




‘Digital pills’ for mental diseases: an ethical and social analysis of the issues behind the concept

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ABSTRACT

Recently, the US Food and Drug Administration has given a landmark approval to the very first digital pill with a sensor embedded in the inside. These are complex systems that include a drug and an electronic tracker that is activated when the patient takes the pill. Accordingly, they might be an excellent tool for monitoring and potentially improving patients’ adherence to prescriptions. This would serve well to avoid unnecessary healthcare costs and reduce the anxiety of patients and their relatives. However, digital pills might also diminish patient autonomy, reduce privacy, or promote inadequate use of pharmaceutical resources. This article is aimed at contributing to adequate use of this new tool by showing the main ethical and social issues they involve and proposing measures meant to address them. Finally, we conclude by defending the idea that these new systems should be seen as means of complementing traditional strategies to promote adherence to treatment, and not as substitutes.

KEYWORDS: Digital health, digital pills, adherence, ingestible sensor, data protection and privacy, patient autonomy

INTRODUCTION: A GAME-CHANGER TECHNOLOGY IS BORN

On November 13, 2017, a pharmaceutical company Otsuka Pharmaceutical Co., Ltd (Otsuka), based in Maryland, USA, and a Silicon Valley company, Proteus Digital Health (Proteus), announced that the US Food and Drug Administration (FDA) had approved a digital medicine system called Abilify MyCite[®] (AMC, aripiprazole tablets

with a sensor). This is a drug–device combination product comprised of Otsuka's oral aripiprazole tablets embedded with an ingestible event marker (IEM) sensor.¹ Aripiprazole is an antipsychotic used to treat adults with schizophrenia, bipolar I disorder, and major depressive disorder. The drug is part of a more complex product, i.e. the Abilify MyCite[®] System, which comprises the Abilify MyCite[®] and the following components: a wearable sensor developed by Proteus, i.e. the MyCite[®] Patch; a smart-phone application (app) called MyCite[®] app, which can display information about the patient on a compatible smartphone, and web-based portals for healthcare providers and caregivers that display a summary of aripiprazole ingestion over time.²

The Abilify MyCite[®] System offers healthcare providers an astonishing outcome: it records real-time medication ingestion by patients and collects data on activity level as well as self-reported rest and mood. The processing is easily described: after the daily antipsychotic pill is swallowed, a digital sensor the size of a grain of sand (made of copper, magnesium, and silicon, which Proteus states are all found in food) functions like a battery by releasing an electric signal to the patch when it has reached the stomach acid. Thus, the adhesive patch on the patient's torso collects information on the date and time the pill was taken, blood pressure, temperature, and level of activity. Then, the patch sends a signal to an app on the patient's smartphone. At this stage, patients can add self-reported mental health data about how they are feeling. The app uploads the data to a secure website on a cloud-based system for viewing by doctors.³ As a final result, all information gathered by the system can be communicated to patients and healthcare providers through the electronic devices incorporated with the product. In this manner, it is possible to obtain an objective summary of drug ingestion over time.⁴ It is good to highlight that patients can decide who has access to their data at any moment among other authorized parties, such as Otsuka and its vendors, their selected healthcare providers, their family and friends, their pharmacy, or their health plan.⁵

At present, there are good reasons to believe that Abilify MyCite[®] will soon be followed by other digital pills. Based on the information gathered, the industry is producing apps for substance abuse treatment, diabetes management, and heart and blood pressure monitoring at a rapid clip. At the same time, studies are underway for digital pills for addressing other mental health pathologies, cancer, cardiovascular conditions, and infectious diseases, such as preexposure prophylaxis medications for preventing human immunodeficiency virus.⁶ Therefore, a new generation of intelligent

1 PR N. Otsuka and Proteus[®] Announce the First U.S. FDA Approval of a Digital Medicine System: ABILIFY MYCITE[®] (aripiprazole tablets with sensor). PR Newswire US [serial online]. Nov. 14, 2017: Regional Business News (accessed Jan. 21, 2020).

2 *Id.*

3 Christopher Rowland, *This \$1,650 Pill Will Tell Your Doctors Whether You Have Haken It. Is It the Future of Medicine?* THE WASHINGTON POST, Apr. 9, 2019, <https://www.msn.com/en-ie/news/indepth/this-dollar1650-pill-will-tell-your-doctors-whether-youve-taken-it-is-it-the-future-of-medicine/ar-BBWorND?li=BBPCQrg> (accessed Jan. 29, 2020).

4 Anthony Ryan Hatch, *Digital Mental Health Drug Raises Troubling Questions*, *PhillyVoice.com* (June 15, 2018), <https://www.phillyvoice.com/digital-mental-health-drug-cyborg-ethics-abilify-mycite/> (accessed Jan. 21, 2020).

5 Otsuka, Ablify MyCite system Terms of Use, Privacy Notice, and Authorization & Consent. Patient authorization & consent, <https://www.otsuka-us.com/media/static/Abilify-Mycite-Patient-Consent.pdf> (accessed Apr. 30, 2020).

6 *Supra*, note 3.

drugs is arriving and we must properly address the benefits and challenges posed by them, while preserving our most valuable ethical principles.

Indeed, digital pills might be an excellent tool for monitoring and potentially improving patients' adherence to prescriptions, which could result in an impressive mechanism for avoiding unnecessary healthcare costs and an efficient and excellent tool for reducing anxiety in patients and their relatives. However, they could also diminish patient autonomy or reduce their privacy. Keeping this in mind, this article is aimed at contributing to the adequate use of digital pills by showing the main ethical issues digital pills involve and proposing measures meant to address them. To this end, we start by showing the main benefits digital pills might provide to us all, mainly their potential toward better adherence to treatments. Subsequently, we focus on the main ethical dilemmas this innovation poses, such as marketing pressures that have contributed to the emergence of this cutting-edge product, as well as other challenges facing patient autonomy.

DIGITAL PILLS: THE PEARLS

As mentioned, digital pills might be an extremely useful tool for reliable identification and minimization of medication non-adherence, a crucial issue in terms of healthcare systems governance. The lack of adherence to treatment causes huge dysfunctions in the healthcare sector. In accordance with internationally recognized standards by the medical profession, a patient is observing a treatment if the average ratio between medication intake and prescription is ≥ 80 per cent.⁷ The World Health Organization considers that, in the case of chronic diseases, at least 50 per cent of patients show poor adherence to treatment in global terms,⁸ a percentage that is even lower in certain cases.⁹ In France, for example, a study has shown very low levels of treatment observation: 36 per cent of heart failure cases, 37 per cent of Type 2 diabetes cases, 40 per cent of hypertension cases, 44 per cent of hypercholesterolemia cases, or 53 per cent of osteoporosis cases.¹⁰ These figures are particularly worrying in the case of psychiatric illnesses.¹¹ Non-adherence causes terrible consequences. Indeed, it causes death or higher complications to a huge number of patients.¹² For example, non-adherence is the largest driver of relapse and hospitalization among patients with disorders such as schizophrenia, diabetes, and asthma.¹³

Furthermore, non-adherence leads to considerable yearly cost overruns. In terms of health from an economic perspective, in the USA, non-optimized medication therapy

7 Grégoire Moutel et al. *Le Médicament Connecté, Entre Bienveillance et Surveillance*, 34 ANALYSE DES ENJEUX ÉTHIQUES, MÉDECINE/SCIENCES 717–22 (2018).

