LIBERAL ARTS AND HUMAN SCIENCES
CENTER FOR HUMANITIES
VIRGINIA TECH

Mellon Foundation

Justice and Safety in Testing of New Therapeutics

Open Access Teaching Case Developed for the Tech for Humanity Pathways Minor

Funded by the Andrew Mellon Foundation

Developed by Kulyash Zhumadilova

Background

You have probably heard of the opioid epidemic. Perhaps it has even affected your life. The number of deaths from opioid drug overdoses has risen sixfold from the early 2000s to the 2020s. The epidemic has killed over half a million Americans over the years, having a devastating impact on individuals and their families. The impact of increased opioid use on communities in Southwest Virginia is well documented in author Beth Macy's 2018 book, *Dopesick: Dealers, Doctors, and the Drug Company that Addicted America* and its follow-up documentary series. As you have already guessed, large pharmaceutical companies and the profits they seek have been instrumental in establishing the situation. Purdue Pharma, L.P. was very effective in promoting its opioid painkillers over the years, including hydromorphone, fentanyl, codeine, hydrocodone—and most famously, oxycodone (best known by its brand name, OxyContin), but they did so while concealing the high addictive potential of the drug from health care providers and the public. This campaign by the company created easy access to legal prescriptions, a driving force in the progression of the epidemic. The progress and key actors of the opioid epidemic are well-documented. But have you ever wondered how new medications are being developed and tested today? What are the tensions within this process, and between which actors? Patients, scientists, doctors, Big Pharma, investors and regulators are the main characters of this case study.

Not many know that the opioid receptor, a very important part of the biological mechanism behind the pain-killing action of opioid drugs, was discovered in 1972 by Candace Pert (1946-2013), a Johns Hopkins University graduate student at that time. The purpose of her

research was to understand the biological aspects of addiction, so that it could be treated medically. She was a part of a new wave of scientists who approached mental health problems from a materialist standpoint. They saw its causes in molecular interaction, rather than immaterial thoughts, morals, and emotions. In fact, she went even further by describing our emotions as a consequence of molecular interactions within our bodies, not just the brain itself. Dr. Pert went on to become an important figure in promoting the body-mind link through her scientific work, a key figure at the National Institutes of Mental Health (NIMH), and a prolific author and speaker on topics in molecular neuroscience. The vision of neurology as just another subfield of biomedical research is changing the way we understand and treat mental disorders. This paradigm has resulted in the making of antidepressants and other drugs aimed at affecting the mental state of the recipient. However, as history of science often shows, a creator rarely controls the life of her discovery. Research initially aimed at understanding addiction has been used to create even more potent drugs.

Discussion Questions

1. Can you name at least 5 female scientists and innovators? What are the barriers women face in the world of STEM? Why do their contributions remain forgotten?
2. How do you think materialist visions of the human mind influenced your culture in the twentieth century?
3. How can we ensure that science is only used for noble purposes? Why do so many scientific discoveries and technologies that are presented as magical solutions to societal problems end up being used for questionable purposes (e.g., the atomic bomb, genetic engineering, etc.)?

Taking mass-produced medications is an integral part of the modern mindset and lifestyle. The contemporary biomedical industrial complex is a billion-dollar industry with an elaborate network of research, production and distribution spread across national borders. The complexity of drug discovery and the process of testing and validation of new drugs might seem overwhelming, but as a college graduate you should have basic understanding of these processes—not only as an informed consumer, but also as a citizen—because a lot of these processes rely on public funding and invoke political tensions that don't involve science, but rather a question of values, fairness and public good.

Candace Pert had an interesting and prolific professional life well worth learning more about; but it is her later discovery that serves as the focus of this case study. While working at the National

Institute of Mental Health (NIMH), she discovered a potential treatment for the little-studied neurological effects of the human immunodeficiency virus (HIV) that caused the AIDS epidemic in the 1980s. Her discovery, however, faced hurdles in the process of validation and approval. The details and analysis of that process are well documented in journalist Pamela Ryckman's 2023 book, *Candace Pert: Genius, Greed, and Madness in the World of Science*. In short, due to agency mismanagement, internal politics, sexism and limited knowledge about molecular action of the proposed treatment, her discovery, Peptide T, failed the official new pharmaceutical validation and testing pathway. However, Peptide T was released to the public under the table, and black market and unofficial use went on for years until an effective AIDS treatment was officially established in the medical industry.

Discussion Questions

1. What are the risks of buying unauthorized medications?
2. On the other hand, how can we provide easy access to much needed medications if official prices (but not cost to make) are high and not many have health insurance or resources to get them. Why do companies and brand names resist going generic and try to protect their patents for as much as legally possible?

