding, a 20% decrease from the year before. This would bring the budget back to the lowest level in 15 years, a time frame unimaginable in the constantly evolving field of research. The Association of American Medical Colleges said the cuts would "cripple the nation's ability to support and deliver" biomedical research. Eastern countries such as China, Korea, and India have started to pour more money into their research programs and public universities, and cuts to American research leave us at risk of getting left behind in the dust.

As a country, we must come together to move forward. Our people have always been our strength, and our commitment to scientific research is imperative in this ever-changing world. A bright future awaits, and we must approach it with open arms. Let's keep asking these difficult questions, encourage our children to think differently and push the horizon, and hold our government accountable. The future is what we make it, and change starts with us.

Article by **Katherine Bruner, PhD** (left) **& Nina Hosmane, PhD** (right)

Graphic Design by **Zane Shah**

HIV: Path to A Cure

In June 1981, the Center for Disease Control (CDC) reported the first cases of autoimmune deficiency syndrome (AIDS) in the United States in five previously healthy young men.[1] Research over the next couple of years uncovered the presence of a virus, the human immunodeficiency virus (HIV), as responsible for this growing epidemic. HIV was shown to preferentially infect specific white blood cells, known as CD4+ T helper cells. Throughout the 1980's and 1990's while the epidemic was expanding, only a few medical treatments were available. Without treatment, those infected with HIV inevitably developed AIDS.

In 1997, the FDA approved combination antiretroviral therapy for treating HIV. This revolutionary new therapy combined a variety of pharmaceutical drugs that targeted the virus at various stages of its life cycle. Despite some side effects, the drugs effectively stopped the virus from replicating, and a standard blood test could no longer detect HIV. These results were so promising that scientists and physicians thought that only a few years of the medication could completely cure someone of HIV. Unfortunately, this enthusiasm was premature. Since HIV has the remarkable ability to insert its own viral genome into the human genome of the cell it infects, the only way to completely eliminate it is for host cell to die. Much to the dismay of doctors and patients alike, when antiretroviral treatment was stopped, the viral load quickly rebounded to high levels. Small amounts of dormant virus persist in immune cells known as resting memory CD4+ T cells. In this dormant state, the virus does not reproduce within the cellular host. Circulating immune cells, which would normally kill virally infected cells, completely ignore these cells since they appear to be healthy. Thus, people who are infected with HIV must remain on antiretroviral treatment for their entire lives, taking a daily pill to keep the virus at bay.

The question then became, how can we eliminate this dormant virus? Unfortunately, the cells that harbor the virus are very long-lived cells. Research has predicted that for these cells to die on their own (and take the virus with them), it would take over 70 years of continuous treatment.[2,3] Since this is not a practical strategy, the HIV research field has taken multiple approaches to cure HIV by aiming to eliminate the dormant virus. The most heavily researched approach is known as the "shock and kill" strategy. This strategy seeks to "shock" the dormant virus "on" so that it can be detected and "killed" by our immune system, as normally occurs when our body detect foreign invaders. Importantly, people remain on antiretroviral medication to block the virus from infecting new cells, so any virus produced from this strategy is not harmful. There have been multiple small-scale clinical trials using this approach with mixed results. Although drugs have been shown to successfully "shock" the virus out

of its dormant state, the infected cells were not eliminated.[4-8] Further research is ongoing to increase the effectiveness of the "kill" aspect of the immune system by pairing the "shock" with a vaccine to stimulate the immune system to kill infected cells. In one recent study, participants received a drug called romidepsin, which was used to "shock" the virus in tandem with a T-cell vaccine to help boost the immune system to eliminate infected cells. Here, the virus was reactivated by romidepsin and a modest number of infected cells were also eliminated.[9] Current studies are applying a similar approach and hopefully these advancements will make this an effective strategy moving forward.

Over the past three decades HIV treatment has come a long way, from a once terminal disease to one that is now treatable with medication. With advancements in scientific research, hopefully one day HIV will enter the realm of becoming a curable disease.

***Check our site for citations.**

DIY DRUGS

3D Printing and the Future of Pharmaceutical Practice

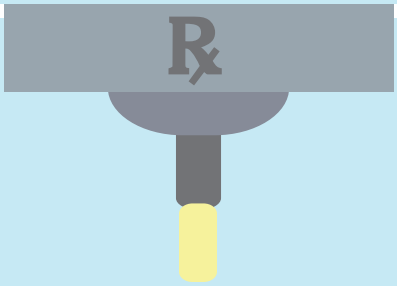
Ethan Wang
editor: Kevin Ye // designer: Parker Spradley

Forget your monthly trip to the pharmacist: In the near future, you may be able to produce drugs from the comfort of your own home. On August 3rd, 2015, a major breakthrough in attaining this reality occurred when the FDA approved Spritam (levetiracetam), an orally-ingested tablet used to treat partial onset, myoclonic, and generalized tonic-clonic seizures in children and adults with epilepsy.[1] Beyond Spritam, barbiturates, calcium channel moderators, and approximately thirty other varieties of pharmaceutical drugs treat seizures as well. In fact, Spritam is not even the only commercial variant of levetiracetam, its generic name.[2] What separates Spritam from its competitors is not a unique chemical composition, but the endless potential behind its production method: 3D printing.

Currently, orally-ingested drugs are produced by power-blending chemicals, crushing particles to decrease particle size, re-forming larger particles with specific chemical proportions via granulation, and heating and pressurizing re-formed particles into a polymer carrier. These final polymer carriers are then condensed into thick capsules composed of gelatin and cellulose.[3] Irrespective of slow production rate and high costs, the traditional mechanism of drug production is impersonal and ineffective in addressing individual differences between patients.[4] Aprecia Pharmaceuticals, the company behind Spritam, utilizes 3D printing to produce its revolutionary drug. Relying on its patented ZipDose® Technology, the first step in the producing Spritam is the release of a thin layer of powdered medicine. Liquid is then added to the powder, and particles are bound together. The process can be incrementally repeated to adjust dosage to individual patients' needs.

3D-printed drugs have the potential to re-define the field of pharmaceuticals. For starters, 3D-printed drugs are porous due to the binding liquid and multiple layers polymerized during printing. The highly porous nature of 3D-printed drugs results in rapid dissolution (within seconds) upon contact with water. Rapid dissipation is essential in ensuring fast and strong dosage delivery. The exterior coat of 3D printed drugs yields improved taste, and is perhaps the most palpable benefit for parents who struggle in convincing their sick children to take medicine. Nonetheless, the ability of patients to print their own medicine presents itself as the most noteworthy potential benefit of 3D-printed drugs. Zipdose's repeated dose addition method allows patients to produce drugs catered to their own specific physiology with exact doses. 3D-printed drugs offer an intensely-personalized, accessible, and cheap alternative to traditional pharmaceuticals.

As 3D printing technology becomes further refined, commercially-produced drugs such as Spritam will soon be produced not in factories but instead in patients' own homes. As long as the patients' home 3D printer is stocked with the necessary ingredients, synthesis of any desired drug is possible. The future of drug production parallels the steps of home cooking: finding the desired recipe, downloading a copy, and cooking the food, except with 3D printing drugs, the 3D printer does all the "cooking" for you. Significant research and development is in progress to make home-printed drugs a reality with in-vitro testing of or-

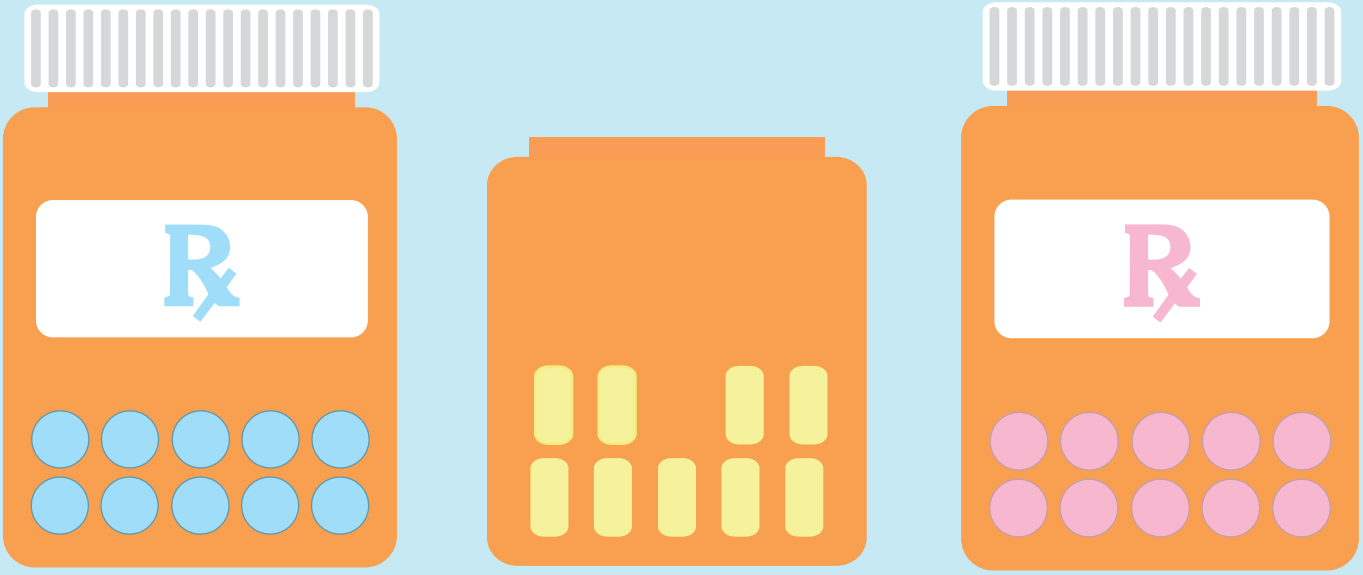


ganic polymers and development of oral films already underway.[5] Moreover, The FDA has been receptive to the integration of 3D printing into medical technology and has dedicated two of its official science and engineering laboratories to study the medical applications of 3D printing. The approval of Spritam itself stands as a compelling example of the FDA's commitment to bringing 3D printing to the forefront of drug production.[6]

The groundbreaking development of 3D printing drugs; however, comes with a host of access barriers. Despite the FDA's declared intent to further 3D printing technology, FDA commissioner Scott Gottlieb has admitted that numerous difficulties exist in regulating such a novel field. In December 2017, two years after the approval of Spritam, Gottlieb remarked that the FDA is still "working to establish a regulatory framework for how… [they] plan to apply existing laws and regulations that govern device manufacturing to non-traditional manufacturers like medical facilities and academic institutions that create 3D-printed personalized devices for specific patients they are treating." Yet, beyond ambiguity in the application of existing laws to 3D printing, Gottlieb does not address what might be the most impactful benefit of 3D printing - integration into patients' households.

Difficulties in the regulation of drugs produced in patients' homes may be responsible for the FDA's inability to fully commit. Currently, the FDA is responsible for the regulation of medical devices, electronics, and both prescription and non-prescription drugs. Categorization of 3D drugs may seem intuitive. But, what if a patient prints a tablet of over the counter aspirin and then prints a tablet of physician-prescribed fentanyl? Both tablets are drugs, but one is a prescription drug and one is an over the counter drug. Extraordinary attention to detail must be exercised in discriminating ideal regulatory practices between different drugs. In addition, the customizable nature of 3D drug production is a problem in and of itself. If patients can print drugs with a theoretically infinite number of chemical combinations, is it the FDA's responsibility to regulate every single combination? Even beyond 3D-printed drugs themselves, the FDA must also address regulation of the 3D printer. Although the FDA regulates medical devices and electronic products, regulation has never been required for personal devices that produce a secondary pharmaceutical product. Questions like these lack clear answers and contribute to the regulatory nightmare surrounding 3D drug production.[7]

However, historical FDA precedent may provide insight into the best method of regulation. Patient-customized tracheal implants produced by 3D-printing have been approved before and are not exceptionally dissimilar to the patient-customized nature of 3D-printed drugs.[8] On the issue of drug categorization, 3D printed drugs can divided into over the counter and prescription drugs and regulated accordingly in each category, and to address the potentially infinite number of drug combinations, the FDA, already responsible for regulating drug strength, could



set upper and lower bounds on acceptable drug combinations and concentrations instead of attempting to regulate all possible combinations individually.[9]

Economic concerns are an additional access barrier. 3D printing is not a cheap process. The cheapest high-quality 3D printers available for commercial purchase cost at least $300, and high-end 3D printers similar to 3D printers used in Aprecia Pharmaceuticals' factories can cost over $10,000.[10] Substantial technological advancement must occur for 3D printers to be affordable for the everyday American. Patients interested in the customizability and accessibility of 3D printed drugs will have to recognize the significant investment involved in buying a 3D printer.