8 Sabate E. *Adherence to Long-Term Therapies: Evidence for Action*. Report 2003. Geneva: World Health Organization, n° 92 4 154599 2 (2003).

9 Aurel O. Iuga & Maura J. McGuire, *Adherence and Health Care Costs*, 7 RISK MANAG HEALTHC POLICY 35, at 4 (2014).

10 Moutel, *supra* note 7.

11 Palazzo P. *Observance Médicamenteuse Et Rechutes Dans La Schizophrénie : Des Neuroleptiques Classiques Aux APAP*, 167 ANNAL. MÉDICO-PSYCHOL. 308–17 (2009).

12 P. M. Ho, J. S. Rumsfeld, F. A. Masoudi, et al. *Effect of Medication Non-adherence on Hospitalization and Mortality among Patients with Diabetes Mellitus*, 166 ARCH. INT. MED. 1836–1841 (2006). doi:10.1001/archinte.166.17.1836

13 Iuga, A. O. & M. J. McGuire. 2014. *Adherence and Healthcare Costs*, 7 RISK MANAG. HEALTHC. POLICY 35–44. doi:10.2147/RMHP.S19801

costs up to \$528.4 billion, which is equivalent to 16 per cent of the total US healthcare expenditure in 2016.¹⁴ For European states, non-adherence is estimated to turn into an economic loss of €125,000 million each year.¹⁵ In terms of medical practice, non-adherence constitutes a fundamental obstacle to adequate practice of good care, as 'When patients do not respond to a medication, it can be difficult to determine whether the lack of response is due to non-adherence or whether the medication itself is not effective'.¹⁶

To date, physicians cannot really do much to solve the adherence issue. They are in general entirely dependent on patients' self-reporting. However, this source is not reliable. Some patients do not report adequately because they are unable to keep good records or they are not willing to do so due to reasons such as failure to understand the instructions, lack of resources, and adverse effects¹⁷.

Therefore, the need to improve adherence to treatment is undoubtedly an essential task for healthcare systems. In recent years, multiple studies have been carried out with the view to achieving this objective. For example, between 2009 and 12, the European Commission financed the ABC research project (Ascertaining Barriers for Compliance: Policies for safe, effective and cost-effective use of medicines in Europe) within its Seventh Framework Program. This and other studies placed the focus of better adherence on the need to strengthen the relationship of trust between patient and doctor, because it is in the direct relationship between the two where it is easiest to assess the actual observance of treatment. Several additional approaches have been developed to support adherence, such as the establishment of therapeutic education groups in healthcare services and patient discussion groups.¹⁸

Traditionally, healthcare providers could use directly observed therapy (DOT) when needed to ensure that patients adhered to the treatment on schedule. Now, new technologies are turning into a useful tool for physicians to measure adherence with the same objectivity rates, while overcoming some disadvantages shown by DOTs. These alternatives include the issuance of follow-up notebooks to be completed by the patient, which allows the patient to check their catches and omissions, and the doctor to advise the patient during consultations. Alternative tools include electronic medication

14 Jonathan H. Watanabe, Terry McInnis, *Cost of Prescription Drug-Related Morbidity and Mortality*, 52 9 ANN. PHARMACOTHER., 829, at 832 (2018).

15 Unidad de Bioindustrias y Farmacia. *Antares Consulting*, https://www.antares-consulting.com/es_ES/main/detallepublicacion/Publicacion/79/apartado/B/idUnidad/1 (accessed Jan. 16, 2020). See: NATIONAL COUNCIL ON PATIENT INFORMATION AND EDUCATION, ENHANCING PRESCRIPTION MEDICINE ADHERENCE: A NATIONAL ACTION PLAN, 7 (2007): Almost half of those polled (49%) said they had forgotten to take a prescribed medicine; nearly one-third (31%) had not filled a prescription they were given; nearly three out of 10 (29%) had stopped taking a medicine before the supply ran out; and almost one-quarter (24%) had taken less than the recommended dosage.

16 C. M. Klugman et al. *The Ethics of Smart Pills and Self-acting Devices: Autonomy, Truth-telling, and Trust at the Dawn of Digital Medicine*, 18 AM. J. BIOETHICS, 38–47 (2018).

17 M. J. Stirratt, J. Dunbar-Jacob, H. M. Crane et al. *Self-report Measures of Medication Adherence Behavior: Recommendations on Optimal Use*, 5 TRANS. BEHAV. MED. 470–82 (2015). doi:10.1007/s13142-015-0315-2. In the case of schizophrenia, see: Peter M. Haddad, Cecilia Brain & Jan Scott, *Nonadherence with Antipsychotic Medication in Schizophrenia: Challenges and Management Strategies*. PATIENT RELAT. OUTCOME MEAS. 43, at 48 (2014).

18 Moutel, *supra* note 7.

container lids¹⁹ or boxes (called pill boxes, sometimes electronic) containing as many boxes as there are doses to be taken in a day, which the patient can program to trigger alerts on their mobile phone.²⁰ Many of these tools raise awareness of new and precise information provided by the device on a daily basis, and during consultations, they provide 'feedback' with the professional and allow for dialogue.²¹ Besides, these medical-device applications not only help patients play an active role in the decision-making process, but also constitute a means of supplying the lack of time not dedicated by the physician,²² as they provide continuous monitoring that allows patients and physicians immediate access to the patient's relevant health data.²³ Yet, they all rely on the patient's will to monitor their adherence to the drug prescribed. Thus, some scholars have pointed out the need for better alternatives for measuring adherence.²⁴

Are digital pills the response to this query? At first sight, it looks like it. Unlike in the previous scenario, in a world with digital pills, a cooperative attitude on the part of the patient is no longer necessary to obtain accurate knowledge of adherence to treatment. It is enough for patients to agree to use the pills (or for the system to force them to adopt them) so that their physicians know perfectly what the real adherence to treatment is. An additional advantage is that this technology could serve to help patients overcome some of the difficulties they face when trying to follow a treatment, a situation that is particularly stressful in the case of the elderly or people with mental conditions.