Case Study

Patient Activism during the HIV/AIDS Epidemic

The HIV epidemic holds a special place in the history of twentieth century medicine because of the power in influencing health policies that patients/activists gained in the process of developing treatment. HIV is a virus that causes suppression of the body's natural defense mechanisms, eventually making the immune system so weak it can't battle even ordinary infections. Before effective treatments were developed, this infection usually led to a fatal condition called Acquired Immuno-Deficiency Syndrome (AIDS). The spread of the disease in the USA dates back to the early 1980s. Even though the virus can infect anyone (via an encounter with another person's infected body fluids through unprotected sexual intercourse, intravenous needle sharing, blood transfusion, or direct contact with an infected person's open cuts, etc.), the disease quickly developed the "gay cancer" label in the homophobic political climate of the era. The demonization of men having sex with men as unhealthy and socially anathema affected general attitudes towards the disease, and by that measure delayed governmental response to the emerging epidemic. By the late 1980s, activists in the LGBTQ

community were pushing for development of treatment options using a variety of political tactics. One prominent political force in the United States was an activist group called AIDS Coalition to Unleash Power (ACT UP). They unleashed a direct action pressure campaign on all fronts of medical research infrastructure, with tactics that included protesting in front of the homes of politicians in charge of funding, disrupting meetings at the National Institute of Health, as well as publicly challenging the procedures of drug approval process and the very logic of double blind randomized clinical trials (RCTs). They argued that some patients didn't have time to wait until the clinical trial was over and the drug was officially approved, as the average time between diagnosis and lethal outcome was less than a year. A proper validation of a drug may take years before it is freely available. Desperate patients were willing to buy unapproved potential treatments from informal networks, but it was hard to tell if those treatments really worked, because of anecdotal evidence and person-to-person variation in disease type and progression. Safety of such unofficial treatments is also a big concern as there is practically no liability for producers and providers.

Discussion Questions

1. As someone who lived through the unfolding of the Covid-19 pandemic, what do you think are the challenges of acting quickly to address an unknown emerging disease? Where did you get your information about the action plan?

2. What are the pros and cons of political action in addressing the spread of a disease?

Getting treatment faster

Candace Pert's invention, Peptide T, was an underground treatment until official treatments caught up in the mid to late 1990s. Over the past twenty years or so, HIV infection and AIDS went from an automatic death sentence to manageable conditions with decades in life prognosis if treated and checked regularly. The story of underground treatments served as the inspiration for a 2013 feature film, "Dallas Buyers Club", but the real story of Peptide T is far more complicated. It is important to examine its legacy, because a similar scenario has been unfolding across different diseases and similar activist tactics are used to bring awareness to existing and emerging diseases such as cancer, Amyotrophic Lateral Sclerosis (ALS)---as shown in the 2022 documentary, "For Love and Life. No Ordinary Campaign"—and "Long Covid".

Besides bringing awareness to the public and raising funds for the treatment and research on diseases of particular interest, many patient advocacy groups seem to push for less regulation

and easier access to experimental drugs. Although buying treatment from underground sellers is not an ideal or sometimes even possible option for a variety of reasons, the action plan in the recent decades has been to try to speed up research and development of pharmaceuticals and shorten the testing and validation phase through legislative action. Indeed, sometimes life-threatening conditions may progress in a matter of days and weeks, so if there is a potential treatment, patients and their families are willing to do anything to get it. They also are willing to risk taking an experimental and unvalidated treatment, if there is even a small chance of getting better. These stories as presented in documentaries, social media posts and personal testimonies in the Congress are usually very convincing and leave you very sympathetic. These narratives, however, often problematically depict federal regulations as obstructive red tape from a system that is too slow and unwilling to help their suffering.

A Need for Federal Regulation

There are good reasons why there should be a federal oversight of new drug validation. Since its establishment in 1906, the Food and Drug Administration (FDA) has overseen the approval and safety-testing of commercially available foods and medicines. It is worth noting that this government regulatory agency evaluates safety data, approves study designs, and also issues warnings and recalls which ensure that commercial companies don't misrepresent their claims—in short, the job of the FDA is stringent quality control. It is important to have a regulatory body whose purpose is public service, not profit, especially since it oversees industries with billions of dollars in circulation across large markets. Having a federally-funded, independent evaluation body is important for the health of the nation. FDA has a long and sometimes conflicting history, but despite its imperfections, it is essential in maintaining safety standards in the world of unscrupulous profit-seeking.