Furthermore, big pharma has taken advantage of consumers before, and may continue doing so by hiking up prices for 3D printers and chemical ingredients. Consider the case of Martin Shkreli, former CEO of Turing Pharmaceuticals, as a warning. Shkreli, who acquired the rights to Daraprim, an anti-infection drug essential in the treatment AIDS, and raised its from $13.50 to $750 a pill, an increase of over 5000%. Though Shkreli later lowered the price of Daraprim to $375, the drug is still inaccessible to lower-income, uninsured patients. Shkreli is not the exception to the rule: Marathon Pharmaceuticals recently raised the price of deflazacort, a muscular dystrophy drug, to $89,000.[11] The nature of pharmaceutical economics itself explains the rampant exploitation of consumers. Pharmaceutical companies' income rises as drug sales and prices increase, regardless of how effective the drugs are. This profit-centric mindset biases how pharmaceutical companies fund medical research and design drugs.

Yet, the unavoidable influence of big pharma may produce certain benefits. Through patent protection, vast economic resources, and significant capital for R&D, these companies are able to sponsor and produce new drugs at a high rate. Even though money may be a significant factor in big pharma's daily operation, a recent study at Columbia University found that "from 2000 to 2009… pharmaceutical innovation added 1.23 years to the average lifespan." The study relied on a causal model to eliminate biased estimates and improvements due to extraneous factors such as income, education, and immunization.[12] Whether beneficial or not, the presence of big pharma begs another question - if 3D printing is patented by big pharma, what happens to the everyday pharmacist? University of Wisconsin professor and executive director of the American Institute of the History of Pharmacy, Gregory Higby, remarks that Aprecia's 3D printing technique sounds "like a return to the days of pharmacy compounding except that a machine is producing the pills instead of a pharmacist. In other words, 100 years ago, any pharmacist could mix together active and inactive ingredients to the specific strength prescribed by a physician for a patient. Now, you apparently tell the 'printer' to do it."[13] In spite of Higby's commentary, 3D printing is far from a death sentence for pharmacists' jobs. Pharmacists perform a variety of middle-man functions including but not limited to ensuring drug safety, providing guidance on side-effects, consulting with doctors responsible for drug prescription, providing pharmaceutical advice to patients with advanced diseases, and checking against the improper sale of drugs for non-medicinal purposes.[14] For now, at least, pharmacists' jobs are safe.

Susceptibility to hackers and black market influence may be the scariest implication of 3D printed drugs. 3D printing, reliant on printers wirelessly linked to a controller PC, is substantially more vulnerable to breaches than traditional manufacturing processes. Hackers can alter preloaded recipes on patients' computers in a manner such that visual differences between the edited and original 3D product are imperceptible. During this process, hackers may not only access confidential patient data, but also mis-produce drugs and harm patients. 3D printed drugs may transform large hacking events into national health crises. Hacked and counterfeited 3D printers can also be purposed for the production of illegal drugs. From basic chemicals, drug dealers can synthesize street drugs en masse in an easily-packaged, dispensable form. Alternatively,

3D printing may replace in person drug deals with printer recipes and mailed ingredients.[15] Two implementable provisions may curtail the impacts of hacking and black market trade. First, recipes sent by physicians to patients could be encrypted such that only the healthcare provider and patient can access them. Second, recipes could be programmed such that they are only printed with doctor and pharmacist authorization. With these two provisions in place, the battle ultimately still rests on two opposing forces: the skill of hackers and the strength of data encryption.[16]

Still, despite these potential issues, 3D printing technology has the ability to extensively improve the processes of pharmaceutical manufacturing and drug development. Personal customizability and drug convenience are huge boons of 3D printing, though understanding risks is essential in moving forward; nonetheless, 3D-printed drugs have the potential be a major turning point in drug production, forever redefining the pharmaceutical industry.

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COMPUTERIZED_MARKETS

Will Artificial Intelligence Take Over Wall Street?

James Kiraly
editor: Kevin Ye // designer: Parker Spradley

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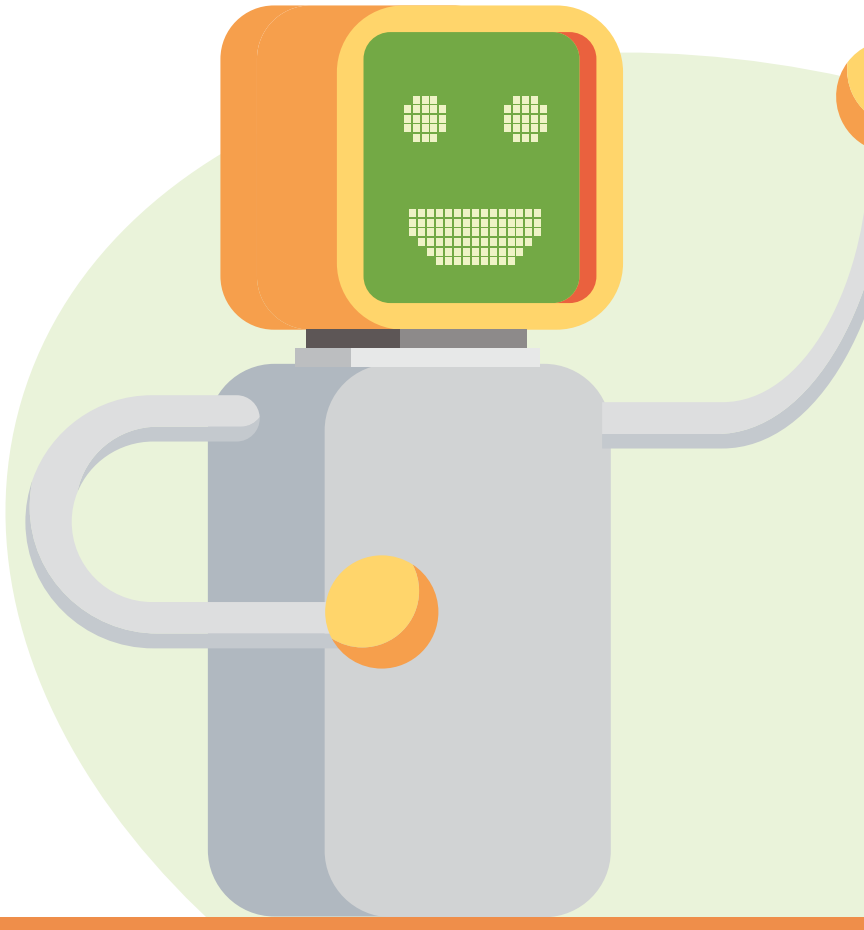
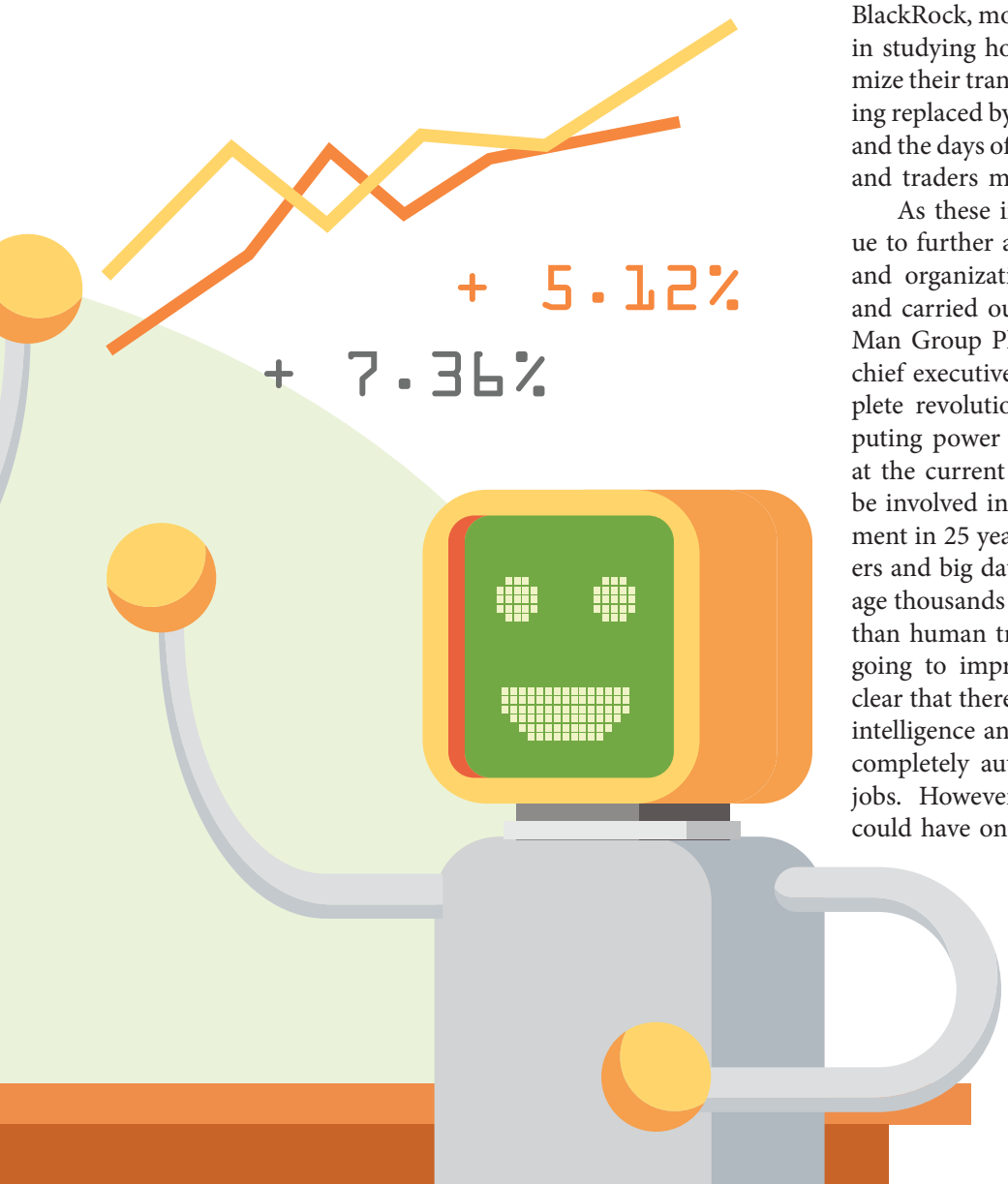
In this day and age, "machine learning", "artificial intelligence", and "big data analysis" are important buzzwords that represent the forefront of modern technological innovation. They have infiltrated almost all aspects of our society, from self-driving cars and automated warehouses to our cell phones, with processes such as Siri or Cortana. However, the greatest question is: what comes next? Artificial intelligence has the potential to revolutionize the corporate landscape, but no one knows the consequences of this technological revolution. What markets or industries will it infiltrate, and what will be the consequences of this "take-over" on the human job market? Automation of jobs could lead to cheap and ultimately more efficient sources of labor, which would result in widespread layoffs and increased rates of unemployment in the impacted sectors. This apocalyptic corporate vision seems almost like science fiction, that artificial intelligence would have the capabilities of emulating or even perfecting jobs requiring human creativity or higher level thinking. However, this future may not be as far off as it seems.

