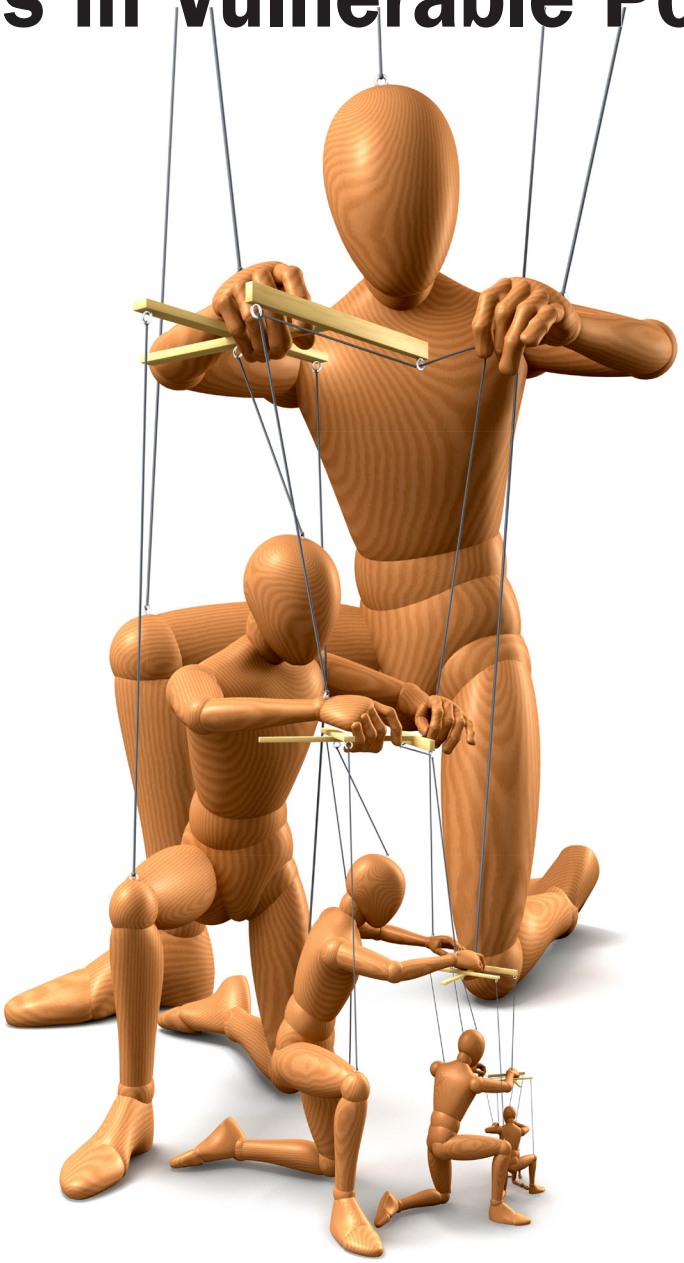
Volume XIII Issue ii

PBJ PENN BIOETHICS JOURNAL

Coercion and Control: Medical Decisions in Vulnerable Populations



Access to Palliative Medication, Autonomy in Anorexia Nervosa Treatment, Homeless Individuals in Clinical Trials, and a Conversation with Dr. Emily Largent and Prof. Holly Fernandez Lynch

PENN BIOETHICS JOURNAL

The Penn Bioethics Journal (PBJ) is the premier peer-reviewed undergraduate bioethics journal. Established in 2004, the Journal provides a venue for undergraduates to make contributions to the field of bioethics. Embracing the interdisciplinarity of bioethics, PBJ reviews and publishes original work addressing debates in medicine, technology, philosophy, public policy, law, theology, and ethics, among other disciplines. The biannual issue also features news briefs summarizing current issues and interviews with eminent figures in the field. Authors and the editorial staff alike have a unique opportunity to experience the peer-review process through the collaborative, rigorous review and preparation of the Journal. With an audience ranging from undergraduates to scholars in the field to the broader public seeking unbiased information, the Penn Bioethics Journal occupies a unique niche in the field of bioethics.

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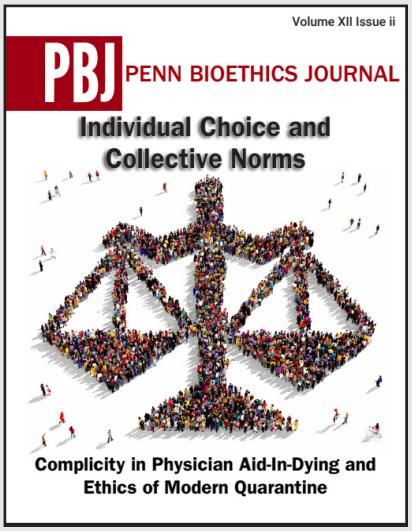

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Letter from the Editor

Claire Fishman
Editor-in-Chief

Dear Readers,

It is my pleasure to present you with Volume XIII, Issue ii of the Penn Bioethics Journal entitled "Coercion and Control: Medical Decisions in Vulnerable Populations." The three articles in this issue explore the power of institutions over the individual, covering topics ranging from access to palliative medication to patient autonomy in Anorexia Nervosa treatment and the involvement of homeless individuals in pharmaceutical trials.

Our first article, entitled "Disparities in Access to Palliative Medication: The Duty of the State to Ensure Opioid Medication Access," argues that governments have a duty to make opioid analgesics available to all patients who require them. Author Brian Cheng from Northwestern University uses a utilitarian framework in his evaluation of the principles of medical ethics to illustrate his claim.

In our second article, entitled "Autonomy At What Cost? Mitigating Patient Autonomy in the Case of Anorexia Nervosa," author Erin Gaudette from the University of Toronto explores the conflicting duties of healthcare providers to both uphold patient autonomy and to promote treatment and recovery. She uses Anorexia Nervosa as a case study to assert that the clinical features of an illness can mitigate the principle of patient autonomy when a life-saving treatment is available.

Our final article, entitled "Involvement of Homeless Individuals in Pharmaceutical Clinical Trials" explores how the pharmaceutical research industry has taken advantage of the situational vulnerability of the homeless population. Author Sharlotte Irwin from the University of Minnesota-Twin Cities uses several case studies to demonstrate her claim, and then presents viable options that would reduce the exploitation of homeless individuals in clinical trials.

In this issue, the Penn Bioethics Journal also had the opportunity to interview Dr. Emily Largent, an Assistant Professor of Medical Ethics and Health Policy and a Senior Fellow at the Leonard Davis Institute of Health Economics, and Prof. Holly Fernandez Lynch, the John Russell Dickson, MD Presidential Assistant Professor of Medical Ethics at the University of Pennsylvania, Assistant Faculty Director of Online Education in the Department of Medical Ethics and Health Policy at the Perelman School of Medicine, and a Senior Fellow at the Leonard Davis Institute of Health Economics. Dr. Largent and Prof. Fernandez Lynch's shared research interests in the ethics and regulation of clinical trials gave them a unique insight into the issues of coercion and undue influence in human subject research.

Furthermore, our Bioethics-in-Brief section, which can be found on the following pages of this issue, includes news briefs that provide updates on recent developments in the field of bioethics. The first brief discusses the reevaluation of the ban on genetic testing in the Navajo Nation. As medical technology continues to progress, the balance between a remembrance of the past and the current wellness of their people becomes increasingly salient in once exploited populations. The next two briefs cover news stories that highlight the consequences that can ensue due to the medical technologies of surrogacy and organ transplantation. Both briefs explore the personal hardships that can result when mistakes are made in these ethically complicated situations.

Finally, I would like to thank Dr. Harald Schmidt and the entire editorial and publication staff for their hard work and dedication to this issue. I have truly enjoyed serving the PBJ community for the past year and am excited to see how this organization continues to promote undergraduate exploration in the field of bioethics. I hope that the content of this issue fosters an interest in the field of bioethics and opens your mind to previously overlooked questions.

Claire Fishman
Editor-in-Chief
University of Pennsylvania C'18

The Navajo Nation and Genetic Testing

Leaders of the Navajo Nation are currently deliberating whether to lift its 15-year ban on genetic testing, according to Sara Reardon reporting for Nature. The reevaluation of the policy follows from the increasing prevalence, accessibility, and utility of genetic sequencing and profiling technologies, which have the potential to personalize and improve the quality of a wide range of medical therapies.

However, the considerations involved in the discussion are numerous, and a new proposal on genetic testing would require a cautious treatment of issues of research ethics. This is because the prohibition in question rests upon a turbulent relationship between Native Americans and the outsider scientists seeking to study them, one characterized by exploitation and abuse.

"Science" has long been misused to justify the subjugation of minorities in America. Most notably, in the era of slavery, constructs of biologically inherent racial superiority and inferiority quelled moral objections to the lucrative use of blacks for labor. Instead, such notions reinforced the institution.

White scientists similarly misappropriated Native American biology through pseudoscientific disciplines such as phrenology, the study of the physical properties of the skull and their ostensible correlations to mental ability. In 1839, Samuel George Morton published a set of lithographs, entitled Crania America, that claimed to provide insight into the biological bases for differing race characteristics via skull examination. On Native Americans, he wrote, "the structure of his mind appears to be different from that of the white man." A magazine published a year later extrapolated upon Morton's findings by describing Native Americans as "adverse to cultivation, and slow in acquiring knowledge" (University of Cambridge 2013).

