Digital Health Policy Lab

Secondo DTx Monitoring Report

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*The DTx Monitoring Report is the result of the work of the **Digital Health Policy Lab**, a research project established in 2022 in collaboration between **Indicon Società Benefit** and the **University of Milan**, aimed at promoting the development and access of digital health technologies (DHT) in the Italian National Health Service.*

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Digital Health Policy Lab

Secondo DTx Monitoring Report

Preface

Prefazione al Secondo DTx Monitoring Report

Senatore Guido Quintino Liris

Con grande piacere e sincero apprezzamento per il lavoro svolto, ho voluto firmare la prefazione del DTx Monitoring Report, redatto da Indicon Società Benefit in collaborazione con l'Università degli Studi di Milano, giunto quest'anno alla sua Seconda Edizione.

Le Terapie Digitali (DTx) rappresentano un'innovazione significativa nel panorama terapeutico globale, costituendo un settore in rapida espansione che sta catalizzando l'attenzione di molteplici attori, sia pubblici che privati. Il DTx Monitoring Report si propone di delineare l'evoluzione temporale di queste tecnologie all'avanguardia, offrendo un'analisi approfondita dello stato dell'arte in Europa in termini di diffusione, quadro normativo e politiche di rimborso. L'obiettivo primario è quello di favorire l'istituzione di un adeguato impianto legislativo anche in Italia, seguendo l'esempio virtuoso di altre nazioni europee.

Ritengo di fondamentale importanza che anche il nostro Paese si apra a questo segmento innovativo, principalmente per tre ragioni di rilevanza strategica. Le terapie digitali si configurano come strumenti di notevole efficacia nei percorsi di cura in numerose aree terapeutiche, apportando significativi miglioramenti alle condizioni cliniche dei pazienti e consentendo al personale medico-sanitario un monitoraggio costante e puntuale dei progressi conseguiti. Queste tecnologie si inseriscono armoniosamente nel processo di digitalizzazione del sistema sanitario, contribuendo a rendere il Servizio Sanitario Nazionale sempre più aderente alle esigenze della popolazione.

In qualità di membro della 5a Commissione Permanente (Bilancio) del Senato ritengo doveroso sottolineare la rilevanza economica di queste tecnologie, sia in termini di opportunità offerte da un mercato indubbiamente attrattivo, sia per la loro capacità di ottimizzare la sostenibilità della programmazione sanitaria nazionale, grazie alla riduzione dei costi e alla possibilità di fruizione autonoma da parte del paziente.

È innegabile che anche in Italia l'interesse verso le terapie digitali stia crescendo in maniera esponenziale. Ne sono testimonianza i significativi progressi compiuti nell'ultimo anno sul fronte normativo, tra cui la recente presentazione di una proposta di legge per la loro regolamentazione e la definizione della normativa ISO 11147, specificamente dedicata alla sanità digitale personalizzata e alle terapie digitali. Tuttavia, persistono numerose questioni aperte che richiedono un'attenta disamina al fine di consentire una piena integrazione delle tecnologie sanitarie digitali nella pratica clinica. Tra queste, emerge la necessità impellente di fornire definizioni normative chiare e univoche per una corretta classificazione di queste tecnologie. È altresì essenziale che il quadro normativo evolva di pari passo con l'innovazione tecnologica, garantendo un accesso equo e universale dei pazienti alle tecnologie più avanzate.

In quest'ottica ho particolarmente apprezzato la scelta di includere, all'interno di questa Seconda Edizione del DTx Monitoring Report, anche i dispositivi medici digitali gestiti dal paziente per scopi medici diversi da quelli strettamente terapeutici. Questa inclusione si propone di fare chiarezza su tecnologie che attualmente occupano una zona grigia e scarsamente regolamentata del panorama sanitario.

È di cruciale importanza che la classe politica e le Istituzioni, attraverso una collaborazione sinergica, si adoperino per rendere accessibili ai pazienti e al personale sanitario tutte le soluzioni tecnologiche innovative che il progresso scientifico mette a nostra disposizione.

Per questo, nella piena consapevolezza che il DTx Monitoring Report possa fornire preziosi spunti a supporto di tutti gli stakeholder coinvolti, voglio ringraziare Indicon Società Benefit e il Dipartimento di Scienze Farmaceutiche dell'Università degli Studi di Milano che, dal 2022 attraverso il progetto Digital Health Policy Lab, lavorano con l'obiettivo di promuovere l'integrazione delle tecnologie sanitarie digitali nel Servizio Sanitario Nazionale e nella pratica clinica, contribuendo in modo significativo al progresso del settore.

Guido Quintino Liris

Membro della 5a Commissione Permanente (Bilancio), Senato della Repubblica

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The Second DTx Monitoring Report expands the research focus from digital therapeutics (DTx) to **digital health technologies (DHT)**, which currently represent a gray area with limited regulation, known as *connected care*.
This report aims to:

1. Clarify definitions of DHT and DTx.
2. Map the evolution of DTx in Europe.
3. Examine the ecosystem of Digital Health Technologies (DHT) and the current framework of DTx in Italy.
4. Define the budget impact of DTx in Italy.
5. Propose operational recommendations developed by the working group.

1. DEFINITIONS: FROM DIGITAL HEALTH TECHNOLOGIES (DHT) TO DIGITAL THERAPEUTICS (DTx)

The working group aimed to clarify the concept of DTx and classify digital health technologies **(DHT) with clinical purpose**, even if different from therapeutic claim, identified as patient-managed digital medical devices (pDMD). These technologies have been categorized based on their medical purpose into **5 categories: Digital therapeutics, Remote Patient Monitoring** (RPM), **Digital Diagnostics and Digital Prevention**. This classification helps in identifying digital health technologies and supports the development of regulations to facilitate their use in clinical practice and subsequent reimbursement.

2. MAPPING OF DTx IN EUROPE

a. COUNTRY SITUATION

The global market revenue for digital therapeutics is expected to reach **$4.68 billion in 2024**, with a compound annual growth rate (CAGR) of 16.61% from 2024 to 2029, reaching a market volume of **$10.09 billion by 2029**. In Europe, **Germany** leads the digital health technologies sector **with 55 reimbursed DiGAs**, compared to 49 in the same period (Q3) of 2023 (+12%), with 20 on the provisional list and 35 on the permanent list. The **United Kingdom** follows with **35 DHTs** approved by NICE (National Institute for Health and Care Excellence), a 150% increase from the 14 devices approved in Q3 2023. **France** with at least **4 DTx** and **3** remote monitoring devices **(RPM)** included in PECAN. In July 2024, **Spain** developed a methodological framework for evaluating digital health technologies in the post-market authorization phase.

b. ANALYSIS OF DiGAs PRICES

A price analysis of 33 permanently listed DiGAs in Germany shows an average DiGAs price of €222, with an **average permanent list price** ranging from **€220 in 2021 to €235 in 2024**. Among the DiGAs analyzed, 30 of them had a price reduction following negotiations, averaging **-47%**. One DiGAs was reimbursed at the same price as on the provisional list, while **two were reimbursed at a higher price** than on the provisional list (an average increase of 33%), both for the treatment of tinnitus.

3. THE ITALIAN CONTEXT

a. MAPPING OF PATIENT-MANAGED DIGITAL MEDICAL DEVICES (pDMD) IN ITALY**

Based on the medical device registry of the Ministry of Health, the CND (National Classification Codes of Devices) related to software as a medical devices were identified with the aim of mapping pDMD in Italy. Out of 344 devices analyzed, **45** met the definition of **pDMD**. Of these, **46%** (n=21) perform monitoring (Remote Patient Monitoring - **RPM**), **38%** (n=17) **therapy** (DTx), 9% (n=4) **prevention** (Digital Prevention), and 7% (n=3) **diagnosis** (Digital Diagnostics). Of the devices analyzed, 31 are registered as **Class I**, 12 as Class IIa, and 2 as Class IIb, while no devices are assigned Class III.

b. MAPPING OF DTx IN ITALY

The number of **Italian companies** developing digital therapeutics is growing significantly: **23** in 2024 compared to 13 in 2023. Of these, **16 are innovative startups**, 3 are innovative SMEs, 1 is a non-innovative startup, and 3 are established companies. The total number of **potential DTx** in Italy is now **41**, compared to 18 reported in 2023, with **17** already registered as **medical devices** with the Ministry of Health. Currently, 7 technologies are undergoing **clinical trials in Italy**, one more than in 2023. Of these, three are also registered as medical devices.

4. BUDGET IMPACT ANALYSIS OF DIGITAL THERAPEUTICS IN ITALY

A budget impact analysis (BIA) was conducted to evaluate the impact of digital therapeutics in the Italian national context. The model considers **17** DTx from the medical device registry of the Ministry of Health, associated with 8 therapeutic areas, over a three-year period (2025-2028). Various scenarios were considered, using the following variables: a) the treatment rate of the target population (5% - 10% - 20% of the affected population) b) the price of technologies (€100 - €200) estimated based on the value of DiGAs currently reimbursed on the permanent list in Germany. The most plausible scenario considers an adoption rate of 10% and a technology price of €200, estimating a budget of approximately **€18.2 million in year 1, €36.4 million in year 2, and €54 million in year 3**. This model provides an indication of the size of a dedicated DTx fund.

5. OPERATIONAL PROPOSAL

Given the complexity and lack of specific regulations on digital health technologies (DHT), the working group of the Digital Health Policy Lab proposes in the Second DTx Monitoring Report an operational model to support policymakers in developing regulations for innovative health technologies. The proposal includes an **evaluation and reimbursement model** inspired by the accreditation process for new technologies being introduced in Emilia-Romagna, a region known for its high concentration of medical devices. This process involves an eligibility assessment (accreditation evaluation) followed by the accreditation process. The procedure includes the involvement of a dedicated evaluation committee and healthcare facilities that intend to adopt the innovative solution.

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GLOSSARY

CEP:	Clinical Evaluation Plan
CER:	Clinical Evaluation Report
CGMs:	Continuous Glucose Monitors
CIP:	Clinical Investigation Plan
CSR:	Clinical Study Report
DHT:	Digital Health Technologies
DHTs:	Digital health therapeutics
DiGA:	Digitale Gesundheitsanwendungen (digital therapeutics in Germany)
Digital Diagnostics:	Digital devices for diagnosis (subgroup of pDMD)
Digital Prevention:	Digital devices for prevention (subgroup of pDMD)
DTx:	Digital Therapeutics (subgroup of pDMD)
EHR:	Electronic health record
GDPR:	General Data Protection Regulation
MDCG:	Medical Device Coordination Group
MDR:	Medical Devices Regulation
mHealth:	Mobile Health
pDMD:	Patient-managed digital medical devices
RPM:	Remote Patient Monitoring (subgroup of pDMD)
SaMD:	Software as a Medical Device

1. AIM OF THE WORK

By Indicon Società Benefit

Digital therapeutics (DTx) represent a significant evolution in therapeutic approaches worldwide and a rapidly growing market. It is crucial to classify these innovative technologies and provide definitions that allow clear identification of digital therapeutics and other non-therapeutic digital health technologies, known as connected care.

In Europe, different countries have established regulatory pathways dedicated to early value assessment of digital health technologies (DHTs), while in Italy there is no specific prescription and reimbursement framework. It is therefore necessary for Italy to define specific policies for digital health technologies and facilitate their integration into daily clinical practice.

The DTx Monitoring Report is the result of the work of the "Digital Health Policy Lab", a research project launched in 2022 in collaboration between Indicon Società Benefit and the University of Milan with the aim of promoting the integration of digital health technologies in the Italian healthcare system.

The DTx monitoring report aims to:

- Map the evolution of digital therapeutics in Europe
- Examine the state of the art of digital health technologies and digital therapeutics in Italy
- Provide concrete proposals for the adoption of digital health technologies

These activities are essential to stimulate the national debate on the integration of digital health technologies in the Italian National Health Service.

2. DEFINITIONS AND FRAMEWORKS: FROM DIGITAL HEALTH TECHNOLOGIES TO DIGITAL THERAPEUTICS

By Professor Paola Minghetti, Director Department of Pharmaceutical Sciences University of Milan and Indicon Società Benefit

Digital Health Technologies (DHTs) are defined as *systems that use computing platforms, connectivity, software, and sensors for healthcare and related uses*[1]. According to ISO 11147 (June 2023)[2], these technologies represent a broad range of products used across the healthcare ecosystem ranging from clinician-facing applications, wellness apps, diagnostic tools, monitoring devices and digital therapeutics.

To help define and classify the full spectrum of digital health technologies (DHTs), the Digital Therapeutics Alliance (DTA) in partnership with Health Advances, has proposed a classification that better reflects the current landscape of DHTs, through the drafting of "Guidance to Industry - Classification of Digital Health Technologies"[3] (2023).

Using the classification proposed by the DTA as a reference, this Report examines a subset of digital health technologies, consisting of patient-managed digital medical devices (pDMDs), a category which is still not universally understood and where major regulatory gaps exist. The aim of the work is to provide clarity and assist decision-makers in defining specific policies to enable the integration of innovative technologies into clinical practice.

2.1 Digital Health Technologies (DHTs)

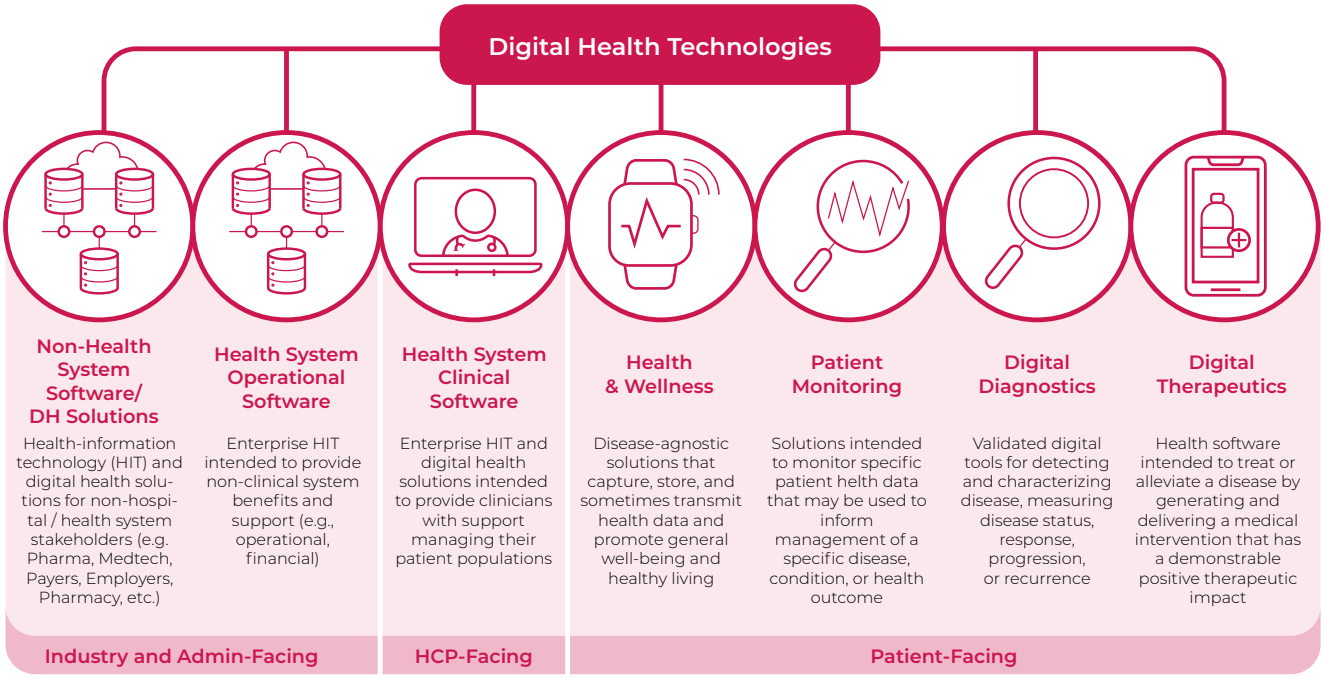
To classify digital health technologies, a categorisation has been developed based on the following segmentation criteria[3]:

1. *End User / Beneficiary:* Industries and admin facing, healthcare professional (HCP)-facing and patient-facing
2. *Intended Benefits / Claims:* clinical or non-clinical purpose
3. *Regulatory Scrutiny:* level of scientific evidence to support benefit claims
4. *Strength of Evidence:* level of regulatory control
5. *Product / Intervention Type:* how DHTs influence the delivery of care

The classification criteria 2,3 and 4 are inherently linked to the claims made by a DHT manufacturer, which have a direct impact on the level of regulatory scrutiny a product is subject to and the resulting strength of evidence required to meet regulatory requirements. These three criteria are extremely important for all stakeholders to understand as they have a massive impact on what a product can and cannot do when used in the real world.

The end user represents the first classification factor; DHTs aimed at patients differ from those aimed at healthcare professionals in terms of acceptance, validation and regulation. According to the end users (industry and admin-facing, clinician-facing and patient-facing) DHTs can be classified in eight multiple categories Figure 1.

Figure 1. Classification of Digital Health Technologies, GUIDANCE TO INDUSTRY: Classification of Digital Health Technologies, Digital Therapeutics Alliance and Health Advances (June 2023). This subset of products is presented from left to right in order of increasing impact on clinical management, which is a core orienting principle for how patient-facing DHTs are evaluated, regulated, and paid for.