Thus, this wirelessly observed therapy offers better features than the supporting technologies already described, which still rely on the patient's capacities and will (what if a patient misuses the notebooks or simply does not take the pill even if they remove it from the box?). Indeed, unlike traditional tools, digital pills register observance automatically, providing patients with the means to ensure optimal monitoring of their drug administration, avoiding missed or duplicated doses.²⁵

Nevertheless, it is important to underscore that reasons behind bad adherence rates can be diverse and multiple (not always they consist on a mere distraction to be solved through a tracking system). When we talk about bad adherence to treatments we are addressing a complex biosocial phenomenon, as health sciences and social sciences literature show us. To this regard, if we assume that the operating mode of digital pills could offer a good solution to solve the adherence issue, we should be aware of the professional perspective we are adopting—in which no report from the patient is needed—since from the non-adherent patient perspective, the system could be far from approaching the true reasons behind bad adherence rates.

19 Klugman, *supra* note 16.

20 B.B. Granger, S.C. Locke et al. *The Digital Drag and Drop Pillbox: Design and Feasibility of a Skill-based Education Model to Improve Medication Management*, 32 J. CARDIOVASC. NURS. E14–20 (2017).

21 Moutel, *supra* note 7.

22 Dimitra Petrakakia, Eva Hilberg, Justin Waring, *Between Empowerment and Self-discipline: Governing Patients' Conduct through Technological Self-care*, 213 SOC. SCI. MED. 146, at 150 (2018).

23 Ho, *infra* note 27.

24 S. Garfield, S. et al., *Suitability of Measures of Self-reported Medication Adherence for Routine Clinical Use: A Systematic Review*, 11 BMC MED. RES. METHODOL. 149 (2011). doi:10.1186/1471-2288-11-149

25 P.R. Chai, Rosen R., Boyer E.W. *Ingestible Biosensors for Real-time Medical Adherence Monitoring: myTMed*, 16 PROC. ANNU. HAWAII INT. CONF. SYST. SCI. 416–23 (2016).

To sum up, digital pills provide health systems with precise data on patients' medication taking²⁶ while informing physicians on whether the failure of a prescribed treatment is due to the ineffectiveness of the treatment or a significant failure in its administration. However, this does not necessarily mean that digital pills must be considered a kind of panacea for adherence issues. Indeed, their use involves relevant issues that should be balanced against their benefits.

THE PERILS: A COPERNICAN TURN IN THE PATIENT–PHYSICIAN RELATIONSHIP

First, one needs to understand that the use of digital pills for monitoring patient adherence constitutes a radical turn in the way we focus this issue. Our current healthcare system is built on a mentality in which trust between clinicians, caregivers, or social workers and the patient is a fundamental piece. The introduction of digital pills replaces this framework with a new policy in which monitoring and control play a key role. It is no longer the patients who reveal data to the physician on a voluntary basis. Instead, the physician becomes a kind of 'Big Brother' who knows everything about the patient even though they are unwilling to share such information.

Of course, one might reply that this does not necessarily have to happen. Indeed, this is hardly the case if the patient is willing to use the digital pill. On the other hand, it is also possible to think that, as the patient will be aware of the knowledge acquired by the physician, it would be much easier for them to discuss the reasons they are not observing their treatment, instead of lying to the healthcare provider. This might indeed happen and it is quite difficult to know in advance whether digital pills might cause a real loss of trust in the physician–patient relationship.

However, the dysfunctions caused by digital pills to the way we approach the functioning of the healthcare system go beyond the loss (or not) of the notion of trust. They extend to the possible erosion of the personal relationship between patients and their physicians. By now, patients usually discuss with their doctor the problems arising from the follow-up of the prescribed treatment. Nevertheless, in the new scenario, patients somehow become the object of inspection of the health system, which watches closely for any deviation from the correct administration of treatment.

It is very important that patients have sufficient confidence in their doctors to discuss with them the reasons they are reluctant to take the prescribed medication. It is also essential that the system provides both with the possibility of building that relationship through adequate means. Thus, with the use of such smart devices, trust would be compromised from both the professional and patient perspectives. First, data generated by the device may cast doubt on the truthfulness of the patient's self-report. Conversely, patients may distrust physicians and their therapeutic recommendations if they receive a different diagnosis from that suggested by the device on which they rely.²⁷ On the other hand, digital pills open a major gateway to distant and mediated interaction between doctors and patients, thereby decreasing the need for face-to-

26 J. Frias et al. *Effectiveness of Digital Medicines to Improve Clinical Outcomes in Patients with Uncontrolled Hypertension and Type 2 Diabetes: Prospective, Open-label, Cluster-randomized Pilot Clinical Trial*, 19 J. MED. INTERNET RES. e246 (2017).

27 Ho, A. & Quick, O. *Leaving Patients to Their Own Devices? Smart Technology, Safety and Therapeutic Relationships*, 19 BMC MED. ETHICS 18 (2018). <https://doi.org/10.1186/s12910-018-0255-8>

face communication. Finally, the use of these new technologies may over-technify the monitoring of treatment or decision-making about a patient. This new scenario, which constitutes a serious challenge in the health care arena, is by no means inevitable, but requires the adoption of an appropriate mentality and measures capable of preventing it. It is essential to keep in mind that technologies should serve to enhance the physician–patient relationship, rather than to replace it.²⁸ For the sake of maximizing the usefulness of these cutting-edge medical technologies in the way we conceive medicine of even the integral care of patients, we must make a proper use of them in terms of both safety and confidence,²⁹ otherwise, a key aspect of the patient–physician relationship would be broken: trust. The question, in short, is whether the possible increase in adherence to treatment would compensate for the decrease in this fundamental value, confidence, if patients were forced to use to this new technology.³⁰ We sincerely believe that this is not the case. That is why we advocate a system that is respectful of patient autonomy and that only allows the use of digital pills in cases in which the patient encourages it, unless the defense of a public good, such as health or safety, makes it essential. We will return to this issue later.

PHARMA BENEFITS VERSUS PATIENT INTERESTS: ETHICAL ISSUES FROM A MARKET PERSPECTIVE

One of the most important ethical dilemmas posed by digital pills comes from the business model on which they are based. Traditionally, the quality of a pharmaceutical product depends on its capacity to improve a patient's health. On this basis, it is possible to draw up cost–benefit analyses, indexes of limitations of coverage in public healthcare, or limits on the provision of funds by insurers. In the case of digital pills, the scenario is much more complicated, as what is offered is not only a medicine, but also a complex pharmaceutical product that combines both that medicine and a monitoring system based on cutting-edge technology. Hence, many challenging dilemmas arise. First, it becomes complicated to compare a system that includes a drug that may not be the most appropriate for a patient with a drug that may be more efficient in treating the patient's specific pathology, but that cannot provide information about adherence. This could obviously be solved by adapting the monitoring system such that it can be incorporated into any medicine, but for the moment this scenario is far from reality.

