the Rutgers Journal of Bioethics

Volume XI, Spring 2020

THE RUTGERS JOURNAL OF BIOETHICS

VOLUME XI, SPRING 2020

The Rutgers Journal of Bioethics is an undergraduate journal exploring the intersection of ethics, biology, society, and public policy. It has been published each year since 2009. While the Journal solicits articles from all persons wishing to participate in the open discussion on bioethics, it is managed by students at Rutgers, the State University of New Jersey. The Journal is published by Premier Graphics (500 Central Avenue, Atlantic Highlands, NJ 07716) and funded through generous contributions from the Rutgers University Student Assembly Allocations Board. The Journal welcomes all unsolicited original essays, book reviews, editorials, and art. To submit, please e-mail a copy of your paper or a high-resolution image of your work of art to <rubioethics.journ@gmail.com>.

Letter from the Editor

Bioethics explicitly pertains to biology and ethics, but in practice spans a vast and diverse array of disciplines, which include law, philosophy, and most STEM fields. American political philosophy emphasizes individualism and personal freedom – of speech, religion, petition, and so on. Historically, these liberties have been protected through both prevention and enforcement of intervention by the government and other institutions. As new biotechnologies and medical practices arise, legal and political thought within bioethics must also evolve. The 11th volume of *The Rutgers Journal of Bioethics* specifically discusses questions surrounding control of these developments by regulatory bodies:

What is the role of these regulatory bodies? Who are they—interest groups, doctors, insurance and healthcare companies, hospitals, the government? Should emphasis be on the individual or the collective? To what degree does self-regulation benefit the individual?

This volume begins with an editorial discussing the legalization of physician-assisted suicide, arguing we should preserve our autonomy not just during life, but also in death. The *Journal* then explores agency, safety, and regulation with respect to novel and established innovations, specifically brain-computer interfaces and assisted reproductive technologies. The next article discusses overdiagnosis of breast cancer and its many stakeholders, and it advocates for analysis of the issue at the population rather than the individual level. The final article analyzes the power dynamics surrounding the control of biological information and technology as well as the forms through which individuals are gaining medical autonomy.

The articles included in the 11th volume of *The Rutgers Journal of Bioethics* expose the line biotechnological applications draw between the vulnerability and empowerment of both the individual and the population. Here, the *Journal* reflects upon on how this line should be treaded, specifically how it should impact policy at the institutional level.

I am thankful to the authors and journal staff for their hard work throughout the editorial and design process. Thank you also to the publishers and the Society for their support in producing this year's volume of the *Journal*.

By understanding our biological realities as well as the politics and laws surrounding them, we are well-equipped to advocate for ourselves and enact change, be it by picketing, voting, or becoming the policymakers. I sincerely hope readers find these works enriching, thought-provoking, and inspiring.

Namrata Pandya
Editor-in-Chief, *The Rutgers Journal of Bioethics*

Letter from the Society

The Bioethics Society of Rutgers University brings students together to raise awareness of bioethical issues facing our generation. Our biweekly meetings feature group discussions of bioethical case studies and prevalent issues in today's global environment. In the 2019-2020 academic year, we have discussed the ethics of a wide range of issues, including bias against minorities in the healthcare system, medical tourism, and biohacking. It is essential to discuss such matters since the "correct" answer in many cases is not always clear nor easy to achieve. Our students gain valuable exposure and knowledge in the real-life issues facing healthcare, research, public health, and law, and our organization equips them with the experience needed to face various ethical decisions.

In addition to our general body meetings, we host a large speaker event in each academic semester, which aim to shed light on current and pressing health issues while allowing our students to learn from respected experts in the field. In the Fall, Dr. Eric Singer, a urologic oncologist at the Rutgers Cancer Institute of New Jersey and member of the Robert Wood Johnson University Hospital Ethics Committee, led an interactive discussion surrounding the intricacies of life support regarding the survival rate of hospitalized patients.

In the Spring, we host the annual Rutgers Bioethics Symposium, in which we welcome a panel of doctorate professionals to share their insights and experiences. In the past, guests have presented on clinical research, population-level ethics, women's health, global health, and neonatal medical ethics. Both events offer real-world examples of the importance and relevance of bioethics. We hope the symposium inspires young minds to examine the world around them and gives them the determination to improve lives. It is a privilege for the Society to host such events, and we thank all our speakers.

As always, we extend our gratitude to the members of the Rutgers Bioethics Society. The dedication and passion shown by our members is the driving force for our organization's success. As they progress in life, we hope that they carry forth the principles and ideas discussed at our meetings and events. We also express our thanks to the executive boards of the Society and the *Journal* for helping with the programs throughout the year. The publication of Volume XI of *The Rutgers Journal of Bioethics* showcases the hard work and efforts of the *Journal* executive board, and we hope that you benefit from reading this volume as much as we do.

Katerina Liu & Shivani Karthikeyan
Presidents, Bioethics Society of Rutgers University

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Editorial

Articles

Cover: Zahren, M. (2017). *Ribcage.* Photograph. Retrieved from https://unsplash.com/photos/Nk7hHi3I__0.

A Right to Die?

by Alona Zunger †

The United States is in a liminal space regarding legislation on physician assisted suicide (PAS). The practice is currently legal in a few states and is intended for people with less than six months to live. On one side of the judicial scale lies the sanctity of life argument, that life is precious and should be preserved at all costs. This teeters in competition with the argument that in order to have individual autonomy, a person's right to die on his or her own terms is necessary. Autonomy is a concept dear to the average American, central to the founding and maintenance of the country, and should be prioritized with respect to PAS legislation. The enumeration of a right to die in pursuit of legal physician assisted suicide for the terminally ill can can occur through the usage of the substantive due process clause; however, this is unnecessarily prevented due to the largely unfounded fear that a legal and social progression will occur.

Substantive due process could be used to establish and codify a right to die as the clause has been used in the past to "create" previously unenumerated rights. Bopp and Coleson point out that "substantive due process is the analytical device employed by the court to declare constitutional rights not enumerated in the Constitution" [1]. This clause of the Constitution is ambiguous and interpretations between different people can differ greatly as it is an "analytical device" and not an explicit list of rights. It is a lens of sorts used by courts to make decisions on what may be rights. Crucially, rights using this clause are not explicitly stated but, rather, are interpreted.

Substantive due process in the fourteenth amendment also vaguely protects people from a withdrawal of rights that exist or ought to exist but are not out-

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wardly stated in the Constitution. The case that legalized gay marriage, *Obergefull v. Hodges*, "emphasized the radical autonomy perspective… relied upon in substantive due process cases" [2]. A person's "radical autonomy" is what allowed gay marriage to pass through as a right. In other words, the right to be married was elucidated by denying the government's constitutional ability to interfere or disallow gay marriage, not by actually saying there is some fundamental right to marriage. This prime example of the power of substantive due process, the idea of autonomy, and the resulting ability to produce rights can be applied to arguments regarding PAS.

Obergefull v. Hodges is an example of a case of substantive due process being applied rather directly to create a new right, but there are similar and important cases that take it a step further with one new right compounding to create an additional new right. An example of this is the famous case of *Roe v. Wade* where the right to privacy stated in *Griswold v. Connecticut* later encompassed a right to abortion [1]. Bopp and Coleson address this idea in saying that "Reaching back to prior substantive due process decisions finding a right to privacy 'founded in the Fourteenth Amendment's concept of personal liberty,' the Roe Court declared that this right to privacy was 'broad enough to encompass' abortion" [1]. This is an example of the potentially problematic idea that rights are interpreted rather than stated. Though substantive due process protects citizens from their rights being infringed upon, it also allows for rights to increasingly be "made" with no explicit upper bound. The right to privacy, which is not explicitly stated, led to what is colloquially known as a right to abortion. If this right was "broad enough" to encompass abortion, the "right to die" could similarly be created based on arguments of similar composition and strategy where one composed right leads to other new rights. If this is the case, some may wonder what is to stop these rights into compounding into something inhumane and nonconsensual?

There is, however, no precedent or evidence to believe that PAS will progress into something inhumane. Lewis notes general public ignorance to the issue in saying that there is "the temptation to assume that the legalization of voluntary euthanasia causes nonvoluntary euthanasia to occur… [and it] should be resisted in the absence of evidence of causation" [3]. Though many

Chains, K. (2019). *Woman holding purple flower bouquet.* Photograph. Retrieved from https://unsplash.com/photos/sw7GX-6KUeg.

are tempted to believe that PAS could lead to danger, it is even more dangerous to draw conclusions and demonize the

Pixabay. (2016). *White hospital beds* (edited). Photograph. Retrieved from https://www.pexels.com/photo/bed-empty-equipments-floor-236380.

practice without the necessary evidence to do so. In fact, one could go further and state *with* evidence that "The rates of non-voluntary euthanasia in Australia, Belgium (pre-legalization [of PAS]), and Denmark were all higher than the rate in the Netherlands, the only jurisdiction in which termination of life on request was lawful at the time of these surveys" [3]. These countries that did not have the termination of life on request legalized all had higher rates of euthanasia without consent. This shows that the slippery slope argument regarding the Netherland's legalization of PAS is not based in evidence and should be looked at with skepticism.

Overall, PAS is an idea that makes many fearful; however, people should be fearful for the right reasons. The primary issue could be the potential risk to the poor and underprivileged due to their lack of resources for care. The efficiency of PAS could pose a problem, according to a California Law Review, that "permitting assisted suicide would increase the vulnerability of all patients without sufficient funds to manage their own health care" [4]. These patients are already vulnerable as it stands, and legalizing PAS could potentially put them further at risk, because "assisted suicide may prove too profitable to resist for American reimbursement systems, eager to discover alternatives to more expensive yet humane palliative care alternatives" [4]. Poor people being vulnerable and reimbursement systems being "eager" to reduce expenses in palliative care would work in tandem against the poor, perhaps pressuring them to choose PAS over palliative care. This presents PAS as a cost-cutting measure that may serve as an immoral reduction of expenses.

The concerns regarding the risks of legalizing PAS may be significant but should not be a deterrent; the autonomy that PAS would provide is essential in being fair and just to citizens of the United States facing their last days.

When looking at the broader picture it is easy to get lost in the kerfuffle that PAS legislation brings and neglect the benefits that PAS provides to many globally. On an individual level "there are terminally ill patients suffering unrelievable pain who competently and voluntarily seek a doctor's assistance in ending their lives" [4]. The people eligible for PAS are suffering unimaginable pain and, as the current legislation states in the United States, will die within 6 months. Importantly, people who seek PAS do so "competently and voluntarily," meaning by their own volition and of sound mind in order to be relieved from what can be described as unnecessary suffering. According to one survey regarding reasons patients would chose to pursue PAS, "more than 97 percent of patients cited loss of autonomy…while nearly 89 percent pointed to the inability to engage in enjoyable activities and 75 percent were concerned about losing dignity" as their reasoning for pursuing PAS [5]. PAS is a voluntary decision that patients should be afforded in order to prevent a patient's loss of autonomy, ability to participate in enjoyable activities, and loss of dignity. Denying their ability to choose death in spite of these negative circumstances is denying a citizen's choice, and more specifically, their bodily autonomy.

PAS may soon find codification as a right as a result of a reevaluation of due process as it applies to a right to die. It is apparent that the stakes are high and that emotions and opinions vary immensely; however, arguments riddled with fallacies harm everybody, especially those that are suffering and being prevented from death with dignity. The rights of the American people are potentially being infringed upon with respect to the right to die, and that must be addressed with evidence and logic, not fear.

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Article

Agency and Accountability: Ethical Considerations for Brain-Computer Interfaces

by Erika J. Davidoff †

Brain-computer interfaces (BCIs) are systems in which a user's real-time brain activity is used to control an external device, such as a prosthetic limb. BCIs have great potential for restoring lost motor functions in a wide range of patients. However, this futuristic technology raises several ethical questions, especially concerning the degree of agency a BCI affords its user and the extent to which a BCI user ought to be accountable for actions undertaken via the device. This paper examines issues of limited agency, consent, and malfeasance that are found at each of the three major parts of the BCI system: the sensor that records neural activity, the decoder that converts raw data into usable signals, and the translator that uses these signals to control the movement of an external device. Due to these concerns, BCIs are not currently ethically viable for widespread use; however, by focusing on improving biocompatibility, increasing recording sensitivity, and developing more transparent algorithms, BCIs could become practical, ethical, and life-changing therapeutic options.

Bionic enhancements—artificial body parts that can be controlled directly by their user's brain—have traditionally been considered science fiction. Recent advancements in machine learning and electrode sensitivity have brought these "fictional" devices remarkably close to reality in the form of implantable brain-computer interface (BCI) assistive technology. BCIs use real-time recordings of brain activity to control external devices. For example, this technology has enabled quadriplegics to perform robust seven-dimensional movements with a prosthetic arm and late-stage ALS patients to communicate rapidly using a computer-based

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interface with a BCI-driven cursor, among many other preliminary success stories [1, 2]. The term *BCI* or *brain-computer interface* refers to any system in which neural activity is measured and used to directly control an external device, such as a robotic limb or a cursor on a screen.