"The idea that Native Americans could not integrate into modern industrial society was central to both Morton's argument and Andrew Jackson's policy of Indian Removal," says James Poskett, of Cambridge University's Department of History and Philosophy of Science. The pernicious repercussions of nineteenth-century pseudoscience provide modern Native Americans with more than ample historical reason for mistrusting white researchers today (University of Cambridge 2013).

Blatantly racist scientific conjectures gradually and rightly became obsolete, but the shadow they cast is long. Exploitative practices continued to take advantage of marginalized people groups in the twentieth century. Infamous examples include the 40-year Tuskegee Study of Untreated Syphilis in the Negro Male, in which researchers intentionally allowed syphilis to persist untreated in hundreds of African-American men without informing them of the exact nature of their affliction (Centers for Disease Control and Prevention 2017), and the astoundingly widespread research use of Henrietta Lacks' cells without her consent, a story that has garnered significant attention in retrospect since the publication of "The Immortal Life of Henrietta Lacks" by Rebecca Skloot in 2010 (Fessenden 2017).

Photo courtesy of The Smithsonian Magazine

Lacks' case hits particularly close to home for Native American tribes, especially those in the southwestern United States. Beginning in 1990, a scientist at Arizona State University collected DNA from the Havasupai tribe, whose members believed the genetic material was exclusively to be used to study Type 2 diabetes. However, the researcher did not stop at diabetes-she also used the samples to make inferences about schizophrenia, inbreeding, and the tribe's geographic origins (Fessenden 2017). From the perspective of Havasupai tribe members, this not only constituted a grave overstep of their rights as human research subjects, but also, by suggesting that the Havasupai people migrated over the Bering Strait land bridge before settling in America, directly contradicted their belief in Arizona as their place of origin and the site of their traditional lands (Blakemore 2017).

The delineation between right and wrong in this story is no clearer than that distinguishing ethical and unethical practices in the consideration of genetic testing. Though the university eventually settled for $700,000 and returned the DNA samples when the tribe sued, the researcher maintains she received informed consent (Blakemore 2017). Regardless, the ordeal of the Havasupai effectively served as a cautionary tale for the Navajo, substantiating the case for a ban on genetic testing.

Native Americans have not forgotten this bleak history. Yet as the Navajo Nation prepares to open its first oncology center in Tuba City, Arizona, leaders have revisited the ban with an outlook oriented towards the future and the wellness of their people. As long as scientists are vigilant to rectify the track record of abuses in research upon Native American populations, the ultimate consequence of lifting the moratorium could be longstanding improvements in health outcomes for the Navajo at large.

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Surrogacy Gone Wrong

Jessica Allen, a mother of two, decided to become a surrogate in order to make some extra money while staying home with her kids. She went to Omega Family Global, who matched her with the Lius (Ridley 2017). At first, everything went according to plan. However, six weeks after becoming pregnant, she found out that she was carrying two children.

Fortunately, the couple was overjoyed at the prospect of having twins and the standard $30,000 payment was increased to $35,000 for the second baby (Wang 2017).

When Jessica gave birth to both babies by cesarean section, she noticed that the babies did not look very similar. However, the babies were quickly taken away, and she did not see them afterwards. She had always heard that newborn babies changed quickly and so decided to think nothing of it (Wang 2017).

Fast-forward one month into the future and Mrs. Liu, the biological mother, contacted Allen saying that one of the children looked nothing like she and her husband. After some DNA testing, it was revealed that one of the twins was actually Allen and her husband's son. In what is believed to be a very rare case of superfetation, Allen's child was conceived after she was pregnant with the Liu's baby (Wang 2017).

This led to a lengthy and complicated legal battle with the Allens trying to get their biological son, Max, back. The Lius demanded $22,000 in compensation from Omega Family Global and the San Diego Agency wanted an additional $7,000 for taking care of the child that the Lius abandoned (Ridley 2017). Omega Family Global also threatened to put Max up for adoption to obtain the money they owed to the Lius. This was all exacerbated by the fact that the Lius were technically the legal guardians of both children.

The real problem, Jessica complained, is that "it was like Max was a commodity and we were paying to adopt our own flesh and blood" (Ridley 2017).

The surrogacy money that Jessica was awarded was mostly spent on legal fees, including $3,000 for a lawyer, and the Allens were now responsible for additional thousands of dollars in compensation. Jessica was also heartbroken that the Lius were letting the surrogacy agency keep her son hostage. She commented that "[we] had a really good relationship throughout pregnancy" and that towards the end Mrs. Liu even said that she loved her (Ridley, 2017).

In the end, everything worked out well in that Jessica's lawyers were able to reduce the fees and bring her son back. However, this does not change the fact that she went through a horrible ordeal. Jasper, Jessica's husband said "The main fact is, our child was kidnapped and held for ransom" (Wang 2017).

Furthermore, Jessica and Jasper are still facing the repercussions of this ordeal. Max, renamed Malachi, was given no social security card or birth certificate that shows his new biological parents (Wang 2017). The only proof that Malachi is theirs is the DNA test that was performed. Despite this incredible hardship, Jessica does not regret becoming a surrogate mother. After all, it did lead to the birth of her son.

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Parole Violation Hinders Father to Son Kidney Donation

Controversy has struck a premier medical institution in Atlanta on October 3, 2017. After initially being cleared to receive a life-saving kidney transplant, two-year-old A.J. Burgess was denied as a patient by the Emory University Hospital after the institution retracted its initial decision. Why? A.J.'s father, Anthony Dickerson, the kidney donor in this procedure, violated his parole for a second time due to possession of a firearm or knife as well as for fleeing or attempting to elude a police officer, according to Georgia criminal records (ABC News 2017). Although the family and Emory Healthcare had made previous arrangements to have Anthony Dickerson escorted from the jail to the hospital for the operation, the hospital changed its mind, requiring proof that Mr. Dickerson would comply with his parole over the next three months before reevaluating its decision ("Toddler hospitalized" 2017). Time is of the essence in such crucial operations, leaving the Burgess family with little choice but to find an alternative solution to A.J.'s ailing health.

Unfortunately, A.J.'s condition deteriorated. On October 29, A.J. was rushed to the emergency room with an abdominal infection, requiring prompt treatment with antibiotics ("Toddler hospitalized" 2017). Without a new pair of kidneys, A.J's long-term prognosis remains volatile. With few options, the Burgess family has taken legal action by hiring an attorney to represent them in proceedings going forward. In addition, the local Atlanta community has rallied behind the Burgess family, garnering support for their cause by starting a petition in hopes of pressuring the hospital to proceed with the transplant (ABC News 2017).

According to experts, major transplant centers like the Emory University Hospital take a variety of factors into consideration when evaluating an individual's donor status, including health risks and accessibility of the living donor. The United Network for Organ Sharing (UNOS), a non-profit organization that administers the only Organ Procurement and Transplantation Network (OPTN) in the United States, states on its website that living donors "should be in good overall physical and mental health and older than 18 years of age." UNOS also lists that individuals interested in being a donor must undergo a "psychosocial and medical evaluation process" to protect themselves and "to help ensure success of the transplant" (ABC News 2017).

Patient and donor rights, rationing of organs, and public policies concerning organ procurement are salient bioethical issues in modern society. Many potential recipients and donors do not get admitted into transplant programs around the world for being too old, not of right nationality, not appropriate candidates due to severe mental impairment, drug abuse, criminal history, or simply because they do not have access to a primary care physician who can refer them to a transplant specialist.

In addition, the ever-increasing gap between supply and demand of organs and the prioritization of patients deemed as being urgent cases has created a core ethical challenge for transplantation (Caplan 2014). Arthur Caplan, professor of bioethics at the New York University's Langone Medical Center expressed his opinions on A.J. Burgess's case.

Dr. Caplan noted that organ transplantation policies are determined by authorities and the transplant centers themselves, not by law. Usually, the transplant center will deny a living donor based on some existing medical condition or because the donor cannot follow up with necessary medical care after the procedure, both of which seem unlikely in A.J.'s case ("A two-year old's kidney" 2017).

In statement, Dr. Jonathan S. Lewin, CEO of Emory Healthcare, expressed Emory's support for A.J. In addition, Dr. Lewin noted that they are considering both A.J.'s potential for receiving a successful transplant as well as a positive outcome for his father, as a living donor (ABC News 2017). The hospital wants to ensure the well-being of both individuals. However, since Anthony Dickerson's medical history is not publicly known, it is difficult to determine the rationale behind the hospital's decision.

Since beginning their efforts, talks have reopened with the hospital. The Atlanta community hopes a consensus can soon be reached so that A.J. can receive the medical care he so desperately requires in order to live a happy and full life.

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Interview

A Conversation with Dr. Emily Largent and Professor Holly Fernandez Lynch

Photo courtesy of Dr. Largent

Dr. Emily Largent, JD, PhD, RN, is an Assistant Professor of Medical Ethics and Health Policy at the University of Pennsylvania. She is also a Senior Fellow at the Leonard Davis Institute of Health Economics at the University of Pennsylvania. She studies the ethics of human subjects research. Her current research focuses on the ethics of paying research participants for their contributions to clinical research and on the ethical and regulatory implications of integrating clinical research with clinical care.