Non-patient facing DHTs

- **Non-Health System Software:** technologies that support non-hospital stakeholders involved in the healthcare ecosystem, such as payers, employers, and industry.
- **Health System Operational Software:** technologies essential for hospitals and health systems to operate efficiently and minimize costs of delivering care. Operational solutions include Integration/ Interoperability Engines, Security/Data Management, Business Analytics, Data Management, and Revenue Cycle Management.
- **Health System Clinical Software:** primarily used by physicians and other healthcare professionals to assist in the delivery of clinical care (e.g., EMR, clinical decision support, telehealth platforms).

Patient facing DHTs

As shown in Figure 2, each class is divided into homogeneous subcategories based on the purpose of the digital health technology and the indication for use (claim).

DHTs without claims

- **Health & Wellness:** largely consumer-based products. These products may promote general wellness or patient experience, any clinical outcomes are not attributable to the DHTs itself.
- **Care Support:** solutions intended to support patient self-management of a specific diagnosed medical condition through educational resources, recommendations, and/or reminders.

DHTs with non-clinical claims

- **Remote Patient Monitoring (RPM):** products intended to monitor patient data to inform management of a specific disease, treatment regiment, medical condition, or health outcome. RPM systems serve as supplementary monitoring devices, aiding healthcare professionals in making clinical decisions. They do not interpret data to diagnose or predict the patient's condition. Instead, they collect highly valuable data (such as patient-reported outcomes or biometric data) and make this information accessible to both patients and healthcare providers, helping with patient self-management and clinical decision-making. RPM technologies do not offer any management recommendations to patients, caregivers, or healthcare providers concerning the disease or condition.

  Characteristics of RPM:
  - The data must be gathered by a patient-facing device that does not require the supervision of a healthcare provider supervision (e.g. genomic or medical imaging data).
  - Monitoring may either be continuous (e.g., continuous glucose monitor) or recorded intermittently at the patient's discretion.
  - Patient monitoring solutions may provide data to inform clinical management but do not interpret that data in the context of a health condition to drive management.

DHTs with clinical claims

- **Digital Diagnostics:** Clinical validated digital tools for detecting and characterizing disease, measuring disease status, response, progression, or recurrence.

  Key features of digital diagnostics:
  - Digital Diagnostics are validated to provide a standalone conclusion about a patient's health status that does not require an HCP to further interpret the result.
  - Algorithmic analysis of data, often from wearables or connected devices, but may also include patient-reported data, imaging, and/or molecular tests.
  - Inform, drive, or deliver screening or diagnostic results by autonomously detecting disease early signs and/or symptoms.

  ### Note

  Patient monitoring differs from digital diagnostics in that a digital diagnostic is a validated tool to detect disease and/or characterise disease progression based on input biometric data. A RPM, on the other hand, deals with the underlying health data but the tool itself does not offer any interpretation, the data must be transmitted to a healthcare professional for analysis and any potential diagnoses.

- **Digital Therapeutics (DTx):** DHTs able to perform a direct therapeutic function (including motor and neurological rehabilitation and secondary/tertiary prevention), and they are defined in the ISO 11147[2] as "health software intended to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention that has a demonstrable positive therapeutic impact on a patient's health". DTx can function independently or integrate with ancillary software and medical intervention components to form a DTx ecosystem. DTx must be clinically validated either through a randomized controlled clinical trial (RCT), real world evidence (RWE), or ideally a combination of the two, to demonstrate product efficacy.

It is important to consider that the increased impact on clinical management means a parallel increase in the level of evidence required for evaluation, approval, patient use and increased regulatory oversight.

2.2 Patient-managed Digital Medical Devices (pDMDs): focus of the Report

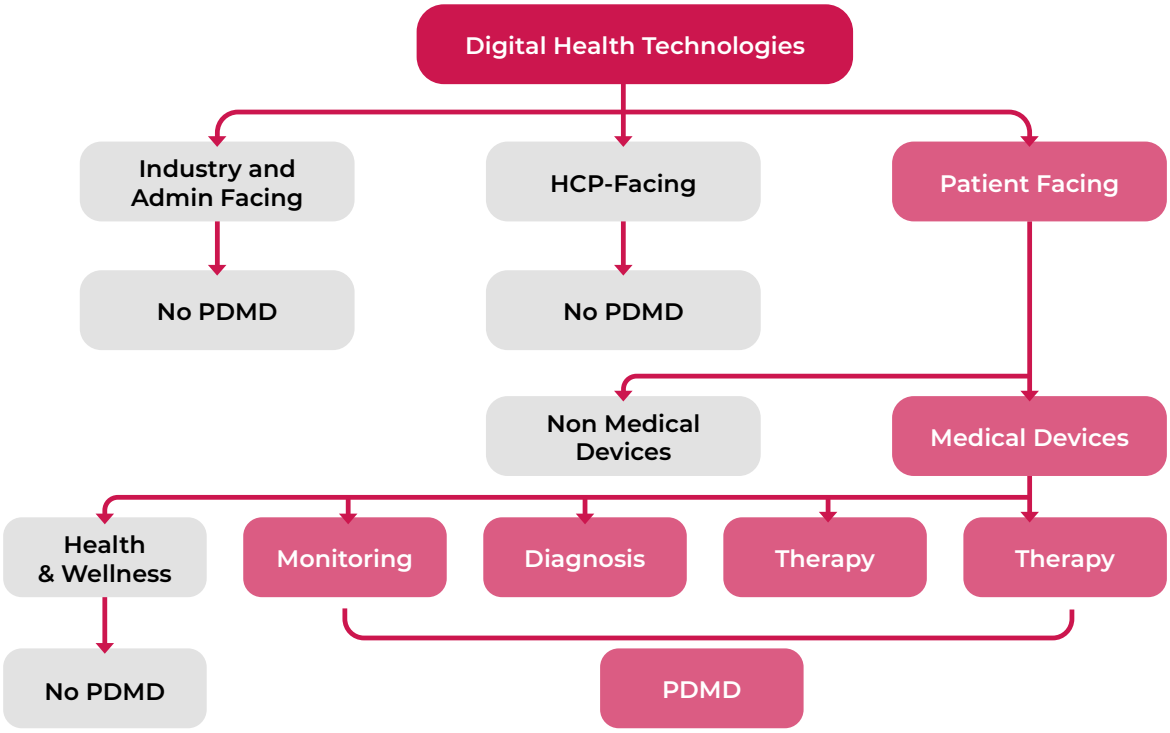
This Report focuses on a subset of DHTs that includes patient-facing Digital Health Technologies certified as a medical device, intended to be used alone or in combination, for one or more of the specific medical purpose (claim) of:

- Treatment (including physical and neurological rehabilitation): Digital Therapeutics
- Monitoring: Remote Patient Monitoring
- Diagnosis: Digital Diagnostics
- Prevention: Digital Prevention

referring to specific pathologies.

These technologies are also known as patient-managed digital medical devices (pDMD)[4].
As a subset of each of these categories is included software support defined as "care support", as the definition of medical device does not consider the concept of care support.

Figure 2. Classification of patient-managed Digital Medical Devices as a subgroup of Digital Health Technologies.



Medical Device Software (MDSW)

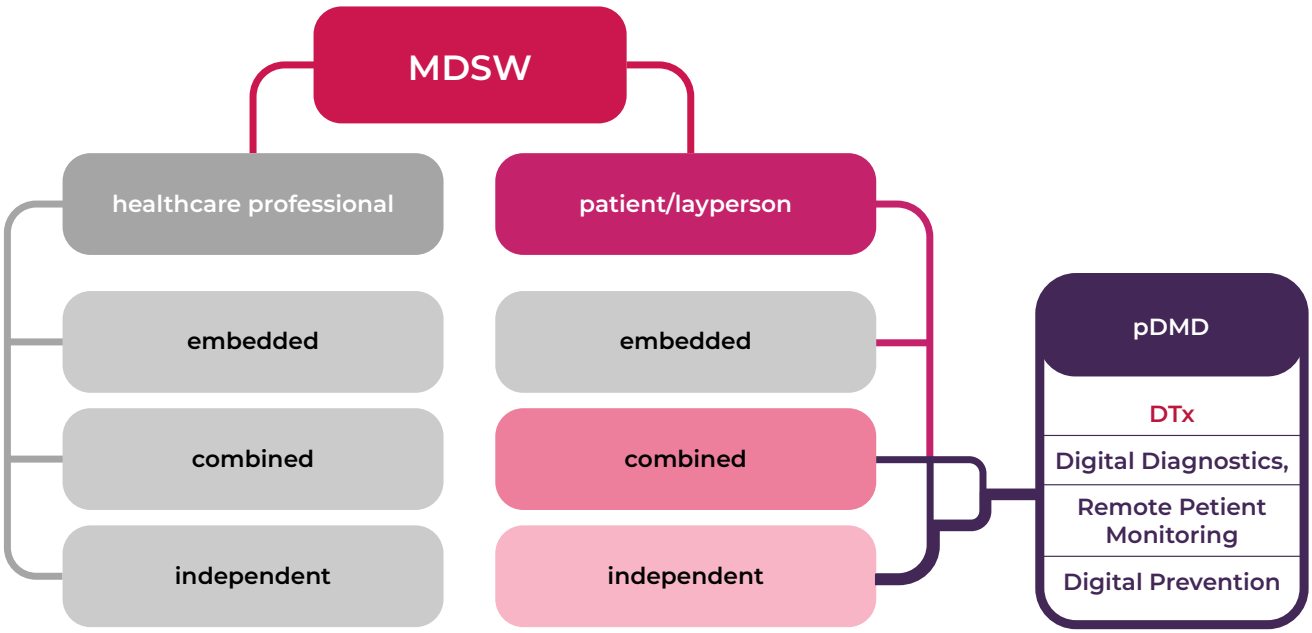
In the European Union, software intended to be used for a specific medical purpose fall under the definition of medical device (MD) or in vitro diagnostic medical device (IVD)[5]. These devices are named medical device software - MDSW - (in the USA: Software as a Medical Device, SaMD) or MDSW applications (MDSW apps) in EU guidance endorsed by the Medical Device Coordination Group (MDCG)[6,7]. Although MDSW are fully covered by the provisions of the Medical Devices Regulation (MDR) or the In Vitro Diagnostic Medical Devices Regulation (IVDR)[8], grey areas still exist regarding the nomenclature for a subset of MDSW, that of MDSW intended to be used directly by patients in the treatment, diagnosis or monitoring of a disease, this group constitutes patient-managed digital medical devices (pDMDs).

Classification of software as medical device

MDSW can be classified according to the final user: MDSW intended for use by a healthcare professional and MDSW intended for use by a layperson/patient, alone or with the assistance of a healthcare professional. This category of MDSW represents the patient-managed digital medical devices (pDMDs) (Figure 3). The category of pDMDs is largely superimposable with that of German Digitale Gesundheitsanwendungen (Digital Health Application – DiGA[9]).

Formally, pDMDs be defined as MDSW apps, not embedded in a hardware medical device, to be used by a layperson, alone or assisted by a healthcare professional, for a specific medical purpose[2], (in the sense of the MDR or the IVDR). Among the full spectrum of medical intended purposes listed in the MDR and the IVDR, pDMDs marketed until now have been mainly used for therapy, diagnosis and monitoring of a disease.

Figure 3. Classification of Medical Device Software (MDSW) based on the MDR2 integrated with MDCG3 and IMDRF7 guidance.



The role of competent authorities

The European Commission centralized competent Authority for MDs and IVDs at the EU level, has both a legislative function - through the adoption of Commission Regulations - and a coordinating function - mainly through Medical Device Coordination Group (MDCG). The assessment and certification of MDs is left to independent Notified Bodies or, in the case of lower risk devices, to manufacturers. Concerning the European Medicines Agency (EMA), for MD which do not contain medicinal substances, its involvement has always been minimal.

At the national level, competent Authorities address market surveillance and reimbursement issues, and the overall picture is fragmented, as different national competent Authorities may be involved in different Member States, and also local regulatory provisions may diverge, particularly concerning pricing and reimbursement.

These products are covered by Regulation (EU) 2021/2282 of the European Parliament and of the Council[10] (2021) on health technology assessment (HTA), amending Directive 2011/24/EU. The HTA process allows competent authorities to determine the relative effectiveness of new or existing health technologies. This assessment focuses in particular on the added value of a health technology compared to other new or existing health technologies. The Health Technology Assessment Regulation will enter into force in January 2022 and will apply from January 2025[11].

Open issues related to the regulation of pDMDs

Rule 11 of the MDR classifies in class IIa or above only software intended to provide information which is used to take decisions with diagnostic or therapeutic purposes or to monitor physiological processes, whereas other software is comprised in class I: "Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause. (i) death or an irreversible deterioration of a person's state of health, in which case it is in class III; or (ii) a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb. Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb. All other software is classified as class I" [2]. As it is, Rule 11 seems to prevent pDMDs specifically intended to treat patients, namely DTx, to access higher risk classes, leaving DTx to class I and self-certification for CE marking, which may not be sufficient for software intended to directly treat a disease. The prevision of at least class II far all the software could be preferable.

Conclusion

The continued development of digital health technologies (DHTs) and patient-managed digital medical devices (pDMDs) represents a major milestone in healthcare innovation. The definition of clear and consistent regulatory and classification frameworks is the first step towards realising the full potential of healthcare technologies and enabling the integration of DHTs into everyday clinical practice, improving patient outcomes and healthcare efficiency.

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3. STATE OF THE ART OF DIGITAL THERAPEUTICS IN EUROPE

3.1 DTx mapping

A. The global DTx market

The global revenue of the digital therapeutics market is expected to reach $4.68 billion in 2024 . The market is projected to grow at a compound annual growth rate (CAGR) of 16.61% from 2024 to 2029, reaching a market volume of $10.09 billion by 20291. User penetration is anticipated to be 1.67% in 2024, with an increase to 3.61% by 20291. The average revenue per user (ARPU) is estimated to be $36.09. Globally, the majority of the revenue will be generated in the United States, with $3.15 billion expected in 20241.

B. The european context

Digital Therapeutics (DTx), as medical devices certified software and authorised for marketing, can be sold in different countries. However, in the absence of specific criteria for evaluating digital software and appropriate pathways for access and reimbursement, DTx are in some cases only available through private channels or require direct user fees, exacerbating inequalities in access to healthcare services. To address these issues, several European and global countries are developing specific access and reimbursement criteria and pathways for Digital health technologies and DTx to ensure equitable access and better integration into the healthcare system.

The evolution of approved DTx and therapeutic areas by country

A. Germany

Germany is currently the country with the highest number of DTx evaluated, reimbursed and made available thanks to the Digital Health Applications Ordinance (DiGAsV - 2019), which establishes criteria for the evaluation, access and reimbursement of digital health applications certified as medical devices (digital health applications, DiGAs), including digital therapies. A special fast-track pathway allows market access for applications that meet safety, usability and technical interoperability requirements but do not yet have complete clinical data. which guarantees reimbursement for 12 months (PRELIMINARY LISTED), a period during which the manufacturer must provide evidence of the product's clinical efficacy. Alternatively, it is possible to apply directly for permanent listing (PERMANENT LISTING). Regardless of whether the reimbursement is temporary or permanent, the price for the first year is set by the manufacturer. After 12 months, the reimbursement price is negotiated with the competent authority. There are currently 55 DiGAs available, of which 20 are temporary and 35 are permanent.

According to a conservative estimate by the SVDGV, patients will have redeemed almost 370,000 activation codes for DiGAs between autumn 2020 and September 2023. With the draft law on the digital modernisation of nursing and care (Digitale Versorgung und Pflege-Modernisierungs-Gesetz - DVPMG), the first steps have been taken to make digital innovations and their benefits accessible also in the nursing environment (DIPA).

The "Law to Accelerate the Digitization of the Healthcare System" (Digital Act - DigiG) came into force on March 26, 2024. It contains numerous and significant improvements for the digital healthcare of patients in Germany. In the future, patients with mandatory health insurance will also have access to digital health applications (DiGAs) in higher risk categories, which include supplementary telemo-

nitoring services. Furthermore, in the future, DiGAss will also be used to provide assistance during pregnancy and will be more closely integrated into disease management programs. At the same time, starting from January 1, 2026, DiGAs manufacturers will conduct a so-called "measurement of application success" (AbEM), the results of which will be published regularly in the list of DiGAs from the Federal Institute for Drugs and Medical Devices (BfArM).

The key figures of the AbEM are particularly:

- The duration and frequency of DiGAs usage,
- Patient satisfaction regarding the quality of the DiGAs,
- The patient's health status during the use of the DiGAs.

Approved DiGAs in the country

The table shows the number of Digital Health Technologies (DIGA) reimbursed in Germany over the years, with a focus on the quarters of 2024.