One market that artificial intelligence and big data analysis has already infiltrated is investment banking. In an effort to optimize their stock market research and investment, more and more funds and large Wall Street firms, such as Goldman Sachs, are turning to artificial intelligence as a way of cutting back unnecessary employee expenditure as well as improve their methods.[4] Hedge funds like BlackRock and larger firms such as Goldman Sachs and J.P. Morgan have already begun pouring more and more money into computer research. As of last year, Goldman Sachs employed around 9,000 computer engineers, around a third of their entire staff, dedicated to improving and maintaining their technological infrastructure.[4] J.P. Morgan has recently hired one of the world's experts in machine learning and natural language processing to help lead their efforts.[3] BlackRock's Scientific Active Equity group, a team centered on studying and using new machine learning methods of investment already manages



$80 billion dollars of the hedge fund's $286 billion active equities, and given the success of their assets in the past few years, more and more funds will be managed by this automated team of traders in the near future.[5] BlackRock's SAE team is an experimental investment group which is currently researching the efficacy of these novel methods, utilizing big data to quantitatively analyze thousands of stocks globally as well as machine learning to create more accurate market models and analyze more qualitative factors such as SEC filings or press conferences. In the past five years, 90% of assets run by BlackRock's SAE team beat their benchmark, as opposed to only 49% run by BlackRock's traditional "Fundamental" team.[7] In London, large firms such as MAN AHL and Winton Capital Management, have also begun investigating the potential for machine learning and big data's role in market analysis and smart investment. "It's at an early stage," Ledford, a chief data scientist at MAN AHL, said. "We have set aside a pot of money for test trading. With deep learning, if all goes well, it will go into test trading, as other machine-learning approaches have."[7] The market of computerized trading through learning machines and macroanalysis of big data is the new frontier for investment firms, and although it is still being researched and tested, the implications of these new technological methods have the potential to revolutionize the markets.



This is only the beginning. Computerized traders and big data analysis are already able to manage thousands of more companies more efficiently than human traders and traditional funds can, and these methods are only going to improve. With increased funding as well as attention from enormous firms such as Goldman Sachs, J.P. Morgan, and BlackRock, more and more money will be invested in studying how artificial intelligence could optimize their transactions. Investment traders are being replaced by computer engineers and machines, and the days of enormous trading floors of analysts and traders may soon become relics of the past.

As these investment firms and funds continue to further adopt these strategies, the structure and organization of how business is conducted and carried out will dramatically change. In the Man Group Plc, a group within MAN AHL, the chief executive officer, Luke Ellis foresees a complete revolutionization of the markets. "If computing power and data generation keep growing at the current rate, then machine learning could be involved in 99 percent of investment management in 25 years," Ellis said.[8] Computerized traders and big data analysis are already able to manage thousands of more companies more efficiently than human traders, and these methods are only going to improve as technology improves. It is clear that there is significant potential for artificial intelligence and its related technologies to almost completely automate the majority of investment jobs. However, despite the exciting potential this could have on how our economy and how it will

function for years to come, there are many important consequences to this revolutionary paradigm shift.

The first, and perhaps most important, result of this change is the implication it has on the job market. Why would firms continue to hire market analyst and traders when their job could be replaced by a more efficient, cheaper AI? At investment firms and groups like at Man Group Plc, there could be a huge impact on jobs. Estimates by Opimas, a research consultant which studied financial firms, say that around 90,000 jobs in fund management, market analysis, and staff will be gone by 2025, around a third of all of those jobs worldwide, due to the implementation of new technology demonstrated by MAN, BlackRock, and more.[8] However, even now, we can see these trends in many firms like Goldman Sachs. Just in 2000, Goldman Sachs' headquarters in New York employed 600 traders, who were in charge of providing for the bank's largest clients. Now, there are only 2 equity traders left, the rest replaced by computers and their caretakers.[4] At BlackRock, two top quantitative researchers left, giving way to more funding for the innovative SAE group.[5] Although not extremely significant at the present, these trends present interesting implications for what is to come, especially as artificial intelligence becomes more ubiquitous in investment banking. Predictions estimate that in the next decade or two, nearly all jobs in analytics have the potential to be replaced, and soon there would be no need to employ human traders. The impact of this replacement is self-evident. The job market for investment banking is about to radically change.

However, the introduction of artificial intelligence in investment banking poses beneficial consequences as well. Increased efficiency in market prediction would allow for greater profits and smarter investment on a faster, larger scale, potentially boosting the economy and providing greater security for the economy as a whole. Improved market analysis could help predict and avoid future economic crashes or depressions. However, as this technology has never before entered the markets in such an impactful way, nothing is for certain about how this technology of artificial intelligence and machine learning will change our economy and our livelihood. For now, it seems that there will be a continuation of hybrid firms of machine and human minds that has a great power to influence the corporate landscape in these next few years.

Finally, this replacement of human jobs with learning machines also brings about interesting ethical considerations as well. Even though computers are becoming more and more efficient in completing jobs than humans, should we allow them to supercede us, or should our jobs ultimately rest in our hands? There must be a limit in which machines should be allowed to replace our economy. Since artificial intelligence is already penetrating higher-level thinking jobs such as analyst positions, it could soon enter even more areas, such as scientific research or management, and although, it seems that this is the logical direction for which our society should head, the unknown consequences are fairly frightening. Economically, what will happen to unemployment rates, and how will people be able to support themselves as the job market grows ever smaller? Right now, our society is in a strange transition state: a hybrid of machine interference and traditional manpower. Though a completely automated society could be utopic, this transition of "power" from people to machine may have many unintended consequences, and as this prevalence of machines in the workplace increases, finding this balance is becoming increasingly important.

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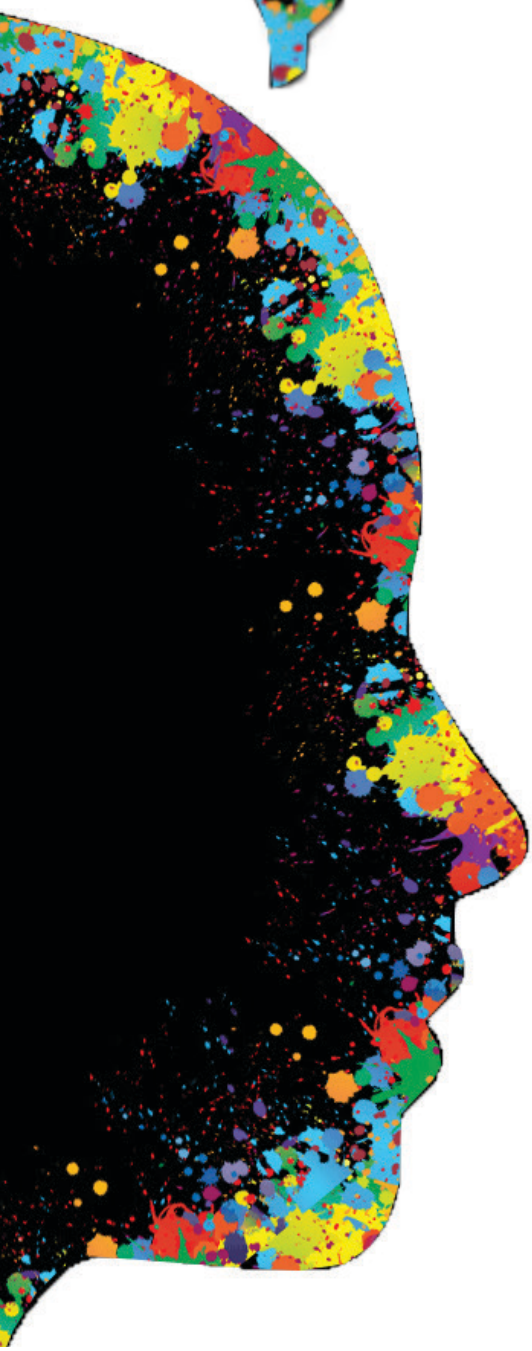
THE EVOLUTION



ALISHA AHMED

editor: Sarah Campbell // designer: Annie Zhang

The Fear of Ghosts and Other Paranormal Creatures

The study of evolution tells us that we are allowed to fear snakes, spiders, and rats. Both snakes and spiders bite us, and rats spread disease. With the advent of the modern age, we learned to fear moving cars, which can hit us, and towering heights, which can lead us to instantaneous death by a simple fall. But what is it about ghosts, about monsters and creatures of the dark, that terrify us so much? Why does something that hasn't even been scientifically proven to exist keep us up at night? The answers to these questions may lie in the field of the most perplexing emotion: fear.

Fear can be described as "an unpleasant often strong emotion caused by an anticipation or awareness of danger."[1] The main function of fear is to act as a natural warning signal for the body. Fear triggers specific adaptive responses to any dangers, threats, or conflicts. This definition of fear implies that a fear of the supernatural entails a direct threat to the human body by some sort of external force. There is a strong sense of unusuality in how the human body can discern such a direct threat from something that has not even been proven to be real. Particularly, supernatural beings are an entity that cannot physically stimulate any fearful response as there is no way that they can interact with any of the human senses. As a result, this fear of the supernatural is a baffling one.

Given that fear is one of the most mysterious emotions, it is no surprise that there have been many theories surrounding the origin of fear and how it is processed by the brain. Specifically, the answers to these questions may be found in theories of emotion. Early on, psychologists and physiologists were concerned with figuring out whether or

not physiological changes preceded or followed emotional experiences. One particular theory of emotion is that of psychologists William James and Carl Lange, who proposed that physiological changes occurr before the emotional perception of a particularly fearful stimuli. Specifically, fearful stimuli, such as the sight of dangerous creatures in the case of fear, reach the cerebral cortex and lead to occurrences of visceral changes.[2] These visceral changes are then perceived as emotion. Many critics of this considered the theory that human emotions could have such a large connection to the physiological body absurd. Some believed that the answers to the question of human emotion lied in a directly neurological basis. Cannon and Bard, two such critics, proposed that the neurological aspects of emotion lie underneath the cortex and involve the thalamus. Others took a more psychological approach. For instance, John B. Watson, known as the father of behaviorism, devised a theory in which all emotion was divided up into three categories and was influenced by three sets of specific stimuli: fear, love, and anger. Despite other theories, the James-Lange theory remains the closest to the truth in describing the origin of fear due to its basis in both physiology and psychology, but cannot explain fears of concepts which have no direct ability to cause a physiological recognition of stimuli. Unsurprisingly, one such concept is that of the supernatural, as the concept of this can not interact with any of the human senses and thus cannot elicit a physical response. As a result, the fear of the supernatural may have to be taken as a completely abstract fear, paralleling other types of fear such as the fear of loneliness and the fear of failure.

Physiologically, we experience fear when our sensory organs detect particular stimuli and transfer information about said stimuli to the brain. The typical symptoms felt in response to fearful stimuli are those characteristic of a "fight or flight" response - a racing heart, fast breathing, and other involuntary physiological reactions involved in the the brain. This response describes the autonomic nervous system, or the portion of the nervous system that is responsible for the control of unconsciously directed bodily functions. The involvement of autonomic activation in the fear response has led to propositions that stimuli leading to fear activate parts of the brain such as the limbic system and the locus coeruleus. Particularly, the locus coeruleus is involved with stress and panic, directly suggesting that the emotion of fear may have a heavy foundation in this location of the brain. Although the supernatural cannot provide any reliable and consistent fearful stimuli to result in such a flight-or-flight response, there must be some psychological reason as to why a fear of the supernatural leads to similar symptoms. Despite this, in the case of the supernatural, there exists no concrete stimuli as the cause of its fear. As a result, the direct cause of this fear may not always

be comprehended consciously.