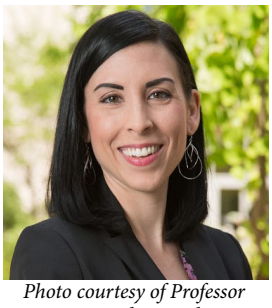

Photo courtesy of Professor Fernandez Lynch

Prof. Holly Fernandez Lynch, JD, MBe, is the John Russell Dickson, MD Presidential Assistant Professor of Medical Ethics at the University of Pennsylvania, Assistant Faculty Director of Online Education in the Department of Medical Ethics and Health Policy at the Perelman School of Medicine, and a Senior Fellow at the Leonard Davis Institute of Health Economics. Her scholarly work focuses primarily on two areas: the ethics and regulation of human subjects research and conflicts of conscience in healthcare.

Penn Bioethics Journal (PBJ): Can you describe your career trajectories and explain what drew you to the field of bioethics?

Dr. Emily Largent (EL): I received an undergraduate degree in Science, Technology, and International Affairs from Georgetown University and then got a second degree in Nursing from the University of Pennsylvania (Penn). I worked as a bedside nurse for several years, and although it was satisfying to help individual patients, it soon became clear to me that there were systemic challenges that needed to be addressed in a more meaningful way. I found that the ethical issues interested me the most, so I applied for a fellowship in the Department of Bioethics at the National Institutes of Health (NIH). After the fellowship, I completed a joint degree program at Harvard, where I received my JD and a PhD in Health Policy with a focus in Ethics. The NIH Bioethics Fellowship was very influential in shaping my interests in research ethics.

Prof. Holly Fernandez Lynch (HFL): As a freshman at Penn in 1999, I found my Introduction to Medical Ethics course very compelling, which led me to a Health and Societies major with a concentration in Bioethics. Then, I completed a joint law degree and Master of Bioethics program at Penn (Class of 2006) because I was most interested in driving policy change. As a private practice attorney focused on FDA-regulated pharmaceutical products, I worked on several issues related to clinical research ethics. From there, I moved to the NIH in the Division of AIDS, where I took a role in their Human Subject Protection branch. This was an important opportunity to better understand how research is conducted, funded, and overseen, especially in the context of developing countries. Most recently, I worked as the Executive Director of a health policy and bioethics research program at Harvard Law School. Emily and I had the opportunity to work on several funded projects together centered on research ethics.

> "Coercion involves a threat to cause harm, whereas undue influence involves an unreasonable offer leading to bad judgement."

PBJ: What inspired you to explore the issues of coercion and undue influence in the process of recruiting subjects for research?

EL: A mentor asked me if I'd be interested in working on a survey of institutional review board (IRB) members on issues related to coercion and undue influence. I agreed, and it became the first national survey on IRB members' attitudes toward coercion, undue influence, and payment of research participants. As a result, the survey opened the door to many other things in my career, and I would regard it as pivotal.

HFL: I was working on a project focused on improving recruitment to clinical trials, which led naturally to analysis of paying incentives to participate. This raised questions about the ethical parameters for paying research participants, and concerns about coercion and undue influence. I read Emily's work and learned that we were both at Harvard together. Together, we conducted a survey of IRB members to learn about the confusion they may face about the concepts of coercion and

undue influence. We also addressed the issue of research exceptionalism, the idea that we need to protect people from payment in research, even though we would generally accept payment as appropriate in other non-research contexts. Our work together seeks to clarify the concepts of coercion and undue influence, in hopes of reducing barriers to paying participants, which we think can be one important step in speeding the conduct of clinical trials.

PBJ: What do you think causes IRBs to be sometimes reluctant to encourage higher payments, and what are your thoughts about this conservative tendency?

HFL: IRB members often have a sense that they should worry about research payment. However, our pilot data suggests that IRB members do not have a clear understanding of key ethical concepts related to payment, and are often confused about coercion and undue influence. Coercion involves a threat to cause harm, whereas undue influence involves an unreasonable offer leading to bad judgment. Our view is that once people have the tools to define these key terms properly, it will become evident that paying incentives to research participants is rarely problematic.

> "It would be over-protectionist if we are denying homeless people the chance to make money just because they have no better alternative."

EL: Another factor that shapes conservatism is that coercion and undue influence are terms from regulatory guidance, and IRBs don't have clear definitions or specific information to apply these terms to offers of payment to research participants. Therefore, there is the attitude of being 'better safe than sorry'—that is, adopting definitions that are quite broad—and hence conservatism.

HFL: Some people may think that there is no harm in keeping payments to research participants low. But we argue that low payment can be harmful when it contributes to the problem of inadequate recruitment, and disrespectful when it inadequately compensates participants for their contributions to science and the public good.

PBJ: What are your specific views on recruiting homeless people for research purposes?

EL: I believe that if researchers launch a general recruitment strategy that the IRB has approved and homeless people come in for screening, there would not be any reason to exclude homeless people specifically. It would be over-protectionist if we are denying homeless people the chance to make money just because they have no better alternative. But if, for example, researchers target their recruitment at homeless shelters because they think the homeless might be more willing to participate given their lack of alternatives, it is more likely to lead to exploitation and it may also affect the validity of the experiment by limiting the representativeness of the study population.

HFL: If we are designing an experiment that studies the effects of certain interventions on the homeless population, it would be fine – and likely necessary – to recruit in shelters. But it is problematic if we recruit there only because homeless individuals are a convenient sample. When homeless individuals are included in research, some may suggest that one ethical protection would be to make sure not to pay them too much or make the research too attractive. However, as Emily noted, if the IRB has determined that the study's risks and benefits are acceptable, it is also important not to exploit their economic vulnerability by paying too little. In other words, just because homeless individuals may be willing to participate for low amounts does not mean low payment levels are appropriate. Study participants should be compensated in accordance with their contributions to research, and in the amounts needed to appropriately incentivize participation in IRB-approved studies.

PBJ: What is your opinion on 'for-profit' IRBs?

HFL: For-profit IRBs are also sometimes called "commercial IRBs", and they are distinct from IRBs housed in research institutions. When commercial IRBs first came onto the scene, there was concern that paying for research review would lead to bias in judgement. However, commercial IRBs have become mainstream today, and their reviews have not been shown to be any worse or different than reviews conducted by more traditional IRBs. Commercial IRBs have good business incentives to make sure the studies they review are compliant with the regulatory standards, since IRBs that fail to do this will develop poor reputations, which will result in few submissions. For example, following a "sting operation" by the Office of the Inspector General in which IRBs were tested with a fake research protocol, the IRB that failed to address significant concerns ended up quickly closing its doors. Commercial IRBs can also make good use of the economy of scale - experienced professionals can work full-time in the approval process. I am generally a proponent of commercial IRBs, and expect them to only rise in stature as the federal government imposes requirements for single IRB review of multi-site trials.

Interview by Henry Hung and Shreya Parchure

Article

Disparities in Access to Palliative Medication: The Duty of the State to Ensure Opioid Medication Access

Brian Cheng*

Opioid analgesics, specifically codeine and morphine, are registered on the World Health Organization's Essential Medicines List, yet these medications are not available to patients in more than 150 countries (Redmond 2014). As a result, more than 5.5 billion people are left with little to no access to chemical palliation, including millions of terminal cancer and end-stage HIV/AIDS patients (Seya et al. 2011). The government of each country must engage with the International Narcotics Control Board to obtain any supply of narcotic medication for its people. However, the high administrative burden to order and track the annual distribution of opioids means the governments of most developing countries cannot attain any narcotics supply. Advocates for ample access to chemical palliation contend that governments have a duty to make opioid analgesics available to the patients who require them. Here, we analyze the proposed obligation in the context of the principles of medical ethics – beneficence, non-maleficence, autonomy, and justice. A utilitarian evaluation reveals that the government indeed has a duty to its people to secure adequate access to opioid medication. As such, countries ought to pass laws to officially recognize their responsibility to close the global disparity in access to palliative medication.

Global Disparities in Pain Medication

"I am in pain 24 hours a day…The pain I have all over my body, it is in my bones. I cannot have a real life without medication." -Mamadou to Human Rights Watch

"Mamadou" is a 47-year-old man who lives in rural Senegal and suffers from stage IV metastatic prostate cancer (Luyirika and Moreira 2013). The terminal sentence his cancer carries is a forgone conclusion. He has given up all hope for a cure, but he still strives to live out the remainder of his life in dignity. Despite his intense pain, Mamadou finds it difficult to obtain his prescribed opioid analgesics because of the unavailability of pain medication in Senegal. He struggles every day to perform simple tasks such as walking, caring for himself, and even speaking. Simply put, without the prescribed pain medication, Mamadou is in too much pain to appreciate the time he has left.

> "Even in countries where opioid analgesics are available, the logistical and administrative obstacles meant to track distribution make them unattainable for wide swathes of their populace."