Table 1: evolution of Digital Health Technologies (DIGA) reimbursed in Germany

	2021	2022	2023	2024 Q1	2024 Q2	2024 Q3
Tot Reimbursed	27	37	52	56	56	55
Permanent Listed	5	13	29	33	35	35
Preliminary Listed	22	24	23	23	21	20
Delisted	0	5	6	6	8	9

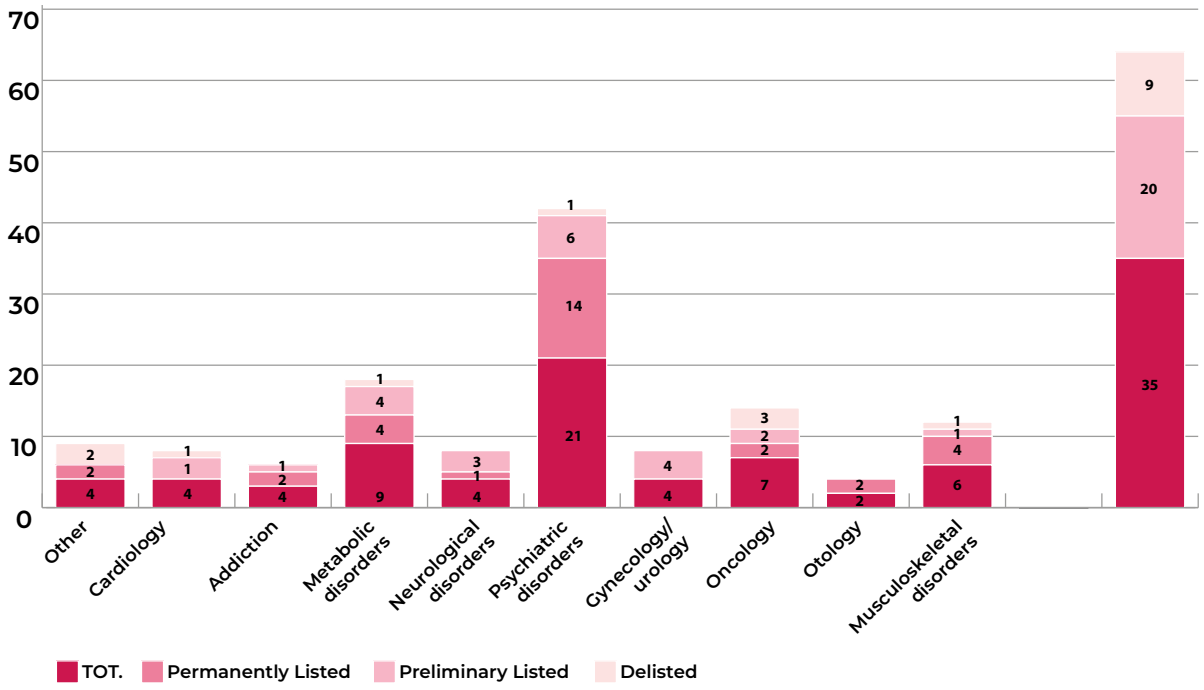
Some key observations

- From 2021 to 2023, the number of DIGAs reimbursed has more than doubled (+103%), rising from 27 in 2021 to 37 in 2022 and reaching 52 in 2023 to stabilise around a value of 56 DiGAs in Q3 2024.
- In 2024, the numbers seem to have stabilised, with values around 56 for the first two quarters and a slight drop to 55 in Q4.
- Rejected DiGAs have steadily increased since 2022, from 5 to 8 (+80%). The largest growth occurred in 2024, with 6 rejected in Q1, 8 in Q2 and 9 in Q3.

Analysis of therapeutic areas

The following chart represents the therapeutic areas targeted by the use of DiGAs broken down by list.

Figure 1: Representation of therapeutic areas treated by the ADI classified by permanent/provisional list



The majority of DiGAs are intended for the treatment of psychiatric disorders, mainly depression (n=7) and panic attacks (n=5), followed by metabolic disorders (diabetes) with 4 DiGAs on the permanent list and 4 on the temporary list (1 rejected), and oncology with 2 devices on the permanent list, 2 on the temporary list and 3 rejected.

There are currently no cardiac devices on the permanent list, 4 on the temporary list and 1 rejected. Only one technology for neurological disorders (specifically multiple sclerosis) is currently reimbursed on the permanent list.

DiGAs for the treatment of psychiatric disorders also represent the largest number of devices on the permanent list.

A. UK

In 2019, the National Institute for Health and Care Excellence (NICE) in England launched the first version of the Evidence Standards Framework, which set out specific assessment criteria for digital health technologies and recognised a subcategory for therapeutic devices, including digital therapeutics (DTx). In 2021, the introduction of the Digital Technology Assessment Criteria (DTAC) established a formal process for assessing these technologies for appropriateness within the National Health Service (NHS). However, in England, there is close no connection between the process of recommendation by the competent bodies and the process of access and reimbursement, which is defined at the level of the regional sub-units of the NHS. For this reason, there is no assurance that a nice-approved device will get reimbursed in the country

La tabella seguente mostra il numero di tecnologie sanitarie digitali approvate dal NICE (National Institute for Health and Care Excellence) per due diverse categorie: l'uso nel NHS (National Health Service) e l'uso limitato agli studi clinici, suddivise per anno dal 2021 fino al terzo trimestre del 2024.

Table 2: number of digital health technologies approved by NICE (National Institute for Health and Care Excellence) for two different categories: use in the NHS (National Health Service) and use restricted to clinical trials, broken down by year from 2021 until the third quarter of 2024.

	2021	2022	2023	2024 Q1	2024 Q2	2024 Q3
DHTs Authorised by NHS	0	1	20	31	32	**32**
DHTs Authorised by NHS for clinical trials	0	0	13	22	27	**27**

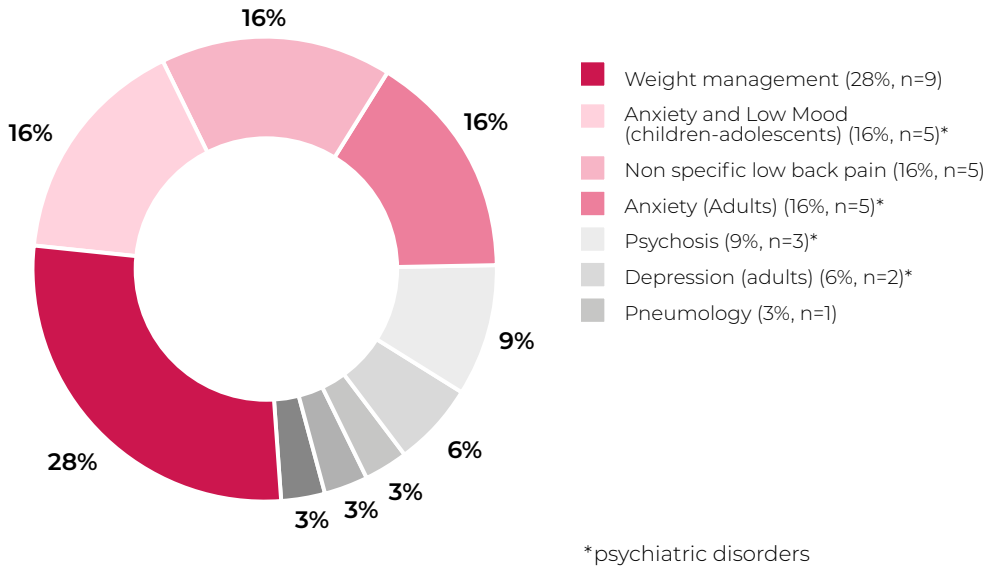
DTx approved for use in the NHS

- NICE approved the first DHTs for use in 2022
- 2023 shows significant growth, 20 technologies approved compared to the previous year's single.
- In 2024, the number of approvals shows 60% growth over 2023, with 31 approvals in Q1, 32 in Q2 and 32 also in Q3.
- DTx approved for clinical trials only:
- In 2023, 13 technologies were approved for clinical trials only.
- 2024 shows growth with 22 approvals in Q1, 27 in Q2 and 27 in Q3, which is more than double the previous year's figure.

Analysis of therapeutic areas

The following table shows the therapeutic areas covered by NICE-approved digital health technologies in the UK.

Figure 2: therapeutic areas covered by NICE-approved digital health technologies in the UK



*psychiatric disorders

The most frequently treated therapeutic areas are psychiatric disorders: anxiety (n=10), depression (n=2), psychosis (n=3), agoraphobia (n=1), with a total of 15 devices, representing 50% of those approved by NICE.
This was followed by devices for weight management (in patients with metabolic diseases): with 28% of the technologies (9 out of 32). The 16% (n=5) is then represented by technologies for non-specific low back pain.

B. France

The German model is inspiring other European countries, such as France, which is working on a similar regulatory framework, the French government introduced a conditional early access process based on the generation of evidence (PECAN), which will enable temporary reimbursement for DTx while further clinical efficacy data is gathered. In 2023, France officially acknowledged the digital classification of a specific subset of medical devices, labeling them as Digital Medical Devices (Dispositifs Médicaux Numériques, DMN). To establish evaluation, access, and reimbursement frameworks for these digital medical devices, two separate pathways were outlined: one dedicated to telemonitoring devices and the other for those with therapeutic purposes, such as Digital Therapeutics (DTx). The French government introduced a conditional early access process based on the generation of evidence (PECAN), which will enable temporary reimbursement for DTx while further clinical efficacy data is gathered.

Unlike in France and England, no lists could be found of the number of devices reimbursed in the country. Based on the research to our knowledge, the following table shows the devices in France.

Table 3: Digital medical devices present in France, classified by the medical purpose

	2021	2022	2023	2024 Q1	2024 Q2	2024 Q3
TOT DTx	1	3	3	3	3	**3**
TOT RMD	0	0	2	4	4	**4**

In 2021, only one DTx device was reimbursed, and none of the RMD devices were covered. In 2022, the number of reimbursed DTx devices increased to three, while RMD devices remained at zero.
For 2023 and the first two quarters of 2024, the number of reimbursed DTx remained constant at three. In 2024 Q3, the number of reimbursed DTx devices stayed at three, while the reimbursed RMD devices increased to four.

Table 4: Therapeutic areas treated by digital therapeutics DTx and remote patient monitoring RPM

	Therapeutics Area	DTx
DTx	Psychiatric disorders (depression)	1
	Motor rehabilitation	1
	Metabolic disorders (diabetes)	1
RPM	Oncology	4

DTx in France are equally divided between the treatment of depression, diabetes and physical rehabilitation, while 80% (n=4) are dedicated to remote patient monitoring in cancer patients and the remaining 20% (n=1) are for physical rehabilitation.

C. Belgium

To the mHealthBelgium initiative was launched in 2018 to integrate health apps certified as medical devices into the Belgian healthcare system. The Belgian model aims to promote the use of apps for diagnostic, therapeutic, or remote monitoring purposes, which facilitate the exchange of information between the patient and healthcare professionals. This system is based on a multi-step pyramid evaluation, where each step is associated with specific requirements:

1. First evaluation level: focuses on technical safety, data privacy, and the app's interoperability.
2. Second evaluation level: includes apps whose clinical trials or cost-effectiveness studies are still ongoing or have been completed. These apps can be considered for reimbursement, but not as standalone technologies. Instead, they are reimbursed as part of an integrated care pathway (using a "bundled payment" model, meaning payment for the entire treatment process and not for the individual app).

As of September 2024, there were 25 certified apps on the mHealthBelgium platform, divided between:

- 12 apps at the second evaluation level
- 13 apps at the first evaluation level

However, despite the presence of these applications, the implementation of the system was considered unsatisfactory, prompting Belgium to reform the model in 2023. The new reimbursement process, approved in July 2023, includes a temporary funding mechanism, similar to the reimbursement models in Germany and France.
The reform aims to make the reimbursement process and the integration of digital technologies more effective, further encouraging the use of these apps within the healthcare system.

D. Spain

In Spain, digital therapeutics (DTx) are becoming a key part of healthcare. The country has developed a specific framework to evaluate these technologies, focusing on their use post-market authorization. Spain, alongside countries like Germany and the UK, is advancing in certifying DTx, with healthcare reimbursement in place. The evaluation considers factors such as safety, effectiveness, cost, and the impact on patients and healthcare systems. A notable focus is on mobile health (mHealth) and artificial intelligence.

3.2 DiGA Price analysis

This chapter presents an analysis conducted on the prices of digital health technologies (DiGAs) in Germany aimed at highlighting the price reduction between provisional reimbursement and permanent reimbursement for digital devices in the pioneering European country in the field of digital health. The analysis is updated to September 2024.

Background

The German system for the evaluation of digital health technologies (in German, DiGA) was established in 2019, is defined as a fast track and provides that a technology that meets all the required safety and efficacy requirements can be included in a temporary list for about 12 months (with the possibility of renewal), during which the manufacturer can begin marketing with reimbursement at the price it sets, with the aim of collecting new efficacy data that has not been previously provided. At the end of the data collection period, if the device has the required data and a favourable efficacy evaluation, it can be registered on the permanent list. The transition from the provisional to permanent list involves the negotiation of the price between the manufacturer and Statutory Health Insurance.

Methodology

The analysis was conducted using the data available on the DiGA Directory (list of digital health technologies, DiGA, present in the German Fast Track) available on the Federal Institute for Drugs and Medical Devices (BfArM) website1.
In Germany, there are 55 reimbursed DiGA, for the purposes of the analysis, the following DiGA were not considered:

- registered on the provisional list (n=20)
- registered directly on the permanent list (n=1)
- for which sufficient information was not found (n=1).

Of the 55 registered, 33 DiGA were therefore included in the analysis.

With the data retrieved from the analysis of each technical data sheet of each DiGA considered in the analysis, a database in Excel format was populated consisting of the following fields:

- Commercial name
- Price on the provisional/temporary list (defined by the manufacturer). In case the same DiGA changed the reimbursement price on the provisional list over time, the first proposed reimbursement price by the manufacturer was considered.
- Price on the permanent list (defined following negotiation between manufacturer and statutory health insurance).
- Therapeutic area.

The analyzed DiGAs and their reference prices are presented in the following table (Table 1):

Table 1: List of DiGAs considered in the analysis with their temporary list prices, permanent list prices, and therapeutic area of intervention, in alphabetical order by product.

Product	Therapeutic area	Temp list price (€)	Perm list price (€)
Cara Care for irritable bowel syndrome	Irritable bowel syndrome	718,20 €	248,00 €
Companion Patella powered by medi	Musculoskeletal disorders	345,10 €	223,49 €
Deprexis	Psychiatric disorders	297,50 €	210,00 €
edupression.com	Psychiatric disorders	357,00 €	224,80 €
Elevida	Neurological disorders	743,75 €	243,00 €
Endo-App	Gynecology/urology	598,95 €	235,80 €
HelloBetter diabetes and depression	Metabolic disorders	599,00 €	222,99 €
HelloBetter panic	Psychiatric disorders	599,00 €	230,00 €
HelloBetter ratiopharm chronic pain	Oncology	599,00 €	235,00 €
HelloBetter Stress and Burnout	Psychiatric disorders	599,00 €	235,00 €
HelloBetter Vaginismus plus	Gynecology/urology	599,00 €	235,00 €
Invirto - the therapy against anxiety	Musculoskeletal disorders	428,40 €	220,00 €
Kaia back pain - back training at home	Musculoskeletal disorders	489,39 €	221,49 €
Kalmeda tinnitus app	Otology	116,97 €	189,00 €
Kranus Edera	Gynecology/urology	552,01 €	235,00 €
Mawendo	Musculoskeletal disorders	119,00 €	119,00 €
Mindable: Panic disorder and agorafobia	Musculoskeletal disorders	576,00 €	245,50 €
My Tinnitus App - digital tinnitus counseling	Otology	250,00 €	260,00 €
Neolexon Aphasia	Aphasia	487,90 €	223,01 €
Non-smokingHeroes app	Addiction	239,00 €	211,00 €
Novego: coping with depression	Psychiatric disorders	249,00 €	199,00 €
Oviva	Metabolic disorders	345,00 €	220,90 €
Pink! Coach	Oncology	535,50 €	234,50 €
Selfapy's online course at bulimia nervosa	Psychiatric disorders	540,00 €	232,00 €
Selfapy's online course for binge eating disorder	Psychiatric disorders	540,00 €	232,00 €
Selfapy's online course for depression	Psychiatric disorders	540,00 €	217,18 €
Selfapy's online course for generalized anxiety disorder	Psychiatric disorders	540,00 €	228,50 €
Somnio	Psychiatric disorders	464,00 €	224,99 €
Velibra	Psychiatric disorders	476,00 €	230,00 €
Vitadio	Metabolic disorders	499,80 €	224,01 €
Vivira	Musculoskeletal disorders	239,96 €	206,79 €
Vorvida	Addiction	476,00 €	192,01 €
Zanadio	Metabolic disorders	499,80 €	218,00 €

Analysis

Considering the data represented in Table 1, the average price of a DiGA on the permanent list is €222, with a minimum of €119 and a maximum of €260.
For each DiGA, the variation between the reimbursed price on the provisional list and that on the permanent list was analyzed, with the aim of understanding the outcome of the negotiations between the manufacturer and statutory health insurance. The study shows that:

- PRICE REDUCTION: 91% (n=30) of the DiGA experienced a price reduction from the temporary list to the permanent list. The average price reduction in percentage value is -47%.
- UNCHANGED PRICE: 3% (n=1) were reimbursed on the permanent list at the same price with which it was present on the provisional list.
- PRICE INCREASE: 6% (n=2) were reimbursed on the permanent list at a higher price than the first price on the provisional list. The increase in percentage value was 33%.

Below are the price variations between the two lists for each of the DiGA considered (Table 2).

Table 2: Price variation between the temporary list and the permanent list.