Since the HIV crisis in the United States and that era's successful critique of the traditional clinical trial model by activists, the FDA developed alternative procedures that can deliver new investigational drugs (INDs) to patients faster. So called "compassionate use" or "expanded use" pathways allow patients with life-threatening conditions who don't qualify for existing clinical trials to get experimental treatment, provided that: (a) their physicians initiate an FDA request and agree to report on progress; and, (b) the pharmaceutical company agrees to provide the new drug on a non-profit basis. In reality, however, not all patients who qualify for the expanded use will receive it. This is for a few main reasons. First of all, a physician would have to be aware of pre-market treatments that might help a particular patient, which is highly unlikely,

unless they are unusually aware of insider-industry news. Usually, doctors stick to reliable, time-tested protocols in their everyday practice. Secondly, the physician would have to be willing and able to take on the additional workload associated with FDA documentations. In addition, pharmaceutical companies may decline a request to supply an investigational drug, because of the concerns about bad publicity in case it doesn't work. Note that also, small biotech companies which develop new pharmaceuticals usually have limited resources for production and distribution as well as administrative work—initiating "expanded use" is like initiating a single-person clinical trial, and that requires a lot of oversight and cooperation with all parties (patient, doctors, FDA, manufacturers, etc.). Therefore, even though "expanded use" exists, and can be approved by the FDA within one day for an emergency and up to 5 business days for regular cases, real-life access to it is usually limited to a few individuals. Those patients will more likely belong to privileged classes that already have access to better care facilities with more informed and less overworked staff, and who can negotiate with pharmaceutical companies effectively in providing them investigational drugs. Unfortunately, in a country where even basic health care is not affordable for everyone, not every eligible patient may benefit from "compassionate use" cases.

Individual vs. Public Good

The tension between individual and public good is at the core of discussions about early drug access. On one hand, we acknowledge a desire of individuals to maximize chances of their survival. On the other hand, we recognize that there should be a balance between individual and collective good. While some individuals may push for change in legislation to get easy access through rapid approval, it might impede progress towards making a time-tested, possibly safer drug for all in need. The human body is incredibly complex; especially if we see it as a collection of molecules. To test just one drug for public usage, researchers need to be very careful, by monitoring its effects over time and in different populations.

A push for an individualistic approach to drug discovery has already happened on the level of biomedical science. Pharmacogenomics is a field of genomics that investigates how individual genetic makeups will interact with medications, or which medications are better suited to a particular genotype. Such personalized, "evidence-based" approaches are becoming very popular. But as a 2023 research monograph, "Tyranny of the Gene: Personalized Medicine and Its Threat to Public Health", by James Tabery shows, that kind of specialized approach comes at the expense of public health. It tends to exclude marginalized populations, since they generally

can't afford expensive lab tests and tailored treatment protocols. Meanwhile, as we train doctors in new, "hot" scientific approaches, methods that worked for the majority are slowly being relegated to the past. In our search for greater efficiency, we might lose universality. It is still important to maintain universality as an ideal for federal regulation of new drugs and treatments. Otherwise, those who lack resources and power (political, social, economic, etc.) will be excluded from getting the treatment they need.

Discussion Questions

1. What entity do you think should regulate the boundary between personal and public interest, and how should they do it?

2. Do you know any examples, where such balance is successfully maintained–or abused?

3. In a climate of reduced federal workforce, how do you think FDA should prioritize review of extended use vs. general clinical trials?

Last but not least, it is important to note that it is not just suffering patients that might wish for less federal regulation. Pharmaceutical companies and entrepreneurial individuals will be a direct beneficiary of deregulation. As of now, in order to comply with USA regulations, those powerful entities spend millions of dollars or more for testing and validating claims of their products' efficacy and safety. Given a chance to sell unvalidated products or decrease the level of safety regulation, they will definitely do so in order to profit. It is worth noting that while in the USA many patients wish they could get experimental treatments, many patients in countries with less regulation and lower safety standards do obtain such interventions—but without their educated consent or full disclosure about possible harms. In 2014, the world of medicine was shaken by the news revealed by four whistleblowers from Karolinska Institutet (the university that gives the Nobel Prize in Medicine). According to their report, Paolo Macchiarini, a famous surgeon and also their colleague, was involved in egregious research and medical misconduct that led to the deaths of many of his patients across the world. Dr. Macchiarini used an untested procedure to perform trachea replacements. Not only did he fail to disclose to his willing patients that the procedure was dangerous and had a low survival rate, but he also used fake images to convince the medical community that his method worked. We see by that example how limiting the legal pathways through which such "experimental procedures" may reach uninformed patients can save lives. Otherwise, we have to live through the Wild West of quack healers and their dangerous "miracle cures".

Discussion Questions

1. Some say that excessive regulation is harmful for innovation. Do you think it is wise to prioritize innovation over some safety concerns? What can be compromised as a result?

2. How can we ensure that patients are truly informed about the dangers and risks of treatments? Doctors underwent years of training and have large experiential knowledge that the average patient may lack. Think of trust and conflict of interests in these cases.