Mamadou's struggle illustrates the global disparity in access to strong pain medication that results in differences in opioid consumption. In 2011, the average American consumed 73.7 mg of morphine, while the average across Africa was 1.03 mg per person (Scholten 2014, Seya et al. 2011, UWisconsin 2011). Moreover, the populations of the US, Canada, and Europe comprise almost 90% of the world's opioid users, while not a single variety of strong pain medication is available in 150 countries (Redmond 2014). A survey of African countries found that none had all seven essential opioid medications available (Cleary et al. 2013). The large disparity is not because of a difference in need: in fact, low and middle income countries account for 6% of the annual opioid consumption, while they are home to more than half of all cancer patients and 90% of the world's HIV patients (Lohman, Schleifer, and Amon 2010). There are over 700,000 new diagnoses of cancer in Africa alone each year, and this number has not been adjusted for the numerous cases that are either misdiagnosed or overlooked entirely (Luyirika and Moreira 2013). The World Health Organization estimates that one million end-stage HIV and 5.5 million terminal cancer patients suffer pain and death because of a lack of access to pain medication (Milani et al. 2011).

Even in countries where opioid analgesics are available, the logistical and administrative obstacles meant to track distribution make them unattainable for wide swathes of their populace. In Guatemala, for example, physicians must write prescriptions on notes that can only be obtained from a central office in the capital city, only 25 prescriptions may be obtained at a time, and the patient must personally travel to the capital city to have the prescription approved by the Ministry of Health (Lohman 2016). Physicians can only write prescriptions for two days in Ghana, while those in Ukraine are limited to one day prescriptions (Cherny et al. 2010, Cleary et al. 2013). Physicians in Latvia, Estonia, Albania, Denmark, Mauritius, Morocco, Sierra Leone, and Tunisia must purchase special prescription order forms (Cherny et al. 2010, Cleary et al. 2013). The World

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Health Organization estimates global opioid consumption would increase fivefold if all countries were to meet their populations' medical need for morphine (No 2008).

Access to chemical palliation is often mistakenly viewed as a small part of the larger problem in distribution of medication to those in poverty; however, treating opioid access as a product of poverty would ignore the underlying restrictions to analgesics access and the historical determinants that have shaped global narcotics policy. Although countries of the Western hemisphere, particularly the United States, have been cracking down on drug addiction and medication use since the early 1950's, the phrase "War on Drugs" was first coined by US President Richard Nixon in 1971. The United States used the 1961 United Nations (UN) Convention on Narcotic Drugs as a platform to promulgate their fear that pain medication in hospitals could lead to an addiction epidemic and their position that narcotics should be more stringently regulated (Lohman and Amon 2009). Because of US advocacy, the UN founded the International Narcotics Control Board (INCB), a regulatory committee with the purpose of ensuring adequate availability of narcotic drugs for medical and scientific purposes and preventing the illicit use of narcotics (INCB 2017).

The INCB has the dual responsibility to ensure accessibility for medical purposes and protect populations against opioid abuse, but through its regulatory restrictions, the INCB has generally prioritized the latter responsibility of ensuring that narcotics are not abused (Groff et al. 2011, Reville and Foxwell 2014). The INCB controls the supply chain of opioid distribution by managing a complex procedure for obtaining pain medication: member governments agree to license manufacturers to INCB standards, oversee trade and distribution, supervise international trade of narcotics, and justify their orders and report consumption to the INCB (Redmond 2014, Groff et al. 2011). Developed countries tend to have the necessary infrastructure in place to comply with the INCB's requirements, but developing nations lack existing political infrastructure to complete the administrative gauntlet. As such, developing nations have been reluctant to engage with the INCB, leaving the hospitals in their countries devoid of the painkillers necessary to relieve the devastating consequences of cancer and HIV infection. The blame for global disparities in opioid access does not lie entirely with the INCB's regulatory restrictions. A recent survey by the INCB identified restrictions imposed by individual countries beyond the INCB requirements that significantly limit opioid availability (Groff et al. 2011). Examples include strict limitations on the prescription duration and dosage, restrictions on the specialties of physicians who can authorize prescriptions, excessive penalties for mishandling of opioids, and limits on the number of supply pharmacies (Groff et al. 2011).

Organizations, such as Human Rights Watch, contend that governments worldwide have an ethical duty to their citizens to ensure adequate access to chemical palliation; for the 170 countries that signed the International Covenant on Economic, Social, and Cultural Rights, which includes a provision for palliative care access, these nations also have a political obligation to fulfill their previous commitment (Simon et al. 2016). Such a bold appeal to government obligations has become fashionable with advocacy organizations seeking to compel nations to invest in their citizens' welfare. Before we can condemn governments for an ethical violation of their responsibilities, we must first interrogate and establish if such a duty does exist for the government to ensure access to palliative medicine.

What does it mean to have a moral duty?

The word "duty" is etymologically related to the word "debt." Thus, to argue that the government has a duty is to contend that the government owes a debt of action to its people because of its position granted by society (Bonde and Firenze 2013). It is necessary to clarify that this analysis will discuss the moral duty of the government, as opposed to an agent-based duty to provide chemical palliation access. An agent-centered duty analysis evaluates whether the stated responsibilities of the government include the provision palliative care, a decision criteria that lends itself more to a legal rather than philosophical analysis. Many developing countries do not have laws related to palliative care rights, so such an analysis of the state's responsibilities would be specious (Husain, Brown, and Maurer 2014). Assuming the duty ought to be pragmatically justifiable and made in the best interest of its citizens, a utilitarian framework is most appropriate to evaluate whether the nation has a moral duty to provide access to chemical palliation.

Does the government have a moral duty to provide palliative medicine access?

Bioethics provides four principles with which to frame medical decision-making, and these are applicable to determine whether States ultimately have the duty to ensure access to chemical palliation. These principles are: beneficence, the duty to act in the best interest of the patient; non-maleficence, the requirement to not intentionally harm the patient; autonomy, the right of the patient to make voluntary decisions about their care; and justice, the fair distribution of goods in society (McCormick 2013).

Beneficence

The relative unimportance of palliative care in public policy likely stems from the misguided belief that medicine is confined to life-sustaining measures. Palliative care, unlike curative treatment, makes no direct attempt to resolve the illness or slow its progress, and so it is preferable from a public health perspective to prioritize spending on diseases with easily verifiable results. It is much easier for health ministers to point at the number of children administered a polio vaccine than it is to quantify the relief and dignity felt by a terminally ill patient during palliative care. Palliative care is the physical, psychological, and spiritual supportive care provided to chronically ill patients, either in the conjunction or absence of curative treatment. Even physicians often equate palliative care with hospice care, leading to the notion that palliative care is only applicable

after the patient has "given up" on his or her condition (Hui et al. 2013). Palliative care, however, is recommended by the World Health Organization to be used in conjunction with curative treatment, and the confusion of the two terms often results in under-recommendation of palliative services. Regarding policy development, the perception of palliative care as merely a supportive, end-of-life measure presents palliative care as a non-essential healthcare service. However, while the person is still alive, curative and palliative care still rely within the responsibilities of the business of medicine.

Forcing a patient to suffer inordinate amounts of pain with no avenue for treatment or relief is – in many ways – torturous. Undertreated pain has been linked to respiratory and cardiac complications, as well as delayed healing (Brennan, Carr, and Cousins 2007). From a psychotherapeutic perspective, patients who live in chronic pain are four times more likely to suffer from depression. The constant pain also interferes with relationships and decreases treatment adherence (Confortini and Krong 2015). Palliative care physicians cite pain medication as a necessary component to their treatment plan because chemical palliation encourages the patient to stick with the prescribed treatment regimen. The constant pain and resulting depression become less acceptable when considered in the context that these patients have little time to live out their lives in dignity.

Beneficence makes a powerful case for the importance of palliative care as a healthcare policy priority. Healthcare is commonly identified as a helping profession, and most clinicians identify providing comfort and pain relief to patients as a moral imperative. As such, adequate supply of opioid medications empowers the physician to ease the patient's suffering and facilitates a better relationship between the physician and patient. Beneficence is upheld when medication is provided to adequately manage pain and avoid the complications of chronic pain.

Non-maleficence

Non-maleficence calls upon physicians and health policymakers to identify the potential harms and refrain from decisions that will inflict harm. As such, non-maleficence is an often-cited principle by opponents to making opioid medication access more widely and readily available. At a clinical level, many physicians and healthcare professionals cite fear of patient addiction and over prescription as the primary reasons for their reluctance to prescribe narcotic medications (Fields 2011). Opioids are admittedly very addictive substances, and users can rapidly become dependent on the medication through a prescription regimen. Withdrawing from opioid dependence generally manifests in intense flu-like symptoms, whereas prolonged abuse of opioids can result in liver damage and painful intestinal blockage (Benyamin et al. 2008). The deleterious effects of opioid addiction are undeniable, and for the government to knowingly harm its people would be unethical, but whether availability of prescription opioid analgesics is the primary determinant of addiction epidemics is unclear. According to the National Survey on Drug Use and Health, 75% of opioid misuse begins with use by an individual using medication prescribed to somebody else (United States Department of et al. 2016). Alcohol or other drug use, not medical availability or prescription, is the largest risk factor for opioid addiction (Miech et al. 2015).