Product	Temp Price (€)	Perm Price (€)	Price Variation
Kalmeda tinnitus app	116,97 €	189,00 €	+ 62%
My Tinnitus App - digital tinnitus counseling	250,00 €	260,00 €	+ 4%
Mawendo	119,00 €	119,00 €	0%
Non-smokingHeroes app	239,00 €	211,00 €	-12%
Vivira	239,96 €	206,79 €	-14%
Novego: coping with depression	249,00 €	199,00 €	-20%
Deprexis	297,50 €	210,00 €	-29%
Companion Patella powered by medi	345,10 €	223,49 €	-35%
Oviva	345,00 €	220,90 €	-36%
edupression.com	357,00 €	224,80 €	-37%
Invirto - the therapy against anxiety	428,40 €	220,00 €	-49%
Somnio	464,00 €	224,99 €	-52%
Velibra	476,00 €	230,00 €	-52%
Neolexon Aphasia	487,90 €	223,01 €	-54%
Kaia back pain - back training at home	489,39 €	221,49 €	-55%
Vitadio	499,80 €	224,01 €	-55%
Pink! Coach	535,50 €	234,50 €	-56%
Zanadio	499,80 €	218,00 €	-56%
Selfapy's online course at bulimia nervosa	540,00 €	232,00 €	-57%
Selfapy's online course for binge eating disorder	540,00 €	232,00 €	-57%
Mindable: Panic disorder and agorafobia	576,00 €	245,50 €	-57%
Kranus Edera	552,01 €	235,00 €	-57%
Selfapy's online course for generalized anxiety disorder	540,00 €	228,50 €	-58%
Vorvida	476,00 €	192,01 €	-60%
Selfapy's online course for depression	540,00 €	217,18 €	-60%
Endo-App	598,95 €	235,80 €	-61%
HelloBetter ratiopharm chronic pain	599,00 €	235,00 €	-61%
HelloBetter Stress and Burnout	599,00 €	235,00 €	-61%
HelloBetter Vaginismus plus	599,00 €	235,00 €	-61%
HelloBetter panic	599,00 €	230,00 €	-62%
HelloBetter diabetes and depression	599,00 €	222,99 €	-63%
Cara Care for irritable bowel syndrome	718,20 €	248,00 €	-65%
Elevida	743,75 €	243,00 €	-67%

Correlation between Price Reduction and Therapeutic Areas

The analysis examined the correlations between the price variations across the two lists and the therapeutic areas treated by the DiGA, with the goal of verifying a potential link between the two factors. The following table (Table 3) represents the considered DiGA, their respective therapeutic intervention areas, and the price reductions following negotiation.

Table 3: Correlation between price variation and therapeutic area

Product	Temp price (€)	Perm price (€)	Price variation
Neolexon Aphasia	Aphasia	-54%	+ 62%
Non-smokingHeroes app	Addiction	-12%	-36%
Vorvida	Addiction	-60%	
Oviva	Metabolic disorders	-36%	53%
Vitadio	Metabolic disorders	-55%	
Zanadio	Metabolic disorders	-56%	
HelloBetter diabetes and depression	Metabolic disorders	-63%	
Elevida	Neurological disorders	-67%	-50%
Novego: coping with depression	Psychiatric disorders	-20%	
Deprexis	Psychiatric disorders	-29%	
edupression.com	Psychiatric disorders	-37%	
Invirto - the therapy against anxiety	Psychiatric disorders	-49%	
Somnio	Psychiatric disorders	-52%	
Velibra	Psychiatric disorders	-52%	
Selfapy's online course at bulimia nervosa	Psychiatric disorders	-57%	
Selfapy's online course for binge eating disorder	Psychiatric disorders	-57%	
Mindable: Panic disorder and agorafobia	Psychiatric disorders	-57%	
Selfapy's online course for generalized anxiety disorder	Psychiatric disorders	-58%	
Selfapy's online course for depression	Psychiatric disorders	-60%	
HelloBetter Stress and Burnout	Psychiatric disorders	-61%	
HelloBetter panic	Psychiatric disorders	-62%	
Kranus Edera	Ginecology/Urology	-57%	-60%
Endo-App	Ginecology/Urology	-61%	
HelloBetter Vaginismus plus	Ginecology/Urology	-61%	
Cara Care for irritable bowel syndrome	Irritable bowel syndrome	-65%	-65%
Pink! Coach	Oncology	-56%	-58%
HelloBetter ratiopharm chronic pain	Oncology	-61%	
Kalmeda tinnitus app	Otology (tinnitus)	62%	33%
My Tinnitus App - digital tinnitus counseling	Otology (tinnitus)	4%	
Mawendo	Musculoskeletal disorders	0%	-26%
Vivira	Musculoskeletal disorders	-14%	
Companion Patella powered by medi	Musculoskeletal disorders	-35%	
Kaia back pain - back training at home	Musculoskeletal disorders	-55%	

Considering the data in Table 3, the two DiGA that showed a positive price variation following negotiation are developed for the same therapeutic indication: the treatment of tinnitus. Specifically, Kalmeda Tinnitus app shows a price increase of 62% and My Tinnitus app - digital tinnitus counseling shows an increase of 4%.

The DiGA that shows no price variation between the provisional and permanent list is for the treatment of musculoskeletal disorders (Mawendo - patella disorders).

The therapeutic area of gynecology/urology is the only one to show a consistent average price variation of -60%, with the remaining therapeutic areas showing no significant correlations with price variation. The greatest price reduction occurred for Elevida, treatment of neurological disorders (multiple sclerosis) with a price reduction of 67%, from €743.75 to €243.00.

Psychiatric disorders, the therapeutic area most treated by DiGA, show an inconsistent price variation ranging from a minimum of -20% to a maximum of -60%, with a peak around 57%.

DiGA price over years

In order to evaluate the price trends of DiGA since the establishment of the Fast Track, a study was conducted on the value of DiGA over time. The analysis considered the following parameters:

- Year of entry of DiGA into the permanent list
- Prices of DiGA entered into the permanent list in the considered year
- Prices of DiGA at point 2 when they were on the temporary list (regardless of the year they entered the temporary list)
- Average price reduction

The average price of DiGA on the provisional list remains constant over the years at around €460, and the average price on the permanent list also remains stable at about €222. The price reduction ranges from a minimum of -34% in 2021 to -42% in 2024, with a peak in 2022 at -49%. The average price on the permanent list ranged from €220 in 2021 to €235 in 2024.

Table 4: Price trends of DiGA from 2020 to 2024

Year of entry into the permanent list	Number of DiGA entered in the permanent list	Average prices in the provisional list (€)	Average prices in the permanent list (€)	Average price reduction
2020	0			
2021	5	468,1	220,8	-34%
2022	8	460,0	216,7	-49%
2023	16	462,6	221,7	-46%
2024	4	459,2	235,7	-42%

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4. STATE OF THE ART OF PDMD IN ITALY

by Indicon Società Benefit

The chapter presents an analysis of the Italian context regarding of patient-managed digital medical devices (pDMDs). It presents (i) a mapping of the Italian players operating in the digital health field, (ii) a mapping of pDMDs registered with the Ministry of Health's medical devices database and (iii) a list of DTx present in Italy with a screening of the DTx-related clinical trials active in Italy. The aim of the chapter is to define the size, and the actors involved within the Italian digital health technologies ecosystem.

4.1 The Digital Health ecosystem in Italy

The entities active in the field of digital health technologies in Italy are described below, divided between public, private and scientific associations, with the aim of defining the digital health ecosystem in Italy and the stakeholders actively working to promote the integration of digital health technologies in the country.

A. National entities

Parliament
In May 2023, *the Intergruppo parlamentare per la Sanità digitale e le Terapie Digitali*, led by the On. Simona Loizzo, was set up with the aim of structuring a regulatory path dedicated to the evaluation and administration of DTx. On 7 June 2023, a draft bill "Regulations on digital therapies" was filed (1208)[13].

Ministry of Health
Within the Ministry of Health, two directorates are involved in the topic of DTx:
-The General Directorate for Medical Devices and Pharmaceutical Service (DGDM), as DTx are medical devices[14] from a regulatory point of view;
-The General Directorate for Digitalisation, Health Information System and Statistics[15].

Agenas
Since 2022, Agenas (National Agency for Regional Health Services) has had the following roles in relation to DTx in Italy[16]:

- National Agency for Digital Health (ASD), from 2022, with the aim of improving the digitalisation of services and processes in the healthcare sector;
- Agency performing study and support activities for the Ministry of Health and the Regions for the medical device sector;
- Agency coordinating Health Technology Assessment (HTA) strategies[17].

Specifically, Agenas has been working with Farmindustria since November 2023 for the following purposes[18]:

- The creation of an HTA evaluation framework and a specific authorisation and reimbursement framework for digital therapies (DTx) to allow access to digital therapies that demonstrate clinical benefit;
- Defining criteria for the use of health data from the application of artificial intelligence systems (guidelines, measurement of outcomes and modalities for access to data by all stakeholders in the supply chain, public and private, consistent and compliant with current privacy regulations). This initiative is in line with the European Commission's proposal for a Regulation establishing the European Health Data Space (EHDS).

Istituto Superiore di Sanità (ISS)
Within the ISS, there are two structures dealing with issues related to DTx:

- National Centre for Innovative Technologies in Public Health[19], which promotes the improvement of the state of public health through research, development, optimisation and evaluation of innovative technologies for public health protection using multidisciplinary expertise. The scope of activities ranges from medical devices, biomedical engineering, radiological health, nuclear medicine, nanotechnology and innovative therapies;
- National Centre for Telemedicine and New Care Technologies[20], whose activity is "to conduct, promote and coordinate research and system governance for social and health applications in the field of new information technologies and telemedicine" (Ministerial Decree 02/03/2016).

B. Universities, research centres, foundations and scientific societies

AFI - Associazione Farmaceutici dell'Industria
Within AFI, in the Regulatory & Medical Devices area, a Digital Health Study Group (GSD) has been set up[21], whose primary objective is to facilitate the adoption of digital technologies applied to health, of which digital therapies are a part, and their integration into normal clinical practice. The group is also dedicated to promoting research, sharing and dissemination of skills, experience and innovations in the context of medical devices.

AiSDeT - Associazione italiana Sanità Digitale e Telemedicina
AISDeT is a national network that brings together experts in digital innovation in the field of healthcare. The association operates with the aim of promoting new interdisciplinary and transdisciplinary expertise, as well as disseminating information on the topics of digital health and telemedicine in a more comprehensive, robust and systematic manner.

In May 2024, AiSDeT signed a collaboration agreement with *Confindustria Dispositivi Medici* with the aim of investigating and promoting digital evolution scenarios in the healthcare sector[22]. In particular, the protocol envisages joint initiatives to analyse and define digital PDTAs, identifying therapeutic areas for further investigation, as well as meetings on the Electronic Health Record (Fascicolo Sanitario Elettronico - FSE) and telemedicine.

ASSD – Associazione Scientifica per la Sanità Digitale
ASSD was founded with the aim of supporting the integration of digital health in the health and social sector and promoting the development of digital skills among health professionals. The association aims to improve effectiveness, safety and innovation in care and prevention processes by facilitating the adoption of digital technologies.

FADOI - Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti
FADOI promotes the development of medical-scientific knowledge. In 2021 it published the text "Terapie digitali: un'opportunità per l'Italia"[23], analysing for the first time the different relevant aspects and problems in the emerging field of digital therapeutics. A new edition of the book is planned for 2024 entitled "Terapie digitali: una necessità per l'Italia"[24], a project promoted in collaboration with *Fondazione Tessa*, which brings together analyses and in-depth studies on taxonomy, regulatory aspects, business models and other updates on DTx.

TESSA - Fondazione Tendenze Salute e Sanità ETS
Fondazione Tendenze Salute e Sanità ETS, (former "Fondazione Smith Kline "), promotes and supports medical research and the improvement of public health by focusing on emerging and innovative trends in health and medicine. It specifically works in the field of Digital Health, Digital Medicine and Digital Therapy. In 2024 it promoted the editing of the book "Digital Therapies, a necessity for Italy"[12] in collaboration with the FADOI association.

ReS – Fondazione Ricerca e Salute
ReS works to promote the integration of digital medicine within the Diagnostic Therapeutic Care Pathways (PDTA) through research projects and publications resulting from collaboration with experts in the field.

Mario Negri Pharmacological Research Institute
The Mario Negri Pharmacological Research Institute, first with the Laboratory of Medical Informatics and now with the Research Unit in Digital Health and Digital Therapies, plays a fundamental role in observing and monitoring the evolution of the digital health context. The Institute is involved in various clinical research projects to evaluate the safety and efficacy of digital health tools and digital therapies.

Polytechnic University of Milan
Polytechnic University of Milan offers several observatories dedicated to digital innovation, including the *Osservatorio Innovazione Digitale in Sanità and Lifescience Innovation*. Among the most recent studies:

- "Business models for digital therapies"[25], published in July 2023;
- "Life Science: Digital to Accelerate Transformation"[26], published in July 2024, concerning the analysis of different digital opportunities (artificial intelligence and digital therapies) with the aim of encouraging their integration into the Italian healthcare system.

SIF – Società Italiana di Farmacologia
SIF – Società Italiana di Farmacologia is interested in the topic of digital therapies (DTx) for their potential therapeutic effect, SIF plans to set up a multidisciplinary working group on digital therapeutics to investigate and promote this field.

AIOM – Associazione Italiana di Oncologia Medica
AIOM is closely following the topic of digital therapies (DTx), recognising their potential to offer a competitive advantage in the treatment of cancer diseases. In 2023, AIOM, in collaboration with the Mario Negri Pharmacological Research Institute, conducted a survey[27] to examine the knowledge, use and attitudes of Italian oncologists towards digital medicine tools.

ANMCO - Associazione Nazionale Medici Cardiologi Ospedalieri
ANMCO, as the National Association of Hospital Cardiologists, developed the position paper "Digital Medicine in Cardiology: Evidence and State of Progress in Italy"[28] focusing on the potential benefits and critical issues associated with the implementation of digital tools, artificial intelligence and telecardiology in clinical practice.

Fondazione RIDE2Med
RIDE2Med is a non-profit foundation with the aim of promoting scientific innovation with a focus on digital health, clinical research and raising awareness among healthcare professionals and the public.[29]

C. Private Entities

Farmindustria
In May 2023, *Farmindustria* published the document "Digital Therapeutics, Farmindustria Working Paper"[30], in which it explains what digital therapies are, discusses the regulatory difficulties affecting these technologies, devotes a section to the analysis of access models in Europe, and then delves into the Italian situation.

Confindustria Dispositivi Medici
Confindustria Dispositivi Medici presents a set of general and specific measures aimed at promoting effective digital governance in the field of medical devices, improving the quality of care and incre-

asing the synergy between the public health system and the production sector. In particular, with regard to digital therapies, according to Confindustria Dispositivi Medici it is important that clear rules are defined as soon as possible for these devices that at the same time guarantee the innovative character of medical devices, following the principles of the new European regulations especially for clinical investigations.

In May 2024, it signed a collaboration agreement with AiSDeT with the aim of investigating and promoting digital evolution scenarios in the healthcare sector. In particular, the protocol envisages joint initiatives to analyse and define digital PDTAs, identifying therapeutic areas for further investigation, as well as meetings on the Electronic Health Record (*Fascicolo sanitario elettronico - FSE*) and telemedicine.

D. Regional activities - the case of Emilia Romagna

Innovative forms of care products or processes based on the use of new technologies. Validation and accreditation

By Dr. Barbara Trevisani, Hospital Care Sector Collaborator, Director of Quality Assurance Service OAOU Modena - Prof. Altini Mattia, Director of the Hospital Care Sector and Regional Co-ordinator Authorisation and Accreditation

To innovate is to implement a product or process characterised by NOVELTY (implying improvement) and TRANSITION TO THE MARKET, with effective application in the company. To innovate, therefore, is to create change in order to improve an existing state of affairs, to bring it closer to the needs of the user and thus to bring about SOCIAL PROGRESS.

In healthcare, innovation - both in processes and products - aims to improve the effectiveness and efficiency of healthcare services in order to offer concrete solutions that respond to real clinical, care and operational needs, improving access, quality and treatment outcomes for patients.

These are positive changes, with measurable impact on public health and overall:

- mproving the quality of care and effectiveness. Each innovation aims to bring about a measurable improvement in patient care and well-being. This includes improvements in diagnosis, more effective treatments, reduced errors, and increased patient safety.
- Operational efficiency. Introduce processes that optimise the use of resources, reduce costs, and minimise waiting times for patients, without compromising the quality of care.
- Accessibility and equity. Ensuring that innovations improve access to health services for all sections of the population, regardless of their geographical location or economic situation.
- Sustainability. Ensure that innovations are sustainable in the long term, not only financially, but also in terms of environmental and social impact.

Every decision, from the development to the implementation of innovative products/processes, should be approached with the aim of improving the quality of life of patients, making care and healthcare services better.

Taking this premise into account, the aim of this project is to make use of the institutional accreditation procedure to enhance innovation experiences based on the use of new technologies in healthcare.

This is because accreditation, in addition to entering into the mechanism of contractual relations between the NHS institution and the health authorities, offers the possibility of activating verification and monitoring mechanisms, which are all the more opportune when the innovation is characterised as such in its life cycle.

In the public sphere, accreditation ensures that innovations comply with current regulations, thus protecting both patients and institutions from legal and reputational risks, and through the verification process that characterises it, accreditation ensures compliance with defined quality and safety standards. It therefore presents itself as a critical process to avoid self-referentiality, ensuring that innovation is objectively evaluated against rigorous and standardised criteria, reinforcing the principles of transparency and accountability of healthcare organisations and highlighting the seriousness with which the organisation pursues continuous improvement.

Through accreditation, it is also ensured that innovative processes and products maintain consistent quality over time, a key aspect in building trust among healthcare professionals, patients and stakeholders, ensuring that innovation can be successfully applied and replicated by promoting continuity and reliability.

Finally, through benchmarking and the sharing of best practices, accreditation provides opportunities for comparison with other healthcare institutions, encouraging the sharing of best practices and stimulating innovation. Organisations can learn from each other by adopting innovative solutions that have proven effective elsewhere. This steers organisations towards adopting innovative approaches that have been validated and proven effective, thus promoting improvement based on a sound scientific foundation.

- From an operational point of view, the technical steps by which the whole process of analysis, evaluation and traceability is developed are described in Figure 1.
- A prerequisite and prerequisite for access to this procedure is that the innovation belongs to a TRL>7.