With this technology comes a range of ethical concerns, many of which relate to BCI users' capacities for autonomy and self-agency. To understand these concerns, it is important to recognize that the basic BCI paradigm of "using brain signals to control an external device" is, in practice, far less straightforward than it sounds. Accomplishing this goal requires three complex systems: a sensor that records neural activity, a decoding algorithm that turns the raw voltage data into meaningful signals such as the activity of specific neurons, and a translation method that turns these processed signals into movement commands for the external device. Developing each of these systems is an extensive design undertaking in which engineers need to make hundreds of decisions, made more complicated by the ethical issues that arise when considering each process. This paper explores the ethical concerns that need to be addressed by these three systems—the sensor, the decoder, and the translator—and some solutions that have been proposed and implemented by BCI designers.

THE SENSOR

Voluntary muscle movement in humans is regulated by neurons in the motor cortex, a strip of cortical tissue located at the back of the frontal lobe, directly adjacent to the parietal lobe. The motor cortex receives input from several other brain areas such as the prefrontal cortex, sensory cortex, and cerebellum. Neurons in the motor cortex compile all of this input into signals they then transmit to the spinal cord, where motor neurons connecting the spinal cord to muscles throughout the body translate these signals into muscle contractions. Paralysis is typically a result of damage to the spinal cord or disease-induced degradation of motor neurons. Critically, the motor cortex is fully functional in the vast majority of paralysis cases.

BCIs make productive use of this brain function by outfitting the body with new hardware that harnesses the activity in the intact motor cortex to drive an external device, which augments or replaces a missing or paralyzed body part. The first step in this chain of hardware is the sensor that records neuron activity data from the motor cortex. Most intracortical BCIs use arrays of approximately 100 needle-shaped electrodes on a platform about 1/15 the size of a dime, with the tip of each electrode exposed and capable of recording signals [3]. These signals have traditionally been transmitted via subcutaneous wires, but concerns about infection and movement restrictions have led to wireless cortical recording technology [4].

Implanting the BCI sensor into the brain raises the same ethical con-

cerns of balancing *beneficence* (benefitting the patient) and *nonmaleficence* (avoiding harm to the patient) as implanting anything into the body does—specifically, the need to balance the risk of infection and tissue damage with the improved functionality the device could provide. Some biomedical engineers have argued that due to the uncertain longevity of the BCI sensor and the high likelihood of needing repeated surgeries to maintain BCI functionality, implanting a BCI sensor represents an unnecessary and unethical risk to the patient given that non-invasive alternative treatments exist [5]. Others claim that these alternative treatments, which range from electromyographic prosthetic limbs to head-tilt sensors for manipulating a screen, pale in comparison to the improved functionality BCIs offer, and that it would be unethical and unconscionable to deprive millions of people who are unable to fully use their bodies of an opportunity for rapid restoration of function [6]. It is true that invasive BCIs, at this stage of their development, have demonstrated superior performance in giving quadriplegia and ALS patients full control over computer software for communication [2]. They have also enabled patients to control prosthetic arms that have more degrees of freedom than ever before—independent movement of all five fingers, for example, which is not possible with any device currently on the market [7]. It is also true that extensive surgical risks abound for any neurosurgery, including CSF leakage, pulmonary embolisms, hemorrhages, seizures, and infection; studies of deep brain stimulation implantations reveal over 12% of patients experience serious adverse effects [8]. While efforts to reduce these risks are underway, including improved biocompatibility and development of modularity standards [9], patients and their physicians need to carefully weigh the benefits and drawbacks of BCI use. It is easy for both patients and clinicians to want to try the "next greatest thing" as soon as it is available, but it is critical from an ethical perspective to temper this excitement with a realistic evaluation of safer treatment possibilities that are already established in the market.

Related to this is the need to ensure full patient agency, as well as a high sense of agency, in acquiring consent for treatment with a BCI. Here, *agency* refers to a person's power to exercise control over their thoughts and movements and produce their desired or intended results, while *sense of agency* refers to a person's feeling that they are in control of their actions. Many potential BCI patients suffer from diseases such as ALS or Parkinson's disease which, in some cases, are comorbid with dementia and other cognitive deficiencies; even if they do not present these symptoms at the onset of treatment, they may develop them over the course of treatment, rendering them unable to provide continuous informed consent. In addition, implanting any device in the brain has the potential to disrupt an individual's identity or sense of self in unpredictable ways [10]; this has been documented in deep brain stimulation and must always be a consideration, though it may be less

likely to occur with a motor cortex implant since the motor cortex is not a brain region typically associated with identity, sense of self, or other higher cognitive functions. Ensuring full decision-making capacity and confirming consent at each stage of the BCI treatment process is critical for preserving users' agency and autonomy.

Other ethical concerns about the sensor hardware relate to its durability and longevity. Human tissues have pre-programmed reactions to the insertion of any non-native object; this is known as *foreign body response*. In the brain, foreign body response manifests as inflammation within the first two weeks after implantation of a foreign device, followed by the continual activation of glial cells that form scar tissue around the implant [11]. As the glial scar builds up, it insulates the electrode and pushes neurons further from its surface, diminishing the electrode's effectiveness. The electrodes are also subject to corrosion, cracking, and other material failures, as well as mechanical failures such as wire damage or dislodgement of the electrode by external forces, which might happen if the user were to fall. These effects combined contribute to one-year microelectrode failure rates that can exceed 50% [12]. Microelectrode failure causes the BCI to malfunction and even completely cease functioning, negating all benefits of BCI implantation; it also leaves patients with scarring in the brain that can lead to further tissue damage. Putting a patient through the rigors of device implantation and training is perhaps ethically questionable given how likely sensor failure is and how devastating the subsequent loss of restored function could be. The only way to ameliorate this ethical burden could be to reduce the device failure rate. Fortunately, research into improving the biocompatibility and longevity of neural implants is well underway [13]. This work is focused on improving the material properties of implants and designing features such as hydrogel coatings and bioactive interfaces to reduce the intensity of the foreign body response.

THE DECODER

The 4x4x0.05 mm volume of brain tissue surrounding the exposed electrode tips of the Utah array contains about 24,000 neurons and half a billion synapses [14], yet all of this activity is captured by only about 100 electrodes. Each electrode can only clearly record from neurons that are within ~0.05 mm of the electrode tip—which is, on average, 3.4 neurons per electrode [15]—so only about 340 neurons, or ~1.5% of the neurons in the array's theoretical volume, are recorded with enough clarity to isolate their action potentials. This represents an extremely small percentage of the population of neurons that would normally contribute to generating movements. The rest of the nearby neurons contribute to background noise in the electrode recordings, so raw microelectrode data is notoriously noisy. The decoder al-

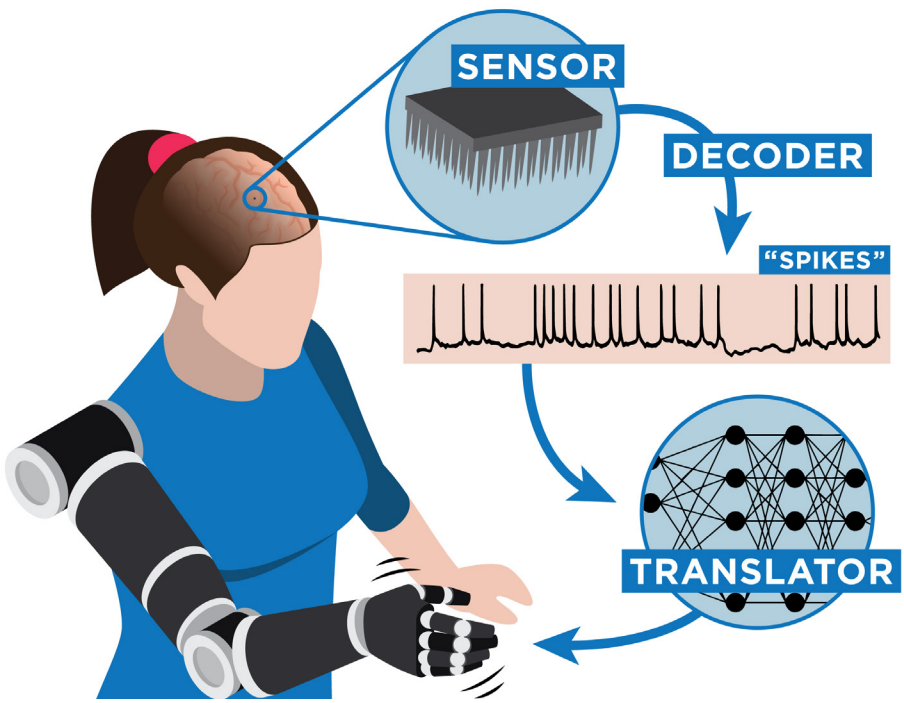
gorithm, which extracts these 340 action potentials from the background noise of thousands of other neurons and converts it into a single output command, represents a serious challenge both technically and ethically. In employing such an algorithm, engineers are claiming that their processing of this small neuron population can accurately represent the activity of the many thousands of neurons that typically generate movement commands, and precise enough that it should be allowed to control a prosthetic device that most would consider to be an extension of its user's body. The ability to do this, from both a technical and ethical perspective, requires a highly accurate decoder in order to capture a person's motor agency via recordings of a small fraction of their relevant neurons.

Neurons communicate with each other and with other cells via action potentials, rapid changes in voltage across the cell's membrane that propagate down the cell. Action potentials are recorded as sinusoidal voltage fluctuations over time which, when converted to the frequency domain, show up as "spikes." From there, assigning the spikes associated with each time step of the recording to particular neurons is essentially a massive linear algebra problem, which is simplified in part by thresholding operations that enable a spike to be counted and analyzed regardless of any drifts in amplitude that can arise from sub-micrometer movements of the electrode relative to the neuron [16]. Only very recently have algorithms strong enough to perform this analysis without human manual verification emerged; the current state of the art has sensitivity and precision both around 95%, which it achieves by breaking down the recordings into smaller samples from about 9 electrodes each and randomly selecting only 50,000 spikes from each sample [17].

Since neuron spikes have a duration of <1 ms, the sampling rate of the electrode must exceed 10 kHz (10,000 samples a second) in order to ensure spike activity is captured. This requires a large amount of energy and makes the system very sensitive to tiny movements of the electrodes relative to the neurons, which inevitably happens due to micromotion in brain tissue from respiration and blood circulation. As such, some researchers have shifted focus to local field potentials (LFPs)—summations of velocity changes in areas exceeding 0.2 mm around each electrode type—instead of relying on spike activity. LFPs are commonly referred to as alpha, beta, and gamma waves and can be recorded using sampling rates less than 100 Hz (100 samples a second). This is promising for reducing energy load and extending the life of the BCI device. However, a major practical and ethical concern is that the precise origin of these LFP signals is, as of yet, unknown [18]. While it is clear that spikes arise from neurons firing action potentials, lower-frequency LFP signals likely reflect many different underlying processes and it is entirely unclear which of these processes relate to volitional movement control. Despite this, a recent primate study showed that LFP data can

provide information about monkeys' reach targets almost as accurately as neuron spikes; combining the two types of data also results in significantly improved accuracy than using either alone [19]. Perhaps the ethical burden of the LFPs' unclear origin can be reduced by only using this data as a supplement to spike data.

To summarize all of the technical information thus far, BCIs record information from a 4x4x0.05 mm volume within the users' primary motor cortex. This information can consist of discrete action potentials from about 340 of the neurons within this volume as well as changes in low-frequency signals, which have no specific or known origin, throughout the volume. This is all of the data available for the translator to use to evoke motion in the prosthetic device. Compared to the amount of data the brain normally has at its disposal—signals from the whole 30,000 neurons/mm^3 in a motor cortex that is roughly 2 cm wide and 2.5 mm thick, plus the millions of neurons in other brain regions that are also involved in movement planning and execution—this is miniscule. Is it ethical for BCI engineers to claim that their devices accurately reflect their users' brain state when they are only recording such a small percentage of it? Relatedly, is it ethical for BCI users to be held accountable for actions performed via the prosthetic device if those actions do not reflect their complete current brain state? Before diving deeper into these questions, let us take a closer look at how the translator turns these decoded signals into actual movements.



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THE TRANSLATOR

The translator is an algorithm that turns the signal extracted by the decoder into commands for the BCI external device, which, in present applications, is generally either a prosthetic limb or an interface for communicating, such as a computer application in which the BCI user controls a cursor on the screen to select and type words. The translator is essentially a large matrix of constants called a linear filter that, when multiplied by a matrix of recorded neuron firing rates, produces velocities that are imparted onto the BCI device.

One critical aspect of the translator is the calibration process, which is how the constants in the linear filter are determined. To calibrate the BCI, users are first asked to imagine moving a cursor on a screen while their neural activity is recorded. As an aid, the user is shown a screen on which a technician moves a cursor systematically through visual targets. These initial recordings "seed" the translator with the first version of the filter, generating a user-controlled cursor on the screen [20]. The user then undergoes several sessions in which they manipulate their cursor to match the technician's cursor. After each session, the linear filter is updated to more accurately synchronize its predicted cursor velocities with the actual cursor velocities the user achieved [21]. The process for calibrating a prosthetic limb is similar, with the participant watching a limb making pre-recorded movements during the initial imagining step and then gaining control of the limb and operating it with gradually less error attenuation [20].