Opponents tend to point to developed nations such as the United States and to a lesser extent, Canada, as examples of how liberal availability of narcotics causes widespread abuse. However, America's healthcare system operates on a fee-for-service health model, which offers a financial incentive for physicians to fulfill patients' requests for opioid prescription because it would likely lead to future visits for repeat prescriptions (Kano and Thiruvananthapuram 2016). Most primary care doctors in Canada also receive reimbursement on a similar fee-for-service model, albeit the payment almost always comes from the government. A review of other wealthy nations reveals that many developed nations are struggling with narcotics abuse, but some, such as Great Britain, lack any significant issue with opioid addicts (Kano and Thiruvananthapuram 2016). Britain's publicly-funded National Healthcare System (NHS) means there is no financial incentive for doctors to over-prescribe, and because of Britain's centralized electronic medical records, a patient "shopping" around to different doctors in search of an opioid prescription would be quickly identified (Kano and Thiruvananthapuram 2016).

Universal access to chemical palliation may make the population more susceptible to narcotics abuse, but evidence points to financial incentives to over prescribe as the primary determinant of misuse. Hence, concern about a resulting addiction epidemic is a reason to evaluate clinician practice and reimbursement, not an argument against opioid access itself.

Autonomy

An argument against the government duty to provide opioid access is the requirement to provide opioids to addicts who request them. Suppose a patient visits his primary care physician, who knows the patient to be a long-time opioid abuser, and requests that his physician write him a prescription for Vicodin, a strong narcotic painkiller. If the government has a duty to provide adequate opioid access to its people, isn't the physician now obligated to give the opioid addict a Vicodin prescription? Does the patient's autonomy supersede the physician's obligation to non-maleficence? The answer to both questions is no, and therein lies a subtle difference between the State's duty to provide adequate opioid access and a human right to opioid access.

If the patient had a right to chemical palliation, this would entitle the opioid addict in this scenario to the aid of a physician and the government in obtaining the chemical palliation he demands. However, the government's duty as described here means it has an obligation to play its part in making the necessary amount of opioid analgesics available to the patients who need them. It does not imply that the government must provide any amount of opioids to any person who demands them. To answer the second question, autonomy generally applies to a patient's right to decline

a recommended treatment or make an informed choice between two treatment options; a patient does not have the right by autonomy to demand a specific treatment that is medically unjustified. Where the principle of autonomy does apply to chemical palliation is when chronically ill patients in pain request medication to manage their pain, the physician can and should comply to provide the necessary pain management. Simply put, the government's duty described here expresses an obligation to align narcotics availability with the medical need for opioid analgesics, not to proffer narcotics in the absence of a medical rationale.

Justice

Suppose two 35-year old male patients check into a hospice with identical cases of aggressive, incurable cancer and both patients are in incredible agony. One patient is unemployed and enrolled on a federal Medicaid plan, while the other is privately wealthy with generous insurance coverage. With just enough morphine for only one of the patients, the hospice physician must choose which patient to administer pain relief. Which patient deserves the opioid dose more? Both have the exact same predicament, yet the scarcity of medication places the hospice physician in the difficult decision of choosing whom to treat. Such a scenario is unfair to the palliative care physician, and it opens the door to inadvertent patient discrimination based on socioeconomic class, sex, race, or another demographic taxonomy. With no medical justification to separate patients who equally need the opioid medication, clinicians are automatically inclined to look for a reason to choose a patient; this situation asks palliative physicians to constantly choose whom to give medication among multiple patients who equally need the palliation. In the presented case, clinicians in the hospice would likely struggle not to allow their subjective opinions of their patients to interfere with their decisions of whether to treat; clinicians may even actively search for any sign of opioid addiction to try and justify the patient they want to treat. In culturally divisive communities in particular, medical opioid shortage makes social discrimination almost inevitable. Such a practice would be a total denigration of the principle of justice, so if opioid medication is available at all, the government has an ethical obligation to ensure that access is adequate to meet the medical need.

The lack of medical narcotics in many developing countries has also led to a dearth of pain management professionals who can diagnose and effectively prescribe pain medication because their skills and training were not needed on a regular basis. In 2000, Uganda became the first African country to declare chemical palliation as an essential provision and has since worked to improve availability of opioid analgesics (Jagwe and Merriman 2007). A key component of Uganda's Strategic Health Plan was investment in a Clinical Palliative Care Course that graduates clinicians to effectively diagnose and prescribe morphine; the nine-month course for nurses and clinical officers has since increased the number of professionals who can prescribe morphine and ensures safe prescription of opioids.

The INCB was founded by the UN because of the war on drugs in some developed nations, and heightened regulation by the INCB has come at the cost of opioid availability in nearly every developing country. Simply put, the INCB prioritizes the developed nations' war on drugs over the palliative needs of the rest of the world. If the government of a developing country decides that the INCB administrative requirements outweigh the benefits of palliative care medication access, the health department essentially lies complicit to the INCB's prioritization of the interests of developed nations. For the INCB, prioritizing the interests of developed nations does not align with the principle of justice, but it is understandable because developed nations wield more political capital in the UN. However, for the governments of developing nations that are elected to represent the interests of their constituents, it is neither just nor ethically justifiable that a government would prioritize the interests of developed nations. Because of its role as a government representative of its citizens, each government has the duty to prioritize the palliative care access of its people over the war on drugs of developed nations.

Implications for developing nations

The quadrumvirate of medical ethics is non-hierarchical, so the support or contradiction by any one principle does not automatically determine what decision is ethically "correct." The aforementioned utilitarian framework defines the ethical decision as the one that maximizes social good for the greatest number of people. A holistic review of the arguments presented with each principle demonstrates that the preponderance of evidence lies in favor of a government's duty to provide adequate access to chemical palliation. An adequate supply of opioid medication allows physicians to provide pain management for chronically ill patients who need it and prevents doctors from having to arbitrarily choose which patients do and do not deserve palliation. The concern that greater opioid medication access will lead to an outbreak in narcotics addiction is well-founded, but not necessarily inherent to universal access to chemical palliation. As such, the government ought to take careful steps to remove financial incentives to overprescribe and track the number of requests for opioids; however, this does not free the government from its duty to ensure adequate availability of opioid analgesics. Adequate medical palliation requires the active commitment of the government. Thus, the government has a duty to its people to ensure adequate access to chemical palliation, particularly in developing nations in which the burden of chronic illness is large.

What steps can the government take to fulfill its duty?

The first step for the government to fulfill its duty to secure chemical palliative access is to recognize access to chemical palliation as important and a government responsibility, which means generating laws that officially declare these statements (Cleary, Radbruch, et al. 2013). Developing nations tend to use the model drug laws and regulations set forth by the UN Office on Drugs and Crime when writing their own legislation, but the model UN legislature does not even mention the value of narcotics for pain relief medication (Lohman, Schleifer, and Amon 2010). As such, countries that rely on these model laws do not enact any pain treatment policies that can drive access

to opioid analgesics (Husain, Brown, and Maurer 2014). Without a full-throated statement that chemical palliation is important, it becomes difficult for the country to enact laws that ensure the availability of opioid analgesics. The curious absence of chemical palliation from the UN's model laws is in direct contradiction with the WHO's inclusion of opioid analgesics on the Essential Medicines List. Instead, the existing INCB system necessitates governments to apply for narcotics, and political determinants continue to restrict access to chemical palliation in most developing nations.

Uganda's success since the turn of the century in ensuring availability of palliative care can serve as a model for implementation in other nations. While other countries can and should learn from the successes and failures of Uganda's recent success, these countries cannot expect that Uganda's palliative care model can be "scaled-up" and replicated in another location. There are unique historical and cultural barriers that would prevent a replica intervention from being successful in a different setting. For example, French colonists historically used opium in Vietnam to make the population dependent on the French, thus facilitating control over the population (Laursen 2016). The Vietnamese and Hong Kong Chinese are generally fearful of opioid medications because of its previous use as a form of control. Similarly, opium spurs fear in Mexico where the illegal narcotics trade has bred extreme violence and displaced many families from gang war zones. Historical stigmas attached to narcotics in such countries as Vietnam and Mexico pose unique challenges that underscore the insufficiency of a technical approach. While many principles from Uganda's palliative medication model can be used to create a successful system in other countries, it would be unwise to expect that the exact techniques used in Uganda can be replicated in another country.

Governments have an obligation to their people to alleviate the global disparity in opioid availability between a few wealthy nations and many developing nations of the world. Although the tangible health repercussions of pain are sometimes difficult to recognize, the poor quality and limited access to palliative care is a problem that requires urgent action. The World Health Organization has strongly urged countries to prioritize palliative care, even adding opioid analgesics to the Essential Medicines List. Countries must also adopt this stance to eliminate the cruel treatment of chronic patients. Nations like Uganda have demonstrated that such improvement and access is possible for developing nations. Although their model cannot be exactly picked up and replicated in another setting, other nations have a duty to analyze what has been done and work toward improving palliative care across the globe.