The following actors are involved in the process: the healthcare facility proposing the innovation that brought about a *value-based* change in the patient care process, supported by the partner company, the regional evaluation commission called **GATE REVIEW**, engaged in the formulation of the suitability/accreditability judgement, and the Technically Accrediting authority for carrying out the external quality audits.

The Gate Review plays the central role when, on the basis of a set of information collected in a structured manner (submitted by the proposing healthcare facility together with the application for an assessment of Accreditability), it is asked to express a competent opinion on accreditability.

The committee's strength lies in the integration of the competencies within it, which are fundamental and decisive in the evaluation process. In fact, its functioning is based on the principle that the exchange of ideas, knowledge, and integration of competences increases the effectiveness of the team in approaching complex issues, where the value of judgement lies precisely in the diversity of competences.

It is proven that teams that combine a variety of skills and perspectives possess greater collective intelligence and are more effective in solving complex problems[32].

The mix of skills and experience, together with transparency, inclusiveness and feedback, represent leadership elements that characterise the Gate Review, to be interpreted across the board to promote a successful and innovative culture[33].

Figure 1: technical steps by which the whole process of analysis, evaluation and traceability is developed

STEP 1: ACCREDITABILITY ASSESSMENT

Submission of request for Accreditation/Validation of innovative process/product — Health Facility proposing the innovative pathway, together with the Partner

Supplementary documents attached to the request

Transposition of the request — Region ER

Appointment of the **GATE REVIEW** Commission

Preliminary analysis and definition of the evaluation date

GATE REVIEW committee meeting and evaluation of the ascertainability of the innovation process (**BASED VALUE**)

Complete documents — NO → Supplementary documents attached to the request

YES

Evaluation OK? — NO → Report with **NEGATIVE** opinion (END OF PROCEEDINGS)

YES

Report with FAVORABLE opinion (Validation of the innovation process)

Delivery of the report to the Regional Accreditation and Authorisation Coordinator.

STEP 2: STARTING THE ACCREDITATION PROCEDURE

Submission of the Accreditation Application — Health Facility intending to adopt the innovative process

"CLASSIC" Accreditation Management Procedure — Hospital Care Sector OTA

Surveillance checks — OTA: every 2 years

INNOVATIVE PROCESS (TRL>7): PROPOSING HEALTH FACILITY:

- Copy of the identity card of the legal representative signing the application and declarations.
- Statement of fulfilment of general accreditation requirements - Self-assessment
- Statement of fulfilment of specific accreditation requirements - Self-assessment
- Substitute declaration concerning the possession of the requirements made pursuant to Articles 46 and 47 of Presidential Decree 445/00
- Population and case history: No. of cases per year and type (case history treated by the proposing structure and also referring to the provincial area)
- Description of the existing care process to be innovated, with specifications:
  - on the reason for the need to introduce Care Process Innovation in the light of the innovation introduced, specifying: the special features of the new process, differences from the usual process, points of improvement
  - whether the introduction of the innovative process will completely replace the existing care process or whether for a certain period of time both will coexist
  - the overall value introduced by the innovative care process and the benefits brought: economic, organisational, patient impact [VALUE-BASED HEALTHCARE - VBHC approach].
  - the impact of the introduction of this change on the organisation and the process
- Attestation of the degree of innovation maturity, with definition of Technology Readiness Levels (TRL), which to be assumed in a non-experimental environment must be at least TRL>7
- Documentation proving the effectiveness and safety of the proposal, accompanying data and references
  - Articles/publications, supporting studies, on efficacy and safety
- Documentation showing the residual risks associated with the innovation and actions for their mitigation.
  - Process analysis in the various settings used, in which the innovative care pathway takes place
- Plan to monitor this change over time
- Monitoring outcomes and results: process and outcome indicators and results
- Costs:
  - Expenditure data for each stage of the traditional care process and expenditure data for each stage of the innovative process
  - With disclosure of Total Costs, Emerging Costs and Discontinued Costs)

PARTNERS

- company view and corporate structure
- general company information: turnover for the last 3 years through this process/product and its ratio to total turnover, number of people, references
- Statement on the degree of maturity of the innovation: Describe whether this product/process is currently on the market or is at the experimental or prototype stage
- product/process brochure
- patents, most important publications related to the product process
- other documentation proving the effectiveness of the proposal
- current use of the same innovative process/product in other facilities
- include which services the

The GATE REVIEW committee:

1. It is appointed by the Director General Personal Care, Health and Welfare
2. It is chaired by the Regional Authorisation and Accreditation Coordinator
3. It consists of a managerial component and a technical component:

- Regional component of the Legal sector
- Regional Member of the Financial Sector
- Regional Risk Management Component
- Regional Component on Accreditation and Authorisation
- Regional component on Clinical Governance
- Innovation Component
- Pharmaceutical Component
- Regional reference component for the HTA topic
- OTA component
- Regional component 'other', depending on the type of innovation for which Accreditation is sought,
- At least 2 professionals in the technical/disciplinary field specific to the subject of the request, participating as experts
- a facilitator, who plays the role of support in the organisational and logistical management of the Gate Review Commission.

The GATE REVIEW meeting is attended by: both the healthcare company that submitted the application and the partner company, for the illustration to the committee of the innovative process and the accompanying data attached to the application (without decision-making power)

The practical side that emerges at the end of the process is of considerable impact, offering the possibility of

- Encourage the diffusion of innovation by offering other structures the opportunity to approach the same operational and organisational mode of care delivery. When an innovation is adopted by an increasing number of users (individuals or structures/organisations), it tends to become an integral part of the operational or economic fabric, losing its novelty character, thus accelerating the innovation life cycle by shortening the time for its routine adoption.
- Encouraging an equitable provision of care/treatment options to the population in the area. When an innovation is accepted and integrated into the culture of a society and/or professional community, it ceases to be perceived as a novelty and becomes part of the way things are done, thus promoting social acceptance.
- Ensure, through accreditation and renewal audits, a monitoring system for the entire life cycle of the innovation applied within the accredited structure.
- Allow for economies of scale: Large-scale production and economies of scale can make innovations more accessible and cost-effective, which in turn accelerates the transition to routine use.
- The possibility of evaluating and investing in innovative processes i.e. processes that can create value in the medium term and allow for a forward-looking approach in terms of sustainability and return, in a "public entrepreneurship" approach, with the aim of pursuing social objectives or providing essential services to all citizens.

Research and innovation are thus the driving force for the evolution of the health system and thus also for the evolution of the Accreditation system. An in-depth analysis of the Innovation-Accreditation binomial makes it possible to emphasise how the Accreditation process is an important facilitator of **RESPONSIBLE INNOVATION** and the adoption of new technologies and processes in the healthcare sector.

In fact, innovations that have passed a rigorous accreditation process can be more easily adopted by other healthcare organisations because accreditation acts as a signal of reliability and effectiveness, making the innovation more attractive and reducing barriers to adoption.
On the other hand, patients, healthcare professionals and stakeholders place greater trust in products and processes that have been accredited. This level of trust is essential for the successful adoption and integration of innovations into everyday practices.
In conclusion, the transition from innovation to routine is a complex and multifactorial process that has a significant impact on society and the economy. Within this framework, accreditation demonstrates a commitment to **SOCIAL RESPONSIBILITY**, ensuring that innovations contribute positively to the community and do not introduce unnecessary risks, and this aligns healthcare organisations with the broader goals of **PUBLIC HEALTH** and **SOCIAL WELL-BEING**.

Understanding the dynamics of this approach is crucial for healthcare organisations that want to maintain a competitive advantage and adapt to changes in the market and the growing and diversifying needs of patients.

4.2 pDMDs mapping

By Indicon Società Benefit

Objective

This chapter presents an analysis conducted on the Italian Ministry of Health's medical device registry, aimed at mapping the presence of pDMDs in Italy (see Chapter 3 – Definitions).

Methodology

The analysis was conducted using the Italian medical device database available on the Ministry of Health's website as a source[1].

The dataset available on the Ministry's website was downloaded on the Access platform. The complete list, updated as of July 16, 2024, includes a total of 1,983,552 certified devices. Subsequently, CND (National Classification code for Devices) deemed useful for identifying patient-managed digital medical devices were selected. Table 1 shows the CNDs considered in the analysis.

Table 1: CND included in analysis

CND codes	Description CND
V92	Software medical devices - not included in other classes
Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software accessory components
Z12069082	Instrumentation for physiotherapy and rehabilitation - software accessories
Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices
Z129092	Various instrumentation for functional exploration and therapeutic interventions - software medical devices
Z12100702	Emg telemetry transmitter units

Once the devices associated with the relevant CNDs were selected, the data was extracted onto the Excel platform for ease of use. A database populated with a total of 344 devices devices was then created, with the following fields reported for each:

- Manufacturer
- Product name
- CND code
- Description of CND code
- Medical device class

Subsequently, each of 344 digital medical device was analyzed by searching the manufacturer's website or the device's website for information regarding its functionality. Using this methodology, medical devices corresponding to the definition of patient-managed digital medical devices (pDMDs) were classified. The analysis revealed a total of 45 were compliant with the definition of pDMDs (13,08%).

[1] Elenco dei dispositivi medici, Ministry of Health [available online at:https://www.salute.gov.it/interrogazioneDispositivi/RicercaDispositiviServlet?action]

The pDMDs were classified based on their medical purpose and divided into the following categories:

- Therapy –digital therapeutics
- Diagnosis - digital diagnostics - software and digital tools that offer diagnostic or prognostic insights for a given disease or medical condition.
- Monitoring - Remote patient monitoring - digital tools intended to track specific health data, allowing physicians to interpret the information for clinical management.
- Prevention - digital prevention - digital tools and software designed to support disease prevention by monitoring health indicators and promoting early intervention strategies.

Of these, 21 are for monitoring (46,67%), 17 for therapy (DTx) (37,78%), 4 for prevention (8,89%) and 3 for diagnosis (6,66%).
Once the size of the pDMDs ecosystem in Italy was defined, the next step involved analyzing the medical device class to which the considered pDMDs belong. The analysis revealed that:

- 68,9% (n=31) are registered as Class I
- 26,7% (n=12) registered as IIa
- 4,4% (n=2) registered in IIb

Table 2: pDMD classified for medical purpose

Manufacturer	Product name	CND code	Description of CND code	Medical purpose	Medical Device Class
Huma Therapeutics Limited	Huma	V92	Software as a devices - not included in other classes.	Monitoring	Class I
Huma Therapeutics Limited	Medopad	V92	Software as a devices - not included in other classes.	Monitoring	Class I
Drop Società A Responsabilita' Limitata Semplificata	Software di servizi medici digitali kalanit rehab	V92	Software as a devices - not included in other classes.	Therapy	Class I
Cineca Consorzio Interuniversitario	Surpass	V92	Dispositivi medici software - non compresi in altre classi	Monitoring	Class I
Precordior Ltd.	Cardiosignal	V92	Software as a devices - not included in other classes.	Diagnosis	Class IIa
Medm Inc.	Pic health station	V92	Software as a devices - not included in other classes.	Monitoring	Class I
Iamhero S.r.l.	Software di servizi medici iamhero	V92	Software as a devices - not included in other classes.	Therapy	Class I
Ada Health Gmbh	Ada assess	V92	Software as a devices - not included in other classes.	Diagnosis	Class IIa
Abbvie Inc.	Myabbviecare	V92	Software as a devices - not included in other classes.	Prevention	Class I
Ethypharm Digital Therapy	Deprexis	V92	Software as a devices - not included in other classes.	Therapy	Class I
Zulu Medical S.r.l.	Zulu meridian	V92	Software as a devices - not included in other classes.	Monitoring	Class I
Valiamo S.r.l.	Realica	V92	Software as a devices - not included in other classes.	Prevention	Class I
Medical Cloud S.r.l.	Visita smart versione 1.0.0	V92	Software as a devices - not included in other classes.	Monitoring	Class I
Morecognition S.r.l.	Remo-dev~remo	Z12100702	Telemetry transmitter units	Therapy	Class I

Manufacturer	Product name	CND code	Description of CND code	Medical purpose	Medical Device Class
Meteda S.r.l.	Did plus	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIa
Laboratori Di Informatica Applicata Di Capasso Giuseppe	Bpcomedia	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class Iia
Sooil Development Co. , Ltd	Any-dana-a	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIa
Me.te.da. S.r.l.	Eurotouch	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Medtronic Minimed	Software solutions cgms	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Diagnosis	Class IIa
Meteda S.r.l.	My dose coach	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Therapy	Class IIa
Amalgam Rx, Inc	Dose check	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIa
Amalgam Rx, Inc	Isage rx	Z12040182	Instrumentation for monitoring and diagnosis in general medicine softwa-re - accessory components	Monitoring	Class IIa
Social Diabetes Sl	App social dia-betes	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIb
Vinehealth Digital Ltd	Vinehealth cancer companion & vinehealthpro	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Persei Vivarium Srl	Caaring	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Diabeloop	Yourloops	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIa
Elekta Solutions Ab	Kaiku health	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIa
Vitalhealth Software B.v.	Engage	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Prevenzione	Class I
Medtronic Minimed	Carelink personal	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Meteda S.r.l.	Diawatch meteda	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Informatica E Telecomunicazioni S.r.l.	Sm@rteven	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class I
Meteda S.r.l.	Metadieta for pre-ventomics	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Prevention	Class I

Manufacturer	Product name	CND code	Description of CND code	Medical purpose	Medical Device Class
Zhejiang Poctech Co., Ltd.	Software per sistemi di monitoraggio continuo del glucosio	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Monitoring	Class IIb
Tech4care S.r.l.	Relab	Z12040182	Instrumentation for monitoring and diagnosis in general medicine - software - accessory components	Therapy	Class I
Jjrent S.a.s. Di Lawrence Spavieri & C.	Allimb	Z12069082	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
Drop Società A Responsabilità Limitata Semplificata	App web app parkinson rehab	Z12069082	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
One Health Vision Srl	Balbus	Z12069082	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
Quicklypro S.r.l. Start-Up Costituita A Norma Dell'art.4 Comma 10 Bis Del Decreto Legge 24 Genna...	Quicklypro-app	Z12069082	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
One Health Vision Srl	Numbers'adventures	Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
One Health Vision Srl	Scrivo bene	Z12069092	Strumentazione varia per fisioterapia e riabilitazione - dispositivi medici software	Therapy	Class I
Euleria S.r.l. Societa' Benefit	Medicrehapp	Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
Euleria S.r.l. Societa' Benefit	Euleria home	Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class IIa
One Health Vision Srl	Turbolettura	Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I
Mindahead S.r.l.	Mindahead active app	Z129092	various instrumentation for functional exploration and therapeutic interventions - software medical devices	Therapy	Class I
One Health Vision Srl	Volo bla bla	Z12069092	Various instrumentation for physiotherapy and rehabilitation - software medical devices	Therapy	Class I

4.3 DTx Mapping

The first DTx Monitoring Report[34] analysed companies involved in the production and development of digital therapeutics in Italy, the aim of this chapter is to update these figures with the most recent data and to highlight the players involved in the production of DTx in Italy.

The number of Italian companies involved in the digital therapeutics sector has increased to 23, compared to 13 the previous year. These include 16 innovative start-ups, 3 innovative SMEs, 1 non-innovative start-up and 4 established companies. The total number of products is now 41, compared to last year's 28 products, there was an increase of 50%.

Of the 41 potential DTx that emerged from the analysis, 17 are already registered in the Medical Devices Registry maintained by the Italian Ministry of Health.
The following table shows the devices, the companies and the reference CE class.

Tabella 1: Italian DTx Mappping

Company	Partnership	Product	Therapeutic Area	MD	Class
AdvicePharma	Chiesi	Churchill	Post heart attack rehabilitation		
AdvicePharma	AstraZeneca	KindeYou	Cronic Kidney Disease - CKD		
AdvicePharma	Theras Lifetech	Liberness / DTXO	Obesity		
ALDATECH		REVIDEO	Glaucoma		
Dally therapeutics		Dally	Diabetes		
DaVi Digital Medicine	Università di Verona	Nyx Digital	Chronic insomnia		
DaVi Digital Medicine	Polifarma	QK-Digital	Hypertension		
DaVi Digital Medicine	DigitalRehab srl	AuReha	Motor rehabilitation		
Develop players		eye-riders	ADHD		
Drop Digital Health	Chiesi Italia	Kalanit Rehab	Muscoloskeletal pain	X	I
Drop Digital Health	Chiesi Italia	Parkinson Rehab	Parkinson	X	I
Euleria Health	Neurab	Euleria Home	Motor, cardiac and cognitive rehabilitation	X	IIa
Euleria Health		MedicRehApp	Cardio-respiratory rehabilitation	X	I
GAIA AG	Ethypharm Digital Therapy	Deprexis	Depression	X	I
HEAPLE		HEAPLE	Mild Cognitive Impairment		
Helaglobe	Roche Italia	MS-FIT	Multiple sclerosis		
Helaglobe		Haemo-fit	Haemophilia - physical rehabilitation		
IamHero		IamHero	ADHD, Neurodevelopmental Disorders	X	I
Jjrent S.a.s. Di Lawrence Spavieri & C.		Allimb	Motor rehabilitation	X	
Meeva	Fondazione Bruno Kessler, Trentino Sviluppo, EIT Digital	Meeva	ADHD, Neurodevelopmental Disorders, Autism		

Company	Partnership	Product	Therapeutic Area	MD	Class
METEDA		My Dose Coach	Diabetes	X	
MindAhead		MindAhead	Mild Cognitive Impairment, Dementia	X	I
Morecognition		Remo	Post stroke rehabilitation	X	I
My Improvement Network		Rita	Cognitive disorders, dementia, post stroke rehabilitation, DSA		
Newel Health		Amicomed	Hypertension		
Newel Health		Soturi	Parkinson		
One Health Vision		Balbus	Stuttering	X	I
One Health Vision		BuildAttention	ADHD		
One Health Vision		Leggo Facile	Dyslexia		
One Health Vision		LogoQuiz	Aphasia		
One Health Vision		Numbers'adven-tures	Dyscalculia		
One Health Vision		Scrivo Bene	Dysorthography	X	I
One Health Vision		TurboLettura	Developmental dyslexia	X	I
One Health Vision		TuttoAscolto	Hypoacusis, Hearing disorders		
One Health Vision		Volo Bla Bla	Phonological disorder	X	
One Health Vision		Voysanalysis	Dysarthria, Phonological disorder		
Paperbox health		Dino	DSA		
QuicklyPro		QuicklyPro App	Motor rehabilitation	X	I
Restorative Neuro-technologies		Mindlenses	Cognitive impairment rehabilitation	X	I
Tech4Care		Relab	Cognitive impairment rehabilitation, Multiple sclerosis, Parkinson	X	I
VRforCare		Drim	Substance use, abuse and dependence		

The following description focuses on devices that were not covered in the First DTx Monitoring Report, presented in alphabetical order[35].