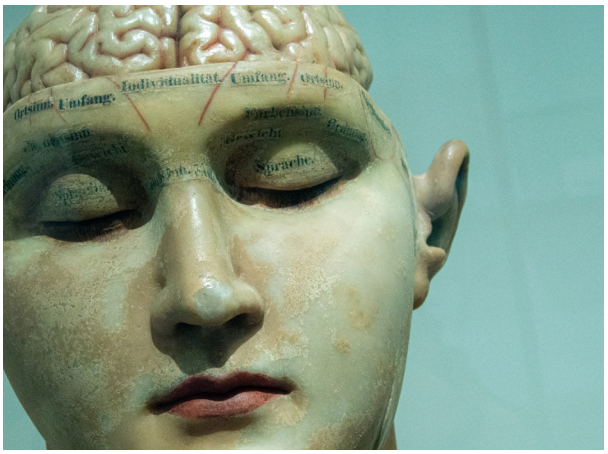
This calibration technique raises an interesting ethical point related to user agency. During the training process, especially early on, much of the movement of the BCI device is controlled by a technician or by a computer and not by the user. Despite this, it is possible for the user to experience a sense of agency over the device. This effect has been investigated in more detail in an experiment in which users were connected to an EEG system and told that their EEG signals were going to be used to control the gestures of a virtual hand [22]. They were given a live feed of their EEG signals, shown how their brain activity affected the hand, and instructed to follow the commands of the facilitator to give one of two simple gestures. However, the virtual hand movements they observed were pre-recorded, conforming to the instructions with a 90% success rate, and had nothing to do with their EEG signals. Despite this, when asked to rate their sense of control of the hand on a scale of 1-7, participants gave an average rating of 5.0. It is ethically concerning that BCI users can potentially have this high a sense of agency when they actually have no agency at all.

In calibrating actual BCIs, of course, users are gradually given full control over the devices. However, this only reinforces the user's sense of agency, and could well lead to users judging themselves as the originators of actions

that their BCI device performed even if these actions do not reflect their mental state. This can affect the BCI user beyond the simple consequences of the mistaken action. Imagine, for example, that Erin, an upper limb amputee who uses a BCI to control a prosthetic hand, goes to shake an executive's hand at a dinner party; her hand, for whatever reason (inconsistent calibration, lack of recording from the appropriate neurons, etc.), grips the executive's hand far too tightly and seriously injures it. Not only is this a major problem for the executive, but Erin is also horrified and feels extremely guilty. She may or may not be legally responsible for the injury, but she certainly feels personally responsible for it—it was, after all, done by her own hand that she has worked with and lived with for years. This greatly affects her emotional state and is bound to affect her personal and professional life; it may also affect her legally and financially. Multiple people are negatively affected despite none of them having any malicious intent—this is clearly an ethically reprehensible situation. Yet without her BCI, Erin would lack the fine motor control that enables her to perform her job and manage other aspects of her full life, and putting her at a serious disadvantage. Is having this device worth the risk of it failing to operate properly? The answer is unclear, but reducing the potential for failure would certainly increase the viability of BCI use.

Linear filter methods produce movement accuracy of about 80%, which is excellent in a laboratory setting but not enough to make these devices viable for constant everyday use, especially considering the possibility of cases like Erin's. To improve calibration and therefore improve integration of the BCI with its user, BCI researchers have begun turning to deep learning. A deep learning algorithm is a series of neural networks—pattern-recognition algorithms that categorize raw data based on its features. Neural networks are made up of interconnected nodes, each of which has a set of weights it assigns to features of the input data. Based on the sum of these weights, the node turns either on or off. The final state of the nodes corresponds to the network's classification for the data. Neural networks are used today in thousands of applications, such as identifying objects in images, distinguishing spam emails from non-spam emails, and recognizing emotions portrayed in photos of faces. In order to do any of these tasks, neural networks must be trained with a labeled dataset—a series of images labeled with the objects in them, for example, or a set of emails pre-sorted into spam or non-spam. The network attempts to sort the data into the correct categories, checks its answers against the input labels, and adjusts weights to minimize error between its answers and the input labels. The network repeats this process many times to approach a final steady state. Deep learning uses several layers of neural networks to produce more precise, fine-tuned predictions. In the context of BCIs, a deep learning translator algorithm can be trained using

neural activity labeled for a certain movement or other device output. The translator would then be able to convert new neural signals into the corresponding appropriate movements.



Matos, D. (2019). *Human anatomy model.* Photograph. Retrieved from https://unsplash.com/photos/xtLIgpytpck.

Though deep learning translators are more accurate than linear filters [23], they raise considerable ethical issues around who or what is ultimately accountable for the device's actions. With linear filters, operators know that the nodes being filtered correspond to individual neural signals; the algorithm is a fairly straightforward conversion from signal to output, and it is possible to look at the individual components of the algorithm's output and trace them back to particular signals. This is not the case with deep learning, where the weights and nodes have no physical counterpart and are defined with no operator input. Deep learning BCIs insert another "black box" into the already complex task of converting neural input into actionable output, which is troubling in terms of user accountability. Not only are the user's intentions derived in a BCI from a miniscule subset of their overall activity, but the algorithm that converts this activity to device action is obscure and virtually impossible to explain, as networks with a large number of nodes can be as complicated as an actual human brain [24]. This makes it difficult to definitively ascribe blame to a user if the BCI device acts contrary to the user's intentions.

There is an argument, however, that this ultimately does not matter in terms of accountability [25]. A BCI, after all, is essentially a tool, and most people use tools like cars and computers every day without knowing exactly how they work. In the same way that people would not use a computer if it constantly crashed and would not drive a car if the steering wheel often locked, people would not use a BCI if it did not work the way the user intended the vast majority of the time. By choosing to use the device, the user accepts responsibility for it in much the same way a driver is responsible for their car, and rare occurrences of BCI malfunction can be treated the same way rare automobile malfunctions are treated. Though it may be impossible to get a perfect analysis of exactly what caused the event, it is typically pos-

sible to determine whether the driver should be held accountable. The same logic can be applicable to accidents caused by BCI use or misuse.

A substantive difference between controlling a car and controlling a BCI, however, is that one is done with the body and the other is done with the mind. Barring medical conditions like epilepsy and paralysis, people have near-complete control of their limbs and it is valid to assume that the movements a person makes with their body are those they intended to make. Conversely, people have no experience controlling objects with their minds. To a large extent, people do not have control over their thoughts. Though it is of course possible to actively think about something in particular, thoughts often arise from the subconscious without willful intent, and some researchers have gone so far as to suggest that the vast majority or even all of our conscious thoughts are non-consciously generated [26]. BCI sensors likely have access to activity generated by these subconscious processes, and this activity may well contribute to driving the action of the external device. It is probably true that subconscious activity affects movement in able-bodied people's limbs; however, most people seem to have the ability to override any unwanted effects and generally feel in complete control of their bodies' movement. It is unclear whether this override ability is rapid enough to prevent unwanted subconscious activity from affecting device movement. Even if it is, the sheer amount and intensity of noise in the sensor's recorded signal likely means that neural activity unrelated to movement will be fed to the decoder and translator, where it may be interpreted into movements that contradict the user's intentions. Should BCI users be held accountable for the translated outcome of their subconscious neural activity despite their lack of control over that activity?

When considering this question, it is also important to remember that BCI users are controlling their device with only a few hundred out of billions of neurons in their brain. This is something like trying to navigate a car through an 0.35 mm square hole in a blacked-out windshield (for reference, a human hair is about 0.1 mm thick). Until a larger percentage of brain activity can be captured and recorded, it seems disingenuous to presume that a user should or will have full agency over their device—and without having agency, it cannot be ethically sound to assign accountability to the user.

CONCLUSION

Brain-computer interfaces are a promising and exciting technology, but they are not yet developed enough to be used outside of strictly controlled clinical trials. Improvements to BCI technology should focus on increasing implant biocompatibility, expanding recording capability and sensitivity, further refining calibration technology, establishing calibration techniques for continual device adaptation and learning throughout use, and reducing surgical

risks. From a basic research standpoint, more knowledge on LFPs and the impact of subconscious thought on neural recordings would be useful in making more efficient and accurate decoders. There is also a lot of potential for algorithm improvement, both in decoding raw neural signals and in calibration and translation processes. These improvements will help alleviate the ethical concerns related to agency, accountability, and safety that make BCIs currently untenable.

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Article

The Fertility Industry: A Dangerously Untouched Market in Health Care

by Caleigh Propes †

The fertility industry is experiencing an unprecedented boom in growth in recent years, with an especially pronounced increase in in vitro fertilization procedures and other assisted reproductive techniques. While these fertility services provide patients with highly meaningful additional means to procreate, the scant regulation of the market poses safety and accessibility threats to consumers. Moving forward, increased oversight by entities like the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology, along with robust state legislation governing clinical standards, will act to increase the safety of these procedures. Other legislative reforms could also increase access to fertility services, lowering the barrier to entry for patients wishing to conceive.

Infertility is a medical condition that individuals and couples face when trying to conceive a child naturally and can be defined as the inability to conceive after twelve full months of unprotected intercourse without pregnancy. According to the National Survey of Family Growth, about twelve percent of couples experience difficulty in conceiving or sustaining a pregnancy in the United States, and 7.4 million women (or 11.9%) have sought out infertility services during their lifetimes. After six months of attempts, only about two-thirds of couples can conceive without any type of medical intervention [1]. Age is one of the risk factors that increases the chance of infertility. Today, many women are waiting until later in their lives to have children, increasing the demand for infertility services [2]. This means that "fertility is one of the fastest growing areas in medicine" [3].

Despite the industry's huge potential for growth, a lack of regulation and

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unsafe practices are commonplace, making these procedures more dangerous for couples wishing to conceive. While some states have laws regulating fertility benefits, there is no nationwide consensus on how these practices should be handled. More federal oversight of the industry, as well as an increase in self-regulation of the market by professional organizations and private insurers, will be critical in moving towards a safer and more equitable future of the industry.

BACKGROUND OF THE FERTILITY INDUSTRY

The most commonly used infertility services among women are counseling services, testing, help in preventing miscarriage, and ovulation-inducing drugs [4]. Other treatments, such as in vitro fertilization (IVF), frozen embryo transfer (FET), and intracytoplasmic sperm injection (ICSI), are more expensive, but they are also more effective for women and their partners who face infertility. It is clear that there is an access issue with infertility benefits in that the women who are most likely to receive these services are of relatively advantaged status. It seems that more disadvantaged groups may be precluded from receiving infertility services due to the high cost of these services and the lack of adequate health insurance to offset these high costs. Women who receive infertility services are also much more likely to be married, non-Hispanic white, educated, and more affluent than the general population [4].

The use of Assisted Reproductive Technologies (ART) has increased since data collection on these techniques began in 1996. ART encompasses all procedures that handle both the sperm and the egg, such as in vitro fertilization (IVF). IVF is a procedure in which a woman's eggs are extracted, fertilized in a laboratory, then transferred back into the woman's uterus. With the rate of successful births done in fertility clinics having risen three times since 1966, it is noticeable that ART is a rapidly developing field [5]. The use of IVF alone has increased, with over 2,000 more babies born from IVF in 2012 than in 2011 alone [6], it is the most widely used ART [7].

REGULATION OF INFERTILITY SERVICES

In general, the fertility industry has been largely untouched by legislators. There are currently 15 states that mandate the provision of some fertility benefits [8]. However, there is little federal involvement with issues of fertility treatment and research, which has led to the development of an incredibly unregulated market and created dangerous environments for patients. It is likely that federal support for treatments like IVF would make the industry safer, as there would be more regulatory measures in place to monitor the quality of care delivered in fertility clinics. However, the federal government's demonstrated apathy has led to an industry that receives mostly

private dollars and experiments on men and women for profit. This is important given that the industry raked in about 25 billion USD in 2018, and this revenue is projected to grow to about $40 billion by 2026 [9].

There is only one piece of legislation concerning fertility clinics, the Fertility Clinic Success Rate and Certification Act of 1992. This act requires fertility clinics to report their pregnancy success rates to the Centers for Disease Control. However, the act does not set forth specific guidelines or consequences to nondisclosure and has had little effect on the industry as a whole [10]. It seems that the only real penalty is that the clinics that are noncompliant are published in the CDC's annual report as not having reported their data. Each year, about 12% of clinics fail to report to the CDC [11], yet are still allowed to provide infertility treatments [3]. The data that clinics report to the CDC can also be inflated or misleading. For instance, some clinics reported numbers of pregnancy success rates in women under 38 years of age, as older women see less success in pregnancy via ART [12]. Also, some clinics did not report the outcomes of prematurely terminated pregnancies or complicated deliveries, giving the clinics inflated success rates [11]. So although the law makes an attempt at regulation, the data that comes from the legislation is imperfect and does not meaningfully contribute to patients' decisions in choosing fertility clinics.