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Article

Autonomy At What Cost? Mitigating Patient Autonomy in the Case of Anorexia Nervosa

Erin Gaudette*

Anorexia nervosa (AN) patients present clinically with a preoccupation on food, weight, and an obsessive worry about being fat, which persists as the patient becomes emaciated due to starvation. When standard treatment courses involving feeding programs (often alongside other therapy) are met with patient resistance or refusal, as is often the case, the patient indirectly risks death as the illness progresses, though not typically presenting with an active death wish. This paper explores how healthcare providers are to ethically balance the duty to uphold and respect patient autonomy and their duty of care in treating the illness. Entailed in this complex question are the following important considerations: To what extent can patients with Anorexia Nervosa be considered competent agents? To what extent do the pathological characteristics of the illness influence both patient autonomy and how it ought to be considered? To what extent, and when, can and should healthcare providers ethically override patient autonomy? Finally, this paper explores how these cases and those of chronic, refractory anorexia pose challenges to our current ethicolegal framework for conceptualizing and upholding patient autonomy in healthcare.

Anorexia nervosa (AN) patients present clinically with a preoccupation on food, weight, and an obsessive worry about being "fat," which persists as the patient becomes emaciated due to starvation. Treatment is typically met with great resistance from the patient, as it involves in some capacity (often alongside other psychological treatment) a feeding program for weight gain. Refusal of treatment, however, risks death as starvation continues, despite a general absence of suicidal ideation in the patient (that is, patients do not actively express that they wish to die). For those who care for the patient — the family and the team of healthcare professionals — there arises a tension between the ability and obligation to respect the patient's autonomy in making their own medical decisions and proceeding with a treatment course that is in the best long-term health interests of the patient's survival. This tension introduces the ethical and legal question that asks in which cases, if any, is overriding a patient's autonomy in choice ethically justifiable. In what follows, I will consider patient autonomy in the unique clinical context of AN patients, examine the extent to which caregivers have an obligation to uphold patient autonomy, and examine autonomy in care decisions for the patient with chronic, refractory AN.

In modern jurisprudence and medical ethics, a hallmark of the Doctrine of Informed Consent is respect for the principle of patient autonomy. It is patient autonomy that allows competent patients the freedom to make their own informed, conscientious choices about what medical treatments they will or will not be subjected to, in accordance with the pursuit of their broader goals and interests (Bratton 2010, Russell 2007). The honouring of patient autonomy requires the condition of patient competence: that their capacity to understand and reason about what is in their best long-term interests is intact (Tomasini 2010). Typically, competence entails understanding of the situation and prognosis, appreciation of their specific circumstances, reasoning, and expression of a choice (Tan 2006). When an AN patient expresses a wish not to undergo potentially life-saving treatment, thereby indirectly risking death, the question often becomes whether this is a wish expressed by a competent decision-maker, since establishing competency of the patient underlies whether or not the patient's refusal of treatment is to be respected or overridden with some form of involuntary intervention. Therefore, considering whether or not the patient with AN, in context of the unique clinical features of the disorder, is able to competently make medical decisions and exercise their autonomy is important in balancing the tension between the patient's wishes and the medical team's life-prolonging recommendations and interventions.

Several research groups have examined AN patients' performance on the Iowa Gambling Task (IGT), a clinical measure for the ability to weigh short-term and long-term consequences related to reward and loss, finding that AN patients performed poorer on the IGT than did matched controls, indicating impaired decision-making (Brogan et al. 2010, Tchanturia et al. 2007). What is troubling in AN patients is that cognitive function typically remains unchanged, despite the values of the patient — especially as they relate to weight, body image, and fatness — being

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changed in such a way that these focuses are prioritized above all else (Tan 2006). That is, the priorities of the patient have shifted in a way which compromises the patient's wellness, though their mental capacity is not obviously impaired in any measurable way. Of course, we may claim any number of belief sets are irrational, but the significance here is that such a set is associated with a harmful illness. With such an obsessive value schema to the visible detriment of patient health, one wonders if someone with such a value schema can be deemed competent, and if perhaps competence assessments should examine both values and emotions, alongside cognitive function (Tan 2006). This is especially true given that, since both the physical and mental characteristics of anorexia are not terminal and are generally reversible, these values are seemingly unstable (Bratton 2010). It has thus been suggested that an additional criterion for competent decision-making capture whether or not the patient is absent of pathological values, or values arising from the disorder (Tan 2006). This, in practice, however may lend itself to medical paternalism, given that there may be no practical, definitive way to clinically distinguish between pathological and non-pathological values that are person-specific. Even if there were some way to neatly identify pathological values, it does not necessarily follow that these values compromise the decision-making capacity of the patient to the point where they may be deemed incompetent (Whiting 2009); that is, possessing pathological values does not necessarily preclude the ability to understand and reason about one's situation in a competent manner. Moreover, categorizing values in this dichotomous way does not account for certain qualities of the patient (self-discipline, austerity, and perfectionism) that may predispose or influence the development of eating disorders.

> "The question then, becomes whether it is defensible to associate irrationality with incompetence."

Perhaps most troubling about the suggestion of necessitating an absence of pathological value is its reference to a normative value schema. When we make such a reference, we associate that which is normatively considered to be irrational (despite being perfectly rational for the patient with AN) with the notion of incompetence, setting a potentially dangerous precedent that restricts acceptable pluralism in self-related beliefs to the confines of what society at large deems rational. Indeed, there are a host of other value sets that we may find equally troubling and irrational (for example, discriminatory values) though we would not deem their holders incompetent agents. The question, then, becomes whether it is defensible to associate irrationality with incompetence (Gans et al. 2003). Importantly, the difference between the two concepts is significant, as legal tradition does not bar, and thereby permits, irrationality. But, the argument for associating irrationality and incompetency in AN may be made given that: 1) the desire not to eat in AN patients undermines a stronger desire not to die and, 2) the desire not to eat may itself be involuntary, grounded in some false belief about the patient's body image (Gans et al. 2003). Thus, categorizing AN patients as incompetent based on their evidenced irrationality may be sufficiently justificatory in overriding patient autonomy in favour of involuntary life-saving treatment. Of further note is that the condition of being anorexic, despite cognitive functioning being unimpeded, may itself represent a failure and loss of autonomy, in terms of the loss of the capacity for self-realization as the disorder progresses untreated (Bratton 2010).

To this point, I have examined factors which may compromise AN patients' competence and ability to act as autonomous agents. But what if we grant the quality of competence to these patients, given the previously discussed problems with assessing competence clinically and the unimpaired cognitive functioning of these patients? Is it, then, ever ethically acceptable to override their autonomy in favour of involuntary, life-saving treatment? When we consider the unique clinical features of AN (including that it is reversible and not necessarily lethal, though progresses to death if starvation continues), refusal of treatment, at some point, becomes commensurate with dying, and honouring this refusal is tantamount with supporting the request to die (Giordano 2010). Is, then, an autonomously expressed choice that will result in the patient's death, by virtue of its autonomous expression, a sufficient reason to honour such a wish? What complicates this matter is that the anorexic patient typically does not actively express a wish to die (that is, they are not typically suicidal), and death is, instead, a foreseen consequence as opposed to the desired end of refusing treatment (Bratton 2010). Here, drawing a distinction between intended and foreseen consequences may be important in understanding the clinical pathology of the disorder. In some ways, this is better conceptualized by thinking of dying as a "side effect" as it were to the patient's ultimate goal of weight loss. However, when we uphold autonomy as a "supergood" in anorexic patients— to be valued and respected above all else — we uphold autonomy as a principle, even though this may mean "dying with their rights on" (Russell 2009). While respecting rights like patient autonomy constitutes a very important means, when placed above all other considerations, especially in the unique case of AN, one wonders what ends patients can hope for.

It is significant that anorexia is a reversible, not terminal, condition; this weakens the strength of the normative reverence for the principle of respecting competent choice (Giordano 2010). Indeed, the excellent

prognosis of the illness, when treated, marks an important moral distinction from other illnesses. Respecting competent choice above all other considerations in the context of anorexia may in fact signify adopting a policy that sanctions premature death in otherwise savable people (Gans et al. 2003). There is a general consensus in society at large that life should not be wasted or at least not disregarded flippantly. Addenda to this that implicate medical aid in dying are circumstances in which there is terminal illness or intractable suffering. Given that this is not the case for patients with AN, is paternalistic medical intervention justified? It ought to be noted that paternalistic interventions are not always immoral. When we legitimately use prudence and consider the value of life, it seems reasonable that if there is a probable chance the patient will later thank you for rescuing them, then you should rescue them (Giordano 2010). This rationale draws an important line with other autonomous medical choices; for example, given that a Jehovah's Witness adherent would likely not thank you after having received a blood transfusion, there is little ground to override this autonomous choice. Such interventions in AN patients are not to disregard patient autonomy, but instead to encourage patient autonomy be treated as a virtue as opposed to a principle. Autonomy should be exercised not just in any manner, but a manner which is responsible and indicates adequate appreciation of consequences and concern for others.

"Respecting competent choice above all other considerations in the context of anorexia may in fact signify adopting a policy that sanctions premature death in otherwise savable people."