My Improvement Network

My Improvement Network is an innovative start up with the objective of helping people with dementia in care centres and has developed:
RITA (Reminiscence Interactive Therapy Activities)[36]: digital therapy aimed at improving the care provided to elderly people, those living with dementia, mental health problems, acute brain injury and learning difficulties. RITA aims to support them by reducing their agitation, isolation, depression and delirium.
It is a relatively new tool in the field of nursing and healthcare; it involves the use of user-friendly interactive screens and tablets to combine entertainment with therapy and to assist patients in remembering and sharing events from their past through listening to music, watching news of significant historical events, playing games, karaoke and watching films.

VRforCARE S.r.l.

Innovative start-up that designed:
Drim[37]: a virtual environment of intense "reality" in which the user can move, interact, make decisions,

and evaluate the consequences of their behavior. A playful, pleasant, and engaging context is created, where the user is immersed and stimulated by visual, auditory, and olfactory inputs. During the exposure, the user is confronted with various substances of abuse (cannabinoids, cocaine, heroin, and alcohol) as well as addictive risk behaviours, such as pathological gambling. The user is invited to "experiment" with them and then face the potential consequences, of which they are often unaware. Alternative choices are presented, allowing the user to assess their impact on internal and external functioning. Throughout the entire exposure in the virtual environment, the user is followed and monitored by a therapist who, based on the responses and variations in physiological parameters—such as heart rate, breathing frequency, and blood pressure—collects rich and up-to-date material for discussion at the end of the VR session. The strength of this tool lies in its ability to deeply explore the sensations, thoughts, and experiences lived in the virtual environment, immediately and directly, without relying on reported or past accounts.

MEEVA Società Benefit

MEEVA is an innovative start-up with the objective of enhancing the social-relational skills of adolescents and young people with special needs (autism, ADHD) through:
MEEVA VR[38]: The proposed solution is based on the latest scientific evidence demonstrating the benefits of Virtual Reality (VR) in the acquisition and enhancement of skills in a safe, realistic and controlled environment. Furthermore, it makes use of multi-player games to promote a sense of belonging to the group and stimulate cognitive and executive functions. During the session, participants will be involved in a series of collaborative challenges designed to improve both their social-relational skills and executive functions through a dynamic and interactive experience.

IamHero[39]

Innovative start-up whose mission is to provide digital therapies based on gamification techniques for a broad spectrum of neurodevelopmental psychological problems. It has developed:
IamHero: a class I medical software device that enables the creation of an advanced game-based therapeutic environment to help young patients with Attention Deficit/Hyperactivity Disorder (ADHD) improve their cognitive-behavioural skills. The child, in fact, by means of such a device, has the opportunity to actively and immediately experiment with his or her own ways of managing emotions, thoughts and behaviour. The therapist, in turn, can intervene directly within the setting to work with the patient with a view to a greater acquisition of awareness of his or her own experiences and a more functional management of them. IamHero, however, like any device, does not set out to replace the therapist in the rehabilitation context, but rather adds to the privileged child-therapist dyad in that empathic and unique bond.

Valiamo[40]

Innovative start-up providing a wide range of state-of-the-art products, including devices, furniture, equipment and integrated systems for hospitals, clinics, nursing homes and communities. Valiamo S.r.l. owns the brand:
REALICA[41]: Virtual Reality visor offering a revolutionary sedation solution as a non-pharmacological and non-invasive approach to alleviate patients' fear, anxiety and pain. Using immersive virtual reality experiences, Realica provides immediate benefits in the management of patient well-being. During treatments that can generate anxiety and pain, Realica guides patients on a total journey into a completely different universe for the duration of the procedure, offering not only immediate relief, but also constant support and distraction. In this context, patients acquire valuable self-management techniques that accompany them throughout the entire medical journey. Realica is backed by rigorous clinical studies and positive feedback from healthcare professionals. Numerous scientific publications attest to its effectiveness in improving patient outcomes across a broad spectrum of medical interventions.

Tech4Care[42]

Tech4Care is an innovative SME offering digital health products and services, aiming to innovate the care and management of frail, dependent and chronically ill people. It has developed:
RELAB: immersive Virtual Reality visor offering rehabilitation solutions for Parkinson's disease, multiple sclerosis and post-stroke cognitive impairment patients. Relab provides a constantly updated library of rehabilitation exercises to ensure patient engagement and adherence, thus adding further value to therapeutic progress. The system also offers the possibility for specialists to monitor patients during their rehabilitation sessions in real time, with accurate data on the number of sessions performed, duration, completed sessions and clinical information.

Jjrent/Allimb

ALLIMB[43]: an app that provides programmes and exercises to support and document the implementation of physiotherapy and occupational therapy plans. At the heart of Allimb's therapy is a multimodal approach based on Cognitive Behavioural Therapy (CBT) and aligned with the standard of care. Supported by artificial intelligence, the app corrects complex movements in real time without the need for additional equipment or an internet connection.

QuicklyPro

Innovative SME that developed:
QuicklyPro App[44]: class I certified medical device that in the form of an application supports the patient in performing rehabilitation exercises at home. Through video tutorials, the app guides the patient through the therapy, providing constant feedback on the progress of individual exercise sessions. In addition, QuicklyPro App allows the patient to manage Q-Walk, the wearable medical devices for gait rehabilitation.

Euleria Società Benefit[45]

Innovative start-up that developed:
Euleria Home: class IIa-certified medical software that accompanies the patient along the entire rehabilitation pathway at home through exercise-therapy programmes customised by their practitioner. Euleria Home allows to configure rehabilitation paths:

- Motor: through an extensive library of exercises for the lower limbs, upper limbs, spine and balance functional to the different work areas including coordination, strength, mobility, proprioception, muscle lengthening and posture. The exercise video guide and real-time audio-visual biofeedback of the movement recorded by the sensor accompany the patient in the correct execution of the assigned exercise.
- Cardiac: aerobic exercises with monitoring of the heart rate by means of a heart rate monitor and of the quality of movement execution by means of an inertial sensor. The rehabilitation programme, created ad hoc by the professional, is administered in the form of exercises that follow one after the other with the aim of keeping the patient's heart rate within a specific range between a minimum and a maximum threshold identified by the professional.
- Cognitive: exercises administered through Neurab's Neurotablet for attention, memory, perception, executive functions, language and a specific set for neglect.

MedicRehApp: a class I medical device developed by Euleria S.r.l and MedicAir, a company operating in the home care sector. MedicRehApp is able to support patients along the entire cardio-respiratory rehabilitation pathway, thanks to the customisable and monitorable exercise programme prescribed by health professionals, which includes aerobic and strength training.

One health vision

Innovative medium-sized company that has developed the following digital therapies.
Balbus: the first web application produced by One Health Vision for the treatment of stuttering.
The device consists of five exercises that enable the patient to gain greater control over their speech. The app also provides audio and visual feedback to help the patient achieve greater fluency. There are individual graphs for each exercise for better patient monitoring. Balbus is certified as a CE Class I medical device. The device is currently on the market and can be purchased from the dedicated website.

Leggo facile: web application for the treatment of acquired dyslexia and reading difficulties.
Reading difficulties. The app offers exercises based on reading texts through a precise speech recognition engine and allows real-time feedback and corrections. It is tailored to the patient's needs and allows him/her to monitor and share the progress and results obtained.

and the results achieved. The software is currently on the market and can be purchased from the dedicated website.
Scrivo Bene: Web application for children who have been diagnosed with dysorthographia or who are learning to write.
spelling skills. Scrivo Bene has been developed according to the principles of the token economy, in which the patient's learning and involvement are stimulated by the dynamics of playing games and completing tests. The app consists of six exercises: 'Read and Write', 'Listen and Write', 'Choose the Correct
Choose the right one', 'Pairs bursting', 'Look for the mistake' and finally 'Dictation'. The app allows you to monitor your child's progress and provides a training report. Scrivo Bene is certified as a CE Class I medical device.

TurboLettura: digital solution for the treatment of dyslexia and reading difficulties
developed as a serious 3D game available for smartphones and tablets. The child
has to read aloud the word displayed on the device, thanks to speech recognition
The app checks the pronunciation and gives feedback in real time. The app allows the child's progress to be monitored and provides a training report. TurboLettura is a CE Class I medical device that can be downloaded on mobile devices through the main download platforms.

TuttAscolto: is the serious game for the rehabilitation of hearing disorders and hearing loss, a technology based on widely used rehabilitation protocols recognised in the literature, suitable for adults and children. It is an application that stimulates not only the auditory aspect but also the neuropsychological one, with the aim of involving the user as much as possible. TuttAscolto allows an intensive daily treatment thanks to the exercises designed and presented within it, based on detection (ability to distinguish whether a sound is present or absent through the presentation of sounds or words), discrimination (ability to distinguish whether a sound is present or absent through the presentation of sounds or words).
presentation of sounds or words), discrimination (identifying 2 sounds as the same or different)
the same or different), identification (identifying a sound or word from a limited set of choices) and sound of options) and sound recognition. Finally, the app allows you to view and share graphs and
Finally, the app allows you to view graphs and statistics on your child's performance and send them to your therapist by email. Already available on the main download platforms.

Volo Bla Bla: a web app designed for patients with phonetic-phonological disorders. This technology is capable of listening to the user's words, analyzing them, and providing immediate feedback. The app allows the user to select the phoneme they wish to practice, offering a highly personalized treatment. The serious game feature lets users collect rewards, increasing patient engagement and motivation through gamification principles and token economy techniques. Results can be shared

with the user's therapist. The app can be purchased via a dedicated website.

Numbers' Adventures: a mobile app for the treatment of dyscalculia and difficulties in the logic-mathematical field. This serious game helps users acquire and consolidate lexical, semantic, syntactic, and procedural calculation skills. The app allows children to unlock and earn rewards that let them customize their avatar, thereby boosting their motivation for treatment. Numbers' Adventures is certified as a Class I CE medical device and can be purchased through major download platforms.

LogoQuiz: an app for smartphones and tablets for the treatment of aphasia and dysphasia. The app helps individuals with language difficulties rehabilitate these functions through exercises focused on comprehension, production, reading, and writing. While performing activities, the app provides continuous visual and auditory feedback within a playful and interactive context. The app can be purchased through major download platforms.

BuildAttention: an app for smartphones and tablets designed to enhance attentional and executive functions, targeting both children and adults. The app treats attentional and executive skills through exercises organized in a hierarchical manner, based on widely-recognized rehabilitation protocols. Users can practice within a playful environment while receiving constant visual and auditory feedback. The app is available for purchase through major download platforms.

One Health Vision also offers other devices such as **Voysanalysis**, **Train Your Memory**, and **Selecteat**. The latter, currently in development, is a mobile app designed to address food selectivity. Additionally, another app is being developed for individuals with conditions that severely impair language, where communication is difficult and problematic due to unintelligible speech. This app, developed using an innovative and effective artificial intelligence algorithm, can detect and transcribe the user's speech. One Health Vision is also developing a new version of **Balbus**, Balbus 5.0. This mobile app provides immediate and personalized feedback, helping patients improve control over their fluency. Additionally, it encourages the restructuring of irrational thoughts through the application of cognitive-behavioral techniques, offering constant support as if each patient were personally followed by a specialist all day long.

Analysis of clinical trials

This section will provide an overview of the current landscape of clinical trials focusing on digital therapeutics carried out in Italy.

Methodology

The analysis was conducted on the digital therapeutics listed in Table 1 to identify which of these have ongoing or completed clinical trials in Italy.
The research was conducted using the global registry of clinical trials, clinicaltrials.gov , as a data source. The process involved searching for each digital therapeutic listed in Table 1 using the following parameters to search for devices

- Intervention/treatment: name of the device
- Sponsor and/or Collaborator: name of the manufacturing company or the partner

For digital therapeutics with ongoing or completed clinical trials, the following aspects has been analysed: product name, therapeutic area, company, partner, trial status, study ID, trial start and end dates, location. The data collected are documented and presented in Table 2.

Tabella 2: Clinical trials on digital therapies conducted in Italy

Product	Therapeutic Area	Company	Partner	Study ID	Start	End	Site	Location
DTX-O/ Liberness	Obesity	Advice-Pharma	Theras Lifetech	NCT05394779	Active, not recruiting	2022	2024	Milano
KindeYou	Cronic Kidney Disease - CKD	Advice-Pharma	AstraZeneca	NCT05286632	Recruiting	2022	2024	Bari
Mindlensis	Cognitive impairment rehabilitation	Restorative Neurotechnologies	-	NCT05826626	Recruiting	2021	2024	Venezia
Remo	Post stroke rehabilitation	Morecognition	-	NCT05416619	Concluded	2017	2019	Venezia
Soturi	Parkinson	Newel Health	Michael J. Fox Foundation for Parkinson's Research, Mediolanum Cardio Research	NCT05904288	Active, not recruiting	2023	2024	Roma, Salerno
Amicomed	Hypertension	Newel Health	-	NCT06091176	Not yet recruiting	2024	2025	N.d.
Euleria Home	Motor rehabilitation	Euleria Health	Università di Verona	NCT06485115	Not yet recruiting	2024	2026	Verona

The analysis shows 7 clinical trials in Italy, of which:

- 28,5% (n=2) active not recruiting
- 28,5% (n=2) recruiting
- 28,5% (n=2) not yet recruiting
- 14,5% (n=1) concluded

Of the 7 studies on digital therapies in Italy, 3 are on technologies already registered as medical devices: Euleria Home, Remo and Mindlensis.

5. PRACTICAL APPLICATIONS OF DIGITAL HEALTH TECHNOLOGIES (DHTs)

5.1 DHTs in diabetology

By Luigi Laviola, Full Professor of Endocrinology University of Bari Aldo Moro

Digital Health Therapeutics in Diabetes

Digital health therapeutics (DHTs) are evidence-based, clinically validated interventions delivered through digital platforms to prevent, manage, or treat medical conditions. Unlike general wellness apps or devices, DHTs are subject to rigorous regulatory oversight and are often prescribed by healthcare professionals as part of a comprehensive treatment plan. In diabetology, DHTs can include continuous glucose monitors (CGMs), insulin delivery systems, mobile applications for self-management, and AI-powered tools that provide personalized treatment recommendations. The advent of DHTs has marked a significant turning point in the management of chronic diseases, particularly diabetes. As the prevalence of diabetes continues to rise globally, innovative solutions are needed to enhance disease management, improve patient outcomes, and reduce the burden on healthcare systems.

Applications of Digital Health Therapeutics in Diabetes Management

1. Continuous Glucose Monitoring (CGM) Systems

CGMs are among the most impactful DHTs in diabetes management. These devices continuously monitor glucose levels in the interstitial fluid, providing real-time data that can be used to make immediate adjustments to insulin therapy. CGMs have been shown to improve glycemic control, reduce hypoglycemia, and enhance quality of life for patients with both type 1 and type 2 diabetes[1]. The integration of CGMs with insulin pumps and mobile apps allows for automated insulin delivery and personalized feedback, making diabetes management more efficient and effective.

2. Mobile Health Applications

Mobile health (mHealth) applications have become essential tools in diabetes self-management. These apps offer a wide range of features, from glucose tracking and dietary logging to virtual coaching and peer support. Studies have demonstrated that the use of mHealth apps can improve glycemic control, increase patient engagement, and enhance adherence to treatment plans[2]. Some apps also include AI-driven insights and personalized recommendations, further tailoring the management approach to the individual needs of the patient[3].

3. Digital Therapeutics for Behavioral Modification

Behavioral modification is a key aspect of diabetes management, as lifestyle factors such as diet, exercise, and medication adherence significantly influence glycemic control. Digital therapeutics (DTx) focused on behavioral modification use evidence-based techniques to support patients in making sustainable lifestyle changes. For example, some DTx platforms use cognitive behavioral therapy principles to help patients overcome barriers to healthy eating or regular physical activity[4]. These programs have been shown to improve both glycemic control and overall well-being, reducing the risk of long-term complications[5].

4. Artificial Intelligence and Predictive Analytics

Artificial intelligence (AI) and predictive analytics are transforming diabetes care by enabling more accurate and personalized treatment strategies. AI algorithms can analyze vast amounts of data from CGMs, insulin pumps, and patient-reported outcomes to identify patterns and predict future glucose levels[6]. This predictive capability allows for proactive adjustments to treatment plans, reducing

the risk of hyperglycemia or hypoglycemia. In addition, these technologies can provide individualized treatment recommendations, thus improving patient adherence to treatment plans and supporting clinical decisions for the health care professionals[7].