Furthermore, we must not forget that the pharma industry is guided by a strong interest in enhancing human health, while making a profitable business of it. It may happen that, for this purpose, it focuses its attention on the monitoring system rather than on the medicine it incorporates, or worse still, the system is used as a means of revaluing a medicine that would otherwise be almost obsolete.³¹

In this respect, the first digital pill approval paves the way for future marketing of similar drug-device combination products, encouraging other applicants to innovate similarly over older drugs. It is important to notice that the way that ingestible sensor can accompany the drug is particularly relevant from the regulatory process perspective,

28 J. Torous & L. W. Roberts. *The Ethical Use of Mobile Health Technology in Clinical Psychiatry*, 205 J. NERVOUS MENTAL DIS. 4–8 (2017). doi:10.1097/NMD.0000000000000596

29 Ho, *supra* note 27.

30 Klugman, *supra* note 16.

31 Hatch, *supra* note 4.

hence for the entrance into the market. Ingestible sensor physically integrated inside the drug, as is the case for Abilify MyCite[®] capsules, requires a New Drug Application approval—since it falls under the Section 3.2 (e) (1) of Title 21 of the Code of Federal Regulations, and the aripiprazole is the combination product primary mode of action. Nevertheless, in case the sensor is not physically integrated in the pill, but embedded separately inside the same capsule, applicant can take advantage of no requirements to undergo a new round of regulatory approval. In this way, no FDA approval was necessary in a recent use of Proteus sensor in a digital oncology pill, within a program developed with cancer patients in cooperation with University of Minnesota and Fairview Health Services, since the sensor was 'loosely packaged' with the drug in the capsule.³² Avoiding a time-consuming and costly regulatory process could therefore constitute a great incentive for applicants to place sooner on the market innovative products as digital pills.

Innovation in the pharmaceutical sector and business strategies are closely linked, all the more so since from the beginning of the last decade, the pharmaceutical industry has been experiencing a phenomenon known as 'patent cliff': a massive expiration of pharmaceutical patents.³³ Even Abilify MyCite[®] developers have mentioned it as a significant factor for their progress. The pharmaceutical market is based on free market and innovation under the umbrella of solid intellectual property regulation³⁴. This translates into a situation where once the patent holder of a blockbuster drug loses the patent, they automatically lose the market gap occupied by that drug. From then on, it will be occupied by generic formulations at a lower cost. Against this background, patent holders deploy various business strategies with the intention of patching the hole in their incomes, or to delay entry of most upcoming generic versions into the market.³⁵

How has this phenomenon affected Otsuka lately? The market for the previous Abilify formulation—without the ingestible sensor—of the digital pill version, entailed a total of \$7.5 billion in the USA for the company,³⁶ and operations with this drug in North America constituted about 40 per cent of Otsuka global sales.³⁷ This put Abilify ahead in the top-selling drugs in the USA between 2013 and 14,³⁸ the year before the patent expired in 2015.³⁹ The entry of generic versions into the market after patent expiry would result in a calamity for the patent holder. And that was the starting point. In 2015, after several attempts to delay entry of the generics (materialized in various

32 Sara Gerke et al., *Ethical and Legal Issues of Ingestible Electronic Sensors*, 2 NAT. ELECTRON. 329, at 331 (2019).

33 Jack DeRuiter & Pamela L. Holston, *Drug Patent Expirations and the "Patent Cliff"*, 37 6, U.S. PHARM. 12 (2012).

34 European Commission, Competition DG. *Pharmaceutical Sector Inquiry. Final Report*. https://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf (accessed May 5, 2020) and World Trade Organization, *Trade-Related Aspects of Intellectual Property Rights*, at 11 https://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm (accessed May 5, 2020).

35 Chie Hoon Song & Jeung-Whan Han, *Patent Cliff and Strategic Switch: Exploring Strategic Design Possibilities in the Pharmaceutical Industry*, 5, 1 692 SPRINGERPLUS 1, at 3 (2016).

36 Otsuka, ANNUAL REPORT, at 17, (2014).

37 *Id.*, at 40 (2014), and Leah Ida Harris, *The Rise of the Digital Asylum*, MAD IN AMERICA, Sept. 15, 2020, at 15.

38 *Id.*, at 17 (2014).

39 The protection period for the substance patent of ABILIFY will expire in Jan. 2016 in Japan (including the 2-year pediatric exclusivity), in Apr. 2015 in the USA (including the 6-month pediatric exclusivity) and in Oct. 2014 in Europe. *Id.*, at 53 (2014).

litigations),⁴⁰ the first generic-version aripiprazole entered the market. In the face of this situation, Otsuka, with cooperation from Proteus, introduced an innovation to the obsolete product—the ingestible sensor—which made it new again, and thus allowed for 'evergreen'⁴¹ patenting. This strategy enabled the maintenance of their leadership in the market, at least for the market share represented by patients that did not meet the proper medication-taking adherence.

The answer to the question of why digital pills have entered the market appears to be clear: non-adherence to medication constitutes a major problem—i.e. especially the case for antipsychotics.⁴² Hence a large market share would demand a product that monitors treatment adherence. But this does not necessarily mean that digital pills constitute the solution for non-adherence to antipsychotics. Some more reasons are needed for that.

In this sense, we find some social factors that would support digital pills' market entry can be added. The first is a favorable public opinion of treatment compliance by such patients, as non-compliance could involve a hazard to public safety in case they behave dangerously toward themselves, their family, or third parties.⁴³ They also have the potential advantage of reducing possible tensions within the family, or reducing family anxiety, about treatment non-compliance. Compliance would warrant public—and private—safety, and digital pills constitute a major step for this purpose, as they are not subject to the limitations shown by previous electronic reminders in ingestion tracking.⁴⁴

The second factor is a favorable attitude from healthcare professionals toward a treatment that would substitute the monitoring ingestion alternative: the long-acting injectable antipsychotics (LAIs)—apart from other advantages they might find for such treatment. LAIs are a means of managing treatment periodically, so taking the medication does not depend on the patient, hence neither does compliance nor non-compliance to the patterns given by the physician. Although LAIs make non-adherence impossible, they have been observed to have some limitations as well—such as difficulties in finding the proper dose—and are not suitable for all patients.⁴⁵ In addition, digital pills overcome the challenges presented by other alternatives posed by professionals for increasing adherence, such as psychosocial interventions (i.e. psychoeducation), electronic reminders (i.e. smart pill bottle, SMS), other service interventions (i.e. access to emergency services, interventions for reducing medicine prices), or financial

40 *Id.*, at 54 (2014); Wolters Kluwer, *Drug Makers Given Green Light to Market Generic Versions of Otsuka's Abilify Drug*, INTELLECT. PROP. LAW DAILY, Apr. 17, 2015 and WCG, FDA, *FDA News*, <https://www.fda.gov/articles/183464-otsuka-loses-again-in-challenge-to-fda-green-light-for-competing-drug> (accessed Jan. 16, 2020).

41 Cosgrove et al. define evergreening as 'a strategy used by industry to effectively extend patent protection by making small changes to existing products, changes that have almost no added benefit to the patient', see *infra* note 49, at 236.

42 Jonathan P. Lacro et al., *Prevalence of and Risk Factors for Medication Nonadherence in Patients with Schizophrenia: A Comprehensive Review of Recent Literature*, 63 *J. CLIN. PSYCHIATRY* 892, at 892 (2002) and Leah Ida Harris, *supra* note 37, at 12.