Having made the argument in support of overriding patient autonomy in the case of AN, it seems reasonable to now examine the extent of the responsibility of medical professionals to ceaselessly urge and promote recovery. This is especially relevant in cases of refractory anorexia that ask another question of us: at what point, if any, is medical futility of further treatment, in addition to an autonomous wish to not undergo further treatment, sufficient ethical grounds for a treatment course focused on end-of-life palliative care as opposed to recovery-focused treatment in patients with chronic AN? Many case studies detail the difficult position medical professionals find themselves in when deciding whether to forcefully, legally override the treatment-refusing decisions of those who have suffered with AN for decades with little improvement. On one hand, a redirection to end-of-life care honours the patient's ability to judge their quality of life in light of the illness and respects patient autonomy. Conversely, some practitioners view such deference to the patient with AN as collusion with the illness and dereliction of their duty of care (Kendall 2014). The concept of medical futility is well-recognized in other chronic pathologies, and denotes a treatment course not considered to be medically appropriate given its marginal chance of success (Geppert 2015). Yet, it seems that even in the most severe cases of AN, the illness does not progress in an inevitable, unstoppable manner that is treatment-resistant (as seen in other medical pathologies). Rather, this notion of treatment resistance in fact conflates resistance with patient refusal, for even in the most dismal prognostic cases of AN, forced, involuntary feeding cannot be labeled as a treatment to which AN will be resistant. Indeed, the physiological consequences of such treatment necessarily include weight gain and some remediation of the clinical features accompanying AN, should a patient undergo such treatment. But for patients who have been hospitalized and force-fed time and time again, who seem absent of any hope for improvement, and whose prognosis does not appear likely to change, is there a point at which medical professionals are resigned to honour the patient's (who appears largely competent despite a lacking dietary competence) directive to refuse treatment and die as a result? Do the experiences of the patient and the indisputable suffering the illness entails warrant that we, at some point, concede to the patient's appraisal of whether or not continuing to live is, in their view, worthwhile? Certainly, in other end-stage illnesses we afford people the right to die when faced with intractable chronicity and suffering due to medical illness. But do the clinical qualities of AN warrant a distinction between such illnesses and AN?

As discussed previously, it is ethically significant that AN is a psychiatric illness that is not terminal in any deterministic sense, despite prognoses varying between patients. Treatment courses for AN, therefore, cannot be considered physiologically futile, as the body will physically respond with due adherence to the course. Even in the most chronic cases of AN, the disorder itself can never have a certain incurability; it does not progress inexorably (Geppert 2015). This poses a problem to labelling AN cases "end-stage"; at what point can responsible medical professionals wager that this is indeed the final stage in an illness that is not terminal and is reversible? When practitioners see little improvement or inclination towards improvement in the patient, it becomes difficult to not conceptualize the illness and the patient as one entity, inseparable. With such a conceptualization, how the illness may be skewing the values of the patient — even as the patient's life is endangered — and what recovery would mean for the patient's quality of life become distant, unimportant considerations. Such sentiments from medical

professionals are understandable; treating an illness that is curable for decades with little improvement almost certainly breeds frustration and a sense of a determinism about the prognostic outcome. Notwithstanding the emotional challenges chronic AN poses to the medical professionals who address it, to insinuate negligible chance of recovery (and support end-of-life measures for the AN patient) is, at best, empirically precarious and ethically premature (Geppert 2015). Chances of recovery are never certain, of course, but our regard for the intrinsic value of life must precede any inclinations (tempting though they may be) to presume the futility of any future treatment in AN.

That the notion of patient autonomy be considered a virtue instead of a principle in AN presents a departure from how standard medical and legal ethical systems value autonomy. This is justifiable owing to the unique nature of AN as an illness that has an excellent prognosis when treated, is not terminal, and is reversible. Ethical action in these cases require prudence, not in the name of disregarding patient autonomy altogether, but in mitigating it with the facts concerning the clinical features of AN. To even suggest such mitigation is, in itself, controversial. Patient autonomy is at the cornerstone of our right to self-determination as it relates to our own health and to be sure, is important. Notwithstanding the value of autonomy, the perspective with which it is exercised in the unique case of AN must also be considered. The ethical and legal system as it exists currently is designed to protect patients from undue influence from medical professionals and institutions; yet, this system is unable to protect patients from the transient influence of their illness itself. Action constitutive of prudent medical ethics in the case of AN is challenging to accommodate within this ethicolegal framework, and demands a case-specific paradigm shift in the way we value patient autonomy, but the unique clinical features of AN demand that we adopt such an ethical shift in order to aptly consider the value of the patient's life.

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Article

Involvement of Homeless Individuals in Pharmaceutical Clinical Trials

Sharlotte Irwin*

In the United States, homeless individuals find themselves vulnerable to many kinds of harm and exploitation, including in relation to pharmaceutical research. This paper begins by identifying the characteristics that make a person both homeless and vulnerable to research. Then, it explores specific incidences of pharmaceutical researchers using homeless individuals for Phase I clinical trials, a practice which first came to public awareness in the 1990s. Ethical principles are then applied to these scenarios, focusing specifically on undue inducement, structural coercion, exploitation, and unfair exclusion. Finally, possible solutions are presented to help resolve the aforementioned concerns, providing suggestions for both the research world and the socio-political context.

Background

Among the wide-ranging problems that plague the homeless population in the United States daily, a lack of necessities seems to be the most problematic. Specifically, a lack of stable housing, access to healthcare, and the inability to secure a reliable income stem from and contribute to a lack of power for homeless Americans. From this lack of power emerges a state of vulnerability, shaped not by homeless people's inherent mental capacity, but by their social situation.

In recent years, the pharmaceutical research industry has taken advantage of this population's situational vulnerability. The relationship between the pharmaceutical research industry and homeless populations raises ethical concerns based on the principles of voluntariness and exploitation. However, pharmaceutical research does benefit homeless people in such a way that categorical exclusion is not an option. Instead, policies must be established to avoid taking unjust advantage of homeless populations, while avoiding imposing paternalistic restrictions on clinical trial participation.

To better understand the ethical concerns of using the homeless as pharmaceutical research subjects, it is essential to first establish the relationship between homelessness and vulnerability. The United States Department of Health and Human Services describes an individual who is homeless as someone who lacks or cannot maintain stable housing, lives in temporary shelters or a single-room occupancy, or lives in another situation that is not permanent (42USC254b(h)(5)(A)). While some scholarly debate exists, this definition encompasses the main idea of homelessness as it relates to the discussion at hand. With this in mind, homeless individuals are said to be vulnerable not because of who they are but because of certain situations that are associated with being homeless (Beauchamp et al. 2002). For instance, approximately twenty five percent of homeless people suffer from mental illness, while many others suffer from addiction or poor coping mechanisms ("Mental Illness and Homelessness" 2009). Additionally, people who are homeless have little power economically or socially and lack a support network (Beauchamp et al. 2002). As a result of these personal and societal factors, homeless individuals are vulnerable to injustice, exploitation, and various forms of harm.

Case Studies

Unfortunately, pharmaceutical research companies prey on the vulnerability of homeless people, a trend that first publicly surfaced in the 1990s. The headlines revealed that Eli Lilly and Co., the producers of Prozac, were recruiting homeless alcoholic men from Indianapolis to participate in Phase I clinical trials, which test side effects and dosage of experimental medicines. As the company argued, the deal benefited both parties: the researchers had easy access to subjects who would most likely not take legal action in the event of harm, and the homeless men received money and free room and board for the duration of the trial (Cohen 1996).

Despite these claims, the scenario ultimately compromised both scientific and ethical values. Scientifically, alcoholism could act as a confounding variable, even though Lilly claimed the subjects were sober. In reality, the subjects hid their alcohol consumption and used insider tricks to appear clean, skewing the trial results while potentially risking their own health. In the same way, the participants often did not disclose side effects they were experiencing, either because they assumed they were associated with alcohol withdrawal or because they did not want to be barred from future studies (Cohen 1996).

The Lilly clinical trials did not hold up ethically, either. While the company insisted it was being philanthropic and helping the homeless, the addicted men often spent

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their compensation on alcohol immediately after the study, blacking out and damaging their health and financial situations even further. While community members witnessed the damaging effects Lilly's trials were having on the city's homeless population, no one spoke up because of the generous donations the pharmaceutical company contributed to Indianapolis organizations, creating a conflict of interest (Cohen 1996).

Although Eli Lilly and Co.'s controversial practices with its clinical trials were exposed more than twenty years ago, little has changed, as Carl Elliott demonstrates in his investigation of pharmaceutical research in Philadelphia. Elliott witnessed firsthand how Phase I clinical trial recruiters specifically targeted homeless individuals by handing out business cards in homeless shelters and putting up flyers. Most commonly, the Phase I clinical trials were for antipsychotics and addiction treatment, resulting in the targeting of people who were not only homeless, but also mentally ill. The recruiters were able to target the mentally ill, homeless population because the FDA does not specifically identify individuals with mental illnesses as needing special protection in or exemption from biomedical research (Elliott 2014).