States have their own standards for the practices that fertility clinics must follow, but there exists a large degree of variation. For example, Louisiana has established minimum guidelines for clinics wishing to provide IVF services, and Pennsylvania requires that clinics file quarterly disclosure reports that are publicly accessible [10]. However, it seems that these types of policies are "the exception rather the rule" [3]. These guidelines, which are few and far in between anyway, do not go far enough in ensuring patient safety. State regulation is a major way in which these clinics could be held accountable for their actions, and the lack of consistent standards across states creates room for error. In addition to the state regulation that exists, there is a degree of self-regulation within the industry through professional organizations such as the Society for Assisted Reproductive Technology (SART) and the American Society for Reproductive Medicine (ASRM). The ASRM is the main body that oversees fertility treatments while SART is an affiliated body that more specifically handles IVF and other assisted reproductive technologies. For one example of this self-regulation, the ASRM released a set of CDC-compliant guidelines for its member clinics to follow. However, the only penalty from not abiding by the guidelines is the removal of membership from the organization, not from delivering treatment on the whole [6]. SART collects data from its member clinics, and in addition to the clinics that chose not to report, 28.1% of clinics reported with an incomplete data set [12]. So while there is a degree of legitimacy at stake for clinics with

regards to following regulations and inclusion in professional organizations, there is no comprehensive check on the actions of the clinics as they may still operate without meeting the guidelines of either the federal government or professional organizations such as ASRM and SART.

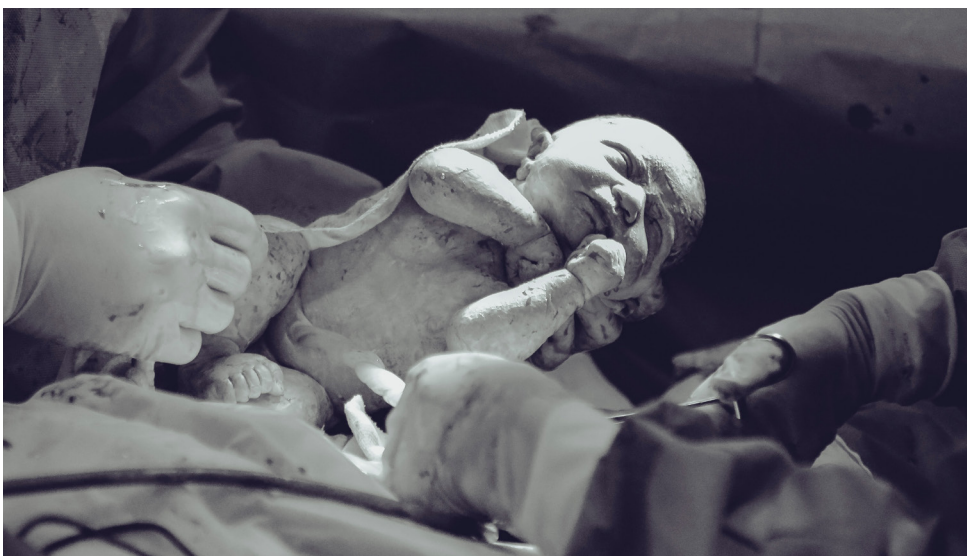
ASRM and SART can play a valuable role in regulating assisted reproductive technologies, as self-regulation can adopt an "education and correction" approach rather than a more paternalistic and inflexible regulatory measure put in place by federal or state governments. In medicine, these kinds of self-regulatory groups tend to foster innovation among new technologies as the barriers are lower to their creation [3]. There are, however, a few specific problems with the current framework. First, checks on clinic participation in the reporting and safety measures only occur every three years. This industry is rapidly advancing, and this time provides a big enough window for noncompliant or unethical behavior. Additionally, not all clinics are members of either the ASRM or SART, the self-regulating group. Even if a clinic is not a member or has their membership revoked, it may still function with little oversight and offer treatments to patients [13]. A lack of full-scale implementation of standards and accountability for clinics leaves the fertility industry largely under-regulated.

EFFECTS OF LACK OF REGULATION

While ART encompasses viable methods that allow women the option of childbirth, the deliveries of babies conceived via ART face more complicated circumstances. One of the most dangerous results of ART procedures is carrying a multiple-birth pregnancy (more than one fertilized egg) to term. Women who undergo IVF or ICSI are also significantly more likely to have preterm births and longer periods of hospitalization. This is largely due to the increased proportion of multiple-birth deliveries. Older women especially have a higher risk of multiple births, as they routinely attempt to have more eggs fertilized during IVF because their chance of success is lower. According to CDC survey results, 8 in 10 fertility clinics routinely fertilize multiple eggs at once [4]. In the United States, only about 73.5% of all births from IVF were singleton deliveries; this number is much lower than the average of a collection of European countries, where the singleton delivery rate from IVF was 82.1%. This discrepancy can be attributed to U.S. clinics' participation in the risky fertilization of multiple eggs at once [5]. This is a clear indication that a lack of standard safety guidelines causes U.S. women to be more likely to carry multiple-birth pregnancies. However, even the average singleton birth from IVF is more likely to be hospitalized than non-IVF singleton births [14]. ART also accounts for a disproportionately high number of low birth weight and birth rate deliveries in the United States [15]. These factors, in combination, make ART relatively unsafe in the United States

as compared to both traditional childbirth and outcomes in other nations where the fertility industry is more highly regulated.

Other flaws within the fertility industry contribute to complicated deliveries and poor outcomes. One of the most concerning practices of this "wild west" fertility industry is that clinics are performing procedures on patients and their reproductive material without evidence of the procedures' safety and long-term results. Instead of amassing data on the effectiveness of the procedures through clinical trials, the clinics use their patients as test subjects, putting both the patients and their potential offspring at risk. For example, in 2010, 283 of 442 surveyed fertility clinics were offering the egg freezing procedure even though at the time its status was labeled as "experimental" [16]. Within the private sector, technology companies such as Apple and Facebook have provided benefits such as egg freezing to their employees after it was no longer deemed experimental, increasing awareness and demand for the procedure. However, even though the egg freezing procedure is no longer experimental, that does not mean it is safe for widespread adoption. The ASRM stated that they "cannot at this time endorse its widespread elective use to delay childbearing," and the organization's motivations for removing the experimental label was to allow women who face chronic illness or other medical problems access to the procedure, not for healthy women to use the procedure as a kind of insurance that would allow for later childbirth [6]. Regardless of this statement of warning from the ASRM that the procedure should only be for women with severe indications that make the procedure more necessary, many fertility clinics still offer egg freezing to



Balielo Jr., V. (2014). *Grayscale photography of unknown person carrying newborn baby.* Photograph. Retrieved from https://www.pexels.com/photo/monochrome-photo-of-newly-born-baby-3376793.

their patients and are even incentivized to offer the service as more insurers cover it on their private plans and more companies elect to include these procedures in their benefit packages.

Besides egg freezing, some other ART therapies also have not been proven to be particularly safe or effective, or used in best practice. Intracytoplasmic sperm injection (ICSI) is a method in which a sperm is directly injected into an egg; this method helps with issues of male infertility. Currently, ICSI is being used in around a third of IVF cycles, even when male fertility is not a contributing factor in the couple's infertility. Moreover, there are questions about the effects of this method on the developing fetus. There are concerns of congenital abnormalities, epigenetic syndromes, and dangerous multiple births [17]. Nevertheless, fertility clinics still continue to offer this procedure as one of the most effective treatments of male infertility and as a procedure to be coupled with IVF. Even with its effectiveness, the potential for harm to the child raises ethical questions about the fertility clinics' ability to offer services. Even if patients elect to have experimental procedures, there are questions as to whether or not they can actually give meaningful consent. New procedures such as egg-freezing have inconclusive long-term effects on a woman's body. It is possible that developing an idea of the relevant risks associated with a certain procedure could take years. In this context, it is hard for a woman to consent to egg-freezing as she does not know the associated risks and benefits to their full extent [18]. The same is true for other procedures such as ICSI, as the definitive long-term health risks have not been properly evaluated. Operating on patients without fully informed consent poses risks for fertility clinics in avoiding instances of malpractice and unethical behavior.

MARKETING OF FERTILITY SERVICES

Another pernicious effect of the lack of regulation is the way that the industry advertises its procedures and the general lack of compliance to the little regulation that does exist. The Federal Trade Commission requires that clinics that post their success rates online also post the way in which they calculated their success rate. Of 193 clinics registered with SART that advertised their success rates, only 62.18% of clinics stated the way they derived them. Many clinics also make statements of comparison for advertisement, and SART dictates that the only allowable comparisons use national averages generated by SART. Of SART member clinics that used comparison statements in their online advertising, only 34.30% of clinics followed this guideline. The most flagrant violations of the rules against comparison came from clinics who compared themselves to others in their region, directly violating the ASRM guideline that "Comparison of success rates between and among practices is invalid" [19]. These insidious advertising practices

that have not been punished by the FTC or SART further complicates the problems associated with fertility industry as it becomes riddled with information inaccuracies and asymmetries.

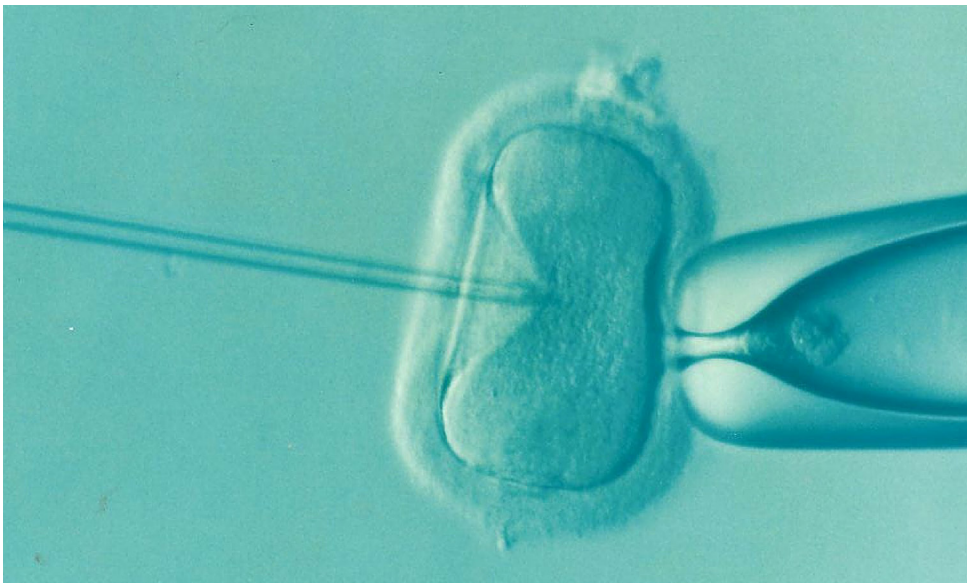
Adverse advertising practices can also contribute to unethical downstream effects in the industry; many scholars think that there is a lack of access to fertility services in minority communities, which is consistent with the findings that 62.93% of clinics only advertise with white babies, and 97.28% of clinics advertise with some white babies. The industry has a homogeneous market as a result of factors like these advertising techniques and the general racial gaps in health care access. By only advertising to majority white patients and making procedures cost-prohibitive, ART procedures exclude lower-income, uninsured or underinsured, and minority patients. In addition, only 2.14% of reproductive endocrinologists at clinics were black, and 4.27% were Latino, representing an obvious dearth in the proportion of minority physicians in the fertility industry. These issues come with the heavy price tags that the procedures carry. While there are obvious barriers to access of treatment here, there is a parallel problem in that married non-Hispanic black women are almost twice as likely to be infertile as married white women due to genetic predispositions [4]. So given that minority couples need treatment to a larger degree than white couples, a lack of regulation in the industry has taken away the opportunity for more widespread access that comes with federal support and funding.

INSURANCE COVERAGE OF ART BY STATES AND EMPLOYERS

Of the fifteen states that have mandates concerning infertility benefits, thirteen of the states require that insurers cover infertility benefits, and two states (California and Texas) have laws that require insurers to offer infertility benefits. However, these laws differ slightly in their scope. Most states include coverage of IVF as it is a standard ART procedure, but Louisiana, California, and New York exclude IVF treatment from their mandated list of covered infertility treatments. Some states go even further in that employers can receive exemptions from covering the fertility benefits if they violate certain religious beliefs [10].

On the other hand, some employers provide infertility benefits in their insurance coverage in order to make the process of childbearing more accessible to infertile employees. However, only about 25% of employers are currently providing these benefits [7]. Even in states where infertility treatments are covered, not all employers are required to provide these benefits to their employees. Under the Employee Retirement Income Security Act (ERISA), employers that offer self-insured plans, meaning that they directly insure their employees, are exempt from state requirements that regulate insurance. The majority of employees covered by insurance are at least

partially self-insured, meaning that a large number of employees that could benefit from mandated infertility benefit offerings are denied coverage [7]. The major pushback from insurers is that providing infertility benefits will be very costly. However, in Massachusetts, the state with the most robust infertility benefits, the monthly cost of these benefits was only $0.26, or about 0.1% of a total family health insurance plan [20]. The incidence of infertility is relatively constant among the population as a whole, so it is unlikely that this figure would rise to an extreme cost after the treatments become available to a wider audience. Even if the utilization rate of IVF rose by 300%, the expected cost per month per patient insured would only see a $9 increase in premiums each year [7]. Overall, many employers opt out of providing infertility benefits under the misguided notion that the cost will be crippling to their bottom lines. This notion is simply untrue, and the projected increase in premiums is minimal in comparison to the number of patients that would benefit from these services.