43 Peter M. Haddad, Cecilia Brain & Jan Scott, *supra* note 17, at 46–47 (2014).

44 Leah Ida Harris, *supra* note 37, at 14.

45 *Id.*

incentives (i.e. payment in return for taking the medicines, although this last option raises ethical issues).⁴⁶

Finally, the third key factor relates to a questionable favorable attitude—already regarded by some as 'spin'⁴⁷—in the scientific literature and news reports that somehow impacts on both attitudes just mentioned: that of the public and the professionals. There is an underlying concern regarding the scientific support and favorable opinion presented in several reports, which revolves around the real comparative effectiveness of this new-generation drug.⁴⁸ Some authors have already highlighted that the approval of this first version of digital pills was based on weak clinical trial evidence. Abilify MyCite is not indicated for adherence, and its impact on it has not been demonstrated. Cosgrove et al.⁴⁹ underscore with their systematic review of clinical trials submitted to the FDA three relevant facts: first, in the reviewed clinical trials, no higher or lower efficacy is proved in comparison with the previous nondigital drug, or with other active drug comparators (approved in the USA for the same indication), or with placebo, while at the same time no clear information about drug safety is provided. Second, the clinical trials could only prove that the treatment fulfilled the purpose for which it is indicated: tracking the ingestion; they failed to prove that fact would increase adherence, and therefore there is no way of knowing for certain if this sort of treatment would improve patient quality of life, symptoms, or relapses. It only succeeds in demonstrating that the sensor works properly.⁵⁰ Third, Cosgrove et al. also point out an emergent scientific and news tide that distorts interpretation of the evidence shown by clinical trials, which is manifestly biased by conflicts of interests, presenting a greater impression of the benefits than that provided by the data.⁵¹

Furthermore, it is important to highlight that medicine prices constitute a barrier to adherence.⁵² Regarding the data between 1999 and 2015 in the USA about cost-related prescription non-adherence, a study reported that millions of people do not

46 Peter M. Haddad, Cecilia Brain & Jan Scott, *supra* note 17, at 55.

47 Cosgrove et al. define spin as 'a specific way of reporting, intentional or not, to highlight that the beneficial effect of the experimental treatment, in terms of efficacy or safety, is greater than that shown by the results', see *infra* note 49, at 232.

48 Leah Ida Harris, *supra* note 37, at 16.

49 Lisa Cosgrove et al., *Digital Aripiprazole or Digital Evergreening? A Systematic Review of the Evidence and Its Dissemination in the Scientific Literature and in the Media*, 24 *BMJ EBM* 231 (2019).

50 Daniel J. Lee. *Center for Drug Evaluation and Research, Application Number: 207202orig1s000 Clinical review(s)*, at 11 https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/207202Orig1s000MedR.pdf (accessed Jan. 16, 2020).

51 Cosgrove et al. showed that 10 out of 14 papers that reported on the two studies taken into account did not address the lack of efficacy of the trials. Thirteen out of 14 did not mention the scarcity of data on safety or the fact that no comparator studies were conducted. In 10 out of 14 papers, authors gave an unsupported impression of benefit, and in eight out of 14 there was at least one author who had economic links with Otsuka or Proteus; moreover, in six out of 14 papers, the authors were employees in those companies. When analyzing news reports, lack of efficacy was not acknowledged in 40 out of 70 cases studied, and 65 out of 70 reports omitted information about the lack of safety data and did not include any nondigital comparator. In 52 out of 70 cases, benefits not supported by evidence were reported. In 54 out of 70 cases, experts were cited, but in 21 of those 54 cases, those experts had economic ties with the companies mentioned. See Lisa Cosgrove et al., *supra* note 49.

52 Maria Kelly, Suzanne McCarthy & Laura J. Sahn, *Knowledge, Attitudes and Beliefs of Patients and Carers Regarding Medication Adherence: A Review of Qualitative Literature*, 70 *EUR. J. CLIN. PHARMACOL.* 1423, at 1427 (2014).

fill a prescription, postpone a prescription fill, take less medication than prescribed, or skip doses to save money. These figures increase among working-aged adults, women, African Americans, the uninsured, people with disabilities, among others.⁵³ This new pharmaceutical product costs nearly \$1700 per month, whereas the generic-version aripiprazole without the sensor costs \$20 per month,⁵⁴ which seems to be relevant inasmuch as access to treatments is important for patients with long-term health conditions. From a funding prescription perspective, it is foreseeable that health insurers will pay for this innovative treatment according to the provided cost-effectiveness. To this regard, they would find digital aripiprazole preferable over the nondigital version if its use translates into reduced costs for the coverage of the patient, hence making it worthwhile to opt for.⁵⁵ Thus far, there is not enough comparative evidence that shows a major ability for Abilify MyCite[®] to improve patient's health over the nondigital version. As highlighted above, we can ensure ingestion will be tracked with a high precision, but we cannot anticipate if this circumstance would translate, in all events, in a patient's health improvement.

In addition, the very characteristics of the final users of these digital pills (surveillance paranoia and similar) appear to be discouraging for the approval of a pharmaceutical product that takes surveillance to a higher level. In this sense, potential hazards over the patients derived from the intake of these pills must be approached in a specific and more in-depth study that has not been performed yet.⁵⁶ But even in the case that these ethical barriers are overcome by the benefit an eventual high adherence rate would generate, then, as already pointed out by some, the lack of effective outcomes or/and harmful adverse effects that high rates of adherence would generate in patients on long-term therapies, should be considered.⁵⁷

All this being said, latest news reveal the short way gone for the once promising millionaire deal between Proteus and Otsuka. Recently, Proteus has announced that it will now focus its interests on some other fields such as oncology and infectious diseases, bringing the agreement with Otsuka to an end. The reason behind its pivoting direction remains, as pointed by some, in the thorny way chosen by Proteus trying to first expand its system between patients and healthcare providers in the area of mental illnesses: not a lot of them seemed comfortable with this new kind of combined product, a circumstance that turned into too low sales for Otsuka, and to an unprofitable and discouraging economic situation for Proteus. Meanwhile, Otsuka would continue

53 Jae Kennedy & Elizabeth Geneva, *Medication Costs and Adherence of Treatment Before and After the Affordable Care Act: 1999-2015*, 106 10, *AJPH*, 2016, 1804-1806, at 1806.

54 Lisa Cosgrove et al., *supra* note 49, at 236.

55 Klugman, *supra* note 16, at 42.

56 Lisa Rosenbaum, *Swallowing a Spy—The Potential Uses of Digital Adherence Monitoring*, 318 2 *N. ENGL. J. MED.* 101, 102 (2018) and Lisa Cosgrove et al., *supra* note 49, at 236.

