

“Apps” for the patient - Medical devices or toys?

Digital technologies for patient health represent an emerging area of medicine. The possibility of improving health outcomes with these technologies - standalone, in addition or in combination with other treatments, such as drugs - has led in recent years to a growing interest on one hand of patients, doctors, researchers, companies and institutions, and on the other to a significant confusion about meaning, research, development, use.

In Italy the level of confusion is even higher, considering the higher “digital incompetence” according to the indicator related to Digital Human Capital in the 2020 edition of DESI - Digital Economy and Society Index of the European Commission⁽¹⁾.

Following the taxonomy offered by the Digital Medicine Society, Digital Therapeutics Alliance and others⁽²⁾, it is first necessary to make a clear distinction between Digital Health and Digital Medicine, the two categories in which the different digital technologies for health are classified.

This distinction is critical, since products classified in these categories have very different requirements in terms of evidence of efficacy needed to support their intended use and need for regulatory oversight for their use.

1. Apps and Digital Health

Digital Health encompasses technologies, systems and platforms that engage consumers on health, lifestyle, wellness or health-related purposes or that capture, store or transmit health data and/or deliver or support health services and clinical operations⁽³⁾.

It is therefore predominantly of interest to consumers, users, who are interested in improving their own well-being by, for example, enhancing certain physiological functions, not patients engaged in fighting a disease. The products represented in this category represent hundreds of thousands of digital applications (“apps”) that can be downloaded from the web and for which - in most cases - no research has been conducted or regulatory approval sought.

It is still infrequent - but rapidly progressing - the case where a physician advises a patient on one of these “apps” to manage a specific health issue, similar to the advice on dietary supplements that the patient can freely acquire at the pharmacy.

Unlike the latter, for which for some years there has been a certain amount of scientific information that allows the doctor to provide informed advice, the doctor’s knowledge about this category of “apps”, their use, their quality is rather poor, sometimes completely lacking. On the one hand, the risk of suggesting “apps” of no clinical validity or even harmful, and on the other hand, the risk of not responding to any requests for clarification or explanation from patients who have found “apps” of interest to them while surfing the web, is certainly not negligible.

In many cases, these “apps” may have attractive and engaging designs and graphics, but without being able to cross the threshold from “toys” to health response.

2. Medical Devices and Digital Medicine

The situation is different for the category of Digital Medicine, which represents a subset of Digital Health and includes evidence-based software and/or hardware products that measure and/or treat in the service of human health⁽³⁾.

These products affect the patient, the physician, and therefore the disease domain. In most cases, they are mobile device applications with both measurement and treatment purposes.

Measurement can be used to support the diagnostic process or to monitor the progression of a disease or therapy, or to guide treatment of the disease with a drug or medical device. Data is generated by the patient in a passive mode through the use of wearable or ingestible sensors or in an active mode by filling out questionnaires or taking online tests.

The treatment delivered by these “apps” can have different modes of execution, such as:

- **Digital Self Management, Education & Support (DSMES):** applications that provide proven training, instructions and guidance on how to interactively manage, for example, Diabetes Mellitus⁽⁴⁾, hypercholesterolemia or hypertension⁽⁵⁾;
- **Digital Drug Supports:** applications that enable the optimal conditions for the use of a drug, with which they are therefore associated or combined, through the reminder of the assumption, the possible dosage calculation of the drug to be taken, the support to the management of any unwanted events, the contact with the doctor or with other patients with previous experience of the same therapy, etc.⁽⁶⁾;
- **Digital Therapeutics:** applications that provide a therapeutic intervention through a “digital active ingredient”, independently from the drug or associated with it or combined in the case of shared therapeutic indication⁽³⁾;
- **Digital Rehabilitation:** digital rehabilitation systems for motor, cognitive, pulmonary, cardiological or other purposes, able to allow the recovery of impaired functions and capabilities through measurements (e.g. with shirts equipped with inertial sensors) and treatment (e.g. with serious games that involve the patient in different motor exercises)⁽⁷⁾;
- **Digital Connected Devices:** devices such as subcutaneous pumps able to infuse the right amount of drug (e.g., insulin) at the right time in response to indications from an algorithm that processes information received from sensors (e.g., continuous blood glucose measurement sensors)⁽⁸⁾.

The use of these technologies requires both the availability of evidence of efficacy generated with clinical trials, depending on the purpose of use, and approval by regulatory agencies.

For the purposes of regulatory classification, when it affects the patient and intervenes in his diagnostic and / or therapeutic pathway, the “app” (and more generally the various tools, both hardware and software, of Digital Medicine) represents a Medical Device⁽⁹⁾ and therefore must be

- designed and produced by a manufacturer with a certified quality management system regarding compliance with UNI CEI EN ISO 13485 - 2016 of these processes;
- developed through clinical research that confirms the effectiveness in the proposed intended use.

For these reasons, it is inappropriate to refer to such products as “apps”, but rather as:

1. medical devices
2. in the form of digital applications
3. with one of the specific measurement or intervention purposes described above.

A Digital Therapeutic therefore should be described as a “Medical Device in the form of a digital application for therapeutic intervention purposes”.

Towards the Bio-Digital Pipeline

There are several companies integrating their drug list with medical devices, with the aim of improving patient health. Research and development of these devices - represented in most cases by products in physical form - are processes well acquired by these companies, as well as the knowledge of their regulatory aspects.

To enable the acquisition of useful data to guide the therapy with their drugs and the treatment of diseases in the therapeutic areas in which they are engaged, today companies with more vision have the opportunity to research and develop new medical devices in the form of digital applications to be associated or combined with their drugs and devices.

It can be Digital Self Management, Education & Support to be associated with an antidiabetic drug to help control the disease, a Digital Drug Support to be associated with an antihypertensive drug to achieve the maximum potential of effectiveness of the same or a Digital Therapeutic to be combined with an antidepressant drug, to achieve levels of effectiveness “beyond the drug”.

These are Medical Devices *by design*, the architecture of which must therefore be designed from the beginning of the project by a team with different skills, including patients with expertise in digital health technologies. They are based on experimental research, which must prove the effectiveness on the basis of which the doctor will prescribe the treatment and the patient - who will hold the smartphone with the application - will take it.

This is a distinctive aspect of the modern pharmaceutical company, i.e. research and development of new Bio-Digital therapies, which will be

able to feed new Pipelines of products able to offer the highest quality and quantity of health today possible to the person with the disease.

This is an ambitious goal, but certainly within the reach of our companies and startups, and the development of this Digital Biotechnology can and should be a key component of the path to recovery and resilience that our countries are now facing.

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