Kontogianni, E. (2016). *In vitro fertilization.* Photograph. Retrieved from https://pixabay.com/photos/ivf-fertility-infertility-icsi-1514174.

Aside from the affordability of these benefits, states may also save money by mandating infertility benefits in their insurance plans. State regulation mandating that infertility benefits be covered decreases the instance of multiple births from infertility treatments, as cited by a study in the *New England Journal of Medicine* focusing on states that mandate coverage of IVF [21]. The average cost of a cycle of IVF is $12,000, and the associated medications add another $3,000 to $5,000 to the total [4]. For infertile couples that wish to have a child, this can be a hefty price, so women will agree to the transfer of multiple fertilized eggs in hopes that the success rate will be higher

and the couple will not have to pay for additional treatments. However, this may actually cause higher medical costs down the road, as multiple births can be a significant financial burden along with the heightened risk of low birth weights and hospitalization that comes with IVF. More widespread access would prevent the woman from riskily implanting multiple embryos through insurance limitations, as successive rounds of IVF would be covered by insurance [21]. Decreasing the instance of multiple births would actually lower the cost of health insurance, as the cost of delivering twins is four times as high as that of a normal birth, and delivering triplets is about eleven times as high as a normal birth. About 34% of all births resulting from ART are multiple births as compared to 3% in the general population, imposing a significant drain on the health care system in the U.S. as these adverse events drive up the cost of care and expend unnecessary resources in trying to accommodate for the riskier multiple-birth pregnancies [7].

While there is significant utility in providing these benefits through insurance plans, opponents have pushed back on the idea that fertile individuals should have to pay for infertile individuals through their increased premiums. Infertility is a disability that is covered under the Americans with Disabilities Act according to United States Supreme Court case *Bragdon v. Abbott*, meaning that there is precedent for recognizing the condition in the field of medicine to be eligible for insurance as it is considered a "major life activity" [22]. The concept of insurance acts to pool risk among a large group of people to subsidize those who are sick, meaning that fertility should be treated as any other disability or malady [10]. As aforementioned, mandating the coverage of these benefits would not raise premiums to a significant extent, and may even lower overall costs.

ROOM FOR FUTURE REFORM

The current state of fertility clinics leaves too much at risk—patients are opting for experimental treatments without knowledge of their long-term side effects, women are facing dangerous and costly multiple births at elevated rates, and clinics fail to be punished for noncompliance with industry standards. The only two sources of regulation for the fertility market are the ASRM, which also includes SART, and a small fraction of state legislatures. In order to make this industry safer and more accessible for consumers, the way clinics operate must be reformed.

The ASRM and SART have enormous potential for self-regulation of the market by enforcing and strengthening their guidelines for clinics while especially considering socioeconomic and racial inequities that exist in the industry. However, the consequences for not following both federal and ASRM guidelines must be of a greater magnitude and more enforceable. Instead of merely marking that a clinic did not report data, following a model

that shuts down noncompliant clinics would be a step towards safer patient outcomes, rather than let these clinics continue to operate. In addition, the self-regulatory power of the ASRM should allow the organization to make changes that will work toward an increase in accessibility to infertility benefits. The ASRM should institute additional guidelines that advertisements online work to increase access amongst racial groups, including representing diverse individuals and children on clinic websites and other advertisements. This idea is similar to the Fair Housing Act which can allow courts to require rental businesses to include diverse individuals in their advertising after instances of discriminatory rental practices [19]. In addition to just advertising, supporting and hiring people of color to serve as physicians is critical in making the sector more equitable.

In addition to self-regulatory groups, private employers have a lot of power to dictate the importance of infertility benefits, especially if they are self-insured. Not only does ERISA allow them to be exempt from state plans, it also allows employers to set a precedent for best practices in health care by specifically choosing the way in which the infertility benefits are distributed. Many employers are changing the way that eligibility for fertility procedures is decided. For instance, Gusto was the first company to provide infertility treatments to employees without requiring an initial diagnosis of infertility, which was monumental for homosexual and untraditional couples, as well as single women who wish to have children. Many states have laws indicating that you must be married or have a diagnosis of infertility for the procedures to be covered; still, more businesses are beginning to offer these benefits in a more open and accommodating way for all of their employees, which could change the status quo for state regulation down the road. In addition, private insurers have the option of not covering certain risky procedures, causing clinics to back away from those procedures in favor of completing those that are covered by insurance and more likely to have a higher volume of patients. As self-insured companies increasingly include infertility treatment in their plans for their employees, this ability to shape the fertility industry is another key tool that does not require government regulation and still allows for flexibility and innovation.

Finally, government regulation could be useful in the fertility industry. Some scholars recommend an approach that both sanctions physicians who transfer multiple fertilized embryos and creates a separate regulatory body that is specifically for ART [3]. Other European nations such as Denmark, Switzerland, and Sweden have set a limit at three transferred embryos at one time, and the United Kingdom only allows the transfer of two embryos. A similar framework in the United States would promote an uptick in singleton births to put the United States on par with European nations in the reduction of multiple births [11]. Recently, the creation of a governing body

for ART has been the focus of debate, as scholars cite that the CDC has limited resources and capability to handle issues of fertility, and that the FDA already concerns itself with a large number of tasks and is more focused on the efficacy of products than the morality of procedures. Finally, states can begin to adopt policies that make clinics abide by CDC and ASRM guidelines more thoroughly and expand their regulatory measures to make them more inclusive to minorities and non-traditional couples. As more states adopt legislation concerning ART, it is likely that the prospect of insurer coverage of the procedures will be more common, driving costs down as women feel less pressure to undergo dangerous procedures and put themselves in positions where they must complete costly multiple birth deliveries.

CONCLUSION

Infertility is a problem that plagues millions of Americans, and assisted reproductive technologies have been invaluable for providing the basic human desire of raising a family to many that would not have been capable otherwise. However, the industry is fraught with questionable practices due to a lack of government and self-regulatory organization oversight. This has left many wishing to conceive without access to fertility benefits, especially in states that do not cover or offer benefits as a necessary part of insurance plans. The ASRM and its partner organization SART serve as useful tools for self-regulation, although their full potential to enforce safety standards within the industry has yet to be realized. Increasing the power of these organizations, along with private insurers choosing to offer equitable and safe benefits to their customers, will be important going forward as the industry continues to grow. Eventually, the U.S. may come to have a system that is regulated more heavily by state governments and covers free infertility treatment to all patients, with fewer barriers to entry and less dangerous outcomes for mothers and their future children.

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Article

Overdiagnosis in Breast Cancer Screening: How a Population Level Bioethics Perspective Can Improve Public Health

by Sofia Barnes-Horowitz †

Excessive screening for breast cancer is a common practice in the United States and often leads to the overdiagnosis of many minimal, non-lethal tumors which cause a multitude of potential harms for patients without reducing breast cancer mortality rates. The issue is increasingly complicated given the current health policy climate: patients are frequently deferred to by their physicians for complicated healthcare decision-making, there is a negative public perception of "rationing" care, and unbiased comparative effectiveness research is not widely disseminated. With these factors and more interacting, the conversation surrounding breast cancer screening can be reframed to focus on a public health perspective instead of an individual one. This would make it easier to see how the system is harming instead of helping and ultimately better protect the health of American women.

The primary claim of this paper is that framing the American approach to breast cancer screening should place more emphasis on a population-level bioethics perspective than an individual perspective. To use scholars and medical ethicists Wikler and Brock's definition in the chapter "Population-Level Bioethics: Mapping a New Agenda" of their book *Ethics, Prevention, and Public Health*, population-level bioethics focuses on the health of groups rather than individuals and "includes consideration not only of health care but also of other social determinants of health, including socio-economic standing, environmental and working conditions, and social exclusion. Its subject… is health rather than healthcare alone" [1]. It is only through a population-level bioethics perspective

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that we can begin to assess more clearly and broadly the problems that excessive screening and subsequent overdiagnosis pose as well as the factors that have led to its prevalence. The current individualistic approach ignores the multitude of potential harms that result from overdiagnosis, such as potential negative consequences of treatment, the financial impact, and negative mental health implications to name a few. As Wikler and Brock assert, adopting a "bird's eye view" for bioethical issues is essential to fully comprehend the complex array of factors that affect how we practice and make recommendations for diseases such as breast cancer and the current screening guidelines [1]. Screening is not a harmless preventive measure; it is simply widely believed that early detection and intervention of disease far outweighs any potential negatives. In actuality, for American women aged 40-49, there is conflicting evidence on whether the benefits of breast cancer screening outweigh its harms [2]. The advancement of screening technology has brought with it the detection of small, benign masses that will likely never bring harm to their hosts, but thus present why screenving poses harm: in detecting any irregularity, healthcare providers are obligated to take action. Major surgery is indisputably not a desirable outcome if it is questionably necessary, but there is also the negative mental health impact associated with a cancer diagnosis (including an increased likelihood of depression and anxiety, among other psychological disorders, which will be discussed later on). Further, thousands of extra screenings, biopsies, and surgeries are not free, and can cause serious financial strain for the patient as well as waste in an already fragmented and wasteful healthcare system. In looking deeper into why excessive screening for this age cohort persists despite dissenting recommendations, it becomes clear that there are health policy factors complicating the process and inhibiting true comparative effectiveness research and population-level health efforts from moving to the forefront of the conversation.

Strukovskaya, V. (2019). *Ancient statue of nude woman.* Photograph. Retrieved from https://unsplash.com/photos/fu3UqXTbGcs.

With all of the aforementioned factors indicating the multifaceted potential harms of screening and the political and social difficulties of scal-

ing it back, it is clear that a population-level bioethics approach is needed over an individual one to better gauge the scope of the ethical issues surrounding breast cancer screening in American women.

PREVALENCE OF OVERDIAGNOSIS

Overdiagnosis refers to the diagnosis of a condition that will in all likelihood never progress or cause symptoms if left untreated [3]. When exploring the bioethical issues surrounding screening and overdiagnosis, it is first important to establish the prevalence of overdiagnosis in American healthcare. The advent of screening brought with it increased detection of many small tumors: lesions that were not detectable in the past but fit the traditional physician definition of "cancer" [4]. However, it is less size and more biologic characteristics or stage that inform whether a tumor will grow, spread, and eventually kill, suggesting that the detection of many minimal tumors (which measure less than one centimeter or in situ carcinomas) is simply diagnosing cancers that will never become significant or harmful, as opposed to eliminating a potentially more lethal tumor [4]. While it is difficult to identify precisely what percentage of American women aged 40-49 who receive annual screening is overdiagnosed, multiple global studies have concluded significant rates of breast cancer overdiagnosis: in Denmark over a 30 year period, it was estimated that approximately 1 in 3 women offered screening were overdiagnosed and that screening itself was not linked to a reduction in advanced tumors [5]. A 2016 American study found that false-positive diagnoses were common, particularly in younger women receiving annual screening, and that various studies utilizing different methods found a range of overdiagnosis rates, with some as high as 54% [6].

Iatrogenesis

Despite the prevalence of overdiagnosis, mortality rates from breast cancer have declined alongside the advent of advanced screening technology [4]. There are dissenting opinions on whether or not this decline can be separated from improved cancer treatments and therapies, but it still asks the question: if screening is playing any role in saving lives from breast cancer, how could it be doing more harm than good? While the answer remains an ultimately personal decision, it is also an indisputable fact that screening is never completely harmless. Iatrogenesis refers to any risk of harm from medical interventions [7]. This is significant because any healthcare intervention presents opportunity for harm: surgery all too often has complications or long, painful recovery periods; hospital-acquired infections, while decreasing in the United States, are still a significant risk; treatment often includes medication with potentially adverse side effects; and in the event of a cancer diagnosis, treatments such as chemotherapy and radiation present

a multitude of consequences ranging from radiation exposure to hair loss [8]. For example, an unfortunately common consequence of surgery or radiation therapy to treat breast cancer is breast cancer-related lymphedema, or abnormal swelling that most often occurs in the arm or hand [9]. Women with breast cancer-related lymphedema have been found to have a lower quality of life; higher levels of psychosocial problems including anxiety and depression; are more likely to experience chronic pain and fatigue; have more difficulty functioning sexually and socially; and may even experience secondary complications of chronic infections, discomfort, and functional impairment [10]. There is also conclusive evidence that women who participate in screening are approximately 20 percent more likely to receive a mastectomy and 30 percent more likely to receive a lumpectomy [11]. Earlier detection does not correlate with improved prognosis or the aforementioned decreasing mortality rates from breast cancer, so it is more likely that improved treatment techniques and therapies have accounted for these figures [11]. For women in the low-risk age cohort and without a family history or genetic predisposition for breast cancer, excessive screening is exposing them to these risks and potential adverse health consequences for tumors that would likely never present any risk or harm.