Particularly, one of these fears is the fear of the unknown, as this abstract fear refers to nothing physical or tangible. The inability of this fear to be understood as connected to any specific stimuli exhibits the conundrum at hand. Specifically, there is nothing set in stone in our knowledge to determine why humans fear the unknown, or in our case particularly, the supernatural world.[2] As a result, understanding the human fear of the unknown may be the first step in bringing us closer to answering the question of how our fears of the supernatural are manifested.

The fear of supernatural beings may be based in the fact that humans are genetically predisposed to fear anything unknown, anything new to them that may pose any sort of threat.[3] Certain studies have shown a negative correlation between a fear of paranormal experiences and a tolerance of ambiguity.[4] In other words, those who have fears of the supernatural world tend to be much less tolerant of ambiguity, or the unknown, than those who do not possess such fears. This suggests that there indeed exists a positive correlation between a fear of the unknown and a fear of paranormal activity.

Specifically, the most probable evolutionary fear that is manifested in the fear of the supernatural is the fear of death. Humans are predisposed to fear anything that has the chance of leading them to death. Reasonably, the fear of death is a rationally based fear, and thus the fear of the unknown or the supernatural can also be described to have this quality.[5] The supernatural world has not been proven to be directly harmful to humans in the way that death can be, but both death and the supernatural have the quality of always being a possible threat. Even though neither are grounded in empirical fact, both manifest a similar general fear of the unknown. Thus, the two are heavily connected.

In an anthropological view, to many religions, death and supernatural beings serve as an entryway to a different world, to an unpredictable place. For example, in Islam, there exist jinns, or creations of God that live in a world parallel to humans and can lead humans astray to this unknown world. In Roman Catholicism, ghosts manifest as malevolent spirits and demons that reside in hell. In Buddhism, ghosts are reincarnated humans that are meant to work out bad karma and live in a distinct, other world. These examples are few of many that demonstrate the unpredictability of the supernatural. As a result, the fear of death may represent the ultimate fear of humanity, that is, of the unknown.

As shown, the themes of death and the fear of the supernatural are found in many cultures, as there exists a large cross-cultural belief in the supernatural world as grounded in religion. Although specific religious beliefs, such as of specific gods and myths, may not all be the same across cultures, universal themes exists, such as that of an afterworld and of supernatural beings.[6] This in turn shows how prevalent these fears are in the global community, and that they are, in turn, a universal fear. It is also possible that humans develop a fear of ghosts and monsters to reinforce their own religions, as humans need a negative force that contrast with the gods they do believe in. In other words, any concept, especially abstract ones like religion, cease to persist steadily without a conflicting ideal or negation. Additionally, belief in opposing forces in religion, such as heaven and hell, can enforce a delicate balance in beliefs, strengthening community and cultural ties in a group.

Understanding concepts of abstract fears such as the fear of the supernatural may help us solve the current issues of the world more effectively. For example, interpreting the human fear of the unknown could allow us to improve mental health diagnoses and treatments. Better understanding our own emotional psychology could provide headway in treating some of the most worrying mental illnesses in society. Many anxiety disorders, such as bipolar disease, panic disorder, and certain phobias have been found to have underlying causes of increased sensitivity to unknown threats, or more generally, of the fear of the unknown.[7] Determining common patterns among such anxiety disorders would allow for more precise treatment, prompting developments of drugs targeted specifically for sensitivities to unknown threats.

On a more global scale, our fear of the unknown can be taken in context of national security. Particularly, the unpredictability of terrorism and the inherent human fear of unknown cultures may have resulted in heightened national security around the world, and particularly in the United States. The events of September 11, 2001 indicated an unpredictable threat that

undeniably resulted in danger, causing elevated levels of fear and anxiety among the population. Particularly, this event was followed by an increased perception and fear of risk, which was further amplified by the media and led to unwarranted hatred and subjugation of certain cultural groups. Consequently, this fear of unpredictable terrorist attacks has been especially significant in today's society given new technologies and a more politically divisive global climate. Thus, understanding this fear of the unknown in the context of both national and international society may be crucial in establishing a more stable and tolerant global community.[8]

Although there exists no concrete or scientifically proven answer to why humans fear the supernatural, the answer may lie in our fear of the unknown. Years of evolution have granted humans the gift of an incredibly complex and intricate mind, which as a result leads to complicated abstract concepts such as the fear of the unknown. Furthermore, the unique human experience shapes our fears, as we manifest fears of absurd concepts and objects. Consequently, our fears of ghosts may just be reflections of our inner complexity that is so inherent in our nature, giving particular concepts, such as the supernatural world, particularly mystifying powers as something to be feared.

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ADDing

Why College Students Are Oblivious to the Reality of Adderall

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"Prescription stimulants can cause tolerance, dependence, and addiction."

In a 2011 study, researchers decided to explore college-student discussion of Adderall® on Twitter.[1] They combed through 213,633 tweets from 132,099 unique user accounts that mentioned Adderall®. Although most tweets were sarcastic, joking, or casual, 12.9% of tweets mentioned an 'alternative motive' in the same tweet; specifically, these tweets concurrently mentioned Adderall with studying, finals, tests, and the like, suggesting a potential for misuse. But regardless of the nature of these tweets, Adderall®, and by relation prescription stimulants, have become normalized, as these tweets demonstrate. And although there is nothing inherently wrong with mentioning these drugs in artforms like rap or in jest, reinforcing the idea that these practices are not only commonplace but also acceptable can have serious effects on how students perceive their use.

Despite how pervasive Adderall is in mainstream culture, the health risks associated with prescription stimulant use are largely unknown. In fact, 81% of respondents from a 2007 survey at a large, public southeastern research university thought that illicit use of attention deficit hyperactivity disorder (ADHD) medication was either 'not dangerous at all' or 'only slightly dangerous'.[2] Additionally, a 2010 web-based survey of over 3400 undergraduates found that 73.1% of respondents were not worried about becoming dependent on ADHD medication.[3] However, these beliefs lie far from reality. From 2004 to 2011, the number of emergency room visits involving nonmedical use of amphetamine-dextroamphetamine (Adderall) increased from 2,303 to 17,202, a stunning 650% increase.[4] The normalization of prescription stimulant use has resulted in students perceiving the drugs to be merely 'tools' that can allow them to thrive and succeed in school, like a set of flashcards or the internet. But in reality, prescription stimulants are incredibly dangerous drugs when used by the wrong people for the wrong reasons.

Prescription stimulants like Adderall® are one of many classes of central nervous stimulants, ranging in the strength of a cup of coffee to that of cocaine. The mechanism of action for these types of drugs involves an increase in norepinephrine and dopamine levels within the prefrontal cortex, the part of the brain associated with decision making and moderating social behavior.[5] Those with ADHD have lower levels of these neurotransmitters, but prescription stimulant use largely compensates this deficiency, allowing these individuals to function as well as their counterparts. For non-ADHD prescription stimulant abusers, prescription stimulant use floods the central nervous system with an excess of neurotransmitters because their baselines are already normal. These users generally report overall increased cognitive function, focus, and wakefulness as well as improved mood. It's exactly for these side effects that students abuse prescription stimulants like Adderall® to boost academic performance.

But despite the potential positives from abusing prescription stimulants, a huge number of both acute and chronic health consequences may also manifest, which, as mentioned above, are largely not known by the public. In addition to enhancing memory and alertness, these same neurotransmitters cause an increase in blood pressure, heart rate, and breathing, while also decreasing blood flow.[6] Users with heart issues can experience irregular heartbeat, circulation failure, and even heart attack. Additionally, prescription stimulant use has been shown to cause mental health issues, ranging from restlessness and tremors to paranoia, aggressive behavior, and hallucinations.[6] Even worse, these prescription stimulants, like many other drugs, can cause both tolerance, dependence, and addiction.[6] Chronic drug use changes the biochemical balances in the brain, resulting in an elevated baseline that increases tolerance to the drug and reduces its efficacy at a consistent dose. Without higher dosages, abusers would be unable to attain the desired effect from the drug. Additionally, developing tolerance to prescription stimulants can also result in a reduced dopamine-receptor feedback loop, which can result in fatigue and depression.[7] Cravings and withdrawal

symptoms are also not uncommon among chronic users, making everyday life difficult to manage without the drug and further fueling the dangers of addiction.

Nevertheless, students will abuse prescription stimulants because the perceived potential of improved academic performance outweighs both the ethical issues and associated health risk factors. From the same 2007 study, researchers additionally recorded undergraduate responses regarding their different justifications for illicit study drug use.[2] One relevant rationalization is the 'minimization argument', in which students 'minimized' the serious nature of prescription by characterising them as 'harmless, benign, and socially acceptable anti-fatigue aid' by comparing these drugs to the likes of coffee, soda, and energy drinks. Another major rationalization was a 'moderation' argument: they believed they were 'responsibly' using them only when needed, rather than abusing the drug like a hard addict. Whether they are minimizing the consequences of their own risky behaviors or that of the drug itself, these students are putting themselves into dangerous situations because they do not understand the severity of their actions.

"Nevertheless, students will abuse prescription stimulants because the perceived potential of improved academic performance outweighs both the ethical issues and associated health risk factors.

Additionally, some prescription stimulant abusers may understand that potential physical and psychological risks exist, but will abuse prescription stimulants anyway out of perceived necessity. A 2005 New York Times article includes anecdotes from students at Columbia University and their struggle to stay afloat in a competitive academic setting.[8] Some students believe that without Adderall® or Ritalin®, they would not be able to maintain their high grades. Other students, aware of study drug abuse by their peers, bring up issues of fairness in the classroom. Some use the "if you can't beat them, join them" mentality as justification for their own stimulant abuse, despite awareness of the ethical dilemmas behind doing so. Although competition and stress can bring out the best in some people, others will crumple under the pressure, turning to these drugs as a save-all and exposing themselves to dangerous side effects.

The reality of prescription stimulant abuse among college students has been driven by a number of hidden factors. One huge component of this phenomenon can be attributed to higher prescription drug use overall in the past twenty years. In one study conducted from 1999 to 2012, researchers observed a sizeable increase in prescription drug use among US adults, from 51% to 59%.[9] Another study came to a similar conclusion, finding a 44% to 48% change in prescription drug prevalence from 1998 to 2008.[10] Additionally, total expenditure on prescription drugs in the United States has increased by nearly nine-fold from 1990 to 2017, ($40.3 billion to $360.1 billion).[11] The considerable spending on prescription drugs and pervasiveness of their use indicate that these drugs, including prescription stimulants, are much greater in quantity compared to the past. Whether this apparent excess is a result of the influence of the pharmaceutical industry or changes in medical practice, the availability and consequent accessibility of these drugs certainly contribute to its normalization, where seemingly anyone can be using them.

It is no coincidence that the increase in prescription drug availability is correlated to the increase in ADHD diagnoses. The National Health Interview Survey, a study run by the Center for Disease Control and Prevention, observed a 66% relative increase in ADHD diagnoses since 2000 (absolute rates: 6% to 10%).[12] One legitimate explanation could be that conditions like ADHD can be detected more frequently now due to improved medical practice and awareness. However, with the definitive rise of illicit Adderall® use and interest, it is completely plausible that some cases are fabricated. Not only are symptoms largely self-reported, but it is also very obvious which responses are associated with ADHD, so patients can easily manipulate doctors by feigning symptoms of hyperactivity and restlessness. And unfortunately, not much can be done on the provider side to stop these patient hijinks. In a healthcare system where prescribers are at the mercy of patients' satisfaction, fear of being sued for mistreatment or negligence may force prescribers into complying.

