Ethical Issues Analysis of Digital Pills

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Plaksha Tech Leaders Fellowship

Team: Manan, Mahathi, Sai Krishna, Neha and Anisha

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Technology Analysis

Digital Health Technology

Healthcare is one of the most important sectors worldwide and a field where there an end to research can't be found. The latest advances in the Health Domain have been developed using digital technologies as they have made health-care feasible for a large fraction of patients with serious mental illness both short-term and long-term. They are now being used to monitor the patient's health status and prompt them to act on it. The technologies include Health-related mobile apps, fitness-tracking wearables, infusion pumps, and digital pills.

Digital Pill Technology

What are Digital Pills?

Digital pills are pills that contain electrochemical sensors that can be ingested by the human body. The pill along with the sensors that transmit data after it is consumed, together constitute the Digital Pill Technology. The sensors used are about the size of a grain of sand and communicate wirelessly to an external device like an app or wearable.

The first Digital Pill approved was manufactured by Otsuka Pharmaceutical Co. that was been working with Proteus Digital Health. They originally embedded the existing antipsychotic drug Abilify (which is used in the treatment of certain psychiatric conditions like schizophrenia, bipolar disorder, and depression) with an Ingestible Event Marker (IEM) sensor. Their product Abilify MyCite is used to determine whether the medicine has been taken or not. There is a patch that is worn on the left rib cage which is the receiver which further transmits the data to a smartphone app via Bluetooth. The data can be forwarded to the doctor according to the user's wish.

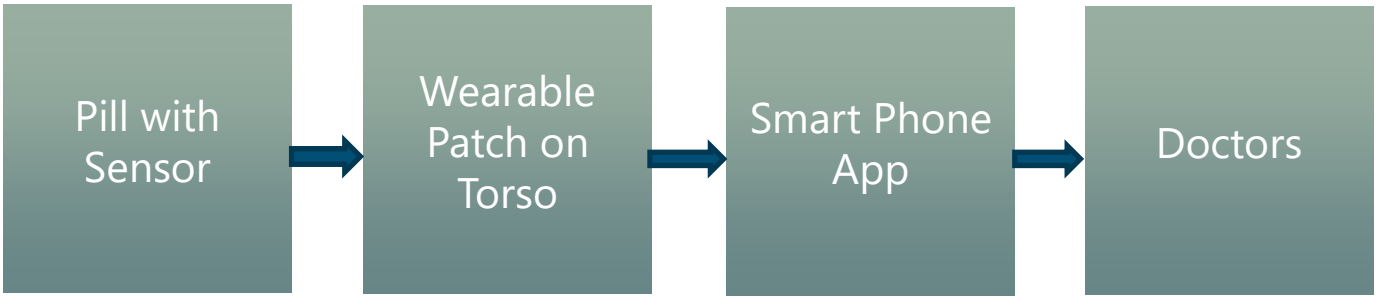

Figure 1: Digital Pills

How do they work?

The sensor gets activated only when it is charged by the stomach acids and then transmits a signal to the patch stuck on the patient's torso. The data transferred consists of the time of the day, dosage size and type of medication.

The sensors are made from biocompatible materials that make up a power supply, microprocessor, controller, sensors that help the device to telecommunication. The Ingestible Event Marker (IEM) Sensor used is made from dietary minerals: copper, magnesium, and silicon, in minute quantities. The sensor comprises three functional components:

- Active layers
- Integrated circuit
- Insulating skirt

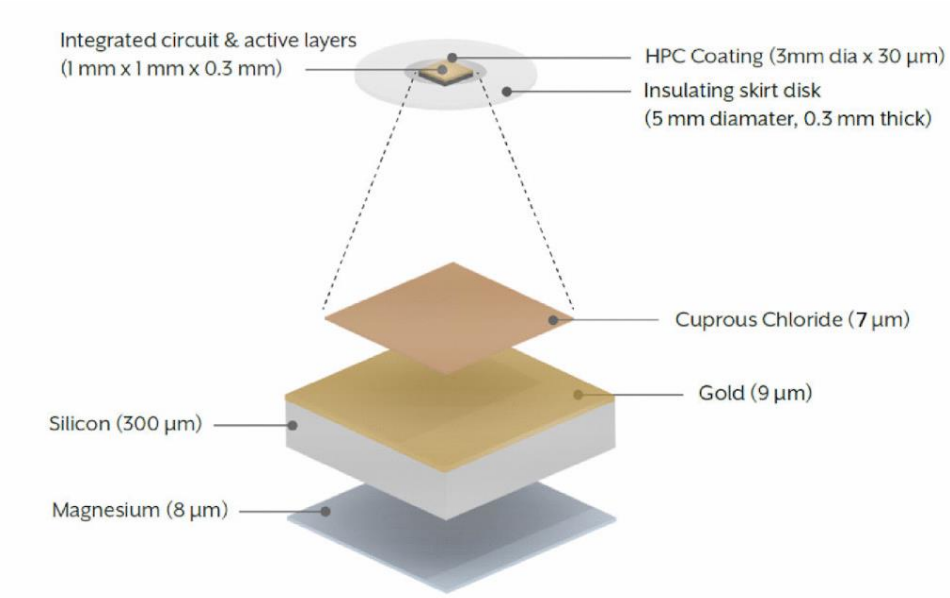

Figure 2: Digital Pills Working

Which group is involved in the use of technology?

The group of users for this technology involves all those who are on medication. But this is more applicable to the groups mentioned below:

- those struggling with forgetfulness (especially elderly people)
- young naughty children who don't like to have medicines
- those suffering from psychological disorders

Why do we need to assess the technology?

Some of the reasons why we need to assess this technology is:

- Some patients may tend to forget finishing their medicine dose (especially in the case of psychiatric conditions) which may worsen their health condition and they may end up in the hospital. These pills help them providing them with the correct nudge. The doctor can be notified in case of any kind of emergency. It is also a personalized medication treatment.
- Looking from the Researcher's perspective, it helps them identify whether the new medication they have developed is effective it not by ensuring that the patient is taking the prescribed.
- The pill can be further developed as it has the potential to tackle other public health issues where medication adherence is required like infectious diseases and antibiotic resistance.

A lot of Smart Pills or Ingestible Sensors have come up recently. Some of these pills can be:

- Used to track whether the patient has taken the medicine or not
- Other Vitals like temperature, pH values can be monitored
- Camera Pills that can take high-speed photos of the intestinal tract

The latest digital pills being developed are digital chemotherapy pills.

What are the ethical aspects that arise in this technology?

Being part of the latest technological advances, digital pills while solving a lot of problems leads to some ethical issues. They are:

- Privacy and data security - the issue of medical confidentiality
- Difficult to ensure data anonymization
- Adverse effects of ingestion of sensors in the short and long term
- Malfunction of sensors
- Reliability on the sensors as they may react differently with different bodies

Stakeholder Analysis

Identification of Stakeholders

Research & Development	Approval	Commercialization
Researchers	Regulatory	Physicians
Pharma Industry	Lobbyists	Patient & Relatives
Manufacturer	Physicians	Marketing Team
Investors	Lawyers	Lawyers
Engineering Team		Insurance
Physicians		