5. Remote Monitoring, Virtual Care Platforms and Telemedicine

Remote monitoring platforms that incorporate DHTs are revolutionizing diabetes care by enabling continuous, real-time data sharing between patients and healthcare providers. These platforms allow for the remote monitoring of blood glucose levels, insulin usage, and other relevant metrics, facilitating timely interventions and adjustments to treatment plans[8]. Virtual care platforms that integrate DHTs also offer features such as teleconsultations, electronic health record (EHR) integration, and automated data analysis, making them a comprehensive solution for diabetes management. The COVID-19 pandemic has accelerated the adoption of telemedicine, highlighting the importance of remote care solutions in managing chronic diseases. DHTs are a natural complement to telemedicine, enabling healthcare providers to monitor patients remotely and adjust treatment plans as needed. For example, data from CGMs and insulin pumps can be transmitted to healthcare providers in real-time, allowing for timely interventions without the need for in-person visits[9]. This integration enhances the continuity of care and can be particularly beneficial for patients in remote or underserved areas. In addition, remotely collected data may help identify patients' attitudes and behavioural patterns in specific conditions[10].

6. Wearable Devices and Smart Technology

Wearable devices, such as smartwatches and fitness trackers, are becoming increasingly popular in diabetes care. These devices can monitor physical activity, heart rate, sleep patterns, and other health metrics, providing valuable insights into a patient's overall health and its impact on diabetes management[11]. Some wearable devices also include glucose monitoring capabilities, allowing for seamless integration with other DHTs and enabling a more holistic approach to diabetes care. The data collected by these devices can be used to personalize treatment plans and improve patient outcomes[12].

Challenges and Considerations

While DHTs offer significant benefits in diabetology, several challenges and considerations must be addressed to ensure their successful implementation and adoption.

Regulatory Approval and Standardization. As DHTs become more integrated into diabetes care, there is a need for clear regulatory guidelines and standards to ensure their safety, efficacy, and quality. Regulatory bodies must establish rigorous approval processes for DHTs, similar to those used for traditional medical devices and pharmaceuticals. Standardization is also crucial to ensure interoperability between different DHTs and healthcare systems, enabling seamless data sharing and integration.

Data Privacy and Security. The widespread use of DHTs involves the collection and analysis of large amounts of patient data, raising concerns about data privacy and security. Healthcare providers and technology companies must implement robust measures to protect patient data and ensure compliance with regulations such as the General Data Protection Regulation (GDPR) in Europe and the Health Insurance Portability and Accountability Act (HIPAA) in the United States13. Ensuring patient trust in the security of their data is essential for the widespread adoption of DHTs.

Patient Access and Health Equity. While DHTs have the potential to improve diabetes care, there is a risk that they may exacerbate health disparities if access to these technologies is not equitable. Healthcare providers and policymakers must work together to ensure that all patients, regardless of socioeconomic status, have access to DHTs and the necessary support to use them effectively14. Addressing barriers such as cost, digital literacy, and access to reliable internet and devices is critical to ensuring that the benefits of DHTs are accessible to all.

Integration into Clinical Practice. For DHTs to be effectively integrated into clinical practice, healthcare providers must be adequately trained on how to use these technologies and interpret the data they generate. DHTs should be seamlessly integrated into existing clinical workflows and electronic health record (EHR) systems to avoid disruptions to established practices. Collaboration between healthcare providers, technology companies, and patients is essential to ensure the successful implementation and adoption of DHTs in routine diabetes care.

Conclusion

Digital health therapeutics represent a significant advancement in the management of diabetes, offering new ways to optimize glycemic control, personalize treatment, and engage patients in their care. The integration of DHTs into clinical practice has the potential to improve patient outcomes, reduce healthcare costs, and address the growing burden of diabetes. However, the successful adoption of DHTs will require addressing challenges related to regulation, data privacy, access, and integration into clinical practice. As healthcare systems continue to evolve, DHTs will play an increasingly important role in the management of diabetes, offering hope for better care and improved quality of life for millions of people living with this chronic condition.

5.2 Applications of DHTs in Oncology

By Tiziana Pia Latiano, executive member AIOM - Italian Medical Oncology Association

Introduction

Cancer is one of the leading causes of mortality globally, with millions of new cases diagnosed every year. Managing these cases remains one of the greatest challenges for health systems[1].
Cancer treatments are no longer limited to drug administration alone but require a multidisciplinary approach. Each patient presents a unique combination of therapeutic needs that vary according to the tumour type, molecular structure, disease stage, response to treatment, and general clinical condition[2].

This complexity makes continuous, personalised support indispensable for patients, who often have to cope not only with disease-related challenges but also with psychological and social difficulties.
Optimal cancer management therefore requires a system that effectively integrates all these dimensions, ensuring that each patient receives treatment tailored to his or her specific needs.

In particular, new therapies, such as immune checkpoint inhibitors and molecularly targeted drugs, have revolutionised cancer treatment[3,4,5]. However, their high cost is placing increasing pressure on healthcare systems. In addition, the need for long-term care for long-term survivors, who often have to deal with late side effects and relapses, further contributes to rising expenses.

In a global healthcare context where sustainability is under great pressure, the transition to digitalisation could be a revolutionary pillar in the field of oncology. The pandemic has accelerated the integration of digital technologies in oncology, leading to an increased use of telemedicine, remote monitoring and digital tools to ensure high quality care also outside hospital facilities.

Although digital care has been seen as a potential solution to make healthcare more sustainable, its concrete implementation has encountered significant practical obstacles.

Continuous Monitoring and the Role of Digital Technologies in Oncology

In recent years, quality of life has emerged as a crucial endpoint in clinical trials in oncology, alongside the traditional goals of survival and tumour response[6].
The increasing focus on the overall patient experience, beyond the mere efficacy of treatments, reflects an increased recognition of the importance of ensuring not only more years of life but also better quality of life.

This new perspective not only facilitates a better understanding of the impact of treatments on patients' daily lives but also encourages the development of more personalised treatment strategies that take into account individual needs and preferences.

The use of paper questionnaires makes it possible to more accurately capture the symptoms reported by patients, facilitating systematic discussions and providing the basis for optimised symptom management. However, while paper questionnaires improve the quality of traditional visits, they do not accelerate the process of symptom management and reporting. In contrast, integrating traditional visits with remote monitoring via electronic tools - such as apps, tablets, or computers - enables near real-time detection of symptoms, facilitating timely intervention compared to standard hospital visit intervals.

Clinical studies published in reputable journals have shown that this approach can significantly improve patients' quality of life by enabling faster management of toxicities and potentially preventing serious complications. Digital questionnaires filled out directly by patients provide a more accurate representation of toxicities than data collected by physicians, allowing for the timely management of issue[7,8].

Despite these advantages, until recently, no official guidelines had been formulated by the major international scientific societies on this subject.
In 2022, ESMO published the first guidelines for integrating patient-reported outcomes (PROMs) into oncology clinical practice, based on scientific evidence and international expert opinions from Europe, North America, Asia, and Australia[9].

Thanks to technological advances, applications on smartphones and computers now allow patients to communicate their conditions between visits, improving quality of life and reducing the risk of serious complications. This approach has been shown to decrease emergency room admissions and hospitalisations, while enhancing the effectiveness of treatments for several types of solid tumours.
The implementation of Patient-Reported Outcomes (PROMs) extends far beyond the use of apps or software for sharing information; it represents a profound transformation in healthcare organisation. Ideally, the information provided by patients should be incorporated into the electronic medical record, just like laboratory data, making PROMs an indispensable part of daily clinical practice. However, this requires the reorganisation of processes to ensure proper handling of reports by healthcare professionals.

In Italy, the adoption of digital therapies is still at an early stage, although efforts have been made towards implementation. In June 2023, a bill was proposed in Italy that clearly defines DTx therapies and their characteristics. This legislation aims to simplify the process of including DTxs in the essential levels of care (LEA) of the National Health Service (SSN), thereby allowing reimbursement for these therapies. For a DTx to be considered for reimbursement, it must be supported by at least two high-quality clinical trials demonstrating its efficacy[10].

The use of digital technology in oncology management allows continuous, accurate, and non-invasive monitoring of patients, offering a patient-centred and data-driven model of care. Observed benefits include significantly improved survival rates, reduced hospitalisation, and enhanced quality of life for patients.

Support, Education, and Monitoring in Oncological Pathologies

A crucial element in cancer management is ongoing patient and caregiver education. Greater awareness of one's condition and available treatments can significantly improve adherence to treatment, symptom management, and ultimately clinical outcomes.

Educating cancer patients about potential side effects, warning signs, and the importance of early communication with their healthcare team is essential for preventing complications and improving quality of life[11].

Additionally, psychological support plays a vital role in cancer treatment. Coping with a cancer diagnosis can be extremely stressful, and emotional support can help patients manage anxiety, depression, and other psychological difficulties associated with the disease. Support programmes, self-help groups, and psychological counselling can significantly improve patients' overall well-being and ability to cope with their illness[12].

Challenges and Opportunities for the Future

Despite the numerous benefits of digital technologies, many significant challenges remain. These include unequal access to these technologies, the need for adequate training for both patients and clinicians, and privacy and data security concerns. Addressing these issues is essential to ensure effective and widespread adoption.

However, the opportunities are enormous. As digital technologies continue to advance, oncology has the potential to become increasingly personalised, with treatments tailored to the specific needs of each patient. The growing integration of digital technologies into healthcare systems can improve resource management and reduce costs, making cancer care more accessible and sustainable.
Overcoming these challenges and harnessing the opportunities presented by technological innovation will be critical for the future of oncology, with the goal of providing more effective, personalised, and sustainable treatments.

The adoption of Patient-Reported Outcome Measures (PROMs) to monitor the symptoms of cancer patients represents a major innovation in clinical management. These tools improve quality of life, increase adherence to treatment, and reduce hospital admissions. However, to achieve full implementation, not only appropriate digital tools are needed, but also an overhaul of clinical processes, staff training, and a significant commitment of resources.

The ESMO guidelines represent a crucial step towards promoting these technologies, but their success will depend on addressing the operational and cultural challenges present in clinical practice.

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6. DIGITAL HEALTH AND REAL WORLD EVIDENCE

By Barbara Meini, Azienda USL Toscana Sud Est

The added value of digital health, and more specifically digital therapeutics (DTx), is connectivity, interoperability and the collection of data in real time, continuously and in a structured (standardised) way, with the caveat that the actual availability of these data to the scientific community is limited if the level of security (cybersecurity) and protection of personal data is not guaranteed.

Software and DTx enable remote patient management, adherence monitoring, behavioural therapy administration, data collection and clinical feedback. This makes them useful in two specific areas, clinical research and prospective observational studies.

The development of DTx can be divided into: design, development, testing and monitoring.
Let's recall that DTx, which are currently considered medical devices as long as they are recognised to have a therapeutic effect, are authorised for sale under EU Regulation 745/2017 and are therefore subject to clinical investigation (testing phase).

The monitoring phase is characterised by the collection of real-world data (RWD) in clinical practice, which enables developers to improve DTx through systematic analysis (real-world evidence - RWE). However, this phase can also provide regulators, regions and health authorities with the elements to support decision making, e.g. for approval or maintenance of reimbursement, purchase and prescription. Both aspects are necessary to ensure the "survival" of DTx on the market, given the inherent risk of obsolescence due to the time lag between design and commercialisation, which is why many ideas generated in the various start-ups do not even reach the testing stage. It should also be considered that, from a regulatory point of view, it will be necessary to define how many software or DTx updates can be considered acceptable, beyond which the software or DTx will need to be re-submitted to a clinical compliance investigation.

It also seems clear that the availability of DTx on the market, and therefore in clinical practice, will become mandatory in order to ensure continuity of care, given that the target group of patients who can benefit from DTx are the chronically ill.

Moreover, if during the monitoring phase a possible loss of efficacy of DTx is observed in clinical practice, due to a kind of subjective "tolerance" to the behavioural therapy itself, the regulatory authorities could then authorise the marketing of DTx for a shorter period, after which a new clinical trial could be required.

If the scientific community and regulators agree that RWE are the method to maintain marketing and reimbursement, benchmarks should be established to assess efficacy and safety, but also to outline from a regulatory perspective the approval pathway for RWE or the possible exemption, and to identify accredited centres for each therapeutic area to reduce potential bias.

In the National Health Service, RWD will be necessary to define eligibility for reimbursement, thus ensuring fair access to those patients who can benefit most.

In addition, it cannot be ruled out in advance that other therapeutic effects worthy of clinical investigation may be observed during the use of a DTx in clinical practice, as well as possible off-label use, so the value of RWE is also evident in these areas.

7. DIGITAL HEALTH AND AI

By Francesca Ieva, Associate Professor of Statistics, Politecnico di Milano

The Life Science ecosystem is evolving, led by the digital innovation which is revolutionizing the healthcare landscape. Nowadays, digital instruments like sensors, health applications and real-world data are already being employed into the remote/home monitoring of patients. Together, Artificial Intelligence (AI) and the so called Digital Therapeutics (DTx) will gain a greater and greater importance in this revolution. Digital therapeutics are health software tools designed to prevent, treat, or alleviate a disease, disorder, condition, or injury by delivering interventions that have demonstrable positive therapeutic effects on individual health and produce real-world outcomes. DTx are often complex interventions as they include multiple components.

According to an audit carried out by Confindustria Dispositivi Medici[1] and Farmindustria, 93% of the health sector companies and 74% of healthcare structures' leaders think that **AI will revolutionize personalized medicine in the next 3-5 years. Digital therapies**, according to 77% of the companies and 55% of clinical structures, **will have a significant impact in the next 5 years.**

Personalized therapies, as well as the improvement of the relationship with clinicians are essential for patients. Both **medical doctors and general practitioners would be keen to prescribe DTx**, if they were really available and patients would have necessary expertise to manage them. In fact, DTx would allow for **a wider amount of relevant data to be routinely collected, supporting clinical research and therapeutic decisions.**

Modern DTx has gradually introduced artificial intelligence algorithms. Despite in theory digital medicine is based on software and hardware solutions which do not necessarily have to use AI techniques, reality says that the number of devices approved by FDA which are complemented by AI tools are exponentially increasing. The main fields which benefit from this are radiology and cardiology, mainly in diagnosis and follow up case.

Currently, artificial intelligence algorithms are primarily applied in high-throughput scenarios such as disease screening and prevention. However, to fully leverage artificial intelligence in the finely managed field of digital healthcare, we should focus on the development of models to properly analyze the information deriving from digital signals and information collected through DTx themselves. It is often the case that a misunderstanding occurs when talking about AI in medicine, confounding AI with digitalization of guidelines. On the opposite, what we should consider when talking about AI and DTx is the algorithms to be included in the DTx technology to exploit the potential of data collected through DTx. This is the **challenge of health analytics and AI technologies**, the extraction, elaboration and synthesis of information carried out by the data to enrich and inform decisions about treatment planning.

In fact, the combination of artificial intelligence and DTx can further enhance the effectiveness and efficiency of DTx. Multiple studies have shown that by utilizing artificial intelligence algorithms to analyze and mine extensive patient data, more personalized treatment plans can be formulated, leading to improved treatment outcomes[2].

Embedding the DTx in an AI framework may enable personalization of the treatment. To make this possible, there are some critical aspects to face: i) AI, by definition, need large amount of data to be trained and ii) exploiting the data coming from DTx in an AI setting means that we need a continuous access to DTx data, as well as to perform a data fusion among DTx data and routinely collected one.

In this perspective, **accessibility and privacy are two big issues**, (not always) addressed in different ways across different territories. Moreover, the accuracy and reliability of artificial intelligence algorithms need further validation and confirmation, and necessitates close integration with clinical research.

Nowadays, there are four main ways AI can be combined with or within DTx:

1. AI as software included in monitoring devices (ex: Medrythm)
2. AI as Machine Learning tools for automatic or self-diagnosis (ex: CognICA for the assessment of cognitive functions, CanvasDx for early diagnosis of autism spectrum disorders, RythmAnalytics, where artimia identification system is based on anomaly identification mechanisms, trained on millions of cases)
3. AI as virtual coach (ex: PivotBreath, for tobacco addiction, Insulia, for Type II Diabetes treatment support)
4. AI as virtual reality tools (ex: Relie Vrx, for chronic pain reduction, Endeavor rx, for improving attention of children aged 8-12)

Aside the relevance of building suitable models for exploiting the information content of DTx data and the outlined role of AI with respect to DTx, AI may also serve for assessing DTx performances.

In fact, it is necessary to design **observational studies enabling the quantitative measure of benefits, impacts and sustainability of DTx** on patients' health, on GPs activity and clinicians practice. This may complement the information provided by health technology assessment (HTA) studies, which not always incorporate the DTx contribution.

To this aim, recent studies have proposed **State Sequence Analysis (SSA)** as a tool to describe different patterns of care in a personalized way[3]. This techniques envises the opportunity to create a sequence of states for each unit (e.g., patient) receiving a treatment, evaluating the quantity of the received treatment and comparing it with the guideline or reference level at each time step. Then, a very intuitive way to describe and summarize such sequence is provided, with the aim of a) comparing sequences, then patients, receiving different treatments, b) grouping similar pathways and c) relate pathways and outputs, so to assess which ones are likely to provide the best outcome. The application of such advanced modeling to dynamic data coming from DTx would be extremely useful to monitor the effectiveness of a given healthcare pathways, as well as to quantify associations among patterns and long-term outcomes.