With how commonplace and easy it is to access prescription stimulants for personal use, it can be hard for students to say no. Competition and fear of failure can also push people to using these drugs. On the other hand, personal moral complications, issues of fair use, and legality may leave students conflicted. But for whatever stance any individual has on the subject, everyone needs to understand the health risks and consequences of use. Prescription stimulants are drugs, and need to be viewed as such. Although there are definitive short-term benefits from prescription stimulant use, in time, the consequences from these ill-advised decisions can have a huge impact on future health and quality of life.

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THE CLONE WARS

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editor: Sarah Campbell // designer: Annie Zhang

The fact that the first successfully cloned primates were born less than 100 days ago serves as a testament to the continuing interest and advancement in the field of mammalian cloning. The birth of Dolly the sheep at the Roslin Institute in Edinburgh over 20 years ago sparked the intense curiosity and debate surrounding the field of cloning that continues even today. Dolly's birth–and more importantly, the way in which she was conceived–is considered a scientific breakthrough, with some even calling it one of the most significant of the century. The commotion surrounding Dolly stems from the pioneering nature of the science behind her conception.

Contrary to popular belief, Dolly was not the first cloned mammal, but she was the first mammal to be cloned using an adult somatic cell. The science behind the technique used, somatic cell nuclear transfer, is relatively simple. Scientists take DNA from the nuclei of fetal somatic cells—any cells in the organism other than the reproductive cells—and implant it into "empty" eggs that have had their own DNA removed. The scientists then stimulate the eggs with an electric shock, and the cells begin to divide and develop into embryos. These embryos are then implanted into a surrogate mother's womb, where they can develop into healthy, viable offspring.[1] In the 20 years since Dolly's birth, scientists have cloned over 20 different species of mammals using the same technique used for Dolly. However, they were unable to successfully clone primates, our closest nonhuman relatives, until recently.[2]

Enter Zhong Zhong and Hua Hua, two genetically identical long-tailed macaque monkeys that were born in Shanghai in late 2017.[3] Like Dolly, the monkeys were not the first cloned primates, but rather the first cloned primates to be produced through somatic cell nuclear transfer. The fact that primates are so closely related to humans makes their successful cloning extremely useful in the study of human diseases. Alzheimer's disease, for example, is a chronic neurodegenerative disease that starts slowly and progressively worsens, following a pattern of both cognitive and functional impairment. Its cause remains a mystery to researchers. Currently, about 70% of the risk of Alzheimer's disease is attributed to genetics, and the other 30% is attributed to external factors such as injury and pre-existing conditions like hypertension and depression. Although researchers have tried to identify specific risk genes, this can be difficult and problematic due to fact that the contributions of each single risk gene is small, and it is often a combination of risk genes that need to be identified. There is also significant overlap in the pathological changes brought about by these risk genes and those that can be attributed to conditions like cerebrovascular disease and depression, often occurring alongside Alzheimer's.[4]

The recent developments in primate cloning could greatly reduce this kind of confusion when

identifying risk genes. The scientists that cloned the macaque monkeys propose the possible pairing of the new cloning technique with existing gene-editing tools (such as the CRISPR/Cas9 complex) in vitro to develop improved animal models of human diseases.[2] Using this technique, the scientists could produce organisms that are born genetically identical with the exception of the specific gene being studied, exclusively testing potential risk genes without interference from the concurrent effects of other health issues. By keeping the clones in a controlled environment and eliminating the external genetic factors associated with Alzheimer's disease, these primate clone models can be used to focus exclusively on the genetic causes of the disease. Scientists could use these gene-editing techniques to investigate and confirm the roles of individual genes and combinations of genes in causing symptoms. Studying two genetically identical primates can reveal the non-genetic risk factors for Alzheimer's through the observation of their effects on genetically identical organisms. If two genetically identical monkeys began to develop differing symptoms when placed in different environments, it would make sense to attribute these differences to purely environmental factors. The benefits and advantages conferred by cloned primate disease models in identifying risk genes is not restricted to Alzheimer's or neurological disorders alone; scientists hope to harness this technology and apply it to a wide variety of diseases, including various cancers.

SCIENTISTS ARE HOPING TO HARNESS THESE TECHNOLOGIES AND APPLY THEM TO A WIDEVARIETY OF DISEASES, INCLUDING VARIOUS CANCERS.

Another useful application of these primate disease models is the option to test any drugs or alternate methods of treatment that might develop on the cloned models before going to clinical drug trials with human subjects. Primates are ideal candidates for the testing of treatments or drugs because of their likeliness to react in a way that mimics the reactions in the human body.[5] Furthermore, cloned primates offer a significant advantage over their non-cloned counterparts due to the fact that in experiments with the latter, it is often difficult to determine whether the differences between test and control groups are caused by the treatment or pre-existing genetic variation. Cloning eliminates genetic background variability, making it easier to tell if the differences between test and control groups are being caused by the treatment being tested.

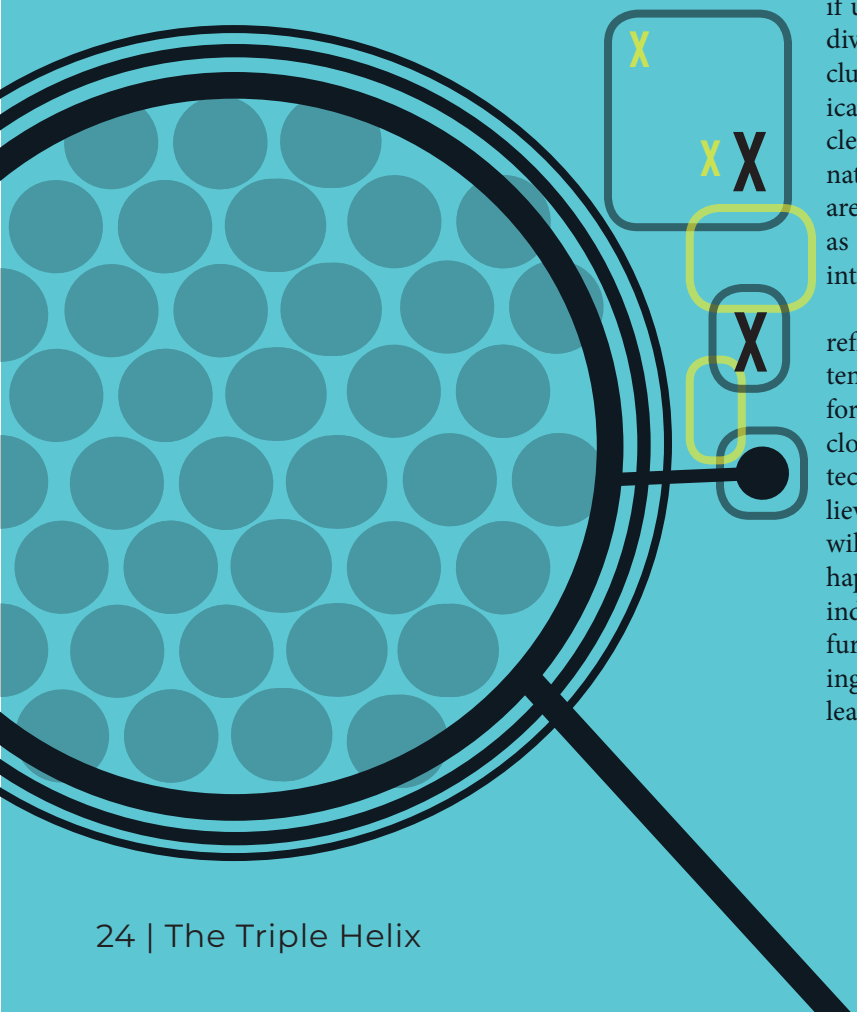
However, the use of primates for drug trials also draws attention to the ethical implications of cloning. Does testing drugs on primates and other mammals before moving on to human clinical trials imply that their lives are inherently less valuable? What effect does cloning have on the value of animal lives? Are clones inherently less valuable than naturally born organisms? While most scientists and researchers would agree that the value of testing drugs on animals comes from a perceived greater degree of dispensability of animal lives when compared to human lives, many animal rights activists disagree with animal testing and believe that it should be discontinued completely. Naturally, it follows that the advent of clones being used for drug testing will also be met with resistance, perhaps even more so because of the fact that many of them will be created and brought to this world for the pure purpose of being drug testers.

Even tougher ethical questions can be raised when the topic of cloning turns human, and this new ethical debate that surrounded possible human cloning started, once again, with Dolly. The novelty of such a momentous scientific feat was also coupled with repulsion and fear associated with the possibility of a cloning a human being. If a mammal as large as a sheep could be cloned from a single body cell, would human cloning be that far off?

Those opposed to the concept of human cloning were quick to take measures against it: countries across

the world banned human cloning and threatened severe punishment to those who even attempted it. In the United States, then-President Clinton called the National Bioethics Advisory Committee (NBAC) and asked them to "undertake a thorough review of the legal and ethical issues associated with the use of this [cloning] technology." Clinton also asked the NBAC to, based on this review, issue a report containing a recommendation of what actions should be taken regarding human cloning. After the report was released, Clinton imposed a ban on federal funding for experiments that involved human cloning.[6] The actions taken by the government reflected the thoughts that many people had regarding human cloning—that it was unethical and needed to be stopped.

However, the scientists that cloned Dolly and the macaque monkeys, as well as most of the other scientists who have attempted to utilize cloning techniques in their research, have maintained that their main goal in cloning mammals was not to potentially clone a human, but rather as a way to study diseases and their mechanisms without endangering human lives.[2] Although the researchers have admitted that "technically, there is no barrier to human cloning," they continue to maintain that their only purpose is to "create genetically identical monkeys" for medical research purposes.[4] However, the fact that a species so closely related to humans was able to be cloned also intensifies the ethical debate and reopens the arguments that surround human cloning, specifically.



The arguments against human cloning are wide and varied, but most seem to make their way back to a central argument against cloning as being a violation of the natural order, tarnishing human dignity.[7] Indeed, the process of cloning would entirely deprive any clone of their own unique identity, which is something that most people highly value as a part of being human. It would be wrong to impose the genetic identity of one individual on another.[7] Clones would be faced with the unfair pressures of living up to the "standard" set by the individual they were cloned from, and might not live up to any talents or accomplishments that cannot be attributed to pure genetics. Many of the arguments against human cloning also carry religious value; a common argument that people use against the implementation of cloning is that it allows scientists to "play God," selecting for and duplicating those traits that they find most desirable. Others argue that cloning, if used widely in the future, would result in a lack of diversity in the population, as people tried to select exclusively for clones with highly desirable traits, physical and otherwise. Our long history of evolution has clearly demonstrated that sexual reproduction and the natural selection that occurs as a result of this process are extremely advantageous for complex species, such as humans, and that it would be dangerous to try to interfere with nature.[8]

As of now, laws in the United States continue to reflect the ongoing ethical debate that surrounds potential human cloning; the ban on federal funding for research using embryonic stem cells from human clones still stands.[9] Just because human cloning is now technically possible doesn't mean that everyone believes it should happen, nor does it mean that scientists will ever have the legal backing or means of making it happen. But, as the recent successful primate cloning indicates, there are now technically no barriers to the further usage and development of mammalian cloning. Where we believe these new technologies will lead is rooted in ethical and moral preconceptions.

For some, primate cloning is a welcome stepping stone toward more sophisticated biomedical techniques and applications. For others, it foreshadows the potential horrors that come with a society of clones.

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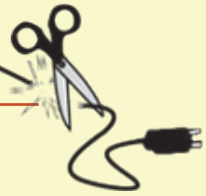

PAS or PASS: Should Helping People Die Be Legal?

Haley Wolf
editor: Lois Owolabi // designer: Christine Mai

The role of a physician is to ease the suffering of their patients, but what if the best way to relieve their pain involves helping them end their life by committing suicide? The media continues to cover stories of triumph over life-threatening illnesses, spreading the joy experienced by the victor and their families. Social norms have allowed these in-depth discussions regarding terminal illnesses, but the final moments of patients that don't overcome these diseases are rarely seen in the public eye. For those patients who aren't lucky enough to broadcast their tales of victory, the end of their stories is often unimaginably heartbreaking. But what if these less fortunate patients didn't have to spend their final moments in agony? What if their friends and family could say their final goodbyes without watching their loved one suffer?

