EXECUTIVE SUMMARY
First DTx Monitoring Report

The objective of the First DTx Monitoring Report is to provide snapshot of the state of the art in digital therapeutics (DTx), from global research stages to commercialization status, and to understand Italy's positioning in the growing field of digital health and DTx in particular.

To date, there is no globally recognized definition of digital therapeutics; for the purposes of this Report, the ISO/TR 11147 definition (June 2023) has been adopted, recognizing DTx as healthcare software designed to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention with a demonstrable positive therapeutic impact on the patient's health.

Horizon scanning delle DTx

A global analysis of over 1200 clinical trials was conducted, from which 224 digital therapies trials were selected. The research revealed a concentration of studies in the US (41%) and Europe (41%), with Germany being the most prominent country in Europe (47% of European studies), followed by the UK (16%). Italy plays a marginal role with only 3 ongoing studies. The most studied therapeutic areas are psychiatric disorders (49.3%), particularly depression, anxiety, and insomnia, followed by diabetes (6.7%). Most of the developed technologies consist of mobile applications.

The State of the art of DTx in Europe

The market overview reflects the status of clinical trials. Globally, the DTx market is valued at $6.5 billion in 2022, with the US leading the way at $2 billion. Europe accounts for only one-tenth of this market ($612 million), and Germany remains the leading country with 49 DTx approved for permanent or provisional listing. The UK follows with 14, and France has 3 reimbursed DTx through the PECAN system.

Innovative Startups in lifescience

From January 2021 to June 2023, innovative startups in lifescience account for approximately 9% of the total innovative startups (643 out of 7,310). Of these 643, 144 (22%) are involved in digital health, and only 6 are involved in DTx. Lombardia region is the leading region with the highest number of innovative startups in lifescience, followed by Campania and Lazio. The lifescience sector has a higher female presence (17%) compared to the average for innovative startups in Italy (13%), reflecting the trend towards greater female representation in leadership positions in this sector.

The financing of Digital Health in Italy

In terms of potential investments in healthcare digitization, Italy can count on investments exceeding 32 billion euros, primarily backed by the National Recovery and Resilience Plan (PNRR), with 1.6 billion euros earmarked for digital projects in Mission 4. The share of privately managed funds, excluding co-investments with public funds, remains limited, reflecting the relatively low presence of Venture Capital (VC) in Italy compared to other countries.

Analysis of DTx Development in Italy

In Italy, 13 companies are involved in the production and development of digital therapies, including 8 innovative startups, 1 startup, 1 innovative SME, and 3 established companies. Out of a total of 28 Italian DTx, 21 are in the development phase, and 7 have already been recognized as Class I medical devices by the Ministry of Health.

Regulatory Aspects

Healthcare software products can be categorized into two groups: technologies with specific medical purposes and technologies for general wellbeing and physical activity monitoring. Software with a specific medical purpose, including digital therapeutics, is defined as Medical Device Software (MDSW) and is subject to the provisions of the EU Medical Devices Regulation (MDR) or the EU In Vitro Diagnostic Medical Devices Regulation (IVDR). As such, DTx that are already registered as devices are listed in the Ministry of Health's Registry of Medical Devices.

The Value of Data

The use of digital therapeutics is subject to strict European regulations on the protection of personal data, including sensitive health data. This requires lawful, transparent, and secure data processing. Software-based digital therapeutics pose a greater cybersecurity threat and need to be supported by robust data protection measures. Personalising treatments improves efficacy and adherence, supports more informed clinical decisions, and opens up new opportunities for medical research. The use of data generated by digital therapeutics can add value to patient health management. The lack of standardization in data collection and management, along with regulatory and technical challenges, are significant barriers.

Digital Therapeutics and pharmacology

DTx, acting as software, do not come into contact with the systemic circulation as drugs do. Therefore, traditional concepts of pharmacokinetic/pharmacodynamic parameters are not applicable. Some aspects of clinical pharmacology can be applied to DTx using quantitative pharmacometric models. Software can also lead to side effects (eye strain, sleep disruptions, risk of addiction), so ensuring optimal exposure is essential for the efficacy and safety of DTx products.

Clinical Efficacy Evaluation Criteria

As medical devices, DTx must achieve high standards, including strong scientific evidence of clinical safety and efficacy. Clinical evaluation of DTx should be structured as a pilot study, as an exploratory phase, followed by a pivotal study. Key elements to be used as criteria for evaluating the robustness of such studies include randomized clinical trials, patient involvement in the development phase, and publications in peer-reviewed scientific journals.

Distribution Channel

To enable DTx to become an integral part of clinical practice, new organizational distribution models that are adaptable to local care will need to be adopted. The distribution channel may involve public payers, and the reimbursability of digital therapies should be similar to that of integrative pharmaceutical care services. It is crucial to ensure adequate funding without affecting existing health expenditure ceilings. Reimbursement can be based on negotiation or a national fixed cost. Reimbursement rates may be negotiated or set at the national level.

Proposals

In the light of these observations, the working group has developed a series of **operational proposals:**

- Definition of a clear classification and accepted nomenclature for various types of software, particularly for software with a direct therapeutic effect, known as digital therapeutics (DTx), with specific terms in the National Classification of Medical Devices (CND) and the European Medical Device Nomenclature (EMDN).
- Definition of health technology assessment through national HTA, eligibility for reimbursement by the National Health Service with a dedicated fund, and the definition of the distribution channel.
- Proposal of a checklist to define the pathway in the light of what has already been done in other countries.