Figure 3: Identifying Stakeholders

Stakeholder Analysis Matrix

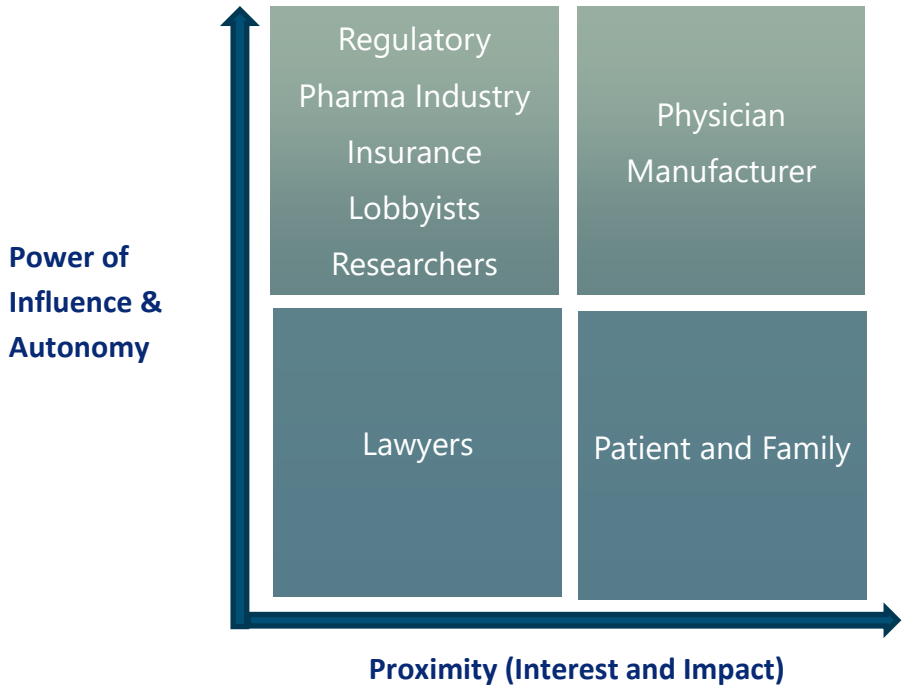

Figure 4: Stakeholder Analysis Matrix

Ethical Matrix Analysis

Principle (Across) Stakeholders (Down)	Beneficence	Non - Maleficence	Respect for autonomy	Justice
Physicians	++	-	-	Neutral
Patients and Relatives	++	-	-	+/-
Regulatory	++	-	-	
Investor	+++	-		
Manufacturers (Tech and Pharma)	+++			
Researchers	+++			

Figure 5: Ethical Matrix Analysis

Physicians:

- The benefit to the physician via digital pills is that they will be effectively able to monitor their patients remotely which will allow them to deliver the best clinical care and overcome the problem of non-adherence. It might also result in decreasing the frequency of patient visits and hence freeing up a doctor's time for more patients
- It will negatively affect the autonomy of the physician and might cause slight harm as well as with this tech coming in more stakeholder will become part of the patient – physician relationship. Device manufactures and insurance player will end up making decisions based on the data from these pills and track physicians on how often they are monitoring their patients
- Overall for the physician community it will be just, as it will help them in their profession

Patients:

- Digital pills will result in beneficence for the patient as the technology will help in delivering better clinical results via better monitoring of vital and increased adherence to medication.
- It will cost the patient some aspect of their autonomy as their confidential health data might now be shared amongst more parties other than the physician. It will also somehow take away the right to deceive physicians in case of non-adherence.
- Although the component of harm is very low, the technology might end up harming patient if the data in provides is used for patient profiling
- Overall since the tech opens options for better treatment results it brings justice to the community but at the same times brings privacy in question so injustice might also propagate

Regulatory:

- The benefit is that patients can get better care in contrast with traditional approaches and the regulatory will able to take better decisions for future product pipelines using data collected
- The technology might result in encroaching upon the autonomy of the regulator as other stakeholders might get access to data that is confidential

Researchers:

- The technology will result in immense benefit for the research community as it will provide them with previously unseen data than will enable a lot of new research in medial field

Manufacturers:

- The machines will provide significant benefit to the manufacturer as they will earn good profit and it will open new revenue streams for them (both pharma companies and tech companies)

Investors:

- The technology will result in immense value generation for the investors if the regulatory climate suits and if the product is marketed effectively
- It can also harm them if the data privacy regulations are not taken care of

Value Conflict Analysis

In this section we try to examine the ethical landscape of digital medicine. As the technology has developed recently, there remains a strong need to think about ethical dilemmas, concerns and risks associated with it.

Based on our understanding of this technology, we feel that out of the four principles of Reflexive Principilism, Respect for Autonomy & Beneficence are far more specific to this context as the drug intake is individual driven.

As with every new technology we had conflicting views on the potential advantages and disadvantages of it.
The positive implications of this technology make us believe that:

- As this technology is meant **to improve individual drug adherence, it acts for both the beneficence** of individuals as well as **for ensuring non-maleficence by reducing disease risk** over long term
- As it facilitates continuous monitoring of data, **it serves as a boon to medical research** for future medical advancements, thus **ensuring better collective justice and beneficence of the society**

On the flipside, the negative aspects point us in the direction of:

- **Compromise on individual autonomy** due to continuous monitoring of data & lack of adequate consent
- Can be **a potential cause of maleficence** due to misuse of sensitive healthcare data to discriminate
- **Malfunctioning and misconceptions** relating to a new technology can cause harm.