These questions echo throughout the debates on physician-assisted suicide (PAS) and euthanasia in the United States. Physician-assisted suicide and euthanasia are alternative end-of-life treatments for mentally competent, terminally ill patients that are not legal in the majority of U.S. states. Voluntary active euthanasia is the process by which physicians administer a lethal agent, or a lethal dose of a therapeutic agent, to their patient, resulting in death.[1] In this case, the physician directly ends the life of their patient, following the patient's request. Physician-assisted suicide, on the other hand, occurs when a physician helps their patients to commit their own suicide, typically by prescribing drugs that will end the patient's life.[1] The most common prescriptions are for oral doses of barbiturates, a class of sedative medication, to be mixed with juice or another liquid for ingestion.[2] However, these practices are not legal in the majority of U.S. states due to the associated ethical and legal uncertainties.

Physician-assisted suicide, unlike the more controversial euthanasia treatment, has been legalized in six states and Washington D.C. The legalization of physician-assisted suicide has been widely debated in the medical community for decades, with varying opinions emanating from healthcare professionals, patients, and patients' families. The American College of Physicians recently noted several groups that strongly advocate for assisted suicide to promote patient autonomy but believed the most compelling arguments on the issue came from the opposition, concluding that it does not support the legalization of physician-assisted suicide.[3] Similarly, the American Medical Association (AMA) officially opposes PAS. However, as of 2018, the Washington D.C. chapter and the AMA chapters in ten states have converted to a neutral position.[2] Physician-assisted suicide is now supported by several associations, including the American Medical Student Association and many others.[2] The complex relationship between physicians and their patients creates a moral grey area in this debate, with both sides citing the legal and ethical implications of these treatments.

Health care professionals are often drawn to their

field because they feel incredible compassion for people in need of help. This may translate into the desire some physicians feel to help their terminally ill patients die with as much dignity and as little pain as possible. In fact, a 2010 study revealed that 40% of physicians, nurses, relatives, and lay people supported the legalization of speeding up a terminally ill cancer patient's death.[4] In 2016, Medscape conducted a survey in which 57% of medical doctors were in favor of legalizing PAS, a marked increase from the 46% found in Medscape's earlier 2014 poll.[2] However, despite attempts by healthcare professionals to minimize their patients' pain, many patients suffering from terminal illnesses endure a difficult end.

The legalization of physician-assisted suicide is often supported in debates by discussing the promotion of patient autonomy and physicians' duty to diminish the suffering of their patients.[2] Allowing patients to decide when, where, and how they will die gives them the power to take control of their lives before their illness makes these choices. A survey conducted in 2000 found that 60.2% of terminally ill patients studied supported PAS and euthanasia in a hypothetical situation.[5] In the U.S., patients' autonomy may be infringed upon in many states in which physicians are not permitted to help their patients end their own lives, giving patients no choice but to forego further treatment or enter into hospice care. PAS is considered by its proponents to be a compassionate way for a physician to help their patient, allowing their patient to die on their own terms. Supporters also often provide criteria for the legalization of assisted suicide that they believe would prevent abuse of this end-of-life care, similar to the safeguards in place in states that have already legalized PAS. Such criteria are meant to defend against the "slippery slope" that many opponents are worried will result from the legalization of assisted suicide.

The "Death with Dignity" laws, which have been legalized in five states and Washington D.C., are meant to help terminally ill patients end their own lives with the assistance of a physician that prescribes them with a lethal medication that they are to administer themselves.[6] The state of Hawaii became the seventh U.S. jurisdiction to legalize a PAS law on April 5, 2018, which will go into effect on January 1, 2019.[7] These laws have many careful safeguards in place to prevent any possible coercion abuse of such legislation. For example, qualifying patients must be mentally competent and have a prognosis of six months or fewer to live, which must be confirmed by two physicians.[6] After the required criteria are met, patients may request to receive a lethal prescription from their physician. The patient may rescind their request at any point in the process, thus protecting the patient autonomy that both supporters and opponents of PAS consider vital.[6] The final decision to end life, using a lethal prescription, can only be made by the patient themselves.

Proponents of PAS often discuss the story of Brittany Maynard, a 29-year-old woman, who was diagnosed with terminal brain cancer and completely changed her life in order to pursue a dignified death in Oregon. After overcoming many obstacles, Brittany managed to establish residency in order to fully qualify for death with dignity.[8] In an article published by CNN she said, "I am not suicidal… I am dying. And I want to die on my own terms."[8] Brittany obtained the medication necessary to end her life but did not take the prescription until several weeks later, after her husband's birthday.[8] Brittany noted tremendous relief when she obtained her prescriptions, and she proceeded to end her life on November 1, 2014, with loved ones by her side.[8] Brittany's hope was that all Americans would have the ability to choose how their life ends and that no one take that choice away from people in similar situations.[8] Those who support the legalization of PAS often look to stories like Brittany's to remind people that this decision cannot be made solely on facts and figures, but real people must be considered.

While stories like that of Brittany Maynard indicate the benefits of legalizing PAS, the opposition considers the possibility of a "slippery slope" to be too great a risk. Opponents often discuss Dr. Jack Kevorkian's actions when describing the possible repercussions of PAS legalization. Kevorkian admitted to helping 130 patients end their lives between 1990-1998 while his actions gained publicity for both him and PAS. In 1998, after many encounters with law enforcement, Kevorkian was charged with second degree murder after injecting a lethal medication into a patient suffering from ALS. Although this patient allegedly requested Kevorkian's help, this crossed the line from physician-assisted suicide into voluntary euthanasia,

which many people believe is equivalent to homicide. Citizens cautious of the slippery slope also note that, of Kevorkian's 130 patients, approximately 60% were discovered to have no terminal illnesses.[9] In some cases, autopsies indicated that there was no physical evidence of any disease in the patient.[9] Thus, opponents often use Dr. Kevorkian as evidence of the possibility of abuse by physicians and other parties.

The possibility of endangering vulnerable groups, including those of lower socioeconomic status, is considered to be a primary reason for opposing this type of legislation. The Washington Times reported a story about a woman who was allegedly denied coverage of treatment for her terminal disease when her state passed PAS laws.[10] Such a story requires consideration of how the economics of health care could be affected, especially when PAS is a more cost-effective option. Surprisingly, though, the interest in PAS was not found to differ significantly among groups of varying age, education, income, length of illness, or physical activity.[5] The safeguards in current legislation are considered to be insufficient by opponents of PAS, leaving too many opportunities for abuse. Some question whether or not the witness present in PAS proceedings could be a family member with some kind of financial or emotional incentive to help the patient die.[11] Despite no evidence to suggest abuse of current PAS practices, opponents continue to cite numerous possible examples in which abuse could corrupt a system that allows PAS.[12]

Oregon, the first state to enact a Death With Dignity Act, provides over twenty years of data and experiences to help shape this debate. While many may predict pain to be a primary reason for desiring PAS in Oregon, this has not been the case. Loss of autonomy, including the loss of physical and mental faculties, and decreasing ability to partake in the activities that made life worth living were the most common reasons patients provided for pursuing a dignified death, with 91% and 89% identifying these as their primary motive, respectively.[13] These patients are often most worried about how losing motor and cognitive functions will affect their quality of life as their illness progresses. Only 26% of patients reported pain as their primary incentive in seeking out death with dignity, while only 4% of patients indicated financial concerns.[13]

Clinical depression has also been found to be a major determinant in the likelihood of a patient to pursue PAS, and it is a major reason why many opponents are fighting for more psychological safeguards to protect patients suffering from mental illnesses as well as physical ones.[13] Many dissenters of PAS legalization call for more support for patients with terminal illnesses, including more psychological support and better hospice and palliative care options. Opponents of the legalization of PAS often agree that autonomy is an important aspect of end-of-life-care, but they continue to believe that physicians should not help patients commit suicide, especially when depression is a facotr.[2] Opponents often suggest that, instead of offering PAS as an easy way out, our society should improve current end-of-life care practices and mental health support for patients suffering from terminal illnesses.

The data from Oregon has also disproved the idea that patients may be more inclined to pursue PAS if they are uneducated or are concerned with finances. With most patients having at least some college education, the results refuted the idea that patients from lower income or uneducated groups would be more likely to pursue PAS to reduce burden on their families.[13] Furthermore, most patients that requested death with dignity were already in the care of a hospice facility, which reveals that other end-of-life care options continue to be considered and accessed by patients suffering from terminal illnesses.[13] This evidence suggests that end-of-life care options are available for patients that do not wish to end their lives, likely providing sufficient care for patients in their final days, which opposes the idea that legalizing PAS would result in a declining hospice care system that drives patients to consider PAS as a more viable option.

Some states have taken action to legalize physician-assisted suicide with many stipulations to prevent abuse, but there are many more that continue to debate this controversial decision. But the question remains, where should healthcare providers draw the line when it comes to assisted suicide and euthanasia? Considering the legal and moral implications of legalizing PAS may seem simple, but what if it were your mother or father that was suffering from terminal cancer? It may be easy to take a stand on the issue from an outsider's perspective, but one must consider how opinions may change when the issue involves their own family or

even themselves. The question of legalization remains controversial because it is not a decision that can be made solely with our heads, it must also be made with our hearts. Physician-assisted suicide will likely remain a controversial issue for as long as we live but, with greater knowledge and consideration, perhaps our society can reach a consensus that satisfies all desires for providing the best ending for terminally ill patients.

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SUPERVISED INJECTION SITES

Helpful or Harmful?

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In the United States, the opioid epidemic claims more than 115 lives every day. 2015 saw 52,404 lethal drug overdoses, 13,000 of which were related to heroin. That same year, 591,000 Americans had a substance use disorder involving heroin. The risks associated with this drug include addiction, heart and lung disease, cancer, mental illness, and infection with blood-borne diseases such as HIV/AIDS and hepatitis. Heroin interferes with normal neurotransmitter function, changing users' ability to control their level of stress, make rational decisions, learn new concepts, and recall old memories. While the drug is damaging enough on its own, it also functions as gateway - roughly 23% of heroin users develop an opioid addiction.1

With an escalating crisis and no clear heading from the federal government, state and local governments are starting to consider supervised injection sites (SIS). In these sites, users bring their own drugs and inject under the watch of a nurse. Proponents of SIS argue that they mitigate the risks of drug use by providing clean needles and emergency care in the event of an overdose. SIS also provide important proactive services, including first and foremost a way to get in contact with drug users, a notoriously difficult group to track, and the distribution of information about rehabilitation services to those who most need them. Critics argue such a facility will encourage drug use and bring drug users to the neighborhood in which it resides, increasing crime and needle pricks in the area.

This article will assess to what extent SIS improve the lives of their patients, if they will be useful in broader societal terms, and how they tie into the national political debate on the opioid epidemic. Two scientific pilot programs, one in Vancouver and one in Sydney, will provide the data for this article's scientific discussion. And to explore the political side of SIS, we'll examine the hurdles surrounding SIS implementation in Philadelphia, a city that opened a legal path to creating such a facility but passed the responsibility for doing so on to the nonprofit sector.

Do SIS help their patients?

To answer this question, we will examine whether SIS prevent overdoses, promote addiction treatment and medication adherence, and/or, ultimately, save lives. While both the Sydney and Vancouver clinics managed thousands of overdose events without a single fatality, neither clinic made a perceptible impact on community levels of overdose nor overdose presentations at hospital emergency wards. Moreover, the sites saw elevated rates of overdosing in clinic as compared to on the streets, suggesting either users of SIS are a high-risk population, or users take greater risk by using more heroin when they are being supervised by health professionals.