57 Thomas Insel, *Post by Former NIMH Director Thomas Insel: Antipsychotics: Taking the Long View* <https://www.nimh.nih.gov/about/directors/thomas-insel/blog/2013/antipsychotics-taking-the-long-view.shtml#1> (accessed Jan. 18, 2020); Lex Wunderink et al., *Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy Long-term Follow-up of a 2-Year Randomized Clinical Trial*, 70 *JAMA PSYCHIATRY* 913, at 919 (2013); Leah Ida Harris, *supra* note 37, at 19.

developing medicines with the use of Proteus system, in a kind of a fully paid-up license conceded by Proteus for a transitional period.⁵⁸

We can conclude that this scenario could anticipate the eventual consequences generated by the entrance in the market of some cutting-edge digital health products.

RESPECT FOR PATIENTS' AUTONOMY

Patients' autonomy is a fundamental value. It might be the most important value in the way we understand medicine these days. It means that we have finally accepted that patients have the last word in making decisions that will have consequences in their own health or life. Therefore, patients' self-determination constitutes a sort of last boundary that should never be violated by physicians, healthcare providers, social workers, or any other person who may be involved in a caring relationship with a patient. This iron rule cannot be overridden by considerations such as the best interest of the patient (beneficence). Otherwise, we would be indulging in paternalism, a practice that has lasted for too long in healthcare. Do digital pills involve a restriction on patient autonomy?

The response to this crucial question is not easy to provide, as many different variables play a role in the answer. Synthetically, we dare say in advance that they neither violate patient autonomy if this autonomy does not exist, nor violate it without justification if there are good reasons to annul it (such as public interest), nor restrict it at all if patients are competent to consent and show willingness to use the tool, as long as they provide a real informed consent—which means they have been informed properly—and freely consent to it. Instead, they would definitively violate such autonomy if the patient would not provide real informed consent, a scenario that might be present under several common circumstances. To this respect we must address very cautiously the information issue in the user agreements these tracking systems imply, since a lack of agreement could translate into a lack of access to the treatment, and then into a pressure over patients to accept some clauses they might not really agree with, thus, making not an optimally autonomous choice. We will approach this question in Section 6.

Starting from the easiest scenario, we concede that digital pills involve no risk for autonomy if the patient consents to their use under such circumstances just mentioned: a really informed consent. This might happen for multiple reasons. For example, patients with memory loss might be willing to use a system that would serve them well to avoid overdoses while reducing the anxiety stemming from the doubt of whether they have taken the pill. Similarly, patients could be looking forward to benefitting from a tool that allows them to demonstrate to their doctors that they are following the provided treatment strictly. Alternatively, they could be proud to use a modern technology that allows them to incorporate their own impressions about the treatment in an agile way.

The reasons for acceptance are indeed uncountable, and we do not think that our mission should be to focus on them. Instead, we should concentrate in cases in which patients are not willing to adhere to the use of digital pills. In our opinion, this would

58 Dave Muoio, *Proteus Parts Ways with Otsuka As It Pivots Toward Oncology, Infectious Disease Treatment Adherence*, MOBILE HEALTH NEWS, Jan. 14, 2020, and Rebecca Robbins, *A Forerunner in 'Smart Pills' Adopts a New Tack as Key Pharma Partnership Unravels*, STAT, Jan. 14, 2020.

not necessarily act as the definitive reason for avoiding their use. First, one must think whether acting against the patient's will violates their autonomy, and then consider some situations that would yet justify this violation.

The first thing to take into account is the patient's legal capacity. In case of legally incapacitated patients, their legal representatives have to decide on whether to adopt digital pills—respecting the ultimate patient's interests and counting with their participation in the decision-making process as far as possible. This would be the case of minors or legally incapacitated people.

More complex is the case of other people who do not have a permanent or lasting restriction on their autonomy, but who find themselves in circumstances that advise the use of digital pills. Imagine, for example, the case of a person affected by a particularly serious contagious disease that requires the administration of a specific medication for treatment; or the case of a mental patient whose pathology is associated with violent outbursts that may endanger other people. In all these cases, the patient poses a threat to public health. It is therefore necessary to adopt measures capable of neutralizing it. At present, this is done through mechanisms such as quarantining or confining the patient in a health facility, where the medication is administered in a forced manner.

The appearance of digital pills promotes an alternative to this situation, as it allows monitoring the administration of treatment without confining the patient (unless the danger of contagion is unavoidable, or patient's values and preferences are in accordance with the confinement, in which cases confinement is legally supported). In these circumstances, recourse to this new technology would undoubtedly be contrary to patient autonomy, but much less than the alternative possibility of confinement. This fact would justify its use even against the patient's will.

Finally, we must consider the case of the largest group of patients, i.e. those who possess full faculties for consenting to a treatment and whose pathologies do not pose a public health or public safety problem. In all these cases, it is not possible, in our opinion, to justify the use of digital pills if it is not through the consent of the affected person. Moreover, consent must be obtained through a process that provides the patient with adequate information and guarantees freedom of choice. This is particularly relevant when we are talking about vulnerable populations, such as the mentally ill, the elderly, or people with low levels of education, as well as in people with very little social support. In these cases, apparent acceptance often hides a desire to not lose the approval of their scarce social links. As Dotolo et al.⁵⁹ wrote, 'When the technology embedded in AMC is introduced to clients and families by prescribers, its use is normalized, if not tacitly endorsed. Although formal policy may require informed consent for AMC prescription use, social workers understand that freely given consent in practice is often complicated by difficulty understanding consent forms and processes (Schenker, Fernandez, Sudore & Schillinger, 2011), power asymmetries (Barusch, 1987), and borderline coercive practices in the context of caregiving (Berridge, 2017). Once the technology is broadly adopted and normalized, it may be featured in mandated treatment or coercively encouraged by family members and service providers in the name of beneficence and safety'.

59 D. Dotolo, Petros, R., & Berridge, C. *A Hard Pill to Swallow: Ethical Problems of Digital Medication*, 63 Soc. WORK 370–372 (2018). doi:10.1093/sw/swy038

In such situations, where using smart devices for healthcare becomes normalized, not participating in such a self-care technological paradigm could even be contemplated as a basis for exclusion from access to health services.⁶⁰ In addition, we may consider that being aware of the risks a person is exposed to appears to condition the person into adopting the necessary measures for safeguarding themselves by controlling those already known risks,⁶¹ a scenario in which smart devices could be extremely useful.

Therefore, we need to be particularly vigilant to ensure that patients have good understanding of the implications of the use of digital tagging. On top of that, we will have to strive to provide a framework that allows them to express their opinions freely and support their decisions, attempting to reduce the hostility they may arouse in their social support networks, family, or friends.

In any case, the dilemma must not be seen as an all-or-nothing decision. It is not true that the alternative to the adoption of digital tagging is the loss of absolute control over the patient's behavior. Today, medication management tools that serve these purposes well even though they limit the patient's autonomy much less are already in use. It is true that they probably do not provide with such exact information. However, it will be necessary to assess in which cases the difference in precision would endorse the imposition of a measure—the use of digital pills—which represents the considerable loss of a person's autonomy.