Some of the principal conflicts that arose while discussing the technology are as mentioned below:

Patient

Respect to Autonomy

Informed consent is the patient's exercise of autonomy by voluntarily agreeing or disagreeing to participate in a test, procedure, or research study.
Traditionally there are two situations under which the patient provides his or her consent

- Non-Invasive: Testing is presumed with patient cooperation. Example- Measure blood pressure
- Invasive: Patient is provided with a description of the process, risks, benefits, and alternatives and must provide written approval on a legal document to give his consent.

In case digital pills, the process of consent generally works differently as it is more of the continuous process rather than a one-time activity. The way it currently works is through User Agreements:

User Agreements: The use of a digital medicine product may be governed by a user agreement. When the patient registers on digital medicine app, he or she will be prompted to indicate agreement. These tend to be long documents written by lawyers, are typically contracts of adhesion and not negotiable.

Some of the issue with User Agreements:

- **Issues of Comprehension**: In traditional informed consent process a provider speaks to the patient and this exchange culminates in the patient's permission or refusal for treatment in a face to face interaction whereas user agreement is framed explicitly as a contract that one agrees to without engaging in a face-to-face conversation which in turn benefits the company.

- A patient using digital medicine will be part **of two overlapping but distinct processes: consent for what the clinician prescribes, and mere acquiescence to the terms dictated by the company**. This may cause confusion and may be a threat to a patient's perception of or actual exercise of autonomy
- **Not agreeing means not receiving this device**, and thus the patient may feel that they have no choice
- User agreements might be written in such a way that companies require access to patient data for technology upgradations, maintenance or medical research purposes. **This raises the ethical question of whether patients should have the option of not allowing data usage for these use cases.**

Maximally empowering patient autonomy would mean giving patients an absolute right to provide or refuse consent for their data to be used in research. However, some scholars from the field believe that at least in the setting of research aimed at expanded knowledge about potentially lifesaving or life-changing treatments, citizens owe an obligation to contribute to the public good by volunteering for research.

Data Management:

In digital medicine, patients have **new responsibilities when it comes to their data**. Consider that the device is recording data both automatically—blood sugar levels, body temperature, ingestion of pill—and manually—patient enters mood, hours of sleep, and energy level. First, **patients must decide who has access to this data**. The **patient may give permission for other individuals to access the data**, whether through an online portal or even through push notifications.

The thornier issue is **whether patients should have the further right to withdraw data they have already contributed**. Doing so would maximally respect patient rights of privacy and data control but poses significant logistical challenges for companies seeking to implement these solutions.

External Influences:

Consent may be further compromised by the beliefs and requirements of another party. In theory, could a clinician state that she will only work with the patient if he agrees to the digital medicine solution**? Currently, clinicians sometimes require patients to agree to certain behavioral conditions in order to continue treating them (e.g., coming to appointments, undergoing urine drug testing). There may be disagreement among clinicians regarding whether such conditions represent a kind of "external influence"—that is, pressuring the patient to do something he or she otherwise would not**. Other examples of potential influences on patient's use of (or clinicians' prescribing behavior) include an insurance company's expressing preference for the digital version of a medication if it has data showing that using such pills reduce their costs, or, conversely, an insurer refusing to cover digital medicine because of a lack of data on reducing costs.

Provider

Digital medicine creates a variety of unique ethical issues for the clinician who will be treating and monitoring patients with these devices. These drugs and devices hold implications for transforming the clinician–patient relationship, patient trust, clinician monitoring, managing expectations, and liability risks. Some of the details under which the provider will be affected:

Transforming the Clinician – Patient Relationship

With traditional pharmaceuticals, the clinician prescribes the medication, the patient has the prescription filled at a pharmacy, the patient takes the drug (or does not), and at some later date, the patient and clinician talk to see whether the drug has worked. Digital medicine is closer to telemetry, where the patient is consistently and closely monitored. **The adherence-monitoring version of the same drug or drug delivery device may change the clinician–patient relationship, a change that can have benefits and concerns**. Closer monitoring could theoretically lead to better patient outcomes and lower costs. A **clinician may have to spend less time with each patient because more data are available before an office meeting**. Perhaps the patient's follow-up appointments could be spaced further apart, as the clinician will know the patient's self-reported mood and automatically logged adherence on a regular basis. This could reduce cost for the patient and the insurer, as well as allowing the clinician to treat more patients.