With regards to referral of users to drug addiction treatment, 11% of clients over 6 years were referred to treatment. This rate has been exhibited as evidence that SIS function as gateways for treatment and criticized as unjustifiably and abnormally low.4 With regards to treatment adherence, a 2014 study of 13 residents of a 24-bed HIV/AIDS care facility concluded SIS are central to a "comprehensive harm reduction strategy," a strategy that improves adherence to highly active antiretroviral therapy as well as survival rates. Additionally, this policy promoted honest discussion of drug use, an important first step to

receiving treatment. While small in sample size, the study suggests SIS do meaningfully contribute to an atmosphere that encourages drug users to seek help.

Calculating lives saved is a tricky business. While there is a debate over the exact rate, there is a consensus that SIS do save lives, but that the rate of doing so is low. While the statistics vary by region and clinic, hypothetically if a clinic hosted 300 injections a day (twice the use of the Sydney site), the clinic would prevent 1 lethal overdose of a patron annually.3 So we can conclude that while SIS do not seem to prevent overdoses, they do promote use of addiction treatment programs and adherence to medication regiments, and they do save lives. To help answer the question of whether the sites do so at an acceptable cost, we will next examine the societal impacts of the clinics.

Do SIS help the community?

To start answering this question, let's first ask: Do SIS decrease public nuisance and the transmission of blood-borne viruses? A decade of data from Vancouver and Sydney have provided us with some preliminary answers to this question. With regards to public injecting, Sydney saw a marginal (at best) decrease in publicly disposed needles and syringes because of their SIS. Furthermore, Sydney saw no impact on blood-borne virus transmission, meaning no demonstrated improvement in Hepatitis B infections, Hepatitis C rates, sharing/reuse of syringe and injection equipment, nor in HIV testing. By these two measures, SIS do not appear to help their communities. We have already shown, however, that they do appear to help their clients. So, it is worth asking if SIS do any societal harm.

SIS have not been shown to increase crime, neither petty crime nor drug dealing, in the area surrounding the SIS. Furthermore, the clinics have not been demonstrated to draw drug users or dealers to their area. So now we are left with a conundrum. The clinics do seem to some good for their patients, and while they fail to really impact community health, they do appear to help their clients in terms of safety and accessing addiction treatment. We thus must look at whether these clinics are efficient tools for societal good.

One way to gauge efficiency is by calculating the medical costs that were prevented (such as ER visits, drug regiments, etc.) due to the implementation of the clinics. Using the conservative estimate that decreased needle sharing was the only effect of the Vancouver supervised injection facility, the facility was shown to be associated with, over ten years, a net savings of $14 million. For every dollar spent on the site, a different calculation found 1.5-4.02 dollars in benefit resulted. Despite these encouraging results, experts agree that more longitudinal studies (studies that track the same variable over years, perhaps decades) are needed. Despite these encouraging results, Australia's health minister stated the money would have been better spent on addiction treatment. As you can see, there's evidence that supports both sides of the scientific arguments for and against SIS. Philadelphia lies in the heart of the epidemic. A quick look at the discourse surrounding SIS in this city will help reveal which arguments carry weight with the public and policy makers.

Politics Surrounding SIS in Philadelphia

In January of 2018, Philadelphia city officials okayed the creation of a supervised injection site. The city, however, will not fund the SIS nor assign it a location – two monumental tasks. The city will not even operate the site, opting instead to help connect users to addiction services. The idea of having a private developer run the site has some community members concerned, including Councilwoman Maria D. Quiñones-Sánchez who represents a district at the center of the crisis. Perhaps even more concerning is the fact that such a site and its workers would not be immune from federal prosecution, an especially concerning possibility given that President Trump has indicated a desire to focus on law enforcement, as opposed to treatment, to combat the opioid epidemic. Further complicating the clinic's legal standing, Philadelphia's police commissioner stated he does not know how the site will affect the policing of narcotics; however, he has declared that those working at such a site will not be criminalized (locally) for trying to stop the spread of disease.10

The government has always controlled the definition and criminalization of drug use, and given the current laws it enforces, the government will have to be a part of any major initiative to treat drug addiction.

bate remains over whether SIS are the path to take. It's worth noting that the economic incentive for SIS (that SIS will save money by reducing the government's net healthcare spending) do not apply in the city, as healthcare savings will primarily go to the federal government (as the federal government funds Medicare and Medicaid) rather than the Philadelphia municipality, the entity footing the bill for the SIS. These economic arguments, similar to those revolving around alleviating stress on penal and mental health care systems, rely on long time scales. Simply put, the returns for public health investments do not come quickly, making these investments difficult for policy makers to sign off on. Amidst scientific, economic, and political debate, the argument that has gained the most traction has been the simple fact that the crisis kills three to four people every day and that the city desperate needs to start acting now, as there is no quick solution.10 While SIS are clearly far from being the silver bullet, they are one of the more implementable proposals and th current models can, of course, be improved upon with time.

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EMERGING MEDICALIZATION & HEALTH CARE

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The course of human history is punctuated by transformative moments of innovation in ideas and technology. The story of medicine is one and the same: from the original text of the Hippocratic oath written in Greece to the development of the germ theory of disease during the Newtonian Age, medicine is a organic machine that changes over geography and time. Societies that define notions of health and design the system by which it treats those considered ill also morph over time. During the Middle Ages, leper colonies were built to quarantine those with leprosy whose physical disfigurations were stigmatized as monstrous and contagious. In the 19th century, mental asylums housed patients deemed criminal or insane, as both qualities were considered synonymous. In modern times, pathologizing disorders has become increasingly practiced through medicalization.

Pathologization refers to the act of determining what is and is not a medical disease - it is fundamentally an exercise in assigning meaning. The 21st century experienced an explosion in rates of new medically legitimized social pathologies: social anxiety disorder, major depressive disorder, panic disorder, anorexia, attention deficit hyperactivity disorder, chronic fatigue syndrome, and so on. This modern process of inventing disorders to describe illness is medicalization. Medicalization refers to the way in which human conditions become defined by and treated as medical symptoms that then require expert intervention. Emotions, bodily characteristics and behaviors once considered non-medical components of human existence increasingly become perceived as undesirable characteristics to be managed through medical treatment, diagnosis, prognosis, and prevention. This paradigm shift occurs within the growth of neoliberalism that emerged in the 70's. Neoliberalism can be defined as a laissez-faire economic system that stresses an unregulated market structure, financial austerity, fiduciary duty, and the privatization of services. The dominant rise in the corporate power of the pharmaceutical industry could be understood through this economic context. Industry, here referred to as the matrix of corporate-patient relationships characterized by continuous drug development, deceptive advertising campaigns and heavy physician marketing, operates through this logic of medicalization, where the incorporation of once human conditions into new disease markets drives market growth, consumption, and innovation. Medicalization transforms the definition of these emotions by framing the illness as an internal issue of the psyche, rather than a symptom of social structures, that must then be resolved through individualized consumption. For example, the effect of social alienation is medically licensed as a pathology that becomes coined as "social anxiety disorder," the implication being an absence of continual communication equals the presence of cognitive deficiency. The mental states that inevitably develop as a result of living in a society plagued with employment instability, unaffordable housing, environmental hazards and materialistic rituals are considered aberrations to be diagnosed and treated. As a result, pharmaceutical companies have an incentive to invest profits into campaigns to convince the population that how they feel is due to medically recognized disorders as opposed to recurring effects of societal failures. This framing results in the belief that disorders are curable only through institutional measures while evading the question of how and why they arose in the first place.

Take depression as an example. The biochemical state of being depressed is not a uniquely modern condition; there have always been individuals who have met the criteria for what would now be considered major depressive disorder. The modern invention here resides in how institutions like the American Psy-

chiatric Association frame that condition as a medical pathology, i.e. major depressive disorder. By normalizing the diagnosis of feelings and behaviors as medical disorders, the country has witnessed a 370% increase in the diagnosis rate of mental illnesses between 1955 and 2000. As the umbrella of what is considered depression widens, more people are incorporated into its label. The treatment response to depression occurs largely through the frame of medicalization and strengthens the idea that response strategies should revolve around medication and individual therapy, as opposed to reconsidering social policies and arrangements.

UNIVERSAL PROPHYLAXIS

Modern medicine emerged after World War I when political leaders placed their faith in science and rationalism as the saviors of human problems. Rationalism is defined as the belief that solutions to social problems should be sought on the basis of calculable measurements. Since science and industrial production won the war, technological progress was believed to be capable of resolving all social ills. Mired in the belief that all aspects of life could be enhanced through rational thought, the human being came to represent an autonomous actor capable of solving issues through individual grit, hard work, and acting in self interest. This logic scales up to the contemporary for-profit health care model, where patients act as rational consumers of plans and physicians, and are responsible for conducting their own research between a myriad of choices. This model is extremely profitable because it stresses consumption as the most accessible avenue for care: in 2015, the twenty largest pharma corporations (after deducting research and development costs) combined to take in a profit of $31,727,491,000. In the 1800's, medicine was similar to religion; doctors were priestly figures who competed for different claims to truth on how to resolve illnesses. Because there was no standardized curriculum for medical school, doctors prescribed different methods of treatment based on individual experience or superstitions. The Flexner Report released in 1910 created the professionalization of medicine by defining scientific knowledge as the principal ethos of the modern physician and introduced the challenge of creating a single rubric for resolving illnesses while simultaneously maintaining the personhood of individual patients. However, the presumption of medicine as a pure science conceptually reduces human beings into medical models to be operated on by expertise driven physicians. Individuals become conceived of as "machines" that must be "monitored" and inevitably "break down" and cease to function. Once people are abstractly reduced to biological machines that either function or do not, they can be fixed, measured, or discarded. The modern metaphors of illness and disease that perceive personhood through functionality emphasize bodily malfunctions and biological deficiencies as indicators of health or lack thereof. The state of suffering becomes explained through a "restitution narrative," the idea that the role of medicine is to return the body to a state of "healthy normality." By stigmatizing emotions associated with abnormality (pain, anger, sadness, loneliness, etc.) as deviant pathologies, the restitution narrative allows experts to maintain jurisdiction by forcing the sick to defer to impersonal forms of authority (i.e. physicians, health commissioners, and specialists) in hopes of regaining normality. However, illnesses and health are much more than top-down models of the body; they're influenced by varying dimensions of class, race, gender, ability, status, and culture.

Since the structural determinants of health are multiple and the perspectives of what health is differs across geography, people have struggled to compile a unitary definition of the subject. For example, Native American ideas of health directly conflict with neoliberal concepts of private property and ownership. For native tribes like the Innu, health is intrinsically tied to land, ecology, and nomadic life. Through the reservation policy, native mobility was confined, spiritual connections to the land severed, and native healing practices discredited by medical practitioners as primitive and self-destructive. Modern medicine and notions of health were used not to strengthen native ties to health, but to replace them. Another example is the way disability activists have challenged the traditional notion of health as synonymous with physical ability and strength. By contesting the notion that disability is an unhealthy illness or a tragedy, activists procured an alternative "social model" of disability that focused on improving disabling environments as

opposed to individual impairments. These example, amongst others, demonstrate that a top-down, one size fits all definition of health and care is inadequate to describe the diversity of social relations and identities in the United States, and that alternative conceptions of health should be understood to formulate policies better attuned to the histories of communities.