Financial Effects

As of 2016, the U.S. Preventive Services Task Force recommends biennial screening for women aged 50 to 74 who are not otherwise deemed "high risk" and selective screening for women below 50 and over 74 based on factors such as family history, genetic predisposition, or dense breasts [2]. Other recommendations, such as from the American College for Radiology, suggest annual screening at as low as age 40. The majority of private insurance companies in the U.S. will cover such extensive, frequent screening for American women [12]. This excess of screening creates a significant financial impact, both for the patient and her family and for the hospital or provider [13]. Offering screening to a larger number of women increases the cost of screening programs without necessarily delivering a significant reduction in cancer deaths [14]. A U.K. study found that the gain in quality-adjusted life years (QALYs) from lowering the risk threshold for screening levels off after a certain point and increases overdiagnosis more than it actually reduces cancer deaths [14]. By increasing the risk threshold (i.e. providing screening for only high risk women) the screening program would cost approximately $648,982 less (in 2018 USD), lead to over 70 percent fewer overdiagnoses, and result in 443 more QALYs gained [14]. Breast cancer itself also poses a serious economic burden for patients, even more so than other cancer types [9]. Common adverse treatment effects, such as breast cancer-related lymphedema, affect approximately 35 percent of breast cancer survivors in

the United States and can result in an estimated $14,877 in out-of-pocket costs in the first two years following a diagnosis [9]. Out-of-pocket costs impact women with both private and public insurance, and are especially significant for those with lymphedema, who not only are faced with double the cost of those without lymphedema but who are also potentially insured by plans that do not cover self-management treatments for the condition [9]. While these adverse consequences would result from surgery or radiation therapy following a diagnosis, less direct but still significant costs include a possible need for psychosocial treatment (an impact of screening which will be discussed in the following section), time off from work, transportation to medical visits and potential visit costs [9]. The latter costs would exist even with just a simple screening, and would increase exponentially in the event of a potential cancer diagnosis regardless of its stage or likely progression.

Psychological Effects

A cancer diagnosis, regardless of a low mortality rate or positive prognosis, still presents significant stress and potential for anxiety, depression, or other mental health consequences for many American women and their families. It is estimated that as many as one-fourth of women diagnosed with breast cancer exhibit signs of psychological morbidity related to both diagnosis and treatment [15]. One study found that women receiving treatment commonly report issues with body image, poor mental health, or difficulty in sexual functioning, all of which impact quality of life and overall mental health and stability [16].

Fragmentation

In the American healthcare system, treatment protocol and decision-making varies widely across states, practices and physicians [17]. As Jay Katz explains in his 1984 book, *The Silent World of Doctor and Patient*, most physicians are uncomfortable with the admission of uncertainty in medicine [17]. For past treatment of breast cancer, providers fell into two potential treatment camps: one of radical mastectomy, and one of conservative surgery alongside radiation [17]. Over the years, relevant and important research on breast cancer and the therapeutic impacts that various treatments have been collected, but to this day there is no absolute consensus on which treatment is best; each practitioner considers their treatment method the most beneficial, the most preferred by patients, and the most effective [17]. Therein lies another major issue with excessive screening: the nature of the current fragmented, convoluted healthcare system means that a woman in a rural hospital in Kentucky may be receiving entirely different options and opinions than a woman in New York City—this could be true even across county or city lines. Additionally, providers are not simply influenced by their mentors

and colleagues, reasons for which will be discussed later on. For example, many physicians practice defensive medicine to avoid malpractice litigation or stand to make a profit from certain treatments in the fee-for-service system [18]. Most importantly, comparative effectiveness research is not valued or utilized by most hospitals or providers, so fragmentation of care is inevitable [19]. There are multiple significant contributors to this, such as the aforementioned perverse financial incentives within the system, inadequate funding for independent, unbiased research, and the influence of stakeholders' (often biased) interpretations of results according to their interests. Not to mention, the results of these studies are often ambiguous and therefore difficult to act on. Finally, the three common biases of confirmation (easily accepting evidence that aligns with preconceived notions and rejecting the contrary), pro-intervention (the idea that some action is better than none at all despite the outcome), and pro-technology (the tendency to accept that the newest technology is superior to previous methods) all influence how information is processed [19]. These contributors make it a near impossible task to fund, publish, disseminate, and put into practice true comparative effectiveness research that would streamline and improve patient care [19]. In the case of breast cancer screening, without these complications it is likely there would be more consistent and accepted evidence utilized across the nation as to what age women should receive screening, insurance companies would offer less liberal screening policies, and subsequently the rate of overdiagnosis would likely decrease.

Fshoq. (2018). *Doctor showing examination results to a patient.* Photograph. Retrieved from https://fshoq.com/free-photos/p/216/doctor-showing-examination-results-to-the-patient.

AMERICAN HEALTH POLICY CLIMATE

Individual v. Public Health Perspective

According to Wikler and Brock, bioethics "at the population level assesses the obligations of societies toward their members and each other and the norms governing complex relationships of individuals, groups, and the state" [1]. In focusing solely on the healthcare system's impact on individuals, we are completely ignoring the issues seen from a bird's eye view; yet, the United States continues to place a greater emphasis on the experience of the individual and values patient autonomy over all else [1, 17]. Judging the importance of the health of the individual against overall population health is a well known trolley problem, and many Americans, particularly when asked about themselves, someone they know, or about a person with an assigned name and face as opposed to a general statistic, may believe that it is unethical to value the lives of many over one individual, regardless of circumstance [20]. This emphasis on the individual plays a role in why overdiagnosis persists: breast cancer patients are all given the same abstract statistics about treatment effectiveness and mortality rates, but the ultimate decision changes significantly when he or she is faced with the possibility that they could be that small percentage of patients with the lethal tumor. When an insurance company debates whether to cover a potentially life-saving treatment or a woman diagnosed with breast cancer is forced to choose between "watchful waiting" or a radical mastectomy, they make decisions based on the health of the individual. In doing so, they are completely ignoring the ethical implications of overdiagnosing thousands of women—physical harm from treatment and hospital visits, potential mental health impacts, and cost. While it is essential to value patient autonomy and the experience of the individual, it is dangerous to completely overlook the underlying bioethical issues related to breast cancer screening and all unnecessary care.

Public Perception

In the United States, healthcare has become increasingly politicized and polarized, and the perceptions of politicians that greatly influence public opinion alongside the power that modern patients have in healthcare decision making has further weakened comparative effectiveness research and created a fear of "rationing," meaning health resources are limited for certain patients based on efficacy, price, or life expectancy [20]. In the U.K., the breast cancer screening guidelines mimic that of the aforementioned U.S. Preventive Services Task Force [21]. The U.K. also has the National Institute for Health and Clinical Excellence (NICE), which provides recommendations on how best to improve health outcomes for all British people, who happen to all be insured under its public National Health Service [22]. In

the U.S., some conservative politicians have touted NICE as a prime example of what an American universal healthcare system would look like: the rationing of healthcare resources, i.e. making decisions not to cover certain treatments because the effectiveness and number of QALYs or lives saved does not outweigh its cost [23]. In fact, healthcare resources are undeniably finite, and the U.S. already rations care; it is based solely on ability to pay, not the effectiveness of the care [20]. Americans who are uninsured or underinsured—approximately 26 million people were uninsured in 2016 and about one-fourth reported having problems paying medical bills—and who cannot afford prescription drugs, life-saving surgeries, or treatments are dying sooner and experiencing a lower quality of life than those who can afford it [20, 24]. Yet this fear of rationing is so pervasive that it is keeping unbiased recommendations for breast cancer screening underfunded and out of the forefront. It also causes the majority of the public to continue believing that when it comes to care, more is always better. For women in the U.K., those under 50 and not otherwise deemed high risk do not have annual breast cancer screening covered by their insurance until they turn 50 [21]. But between the U.S. and the U.K., mortality and five-year survival rates are relatively comparable [25]. Given the data on the prevalence of overdiagnosis, unbiased recommendations to wait to screen until age 50 for average risk populations, and the myriad of negative effects of excess screening, it seems that breast cancer screening is an acceptable place to "ration" care.

Interest Group Influence

While there is some debate whether "American exceptionalism" can truly account for why we never developed some form of universal healthcare, it remains that the American political system is relatively unique in its multitude of veto points that interest groups and other external influences can have on policy making [26]. In our healthcare system, there are many stakeholders who stand to gain from excessive screening. For example, the American College for Radiology rejects the U.S. Preventive Services Task Force's recommendations and instead argued that decreasing screening would result in thousands of unnecessary breast cancer deaths [12]. In our fee-for-service system, radiologists depend on the breast cancer industry as a source of profit and are not independent or unbiased, yet this is information unlikely to be broadcast when a patient interacts with his or her radiologist [27]. Thus, regardless of the validity of their claim, it is important to note that the information is coming from a clearly biased source, whereas the U.S. Preventive Services Task Force receives no monetary benefit for its recommendations. Other groups, such as the Susan G. Komen foundation, have hugely influenced public opinion with campaigns suggesting that early detection always saves lives and listing surgery and radiation as the first treatments for

treating early-detected breast cancers [28]. While it is not to say that these groups do not have the interests of women and their patients in mind, they do have either other motives or misinformation [29]. An independent third party such as the U.S. Preventive Services Task Force should not be received with skepticism when its purpose is to make unbiased recommendations for the health of women using peer-reviewed evidence [29]. Yet, the recommendations of the previous biased groups influence what is covered and recommended, as radiologists work with patients and groups such as Susan G. Komen reach large numbers of women with their campaigns, and help in part to explain why overdiagnosis still exists [27, 28].

Physician Perspective

Continuing in the vein of the American College for Radiology's presumably less-than-altruistic intentions, the American healthcare system is based on a fee-for-service system [27]. Physicians are paid based on services rendered, not outcomes, leading to perverse financial incentives that can lead many to make treatment choices based on personal financial gain and not the genuine health of their patient [27]. This is not necessarily a conscious effort—for example, if a group of physicians purchases a CT scanner, they will likely use the scanner more than necessary to pay off its cost [30]. But there is little evidence that CT scans are better than older, cheaper tests and can also expose patients to unnecessary radiation [29]. Given the previously mentioned technology bias and the revenue the scanner would bring in for a clinic, it is understandable why many physicians would choose such a route. Physicians are also susceptible to defensive medicine, or practicing unnecessary testing or treatments to avoid malpractice litigation [18]. In the current legal system, patients can sue relatively easily for negligence, and patient perception of negligence often depends on what the doctor did not do, not complications from actual interventions [18]. The belief from both physician and patient that more is better and that beneficence depends on doing the most is a significant factor in rates of overdiagnosis. By offering early screening, physicians are paid more, avoid being sued, and feel that they are providing the best possible care for their patients [27]. Thus, it is not difficult to see why so many support and themselves recommend such frequent, early screening and contribute to the high rates of and complications from overdiagnosis of breast cancer.

CONCLUSION

Ultimately, the current approach to breast cancer screening focuses too much on the individual level, thereby ignoring the dangers of overdiagnosis and the complicated, biased factors and influences that are negatively impacting women's health. A "bird's eye view" approach is clearly needed to improve

the health of American women who are not at serious risk for developing breast cancer, as it is unethical to continue to put any woman through the physical, mental, emotional, and financial strain that overdiagnosis causes, and it is only through more selective screening that we can reduce these harms. While few contest the benefits of shifting away from the paternalistic traditions of American healthcare and into a newfound and widespread respect for patient autonomy, the complexity of our healthcare system means that conversations about care are never as simple as between physician and patient. All parties need to look more broadly at what factors are influencing care decisions and how to improve overall health. In the case of breast cancer screening, that likely means becoming comfortable with doing and knowing a lot less.

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Article

"Technologies of the Self" and the Politics of Empowered Biocitizenship

by Katie Gu[†]

Biotechnological innovation is demonstrating, with accelerating momentum, our abilities to hold power and control over life. Recent innovation has conferred a higher degree of biological agency to the individual citizen, rather than solely relegating control to centralized scientific or governing bodies. The present paper analyzes new processes of empowered biocitizenship that are reshaping biological knowledge to be more distributable, actionable, and centered around the individual self. I conclude with a discussion on responsibility thus necessitated by twenty-first century movements towards democratic and empowered models of biocitizenship.

Between 1975-76, the French philosopher Michel Foucault, upon his appointment to the chair of History of Systems and Thought at the Collège de France, delivered a series of public lectures titled "Society Must Be Defended" [1]. Foucault first presented his ideas on biopower in his eleventh lecture, in which he said:

> It seems to me that one of the basic phenomena of the nineteenth century was what might be called power's hold over life. What I mean is the acquisition of power over man insofar as man is a living being, that the biological came under State control, that there was at least a certain tendency that leads to what might be termed State control of the biological [1].

Biopower, or *biopouvoir* as coined by Foucault, examines the shifting balance of modern power relations with the increasing role political systems of power began to exert in governing and modifying biological phenomena of their populations. Tracing the development of biopower back two centuries, Foucault discusses the emergence of "techniques of power that were essentially centered on the body, on the individual body," such as systems

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of "surveillance, hierarchies, inspections, bookkeeping, and reports" introduced in the seventeenth to early eighteenth centuries [1]. These systems were used as a means of controlling an individual's labor and productive capacities within the workforce [1]. From this earlier "disciplinary technology of behavior," Foucault notes that the latter half of the eighteenth century saw the emergence of a "new nondisciplinary power […] directed not at man-as-body but at man-as-species" [1]. In this period, European states (most notably Germany) began linking population health and its management with the maintenance of political and economic security. Foucault writes that this shift towards biopower "exerts a positive influence on life, that endeavours to administer, optimize, and multiply it, subjecting it to precise controls and comprehensive regulations" [1]. Thus, a state's public health efforts and policies directed at regulating population birth rates, mortality rates, disease burdens, longevity, and disabilities can be viewed as exertions of biopower over its constituents.