Monitoring the Clinician

There is also a different kind of trust relationship at stake—the relationship of industry and clinicians. Insurers may use digital medicine devices to monitor and evaluate clinicians. Medical device manufacturers and pharmaceutical companies—which have always had access to patient prescribing patterns through the American Medical Association (AMA)—will now have access to when and how their products are used, not just whether they were prescribed. Data portals will require usernames and passwords, which will track when a clinician logs on, how much time is spent looking at information, and perhaps whether any adjustments were made to the digital medicine device (e.g., the app's settings). Some of this information may be helpful for designing user-friendly and easier-to-use software, but it **could also be designed to determine whether clinicians do keep closer tabs on their patients.** If a company wants to demonstrate that its digital medicine technology improves health outcomes and reduces costs, **it may require (in the user agreement) access to corroborating medical records. Clinicians may find themselves subject to greater oversight monitoring and further erosion of professional autonomy at the hands of insurers and manufacturers.**

Liability Risks

Even if user agreements and consent forms spell out that the clinician is under no obligation to check the data, the patient may expect this. The insurer may also expect it— after all, why pay more for digital medicine if the tool goes unused? For some of these technologies there may be an expectation that the information will be incorporated into clinical records. The use of these technologies may also trigger the need to comply with the federal privacy rules under the Health Insurance Portability and Accountability Act of 1996 (HIPAA)**. Could a clinician who does not keep tabs on the data be liable for failure to do so if there is a bad outcome?**

Proposed Innovative Options

We have identified some ethical issues that we considered whilst development, testing, verification and validation phases of digital pills.

Development:

- Biocompatibility of sensors
- Possible malfunction/ absence of the transmitted signal
- Anxiety of Ingesting sensors into the system
- Adverse reactions within the body
- How is the pill excreted?
- Toxicity and Maximum dosage
- Adverse effects of ingestion of sensors in the short and long term
- Irreversibility of ingestion in the case of change of mind

Testing:

- Most of the clinical drug trials are carried out in low-income countries largely on poor, illiterate and uninsured people.
- Different demographics being affected differently by the pills

Verification:

- Using preclinical studies to verify results.

Validation:

- Compare results of normal drug results with digital pill

Design Specs/ Engineering Solutions:

- Cost-effectiveness of the drug trials in developing nations over the US.
- Importantly the effectiveness of those drug trials.
- Testing drugs which need to be produced for Latinos tested on Indians

Innovative Solutions:

- Ensuring warning mechanisms and notification processes in the sensory patch won on the body to detect any malfunction of the pill.
- Check the patient's conditions (like pH value of stomach acids) before ingesting the pill to prevent effects of the sensor
- Integrate the medication with other edible substances like chocolates to make it easier for patients to consume and reduce the level of anxiety. We can also think of different form factors for the medication to suit patient choices.
- Monitor the levels of the raw materials of the sensor substance to ensure that there is no overdosage of those substances in the body.
- Trying to get control over the pill in case the patient suddenly decides he doesn't want his vitals to be monitored.

Pathway and Justification

Our team believes in the potential merits of the technology and the impact it will have on the patients and their health. Anisha, Manan, Neha believed in the technology benefits from the start, however Mahathi due to her phobia of ingestion of pills of wanted to have more checks in place. Sai Krishna agreed. We realized that the beneficence far outweighs the non- maleficence because the patients would now be in a better state with drug adherence and disease management.

Anisha, Manan and Neha believe that these pills will reduce the adherence cost in-case a patient forgets to take their medication. The patient visits to the physician will reduce thus freeing up more time for the physician. The continuous monitoring mechanism available helps in medical research and the data that is generated can be used to advance medical sciences and prevent diseases.

Along with the advantages we realize that the data that is generated needs to be managed and protected effectively and we have a responsibility to do so in a secure and scalable manner. We understand that the data can be misused and hacked but having proper checks and balances in place to mitigate these issues helps. Also having access to a sounding board that can help us think through various challenges as they come about.

We will market the device in small batches initially and then partner with institutions and dealers who will help take the pills to a larger market. The reason we grow from a small batch of users is so that we provide a high-quality product and build on its success

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A special thank goes to our colleagues who helped us out in completing the project, where they all exchanged their own interesting ideas, thoughts and made it possible to complete our project with all accurate information.

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