REIMAGINING CONTOURS OF HEALTH

It is difficult to programatically establish national health insurance without a prior understanding of what "health" is, because after all, health is ostensibly the object being insured. The nucleus of the modern medical system is the belief that health is a marketable "commodity" – that is, health is a quantifiable and scientifically measurable state of being that can be formulaically achieved with the right medical prescriptions, diagnostic tests and technological advancements. As a commodity, the distribution of health should be left up to markets with the underlying philosophy being that those who cannot afford services should remain without them. Yet, health is not a commodity. It is not a car where consumers rationally decide between competing options in full knowledge of associated pros and cons – much of this knowledge stays insulated within the medical profession. There is also no single definition of health. Health is not a uniform reality that transcends geography and time. It is socially constructed and medically conditioned; its definition has changed over time and will continue to morph in the future. The modern ideal of a healthy body is a conceptual product of a neoliberal society. It is precisely this idea of health as profitable commodity that generates a defunct, inequitable health care system marked by skyrocketing premiums, malpractice lawsuits, depersonalization of the doctor-patient relationship, medical fraud, and profiteering conflict of interests. The market approach transforms patients into avid consumers, generating two noticeable paradoxes. Firstly, the consumer oriented model drives health care costs way up. Individuals actively seek out excessive goods and specialized services for often medically unnecessary reasons. Consumption in turn drives endless production, overprescription, and drug innovation untied to necessary medical progress. Secondly, medical consumption operates by engineering the desires of the population. Inundated with societal demands to attain achieve certain standards of beauty, health, and body (the alternative being cased as an unhealthy, diseased body), an expansive market structure is established to deliver health to insecure consumers. What remains absent from the political economy of health, care, and insurance as an individualized solution to society's disorders is an analysis of the systematic, cultural forces that symptomatically produce illnesses. Societal incubators of illness that reflect particular power relations such as poverty, inaccessible gender norms, and unprecedented levels of wealth inequality remain unaddressed in order to export the responsibility of fixing health concerns onto the individual consumer, which leaves society in a web of rising rates of medical disorders. In conjunction with analyzing systematic, neoliberal arrangements of society that actively produce health concerns, a revaluation of health as an idea must take place if society is to envision a democratic spirit of care. Is health merely a commodity available to those who can afford it or a human right that all are born entitled to? Are the ways institutions define and treat illnesses neutral or a reflection of particular arrangements of incumbent power interests? Are human beings dignified individuals with the right to a reasonable expectation to a healthy life or productive machines that function and wither away? Reconfiguring the values and conditions of health is critical to formulating politics, because government policies are not abstractly created in a vacuum but rather represent the final trajectory of contingent articulations of value. Only once those who inhabit societies collectively engage in dialogues over a common set of values and what it means to be a healthy body can health concerns become a social priority.

***Check our site for citations.**

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A picture is worth a thousand words, but the phrase "genetic engineering" is worth a thousand pictures. The images conjured by genetic engineering (GE) are optimistic, pessimistic, intriguing, terrifying, and controversial. But few know what GE can currently do in humans, whether and where such things are legal, which applications may be forever out of reach, or just how ineffective our current regulations can be.

Most GE talk surrounds enhancing food, but some research deals in modifying humans. Currently, our only GE application in humans is through gene therapy: injecting patients with modified DNA to help cure their genetic disorders. These therapies target only specific parts of the body and cannot be passed onto the patient's children, because they don't modify sperm or eggs[19, 27]. Some gene therapy successes have been achieved in patients with immunodeficiency disorders, Parkinson's disease, hereditary blindness, hemophilia, and more; but the premier examples emerge from the fight against cancer. There have been several instances of "incurable" patients going into remission after highly-experimental, last-resort gene therapies in the USA, UK, and China[14, 16, 35, 42]. In these cases, doctors harvested the patients' immune cells and modified them with the ability to recognize and destroy cancer cells, making the treatment systemic, yet non-hereditary.

Gene therapy is not widely used because the technology is still in its infancy. Most gene therapies have only reached clinical trials, though a handful of gene therapies have been approved for general use by the FDA[15, 21, 22]. Every nation has a unique set of rules defining what types of gene therapy are legal and under what conditions; generally, though, some type of somatic cell gene therapy is legal for clinical trials in most researching countries[5, 37]. Clinical trials have been conducted in 36 countries worldwide, and the USA accounts for more than half of them[17].

But synthetic biology gains most of its controversial undertones not from medical purposes, but from other theoretical applications, such as human cloning, embryo editing, and trait enhancement beyond normal levels. While creating a copy of someone doesn't involve editing any genes, it does evoke many of the same controversial pictures as GE does. In theory, cloned human beings could be used to study disease, which was the purpose of cloning rhesus monkeys[23, 25, 41]. However, cloning or not, human experimentation without consent has exhaustive bans worldwide, including the United Nation's International Covenant for Civil and Political Rights, which was enacted as law in 170 of the signing countries[2, 20, 32]. About 70 countries have explicitly banned human cloning, though some still allow cloning of non-viable human embryos for stem cell research[8, 28]. The United Nations also passed an ambiguous, non-binding agreement by split vote discouraging human cloning[43]. Thus, cloned human beings, while feasible, are a rare instance of international legislative cooperation and likely won't be appearing anytime soon.

Obviously, technology is rapidly catching up to our wildest imaginations. For instance, it may soon be possible to genetically engineer a human in the womb. In 2015, Chinese scientists edited hu-

man embryos in an attempt to cure a form of blood disease, though the embryos were intentionally non-viable[7, 45]. No one has ever attempted to genetically engineer a viable person in this fashion, but it's theoretically possible to fix simple diseases like cystic fibrosis or sickle cell disease that are caused by a single, well-studied genome mutation. In contrast to gene therapy, which is conducted in adults or children, changing the genes of an embryo would affect the resulting person's entire body, and would be heritable by that person's children, opening entirely new controversies and legislation[30, 40]. Today's doctors avoid this practice in part because gene editing technologies such as CRISPR, homologous recombination, TALENs, and zinc fingers are currently too error-prone for such medical uses. But their accuracy is rapidly improving[4, 12, 24, 45].

The Chinese team's study was received with international outcry from the scientific community, partly because of worries that their study could eventually lead to the enhancement of human traits for non-medical purposes[7, 45]. Many researchers warn against ever using gene editing for anything besides curing disease[38], but sometimes curing a disease may accidentally lead to non-medical advantages[30], as demonstrated when other Chinese researchers recently modified beagles to study Parkinson's and muscular dystrophy: the gene they are targeting also causes both dogs and humans to become unnaturally strong[18].

While it may soon be to enhance strength or cure muscular disorders, it is exceedingly more difficult to predict the future of enhancing or curing complex traits like height, intelligence, autism, mood disorders, or creativity. "Complex traits" are controlled by many genes. For example, combined studies of over 27,000 genomes have found 44 genetic factors that are correlated with height, yet estimate that 95% of the factors are still undiscovered[13]. Similar studies estimate that intelligence could be controlled by hundreds or even thousands of different genes[10, 24, 45]. Thus, the first problem with enhancing or fixing complex traits is finding the sheer number of genes that influence them[6, 13, 24, 45].

The second barrier, assuming all these genes are located, involves tradeoffs[45]: scientists postulate that a vast majority of genes affect multiple traits at once, often leading to both positives and negatives[6]. The same genes that increase height also correlate with shorter lifespans, and intelligence and creativity are correlated with conditions such as autism and emotional disorders like schizophrenia[10, 36, 39]. Trying to eliminate autism from the human population would eliminate many of society's geniuses, just as erasing certain mood diseases such as bipolar disorder would likely reduce the number of great authors[24].

A third obstacle to modifying complex traits is deciding which traits to enhance and which to eliminate. Whereas editing complex traits may mean balancing positives and negatives, it may also mean deciding between two different positives. For example, there are different kinds of intelligence that are inversely correlated with each other: highly-detailed memory displays in individuals with deficient big-picture memory, and abnormally-high intelligence is often correlated with abnormally-low creativity[10]. Some forms of mental capacity are mutually exclusive. It might be easy for the world to decide that cancer is an objectively undesirable characteristic, but the pros and cons of some traits may be incredibly, if not entirely, subjective[24]. This is not just a matter of individual opinion: to effectively change such complicated traits, the edits would need to be made to an embryo, and not to a consenting adult.

In summary, it is not currently possible to achieve our wildest dreams of curing complex diseases, nor can we achieve our wildest nightmares of superhuman enhancement: there are too many genes to find, and each gene may have both positive and negative effects. Even years in the future, enhancing or eliminating complex traits may never be possible, because there is not an obvious definition of good or bad[24]. Many human traits have natural variability because different traits are "superior" in different situations[24].

Taboos, ethical controversies, and a simple lack of technology all contribute to the current lack of genetically-engineered humans, but some countries have also attempted to instate laws against GE in unborn humans[7, 26, 38, 46]. There are two types of GE: somatic cell editing and germline editing[30]. The germline includes reproductive cells such as sperm and eggs, which can be passed onto offspring[40]. Somatic cells make up the rest of the body and cannot be inherited[40]. Gene therapy is conducted on the somatic cells of consenting adults or children[19, 27.] But in order to change an entire human body, and not just a subset of tissues, the modifications would need to be made during early development in the womb, when a single injection could reach every cell in the forming embryo, affecting both somatic and germline cells[30]. Thus, countries differentiate between regulations on somatic modifications like gene therapy, and the permanent germline modifications.

Laws forbidding germline editing for any purpose, be it medical or enhancement, have been enacted in Canada, Mexico, Brazil, Australia, and most of western Europe. China, India, Japan, and Ireland have "guidelines" discouraging this, but they are not well-enforced and are subject to amendment or exception (hence China's human germline edit in 2015)[7, 26, 46]. The rest of the major players, including Russia, South Africa, South American countries, Iceland, and the US, have unclear legislation regarding germline editing[26, 46]. The United States government effectively brought GE embryonic research to a halt by imposing a temporary moratorium on government funding, and several states ban it by law[11, 26, 31, 46]. However, many states still allow private funding for such research[31].

There are currently no binding international agreements on genetically engineering humans[37, 46]. Some scientists and NGOs have attempted to set some guidelines for future regulations,

calling for an international moratorium on funding for clinical trials until more data is gathered from research[30, 37].

This abundance of international confusion on the issue is concerning scientists worldwide. For if a country ever did decide to allow human engineering, there would be nothing stopping those engineered humans from crossing international borders. In 2016, an American couple wanted to conceive, but knew their kids would inherit the mother's mitochondrial disease[29]. Scientists had recently developed a technique that would allow parents to conceive a child while using a healthy surrogate donor's egg, thus replacing defective mitochondrial DNA and technically giving the child three parents[29]. The United States banned this technique due to its lack of precision, but the UK has already green-lighted the process, and Mexico does not enforce its restrictions on the technique[3, 9, 29, 33]. So the couple simply had the procedure done in Mexico, and their baby boy was born nine months later in New York[9, 29]. This illustrates the problem with different countries having different legislation: people move. If countries with lax legislation would allow some parents to cure their children of debilitating diseases, there is nothing stopping people from traveling in order to do so. And, once the modification is made, there is nothing stopping them from returning home.

The world must realize three things: firstly, that all countries are interconnected and must standardize their GE rules if they are going to be worth anything at all, because neither somatic nor germline editing respects national borders[5, 27, 45].

Secondly, GE technology is not simply going to stop advancing, even if funding is cut, techniques are banned, and the public refuses to pay attention to it[45]. The desire to cure devastating diseases will always tempt desperate patients and parents worldwide[45]. Instead, whoever offers treatment to these desperate individuals will make the rules. Countries that fund research set the safety guidelines, gain oversight and control over procedures, and provide a safe environment for patients to seek treatment. And only through research will the world be able to foresee the benefits and pitfalls of treatments.

Lastly, people need to stop treating these things as science fiction meant only for Orphan Black, comic books, and Gattaca. Scientists and governments have so long ignored GE's ethical implications because it was not yet possible, but science is rapidly breaking down barriers that previously seemed insurmountable[40, 45]. Some imagined GE techniques may never be possible, and others may completely blindside humanity, so when it comes to international agreement, it's better that gene editing brings to mind an in-focus, universal picture, compared to the diverse collage we have now.

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