Biopower and the State

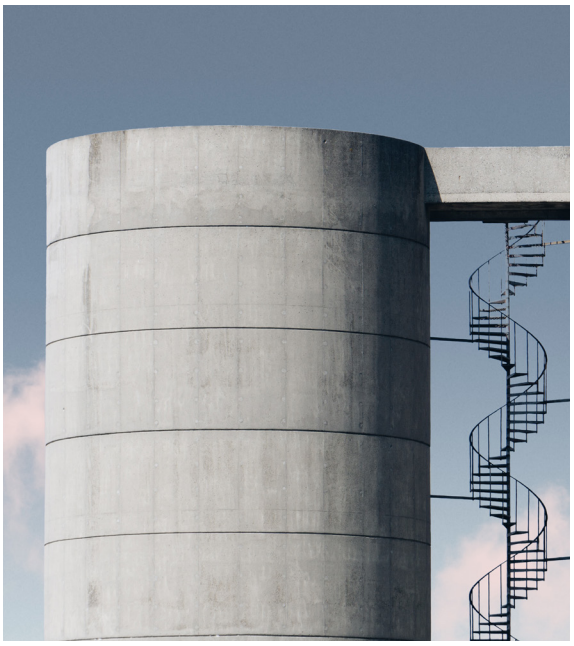
An emphasis of biopower as a "technology of power," involving the objectification and subjugation of a subject, helps uncover further implications of Foucault's thesis [1]. With biopower, Foucault submits:

> [W]e now have the emergence, with this technology of biopower, of this technology of power over "the" population as such, over men insofar as they are living beings. It is continuous, scientific, and it is the power to make live. Sovereignty took life and let live. And now we have the emergence of a power that I would call the power of regularization, and it, in contrast, consists in making live and letting die [1].

The framework Foucault develops here opens fascinating political, social, economic, and biological questions. First, biopower reevaluates fundamental aspects of the social contract. Can an individual's life, in a purely biological form, be put under a government's control when social contracts are drawn? How justified are governments in controlling biological phenomena using underlying economic or efficiency rationale? In considering public health efforts, how much control is delegated to governments through these technologies of power? Examples of contemporary exertions of biopower include Germany's vaccination campaigns, China's former one-child policy, and the UK's emphasis on biopower as a regulatory technology of power exerted to manage populations. In each country, different socio-political dynamics are exerted between state and constitutive populations with biological life as their foundation.

Biopolitics and Liberal Government

Biopolitics, in turn, refers to the dynamics of biopower between populations and their governments, in which the biological lives of citizens become objects of political strategy. Foucault considers biopolitics within "Society Must Be Defended" in the following manner: "Biopolitics deals with the population, with the population as a political problem, as a problem that is at once scientific and political, as a biological problem and as power's problem" [1]. If we consider biopolitics as a modern form of exercising power, then the proliferation of genetic, reproductive, and synthetic biology technologies holds immense implications not only in transforming health outcomes, but also in political strategies of governance by states.



Châtel-Innocenti, P. (2018). *Gray building.* Photograph. Retrieved from https://unsplash.com/photos/KY-opXSvJsU.

In his foundational work, *Biopolitics: An Advanced Introduction*, Foucauldian scholar Thomas Lemke emphasizes that the nascence of Foucault's biopolitics occurred alongside the emergence of liberal forms of government in Europe [2]. As Lemke discusses, European governments in the mid-eighteenth century shifted from a focus on maximizing state power to a new operation "through an 'economic government' that analyzes governmental action to find out whether it is necessary and useful or superfluous or even harmful" [2]. In a later lecture series, Foucault speaks of liberalism in the following manner:

> But what does "the self-limitation of governmental reason" mean? What is this new type of rationality in the art of government, this new type of calculation that consists in saying and telling government: I accept, wish, plan, and calculate that all this should be left alone? I think that this is broadly what is called "liberalism" [2].

Following this definition of liberalism, Foucault asserts that the "general framework of biopolitics" is informed by liberal forms of government [2]. Just as biological systems have "a basic principle of organization," or the capacity to self-regulate, so too can society be left to natural regulating forces.

Given these parallels, Lemke argues that Foucault's biopolitics in modern Western societies, through its fundamental reliance on liberalism, is a "technology of the self" as a result of its emphasis on the freedom of the individual [2].

A "technology of the self" enables an individual to "effect … a certain number of operations on their own bodies and souls, thoughts, conduct, and way of being, so as to transform themselves in order to attain a certain state of happiness, purity, wisdom, perfection, or immortality" [2]. The concept borrows heavily from the Greek practice of *epimelesthai sautou*, "knowing oneself", in order to take care of oneself. In framing biopolitics as a "technology of the self" involving greater care and knowledge of oneself, ongoing personalized medicine initiatives and biocitizenship efforts lend themselves well for contemporary Foucauldian analysis.

A Concluding Note on Power-Knowledge

Foucault's foundational concept of *savoir-pouvoir*, power-knowledge, is integral to his definitions of both biopower and biopolitics. In *Discipline and Punish: The Birth of the Prison*, Foucault writes: "There is no power relation without the correlative constitution of a field of knowledge, nor any knowledge that does not presuppose and constitute at the same time, power relations" [3]. Thus, in Foucauldian theory, power and knowledge are inextricably related—knowledge is an exercise of power and power, an exercise of knowledge.

The connections between biopower, biopolitics, liberal government, "technologies of the self," and power-knowledge lead toward the motivating questions of the present paper. What are contemporary examples of expanded, personalized access to biological knowledge shaping twenty-first century biopolitics around "technologies of the self?" In turn, what are the politics of these new "technologies of the self" that represent individuals as active, free, and self-governing citizens?

ASSERTIVE BIOCITIZENSHIP AS DEMOCRATIZING ACCESS

For contemporary Western societies, ongoing movements for individuals to regain control over personal health information and decisions are shifting biocitizenship from a "technology of power", controlled by the state, to a "technology of the self," exerted by individuals. Contemporary efforts for democratizing access to biological knowledge will be discussed in this section within the context of biocitizenship as a "technology of the self." The twenty-first century move from reactionary to assertive biocitizenship is further interpreted in the context of the evolving contemporary dynamics of Foucault's biopower and biopolitics.

Majia Nadesan, in her 2010 book *Governmentality, Biopower, and Everyday Life*, underlines the sociopolitical aspects of the "technology of the self" inherent in twenty to twenty-first century forms of biopower in Western societies:

> In achieving securitization, private and public governmental authorities not only produced and disseminated new disciplinary spaces (hospitals, clinics, institutions, public schools) and practices (sanitary science, hygiene, exercise) constituting everyday panopticons of surveillance and social control, but also generated technologies of the self premised in the idea of individuals as self-governing agents [4].

Individuals acting as "self-governing agents" in the monitoring, diagnosis, and treatment of their bodies are engaged in an act of biological citizenship, or what scholars such as Nikolas Rose and Carlos Novas have discussed as biocitizenship.

Reactionary Biocitizenship

The concept of biocitizenship was first used by Adriana Petryna in her 2002 work, *Life Exposed*, a book analyzing political action taken in response to the Chernobyl disaster. Petryna's discussed forms of biocitizenship were reactionary—Petryna writes of the "massive demand for but selective access to a form of social welfare based on medical, scientific, and legal criteria that both acknowledge biological injury and compensate for it" [5]. She explicitly notes the interwoven biological and political interests of biocitizenship, and how the discussed acts of biocitizenship occurred alongside the rise of democracy for the Ukrainian citizens affected by Chernobyl. In discussing the role democracy and political systems play in biocitizenship, Petryna states:

> The collective and individual survival strategy called biological citizenship… is also part of a broader story of democratizing processes and structures of governance in post-socialist states… Only through concrete understandings of particular worlds of knowledge, reason, and suffering, and the way they are mediated and shaped by local histories and political economics, can we possibly come to terms with the intricate human dimensions that protect or undermine health [5].

Petryna interprets acts of "biological citizenship" as democratizing tools through which individuals sought medical, social, and human rights-based compensations for the Chernobyl explosion. Such examples of reactionary biocitizenship remain abundant in contemporary societies. In the UK, for example, a citizen science project called the Parenting Science Gang (PSG) overturned a National Health Service (NHS) guideline on detergents for baby cloth diapers. In reaction to a NHS-issued recommendation of biolog-

ical over non-biological washing powders for diapers, PSG ran a 2015 study sponsored by the Wellcome Trust and the UK Royal Society of Chemistry. The study determined that no evidence existed for the NHS' previous assertion that non-biological detergents cause more skin irritation over biological alternatives, ultimately leading to the previous NHS statement being rescinded [6]. The group's impact on NHS guidelines has been interpreted as a successful biocitizenship effort to decentralize control over the direction of scientific research.

The 2016 water crisis in Flint, Michigan is another example of citizens setting the scientific agenda when public government responses are deemed inadequate. When a 2014 Michigan ordinance rerouted Flint's water supply from the former municipal water system to the Flint River, inadequate water treatment measures led to an increase in lead levels for the city's water. Initial citizen concerns were dismissed by city officials until Flint residents along with researchers from Virginia Tech ran an independent study, which found that 40% of measured Flint water samples had above 5 ppb of lead, a level considered to be a "very serious" public health danger [7]. In these two acts of reactive biocitizenship, individual citizen groups directly initiated studies to tackle underfunded or under-prioritized research topics. Increasingly, citizens have been involved in a form of biocitizenship that is more assertive than reactionary, and more focused on the individual rather than the community. This trend towards an assertive democratization of access involves the engagement of not only the biopolitical citizen, but also the commercial biotechnology industry.

Expanded Access, Compassionate Use, and Right to Try Programs

In the context of clinical trials, patients simultaneously produce and consume medical information relating to the development of new biotech and biopharma products. Unfortunately, due to capped enrollments, physical constraints (distance from clinical centers), time constraints (time needed for follow-up visits), and affordability of participation, there is limited accessibility to experimental therapeutics in development via clinical trial access. More recently, partnerships between the individual biocitizen and the biotechnology industry have attempted to expand access to the usage and production of health-related information. For example, Genentech, a leading biotechnology company that houses the largest single-site biotech research facility in the world, has begun expanding access to investigational or unapproved treatments for patients outside the constraints of the traditional clinical trials process [8].

On Genentech's website, apart from clinical trials, there is explicit mention of the potential for access to experimental drugs via expanded access programs (EAPs) or compassionate use (CU) programs. While the two

terms are often used interchangeably, Genentech defines EAPs as expanded access for a limited group of patients, while CU programs are granted on an individual patient-by-patient basis. Merck & Co., one of the largest pharmaceutical companies in the world, similarly has a public page where options for expanded access to investigational medicine via EAPs or Country-Specific Authorization to Use programs are discussed [9]. Johnson & Johnson further lists CU, Pre-approval Access Programs, and Single Patient Requests as routes for accessing investigational medicines outside the context of clinical trials [10].

Through these programs, patients are given increased agency over their own disease management and treatment. In the context of CU and Single Patient Requests, patients reassert their rights to clinical resources, knowledge, and action away from centralized systems and back to the individual. In receiving access to such programs, patients must ask their doctors to contact the manufacturing drug company and submit an application to the FDA for expanded access. More than 90% of requests for EAP applications between 2013 and 2016 have been approved [11, 12]. Crucially, the patient's expanded ability to initiate action in order to gain access to investigational drugs is a powerful contemporary tool for self-governance and self-regulation. The dissemination of risk and responsibility from manufacturing drug companies back to patients is a biopolitical transfer of power back to the individual at his most desperate, vulnerable health state.

While the previously discussed CU, EAP, Pre-approval Access Programs, and Single Patient Requests all require FDA permission for use, the federal Right to Try Act, signed into law in May 2018, does not require prior FDA approval or IRB review [13]. The act allows terminally ill patients in the US to access medications that have passed Phase I of the FDA approval process through their physicians [14] and further represents a transfer of biopolitical agency to the individual from the state. Previous Right to Try laws had been passed in individual states, but the passage of the federal bill in 2018 codified the transfer of medical decision-making power to the terminally-ill individual without other treatment options. The passage of the Right to Try Act comes along the heels of recent death with dignity statutes. Six total states and Washington, D.C. have since enacted such statutes, with Hawai'i passing the most recent Our Care, Our Choice Act in 2019 [15]. Together, these twenty-first century laws hearken back to Foucault's discussion of biopower as "the power to 'make' live and 'let' die" and have reasserted access to biopolitical power as an individual right.