Finally, it is good to remember that, in general, people are allowed to refuse a medical treatment due to a number of reasons that are not necessarily rational. It would be unusual to make an exception in the case of digital pills. It is widely accepted that choosing between welfare and peace of conscience is a decision to be taken from one's own deepest autonomy, as an expression of the ownership of rights, without the State or third parties playing a role in the decision-making—except legal incapacity cases.⁶² We could consider the paradigmatic example of a Jehovah's Witness's decision in rejecting a blood transfusion, and hence deciding to preserve their freedom of consciousness at the expense of their health or even their life. To support this, we can follow Stuart Mill: 'The only part of the conduct of any one, for which he is amenable to society, is that which concerns others [. . .] Over himself, over his own body and mind, the individual is sovereign.'⁶³ This is the idea that has constituted the guideline in designing a healthcare system based on autonomy, stripped of paternalism patterns.

AUTONOMY AND USER AGREEMENTS

The use of digital pills implies the need to address a particularly complex issue in terms of informed consent, which is not present in all physician–patient relationships. As we have explained, digital pill systems include both a drug and a digital tracking system, i.e. three electronic devices: the IEM, the patch, and the mobile app. The issue is that the use of these devices requires the acceptance of some conditions of service, i.e. of a consent that is unrelated with the consent related to the administration of the drug.

60 Dimitra Petrakakia, Eva Hilberg & Justin Waring, *supra* note 22, at 149.

61 Sonja Erikainen et al., *Patience and Participation in the Digital era*, 5 DIGITAL HEALTH 1, at 6 (2019).

62 Francisco Bueno Arús, *El consentimiento del paciente en el tratamiento médico-quirúrgico y la Ley General de Sanidad*, in ESTUDIOS DE DERECHO PENAL Y CRIMINOLOGÍA, 163 (UNED, 1989).

63 J. Stuart Mill, ON LIBERTY, at 13 (1859).

Here, we may find the first concern about this issue: this privacy policy is sort of a take-it-or-leave-it contract (usually termed an adherence contract). These agreements often consist of hundreds of pages written in technical language. Sometimes they hide clauses that enable manufacturing companies to manage the data collected for purposes other than monitoring the treatment of the patient involved.⁶⁴ In these—mostly common—situations, the patient may be authorizing uses they would not be able to understand due to the complex terminology. This question keeps the door open to a wider discussion about data privacy: future data use, eventual collections of identifiable patient information, access by stakeholders to patient and physician data collected the mobile app, and the web portal used by them, etc. The second concern we find is that when the privacy policy is provided only by the mobile app, there is a risk that document only refers to the app, overlooking sensor and patch privacy issues about which the user should be informed.

In both situations, the patient would not be making a properly informed decision: in the first situation, it is because of the lack of understanding about what information is collected and how it is used; in the second situation, because the patient has no way of knowing the risks implied. Hence, such privacy policies fail to protect the consumer that, in this case, meets a patient status whose autonomy is infringed.⁶⁵

Moreover, such consent is far removed from the norm in the practice of medicine, as it is not based on face-to-face information and a negotiation of the terms of treatment, but on a user agreement that cannot be discussed with the provider. Pretending that a person can, by their own means, provide informed and free consent to the use of these devices is, in these conditions, not very credible. Although some of our current regulations (such as the General Data Protection Regulation in the European Union context) accept that a mere 'box ticking' serves to capture the existence of consent, the truth is that this rarely happens. What really happens is that very often we sign a consent form to access a service without having any idea of the terms of the contract. This, which is worrying in any sphere of human life, is even more so in the field of health. This might become even worse if acceptance of the use agreement becomes a condition of access to the drug. In such cases, we could think about an absolute perversion of the system of consent to treatment.

It is therefore necessary to create new mechanisms capable of tackling this problem effectively, ensuring an effective defense of the patient's interests. Some authors have postulated an adaptation of the traditional informed consent.⁶⁶ This way, healthcare providers would be the player committed to informing the patient about such privacy issues. There are some advantages to this proposal: the patient will be informed before buying the treatment, and will likely better understand when that information is communicated face-to-face by a trusted person (doctor) instead of from a legal document. Some would say that studying privacy policies would take a long time for physicians, apart from exceeding their competences, but, that is, when doctors may

64 Klugman, *supra* note 16.

65 Amelia Montgomery, *Just What the Doctor Ordered: Protecting Privacy Without Impeding Development of Digital Pills*. 19 *VAND. J. ENT. & TECH. L.* 147, at 168 (2016).

66 Article 29 Data Protection Working Party, *Opinion 8/2014 on the on Recent Developments on the Internet of Things*, at 7, <https://www.dataprotection.ro/servlet/ViewDocument?id=1088> (accessed 5 May, 2020).

ponder the sacrifices they must make and the benefits obtained by prescribing a digital pill treatment.⁶⁷

We could certainly think of many other alternatives, which should be carefully explored in the future. This may well result in a form of paternalism, but in our view, it would not be an immoral type. Paternalism is only reprehensible when someone tries to supplant the will of the patient on the basis of the alleged pursuit of his welfare. However, if the patient is incapable of giving consent because the process makes it impossible in practice to be adequately informed, then we are faced with a situation of vulnerability, in which the intervention of a third party to protect their interests is unavoidable from an ethical point of view. Thus, an administrative intervention capable of putting conditions on use agreements and their updates, or a system that allows patients to access reliable information on the real content of these agreements, seems to be a more than reasonable option.

THE ISSUE OF PRIVACY

The use of digital pills has strong implications on patient privacy. To begin with, it is necessary to stress that the introduction of this technology puts an end to the monopoly of power over information on the observance of the treatment possessed by patients. Up until now, and despite the existence of mechanisms that allow adherence to treatment to be monitored in some way, the truth is that patients are still the only ones who know for certain whether they are following the indicated doses. This is due to the simple fact that, ultimately, only the patients know whether they are taking the prescribed tablet and when. With the inception of this technology, however, that monopoly was broken. There is an alternative source for the doctor capable of providing extremely accurate information. Consequently, the patient's privacy is unavoidably threatened. The security of secrecy is no longer in their hands alone. To begin with, their doctor will have direct access to the information without having to consult with the patient. This in itself is not the worst threat to the patient. Healthcare professionals have been used to professional secrecy for generations and the law protects patients against indiscretion.

Nevertheless, this scenario introduces, in addition, a third party to play a role in between physician and patient, and who will have access to all the data collected by the device: the device developer. Developers need that access to procure the minimum safety and effectiveness levels for the service they are offering. When using that data properly anonymized and for legally contemplated purposes (such as investigations), no explicit consent is needed as long as developers comply with the applicable laws. But when we talk about highly protected information—health data—this circumstance raises serious challenges related with data breaches and deanonymization.⁶⁸ Consequently, while they are accessing the same data as the physician, developers should not abdicate the same secrecy and confidentiality responsibilities demanded of healthcare professionals.