As for drug addiction treatment trials, Elliott learned that many homeless people would begin using drugs to qualify for the studies because they were so desperate for the accommodations and the compensation. Highlighting this desperation, Elliot describes cases of mentally ill homeless people who viewed their participation in over twenty Phase I trials to be "worth it," despite the long-term side effects they experienced. One might think that provisions would be in place to prevent taking advantage of homeless individuals, but Elliott explains that Institutional Review Boards are often for-profit, at least in the context of pharmaceutical companies. As a result, they may avoid rejecting studies that are ethically questionable for fear of earning a bad reputation and losing future clients, thus further perpetuating the unethical conflicts of interest that are rife in the pharmaceutical industry (Elliott 2014).

Ethical Analysis

Thus far, case studies of pharmaceutical research involving homeless individuals have only been examined at face value; it is essential, however, to apply universal ethical principles to these scenarios to understand the underlying complexity of the issue. First and foremost, informed consent is a requirement for all research involving human subjects. The Belmont Report asserts that "information, comprehension, and voluntariness" must be present for informed consent to be valid (The Belmont Report 1978). While one could question whether comprehension is always present in mentally ill homeless individuals, the main subject of dispute is voluntariness, which can be violated in multiple ways in the homeless population.

While the recruited homeless individuals do technically volunteer to participate, this voluntariness is diminished in the presence of undue inducement, such as offering money and shelter to homeless individuals. The main reason that researchers offer shelter is to conduct the trial in a controlled environment and closely monitor the participants, but the practice still raises ethical concerns. While a person with a stable home would probably not feel tempted by the promise of shelter when deciding whether or not to enroll in a clinical trial, the offer would be essentially too good to refuse for someone lacking it (Fisher 2013). Does this situation still allow for free choice, or does it invoke undue inducement that compromises voluntariness? In the case of the homeless alcoholic men who depend on clinical trial earnings to meet their daily needs, or in the case of the mentally ill homeless individual who continues to enroll in clinical trials despite side effects, voluntariness seems to be lacking. Instead of offering a chance to rebuild their lives, as some researchers insist, promising money and shelter to homeless participants in Phase I clinical trials fosters a cycle of dependency that constrains voluntariness, leaving the participants feeling unable to refuse (Beauchamp et al. 2002).

"While the recruited homeless individuals do technically volunteer to participate, this voluntariness is diminished in the presence of undue inducement..."

The threat to voluntariness does not only stem from the side of the research institution in the form of undue inducement; societal factors are largely to blame for negating the voluntariness of consent, ultimately leading to the exploitation of the homeless. The term "structural coercion" refers to the threats associated with a homeless individual's social and economic situation that ultimately force him or her to agree to something, i.e. a Phase I clinical trial. Traditionally, coercion is thought of as one individual directly threatening another individual in order to force compliance. In the case of structural coercion, homeless people are coerced not by the researcher but by the threat of structural violence, such as lack of access to food, shelter, and healthcare (Fisher 2013). They feel that they have no option but to participate in the trial if they want to temporarily escape from the daily harms they face.

While pharmaceutical researchers are not the ones responsible for coercion, they exploit homeless individuals who experience structural coercion, taking advantage of their utter lack of power or options. Exploitation involves taking advantage of someone in a way that is harmful, disrespectful, or unjust. Instead of trying to promote justice

and respect for the homeless by acknowledging structural violence and coercion, pharmaceutical companies intentionally prey on society's victims. Specifically, the fact that researchers in Philadelphia recruited participants at homeless shelters is undeniably exploitative, considering the researchers intentionally sought out vulnerable homeless and mentally ill individuals seeking refuge for a night. The researchers also exploited the fact that the participants were powerless to file lawsuits, making it even easier to cause harm.

While homeless research subjects may temporarily benefit from participating in these clinical trials, they are often ultimately harmed in the form of physical, mental, or economic side effects. As aforementioned, the Lilly clinical trials involved taking advantage of homeless people's need for shelter and money but caused immense harm when the subjects immediately spent their compensation on alcohol. The mentally ill homeless population is especially at risk for exploitation, because researchers fail to respect their diminished mental capacity, which may make it difficult for them to make rational decisions that are in their own best interests. Instead, the researchers take advantage of this vulnerability for their own scientific gain (Resnik 2003).

The exploitation of the homeless in research also is largely an issue of justice; specifically, the unjust distribution of risks and benefits. Disadvantaged homeless individuals take on a relatively large amount of risk in Phase I trials but will most likely not be the population benefiting from the results of the research because of their limited access to healthcare. Even during the trials, most studies do not provide free care or treatment if the subjects are harmed as a result of the testing. A final point of contention is the payment the homeless receive for these clinical trials. While they are often paid more than minimum wage, they receive no extra benefits, especially considering the amount of risk they are encountering (Elliott 2008). Unfortunately, trying to strike a balance between exploitative under-compensation and undue inducement is challenging.

“ The homeless are already victims of an unjust system that makes earning a livelihood difficult, so completely barring them from paid research is just another form of unfairly limiting their options.”

While including the homeless in pharmaceutical research does raise many ethical challenges, completely excluding them is not an option, either. Since homeless individuals do possess autonomy and the freedom to consent, excluding them from clinical trials would be paternalistic and unreasonable. The homeless are already victims of an unjust system that makes earning a livelihood difficult, so completely barring them from paid research is just another form of unfairly limiting their options (Dickert 2009). Many homeless shelter directors actually encourage some residents to enter into clinical research as a way to avoid the exploitation of day labor. Without this slightly better alternative, homeless individuals would be forced to endure more severe forms of exploitation and structural violence in the form of day labor. Complete exclusion of the homeless from clinical trials would even further deprive them of opportunity and would unfairly discriminate against an entire group of people (Beauchamp et al. 2002).

Proposed Solutions

While the unethical payment practices in pharmaceutical research are numerous, some more ethical forms of compensation have been developed in the research community. An ethical payment method is one which neither unduly induces nor exploits the subject, and respects the process of informed consent. To achieve these goals, some scholars have suggested using payment-in-kind, or PinK, as an ethical payment method. PinK is an alternative to monetary compensation, which offers payments in the form of goods. Proponents claim that payments-in-kind protect mentally ill participants from misusing funds. In reality, PinK is often worth less than cash, which is exploitative, and also does not promote equality because it is only offered to disadvantaged groups of people. As a result, PinK limits homeless individuals' autonomy by constraining their options. While the upper class is free to spend its money how it chooses, PinK imposes a paternalistic double standard by not allowing homeless individuals to choose how to spend their earnings. Some people say the mentally ill need special protection and should receive necessary material goods as payment, but that would imply that they are unable to give valid informed consent in the first place. Ultimately, PinK is as coercive, if not more, as monetary compensation. If, for instance, the payment-in-kind for a study is three hot meals, a homeless person would have a much more difficult time saying "no" than a person with stable housing and access to food (Schonfeld 2003). Consequently, PinK is not an effective solution, and instead just creates more inequality and exploitation in the research setting.

With so many ethical concerns to consider, it seems as if the fair inclusion of the homeless in pharmaceutical research is impossible. However, there are specific steps that both the research community and policy makers can take to improve the situation. Within the research

community, one of the most effective solutions would be for researchers to not specifically target the homeless, reducing exploitation by not intentionally seeking out vulnerable individuals. Phase I trial recruiters do not recruit participants in country clubs, so they should not be practicing this in homeless shelters, either. In a similar way, a limit should exist on what percentage of a study's participant pool can consist of homeless individuals (Dickert 2009). While, as stated previously, it would be unethical and unbeneficial to entirely exclude the homeless, having a trial consist of a large percentage of homeless individuals puts a disproportionate, unjust burden on them, while also skewing scientific results.

For those that still do choose to participate in clinical research, the homeless should be encouraged to participate in Phase II and III trials, where they would actually be receiving treatment, unlike in Phase I safety trials. This way, exploitation via unjust distribution of risks and benefits would be reduced because they would be enduring less of the burden and receiving more of the benefit. Their health may actually improve, instead of being harmed as a result of long-term side effects. Additionally, researchers need to stop offering housing as compensation, unless it is essential to the accurate scientific results of the trial, because this practice specifically entices homeless individuals with no other options. Undue inducement could be drastically reduced if researchers only offer monetary compensation, which is desirable to the general population instead of to solely a particular group. Once participants are already enrolled in the studies, however, researchers could offer vocational and educational services such as career counseling, or meetings with community college or GED program representatives. The research institution could take the opportunity to provide more benefit to participants without creating undue inducement beforehand.

In conclusion, the involvement of homeless populations in pharmaceutical clinical trials raises issues of informed consent and exploitation, but viable options do exist that could lead to improved circumstances. Instead of exploiting homeless participants or offering undue inducement, researchers could utilize their participation to offer them treatment and necessary services that would be beneficial in the long run. At the same time, a balance must be achieved between homeless people's needs and monetary compensation so as not to deny them a potentially significant source of income. Still, because of the situational vulnerability of the homeless, structural violence can act as a form of coercion, limiting their options. The true solution to this, then, is to tackle the societal issue of homelessness by eliminating the structural violence that motivates them to participate. If homeless individuals feel like they have equal opportunities outside of the research domain, less coercion and more autonomy would result. In the grand scheme of trying to promote autonomy and avoid exploitation, it is vital to respect the dignity and personhood of the homeless, so that they may be active participants in both research and society.

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