KNOWLEDGE PRODUCTION

Contemporary trends towards assertive biocitizenship actively promote individual production of and engagement with biological knowledge. Bio-

hacking, also referred to as do-it-yourself (DIY) biology, is a growing social movement that is broadening access to biological research. Whether through open source laboratories, informational resources, or advocacy, these biohacking movements have worked to democratize participation in the production of biological knowledge. Similarly, several federally-initiated movements have witnessed a shift in engagement from the level of the population to that of the individual. The following section will focus on several citizen and federally-initiated efforts to transfer the locus of control in knowledge production and consumption back to the individual. These efforts collectively emphasize the individual as actively responsible for the knowledge and care of his own health, an emphasis that is resonant with Foucault's liberal models of citizenship.

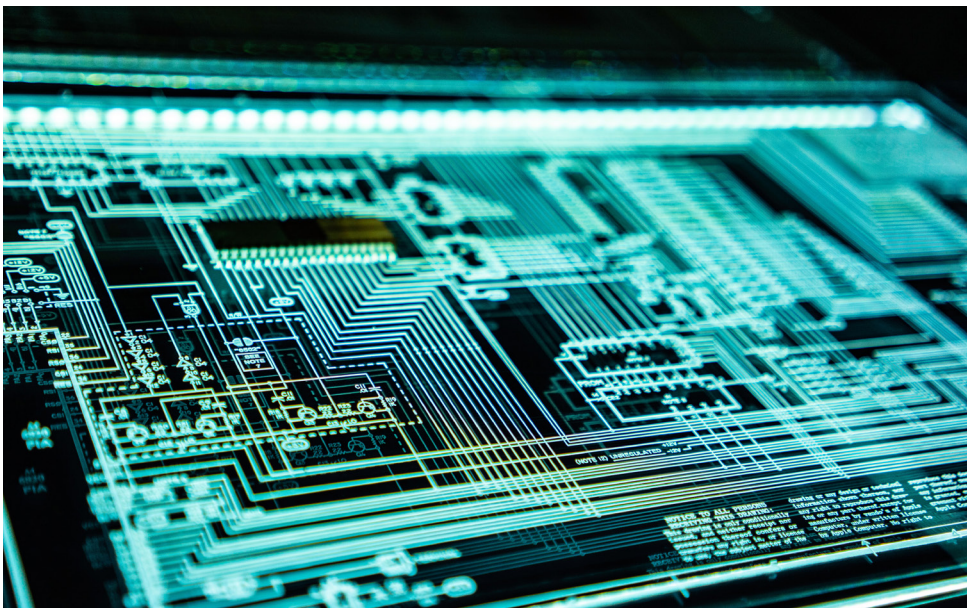
Biohacking and DIY Biology

Biohacking is built upon a belief that the individual citizen should have democratic access to the exploration of biology and health. Across all categories, biohackers apply an open source model of biology in order to democratize access to scientific innovation, giving the citizen the "right to know" about his own health and biology as well as the right to act on that knowledge. This structure requires fundamentally redesigned models for scientific outreach and community engagement. For example, to provide laboratory and equipment infrastructure to support open source science, about 44 biohacking community labs have developed in North America, 31 in Europe, and 19 in Asia, South America and Oceania [16].

Efforts to engage the average citizen in health innovation and therapeutic development are taking place in community labs around the world. Biocurious, one such community lab based in Santa Clara, was discussed in a 2018 *Scientific American* article titled "The Rise of Citizen Bioscience" [17, 18]. The article featured Elodie Rebesque, a high school student whose brother suffers from pneumothorax, a disease which involves the collapse and separation of the lung from the chest wall and currently lacks safe, non-invasive treatment options. Motivated to expand treatment options for these patients, Rebesque has proposed a "biological velcro" matrix design that could reattach collapsed lungs to chest walls. Similarly, Counter Culture Labs, based in Oakland, is attempting to broaden access to cheaper solutions for diabetes patients via options like closed-loop continuous glucose monitoring systems and DIY insulin pumps [19].

Another DIY bio initiative within the diabetes space is the Open Insulin Project (also based in the Bay Area), which is developing the first freely available, open source protocol for insulin production. On their website, the Project states: "Pharmaceutical companies patent small modifications to previous insulins while withdrawing those previous versions from the market

to keep prices up. We're doing the scientific research necessary for a generic drug company to make a low-cost insulin and open up access to this crucial drug" [20]. Here, the Project explicitly expresses a need for individual citizens to participate in the production of biological knowledge, as a means of democratizing public access to therapeutics. Such citizen-driven research taking place in community labs across the world reintroduces concepts of the neoliberal, rational citizen as an active participant in the production, mobilization, and instigation of new biological knowledge.



Goldstein, A. (2019). *LED panel.* Photograph. Retrieved from https://unsplash.com/photos/EUsVwEOsblE.

Self-Experimentation

A subcategory of biohackers, those engaging in self-experimentation, subscribe to the most radical belief in the individual's responsibility to health, one that potentially subverts larger public health obligations. The range of self-experimentation has reached extreme fringes. Famous instances of biohacking self-experimentation involve Aaron Traywick, former CEO of the DIY bio company Ascendance Biomedical, who publicly injected himself with an experimental gene therapy for herpes virus at the February 2018 BioHacking Con [21].

Josiah Zayner, former NASA researcher, is one of the most public biohackers. His most publicized feats include a full-body fecal microbiome transplant, performed in an airport hotel, and his self-injection with a CRISPR-Cas9 system to modify myostatin, a gene responsible for muscle growth,

at the live-streamed conference SynBioBeta 2017 [22-25]. He also produces DIY genetic editing kits through his company ODIN, which in 2016 sold about $200,000 worth of products [26, 27]. Self-experimenting biohackers like Zayner have been operating under a regulatory loophole within the FDA—while compounds that have not yet been FDA-approved cannot be marketed or sold as therapies, self-experimentation and self-usage are not technically illegal. The FDA has, however, published the following statement on the practice of self-experimentation in November 2018: "FDA is aware that gene therapy products intended for self-administration and "do it yourself" kits to produce gene therapies for self-administration are being made available to the public. The sale of these products is against the law. FDA is concerned about the safety risks involved" [28].

Within this group of self-experimenting biohackers, the paradigm of control by the individual of his own biological processes and body is asserted to an extreme. The individual places himself at the immediate locus of biological knowledge production and consumption and assumes full responsibility for this power. Transfers of power from state control to the individual certainly carry real risks that can be of immediate private and public concern. Most notably, the recent rise in self-experimenting biohackers proposes a potentially dangerous radical new medium for the direct engagement of individuals in biopolitics and biocitizenship.

Real World Patient-Generated Data and the FDA

While biohackers, DIY biologists, and self-experimenters are initiating citizen-driven efforts to democratize biocitizenship, the FDA's incorporation of real-world evidence (RWE) into the development and approval of new medicines further increases the individual's agency in producing and consuming new biological knowledge. By incorporating patient-reported outcomes and patient preferences more formally into the agency's regulatory approval process, the FDA is moving towards more patient-centric approaches to the development of medical products.

RWE includes forms of health data collected outside the context of traditional clinical trials. These data relate to both patient health status and the delivery of clinical care. Sources of RWE include electronic health records, claims and billing activities, product and disease registries, and patient-generated data (e.g. from wearables and other mobile devices) [29]. Several legislative mandates, including the 21st Century Cures Act, the FDA Reauthorization Act of 2017 (FDARA), and the Prescription Drug User Fee Act Reauthorization of 2018 (PDUFA VI), have all underscored the FDA's new focus on RWE. The *All of Us* Research Program, funded by the 21st Century Cures Act, is an effort to gather health data (via survey questions, electronic health records, biological samples) in order to better understand individual

disease and health profiles [30]. Dr. Francis Collins, director of the NIH, stated: "The *All of Us* Research Program will change the way we do research. Participants will be partners in research, not subjects, and will have access to a wide range of study results." Collins' focus on framing patients as not only subjects but also "partners in research" builds upon a larger transition in regulatory discourse around patient empowerment and autonomy. The PDUFA VI, for example, has extended the Patient-Focused Drug Development (PFDD) program established in PDUFA V to emphasize the importance of patient and stakeholder perspectives in guiding regulatory processes [29]. The December 2018 testimony published on PDUFA VI notes:

> Central to PDUFA VI, and its largest single investment component, are plans to elevate patient voices in developing new drugs to treat their diseases... Under PDUFA VI, we look forward to engaging in a transparent, multi-stakeholder approach that will lead to development of the methods and approaches to ensure patients not only become active participants but informants to industry drug development and agency review [31].

The 21st Century Cures Act further directs the FDA to focus on two types of RWE uses: 1) RWE for post-approval safety and efficacy analyses, and 2) RWE for the approval of new indications and of drugs for rare diseases [32]. The FDA's Sentinel Initiative, launched in 2008, is another example of FDA's efforts to incorporate RWE into its review processes. Specifically, the initiative uses safety analyses of claims data, hospital stays, outpatient visits, and pharmaceutical dispensings to assess post-market evaluations of medical products. Sentinel's distributed data network currently contains health data covering over 100 million individuals [33]. The Initiative's collection and analyses of RWE have not only informed the FDA's regulatory decisions, but also shed insight into patterns of medical product usage (e.g. patterns of

Adams, M. (2018). *Incandescent bulb.* Photograph. Retrieved from https://unsplash.com/photos/sq1dNSxyGdU.

opioid use, usage of medications during pregnancy, quantification of medication errors) and eliminated the need for expensive, lengthy postmarketing studies [33]. Collectively, these efforts to include RWE into FDA's regulatory review processes allow for a greater depth of patient representation and engagement to be incorporated into regulatory decisions.

More importantly, the individual patient's abilities to inform and direct ongoing drug development efforts are reinforced by legislative mandates revolving around RWE evaluation. The integration of patient-generated real world outcomes into the creation of new medicines re-emphasizes the agency of the individual, outside of the regulated confines of a clinical trial, to participate in the creation of knowledge of the body and biological processes. Shifting away from Foucault's late twentieth-century description of the "State control of the biological," newer contemporary outlets for de-institutionalized participation in biological knowledge production, whether through RWE production, biohacking, DIY biology, or self-experimentation, each represent efforts to return biopolitical power back to the individual [1].

CONCLUDING REMARKS

Assertive biocitizenship, expanded access programs, biohacking, community labs, and the incorporation of real world evidence into the production and consumption of biological knowledge are collectively redistributing control of biopower back to the individual. Returning to Foucault, political notions about individual responsibility, coupled with biological notions of self-regulation, are re-emphasizing contemporary biopolitics through many "technologies of the self." At the extreme ends of these "technologies of the self," most notably among self-experimenting biohackers, the citizen who engages in radical modes of assertive, self-regulating biopolitics contributes to a passionately empowered form of biocitizenship.

As discussed thus far, not only are citizens themselves becoming active participants in these transfers of power, but new regulatory procedures and policies are also enabling individuals to participate more directly in their biological citizenship. Combined, the shifting locus of biopower away from centralized control and towards the empowered individual, introduces new responsibilities for the self-monitoring biocitizen. Such responsibilities imply a liberal interpretation of the human body's political autonomy and capacity of self-regulation. As the mantras of personalized medicine, democratic access, and empowered biocitizenship continue to inform direct citizen engagement and new regulatory efforts, the individual will increasingly encroach on existing regulatory frameworks.

In early May of this year, Josiah Zayner was sent a letter for "practicing medicine without a license" from the California Department of Consumer Affairs. The relevant California law (Business & Professions Code 2052:

Unauthorized Practice of Medicine) specifies that such an act constitutes a public offense [34]. Zayner has in turn claimed: "I have never given anyone anything to inject or use, never sold any material meant to treat a disease and never claim to provide treatments or cures—because I knew this day would come" [35]. Whether Zayner's self-experimentation with body-altering compounds for both therapeutic and non-therapeutic purposes should be considered "unauthorized practice of medicine" is still up for debate.

Despite this ambiguity, Zayner's awareness that his acts would inevitably lead to questions of legal transgression directly address underlying questions about the politics of empowered biocitizenship. In his Instagram post concerning the California Department of Consumer Affairs notification letter, Zayner described his acts as "showing people how to access publicly available knowledge" [36]. Biohackers and self-experimenters certainly galvanize public engagement with biologically-relevant knowledge, but does this broader engagement promote the common good? Should Zayner's Youtube video outlining the process of self-administering CRISPR-Cas9 systems for human experimentation remain a publicly-accessible resource [37]?

Empowered biocitizenship now encompasses unprecedented public and private grounds, as Zayner's actions demonstrate. While Foucault's conception of a "technology of the self" was once circumscribed to the individual's practice of knowing oneself in order to take care of oneself, current forms of biocitizenship further necessitate the practice of knowing one's place, power, and responsibilities in society. Within each of the present paper's discussions of contemporary biological "technologies of the self," new sociopolitical responsibilities must be assumed by the twenty-first century biocitizen. The need for responsible science in the era of empowered biocitizenship and personalized healthcare will require new definitions of responsibility for not only the biocitizen, but also scientific communities, regulatory bodies, and political bodies. As individuals assert greater degrees of biopower, biopolitical knowledge, and biocitizenship, policies should be focused on not only how to best regulate individual bodies, per Foucault's original conceptions of biopower, but also how to best enable individuals to assume responsibility and care in the acquisition of new biopolitical power.

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