Furthermore, we must keep in mind that friends or relatives around patients might access the data. Different from healthcare providers, they are not legally obliged to keep

⁶⁷ *Id.*, at 173 and 174.

⁶⁸ Glenn Cohen et al., *The Legal And Ethical Concerns That Arise From Using Complex Predictive Analytics In Health Care*, 33 *7 HEALTH AFF.* 1139, at 1141 (2014).

the data confidential, nor have they been trained to do so. On the other hand, it is quite obvious that the mere knowledge that patients are using this type of device can lead to great pressure being exerted from their environment to share the data. Take, for example, the case of a bipolar person living in the house of a brother, son, or their parents. Do we not think that there will be many cases in which the relationship of economic dependence is used to gain access to data? Even more dangerous are the pressures that insurance companies could exert on their policyholders to gain access to the data. If it were legally possible, it is likely that some would try to condition the funding of these devices based on the possibility of appropriating the resulting information, or at least, offering discounts to policyholders who allow it. Data provided by tracking devices could be used in health decision-making, either for ensuring compliance with therapeutic recommendations, or as a consequent fairer distribution of health resources ('if you don't lose weight/don't take the pills on schedule, then you lose the right to undergo a surgical procedure/to be covered up to this insurance policy').⁶⁹

Finally, we must not underestimate the possibility of the stored data being used in police/judicial instances, perhaps as a condition for a convict to be released on bail ('you take the pills on schedule, or you go back to jail'), or perhaps as evidence against the patient himself. Some bioethicists consider this method more reliable than just trusting a detainee/convict's word.⁷⁰ This judicial use has already happened in some cases, for example, 'in one reported case, police sought a search warrant to access pacemaker data of a patient they suspected of arson.'⁷¹

THE SOCIAL PRESSURE FACTOR

Finally, it is important to bear in mind that the existence of an objective measure of adherence to treatment can lead to moral, social, or even legal censorship of patients who sustain in general a lack of adherence to treatment. Lack of adherence to treatment constitutes, thus, a neglect of responsibilities assumed by the person once they are aware of their behavior and the risks derived from it. In addition, datafication of patients provides the possibility of creating new categories of patients according to the information they generate;⁷² consequently, we run the risk of constructing a scenario in which it is possible to distinguish between 'good' and 'bad' patients depending on their adherence to treatment. We might even be tempted to impose sanctions on the second group, a temptation that has already given rise to action in this regard.⁷³ We could assume that if the individual behavior generates harm over the interests of others, without the existence of a higher duty that obliges a person to behave that way, they deserve moral disapproval. Not so if the consequences of that behavior only affect their own interests.⁷⁴ The question is whether (or when) this behavior—not taking pills when prescribed by the physician—constitutes a damage of the interests of others, and hence could be punished by the community.

69 Sarah Chan, *Bioethics in the Big Data Era: Health Care and Beyond*, 41 REV. BIO. Y. DER. 3, at 11 (2017).

70 R. Brandom, *The Frightening Promise of Self-Tracking Pills*, THE VERGE, Oct. 7, 2015, at 1.

71 *Telltale Heart: Pacemaker Data Leads to Arson, Fraud Charges*, Fox News U.S. (2017), <http://www.foxnews.com/us/2017/02/08/police-use-data-on-mans-pacemaker-to-chargehim-with-ohio-arson.html>

72 Sonja Erikainen et al., *supra* note 61, at 6.

73 Moutel, *supra* note 7.

74 Stuart Mill, *supra* note 63.

In our view, differentiating between 'good' and 'bad' patients and imposing sanctions on the latter would be a fatal mistake for many reasons. In general, constructing the figure of the 'guilty patient' is a mistake, a moral injustice that can eventually lead to State interference in private life. Second, this vision of the world sacralizes science, thinking that it is possible to objectively set optimal treatment guidelines that everyone should follow faithfully, although this is not how things work. As we have mentioned, reasons for non-adherence could be multiple and complex, and we should not fall into the error of thinking that this phenomenon is only understandable and approachable in one way. If there is one thing the evidence shows us, it is that each patient responds individually to a treatment, so unless we are able to optimize the doses for each patient, we will have to assume a margin of error. Moreover, we have to assume that this margin empowers the patient to deviate from the intended dosage without there being any evidence that this will lead to worse treatment performance. Moreover, we must keep in mind that there are times when strict adherence to treatment can be very difficult or even harmful for the patient, either because of the physical adverse effects it causes or because of the lifestyle changes it inevitably imposes. While the healthcare professional may prioritize healthcare understood to mean perfect adherence to the treatment, the patient may prioritize well-being in a wider sense, more related with a quality of life concept.⁷⁵ Therefore, it seems reasonable to assume that patients would know better how to deal with a treatment so that their lives are improved effectively instead of the opposite. This is usually known as 'self-efficacy', a concept developed by Bandura,⁷⁶ which shows the need to pay attention to the circumstances at stake and the wisdom of the patient's decision.

FINAL REMARKS

It is quite difficult to deny that smart pills could be useful for increasing adherence to treatment. If we are able to force patients to consume a medical device that inform healthcare providers if they have taken the pill, and combine this with the threat of punishing any lack of adherence with forced confinement of the patient, surely the intended objective will be achieved. However, this is not, in our view, the ideal way of ensuring better adherence. If studies show anything, it is that adherence improves with better understanding of the need for medication and a fluid and permanent dialogue between the patient and healthcare workers, which makes it possible to reduce harmful adverse effects. Obviously, there will be patients for whom all this is impossible. There will also be others where resistance to treatment is irrational. But, in general, we believe that these new systems should ideally be seen as a means of complementing traditional strategies for promoting adherence to treatment, and not as a substitute. Only in this manner can we obtain a final result that is not reduced to an increase in adherence rates subject to inadequate limitation of patient autonomy. As stated, 'Automatic and computerized data collection, related to the follow-up of a treatment, will require us to consider the following the question of benefit/risk assessment. The evaluation of

75 Victoria Camps, *UNA VIDA DE CALIDAD. REFLEXIONES SOBRE BIOÉTICA*, at 72 and 73 (2001) and Rosana Triviño, *EL PESO DE LA CONCIENCIA. LA OBJECCIÓN EN EL EJERCICIO DE LAS PROFESIONES SANITARIAS* (2014).

76 Bandura A. *Health Functioning*, in *SELF-EFFICACY: THE EXERCISE OF CONTROL*, 259–318 (SF Brennan ed., 1997). W.H. Freeman and Company.

a connected device will require to study how its use improves or not the quality of the follow-up and, ultimately, the patient's quality of life. And to analyze if risks would not offset these potential benefits (whether or not fundamental freedoms are infringed, psychological impact of fear of surveillance, increased anxiety, etc.).⁷⁷

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⁷⁷ Moutel, *supra* note 7.

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