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8. DEVELOPING DIGITAL THERAPEUTICS (DTx)

By Massimo Beccaria, AFI Study Group Coordinator - Digital Health

The aim of this chapter is to describe a process for building a digital therapy. The process leading to the construction of a digital therapy can be carried out in different ways, particularly depending on the country in which the digital therapy is being developed and the type of software that is being built. The assumption of this chapter is that a digital therapy will be built in the European area (thus using the MDR constraints), describing the main steps that this software-based technology must have.

In particular, we would also consider the broader definition of digital therapy as defined in ISO 11147, the description we quote:

"Health software that is intended to treat or alleviate a disease, disorder, condition or injury by generating and delivering a medical intervention that has a demonstrable positive therapeutic effect on a patient's health".

Following this definition, it must be understood that, in general, software is made up of several components (or modules) that have different purposes, and that therefore only some parts of the software are designed to "cure" (or improve the patient's health), while other parts are functional to achieve other purposes, such as engaging patients or managing their data and access.

In digital therapies, we will therefore have a so-called "therapeutic algorithm" (understood as a sequence of instructions or steps defining the operations to be performed to obtain the expected results), which will also be patentable, and which will ensure that the patient's state of health is improved by means of software. Then there will be accessory functions configured as "value-added services" integrated into the digital therapy platform (reminders or motivational messages, for example).

Formally, digital therapy software is recognised and reimbursed as a digital medical device in Europe, so the route to market must include CE marking as a software-based medical device. Medical devices are classified on a scale of 1 to 3 based on the risk to the patient, with class 1 being the least risky for the patient. In general, digital therapies are class 1 and 2, and since they have to deliver a therapy, they are born with solid scientific evidence from clinical studies of the device.

After this necessary premise, we will identify five steps that will allow us to build a digital therapy, from the identification of the project to the commercialisation of the technology.

Phase 1: The R&D pathway (and project identification)

In order to produce a digital therapy, it is necessary to follow a research and development path that, starting from a feasibility analysis to develop the specific business case, includes a series of technical phases (such as software development and instrument usability); a clinical validation phase to assess, document and confirm the product's validity; and a phase to monitor the impact of the technology after it has been placed on the market, through the collection of real-world information.

The first phase in the R&D of a digital therapy is usually preceded by a preliminary step, which could be called "zero phase", in which the project is identified, market demands and "unmet needs" are analysed and the requirements to meet them are outlined. Once this scope has been outlined, the partners involved are identified and a Board of Experts (BoE) is set up, comprising various experts, including: one or more Key Opinion Leaders (KOLs), physicians, patient associations, technical experts in medical devices, cybersecurity, software architects and device usability experts.

The pre-development phase of the DTx therefore involves close collaboration between the Boe, who provides feedback and clinical requirements to the key person who will manufacture and be responsible for the product, or the legal device manufacturer, who provides the technical, regulatory and quality strategy.

In general, it is possible to act for a third party, typically when a pharmaceutical company commissions the product or wishes to market it. In this case, a distribution contract is drawn up between the legal manufacturer and the pharmaceutical company, in which the relationship between the economic agent and the legal manufacturer is defined, depending on the business strategy of the economic agent. The elements identified then allow the detailed design and development phase of the software to proceed.

Phase 2: Software Design and Development

The development of a DTx follows well-defined models, both from IT literature (software lifecycle) and from project management (with "agile" project management, which involves an incremental and iterative approach).

Firstly, this activity involves the collection of user requirements and the definition of technical documents, in which the intended use of the medical device is made explicit. The technical documents contain the technological solutions and computer architectures that the researchers intend to develop for this purpose. This is a complex activity that also requires a risk analysis to identify any technological criticality and potential impact on patient health.

As with any other medical device, DTx manufacturers are required to manage the software lifecycle in accordance with ISO 13485 guidelines[1]. Functional and usability testing is performed during the development and design phases. In particular, usability testing refers to the evaluation of a product or service through a test involving representative users (such as individuals affected by the pathology for which the DTx is being developed).

This allows researchers to gather qualitative feedback on the most relevant aspects of the application. Other important phases are those related to security analysis, which are applied throughout the software lifecycle and fall under the specific regulatory requirements for cybersecurity. Vulnerability assessment and penetration testing are among the activities performed during these phases, in addition to the review and validation of the source code and libraries used in the development phase.

Phase 3: Regulation

Similarly, the regulatory compliance analysis is not a stand-alone phase but runs parallel to all the steps leading to the creation of a digital therapy. The reference regulation is Regulation (EU) 2017/745 (Medical Device Regulation - MDR)[2], which defines the safety and performance requirements that all medical devices placed on the European market must meet to ensure a high level of quality.

MDR also clarifies the responsibilities of stakeholders in the supply chain and reinforces control obligations, in particular with regard to the performance of the medical device throughout its lifecycle, including the management of communication with all stakeholders.

In order to guarantee this commitment, DTx companies use the harmonised and international standard ISO 13485, which defines the requirements for a specific quality management system for medical devices. It should be noted that this certification is not mandatory, but the application of the standard allows a "presumption of conformity" with the essential requirements of the MDR.
In addition to ISO 13485, the other international standard to follow is ISO 14971[3] on risk management, which is particularly important for software design, testing and updating activities. These two standards are essential for medical device.

Closely related to the two system standards, DTx developers also refer to the harmonised standard En ISO 62304[3], which lists the principles for managing the entire software lifecycle (as per essential requirement Art 17 MDR), enabling the correct technical validation of software and the correct handling of development problems. The reference standard for evaluating and testing the usability of the device in a simulated environment and with simulated patients is IEC 62366[5].

Then, to demonstrate clinical utility, the reference standard is ISO 14155[6] on good clinical trial practice for medical devices. Throughout the software lifecycle, it is also necessary to integrate the principles dictated by the General Data Protection Regulation (GDPR)[7], where applicable. A series of documents that provide a valuable tool to help stakeholders implement the MDR are the technical standards developed by the Medical Device Coordination Group (MDCG).

Phase 4: Clinical investigation

The clinical investigation of a DTx includes a first evaluation step with the preparation of a clinical evaluation plan (CEP) and a clinical investigation (CI), both of which are regulated by the MDR.

In the first step, the objectives of the CEP are:

- Confirm compliance with the relevant general safety requirements;
- Confirm the safety and performance of the medical device;
- Assess adverse effects;
- Assess the acceptability of the risk-benefit ratio.

The clinical investigation phase, taking into account the innovative nature of the DTx, which is classified as a Software as a Medical Device (SaMD), includes the preparation of the Clinical Investigation Plan (CIP) and all the documentation confirming the CEP in order to clinically demonstrate the intended use of the device.

The clinical investigation can begin once the ethics committee has given its favourable opinion and the Ministry of Health has validated it. It provides for:

- Activation of hospital centres;
- Patient enrolment;
- Clinical data collection and analysis.

All activities planned in the Cep for the purpose of clinical evaluation and CCI must be reflected in the Clinical Evaluation Report (CER) and in the Clinical Study Report (CSR), which will be submitted to the notified body for CE marking.

Phase 5: Post-marketing surveillance

The final step after the DTx has been placed on the market is post-market surveillance. This includes application maintenance of the systems and services involved, aimed at keeping electronic data collection and communication stable and secure. In the IT field, maintenance operations also include important aspects of computer threat prevention, bug-fixing activities and the application of security patches (updates that correct possible vulnerabilities in the system). As described at the beginning, these are the essential steps to create a digital therapy.

A practical suggestion is to anticipate the go-to-market strategy as much as possible, to have a clear idea of the business model to be adopted, and to carefully evaluate the benefits (not only economic) of launching this type of technology.

References:

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9. OPERATIONAL PROPOSAL

Given the lack of specific regulations for digital health technologies (DHTs), the Digital Health Policy Lab working group proposes an operational model aimed at supporting policy makers in managing the reimbursability of innovative health technologies at national level. This proposal is based on the most recent process dedicated to new technologies under development in Emilia-Romagna, region with a strong Medtech company concentration, following HTA rules.
Below are the main features of the proposed process.

WHAT - Technologies eligible for the HTA assessment

Eligible technologies for the process include patient-managed digital medical devices (pDMDs - see Chapter 3, Definitions) with a Technology Readiness Level (TRL) of 8 or higher. Each device must submit an HTA report to a dedicated evaluation committee, called Innovation Commission, containing all necessary information to verify its eligibility for inclusion in the process.
WHO - Assessor
The Innovation commission is dedicated to assessing innovative technologies. It is established by the relevant authorities (i.e. Ministry of Health, Agenas, Regions) and comprises a business-related component and a technical component. It includes representatives from specific sector, such as:

- delegates of Ministry of Health
- delegates of Agenas
- experts in HTA,
- pharmacists,
- nurses,
- patients
- medical doctors with specific competence for the considered pathology.

HOW - The HTA assessment process

The HTA assessment process can be organised in the following steps:

1. Process start: request from a SSN entity for assessment
2. Document submission: manufacturers wishing to participate in the process must submit an HTA report to the Innovation Commission.
3. Innovation committee assessment.

During the Innovation Commission meeting, both the proposing healthcare company and the partner company will be in attendance to present the data and documentation attached to the application.
The Innovation Committee has the key role of determining whether a technology is eligible for reimbursement. While all pDMDs are eligible for the process, the Commission assesses which devices can actually be reimbursed, and at what price, based on criteria such as:

- The existence of clinical trials and their design
- The impact of the technology on patient health
- Care context (community or hospital)
- Therapeutic function (diagnosis, monitoring, therapy, prevention, etc.)
- Presence of competitors and their prices

4. Final decision issuing: in positive case the technology will be approved at national level under a specific and dedicated budget
5. Reassessment every two years: during the second evaluation, the manufacturer may submit to the committee an updated dossier containing the results of trials conducted in the meantime or RWE data collected during the time the devices have been on the market.

Technologies that are deemed eligible for the HTA evaluation process are granted reimbursement and access to the healthcare facility that supported their entry into the process.

Table 1: overview of the key elements of the HTA evaluation process.

KEY ELEMENT OF THE HTA EVALUATION PROCESS	
Assessment Requirements	Technologies: pDMD
	TRL >8
Submission Documents	HTA report
Evaluation Commission	Innovation Commission
	It is established by the relevant authorities and comprises a business-related component and a technical component. It includes representatives from specific sector nominated by Ministry pf Health, Agenas, regions, comprensive of experts in HTA, pharmacists, nurses, patients, medical doctors with specific competence for the considered pathology
HTA Assessment Process	1. Process start: request for assessment from SSN entity or product manufacturer 2. Document submission 3. Innovation committee assessment 4. Final decision issuing: in positive case the technology will be approved at national level under a specific and dedicated budget 5. Reassessment every two years: the manufacturer may submit to the committee an updated dossier containing the results of trials conducted in the meantime or RWE data collected during the time the devices have been on the market.

10. BUDGET IMPACT ANALYSIS OF DTx IN ITALY

By Indicon Società benefit

This chapter presents a budget impact analysis (BIA) of digital therapies (DTx) in Italy, conducted with the goal of evaluating the economic sustainability of these technologies in the national context. The model considers 17 DTx listed in the medical device registry of the Ministry of Health and associated with 8 therapeutic areas, over a three-year horizon (2025-2028).

Model description

The model analyzes the expected impact of digital therapies in the Italian context for the 2025–2028 time horizon, the parameters used in the model, their descriptions, and the rationale used have been summarized in Table 1.

Table 1: Schematic representation of the model.

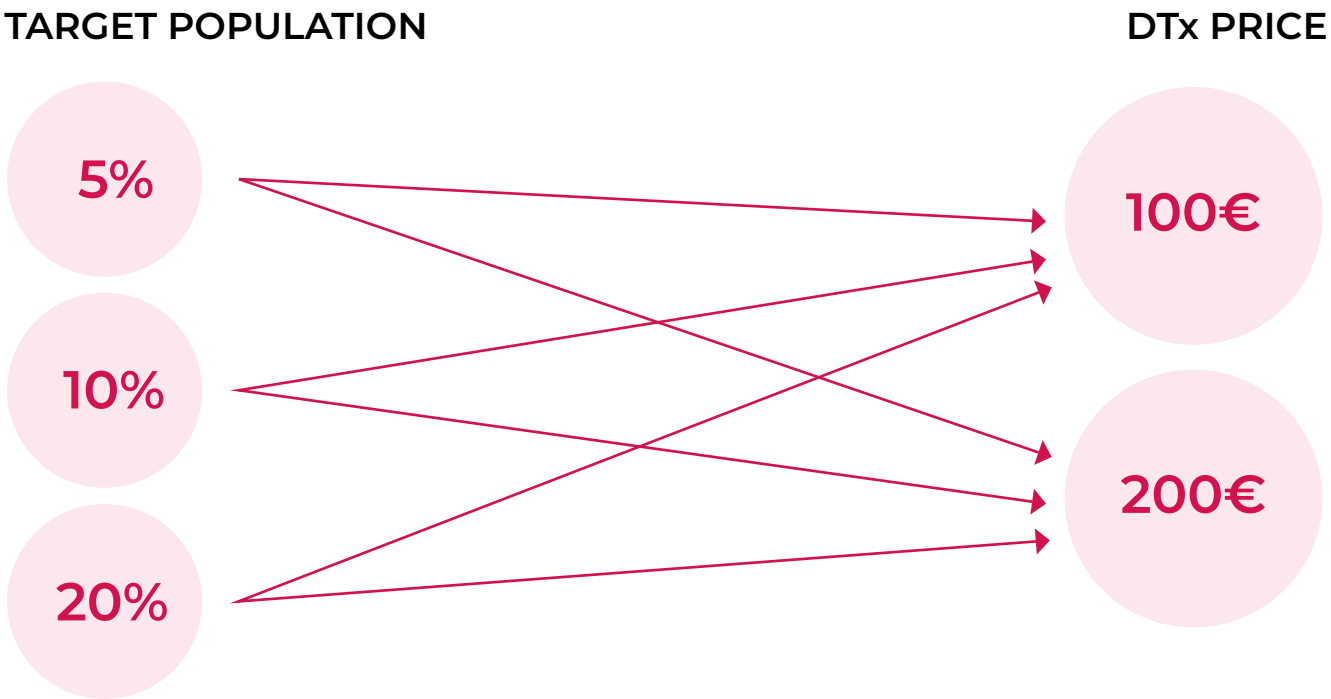
INPUT	DESCRIPTION	RATIONALE
DTx	Digital therapies (DTx) included in the model	Included in the analysis are devices with the following characteristics: - Devices listed in the "Medical Device Database" of the Ministry of Health - Classified with CDN codes (see chapter 5.3 - mapping of pDMD in Italy) - That meet the definition of DTx (patient-managed digital medical devices for therapeutic purposes, see chapter 3)
THERAPEUTIC AREA	Therapeutic area for which DTx usage is intended	Each DTx was considered for the therapeutic area for which it is intended.
POPULATION AFFECTED BY PATHOLOGY (ITALY)	Population of subjects affected by the pathology in Italy	Epidemiological estimates were conducted through literature analysis, preferably using Italian sources. Two methodological approaches were adopted based on the available sources: - Research on disease prevalence. The percentage value of prevalence was subsequently applied to the Italian population of the year 2023 (equal to 59,000,000 individuals according to ISTAT data). This represented the population of affected individuals in Italy. - Literature review regarding the population affected by the disease in Italy (in case prevalence data is not available).

INPUT	DESCRIPTION	RATIONALE
TARGET POPULATION	Population of subjects who can benefit from DTx for specific clinical condition	Two scenarios were considered based on the following estimates: 1. Target population= 5% of the population affected by pathology 2. Target population= 10% of the population affected by pathology 3. Target population=20% of the population affected by pathology
ADOPTION RATE	Percentage of target population that adopts the use of DTx per therapeutic area	An incremental treatment rate has been estimated for the years considered: 1. FIRST YEAR (Y1): 5% of the target population 2. SECOND YEAR (Y2): 10% of the target population 3. THIRD YEAR (Y3): 15% of the target population
PRICE	Cost per considered DTx	Based on the value of DiGA (digital health technologies) currently reimbursed on the permanent list in Germany, two potential scenarios were considered: 1. COST PER TECHNOLOGY EQUAL TO €100 2. COST PER TECHNOLOGY EQUAL TO €200

A sensitivity analysis was conducted using the following variables:
a) Target population
b) Price of DTx

The analysis allowed for a deeper understanding of six different scenarios represented in the following diagram (Figure 1):

Figure 1: Graphic representation of scenarios analyzed in the Budget Impact



The objective is to study various scenarios and evaluate the most reliable one.

Input data of the model

DTx included in the model and related therapeutic areas

The analysis considered digital medical devices managed by the patient (pDMD) for therapeutic purposes (DTx) identified through the analysis of the medical device database of the Ministry of Health (refer to chapter 5.3 – mapping of pDMD). Overall, the model included 16 technologies associated with 9 therapeutic areas, which are represented below along with their respective therapeutic areas (Table 2).

Table 2: Schematic representation of digital therapies (DTx) included in the model and their therapeutic intervention areas.

N.	DTx Considered	Therapeutic area
1	Allimb	Motor rehabilitation
2	Balbus	Speech disordered (stuttering)
3	Deprexis	Depression
4	Euleria Home	Motor rehabilitation
		Mild cognitive impairment
		Cardiac pathologies
5	Iamhero	ADHD
6	Kalanit Rehab	Motor rehabilitation
7	Medicrehapp	Cardiac pathologies
		Chronic respiratory diseases
8	Mindahead	Mild cognitive impairment
9	My Dose Coach	Type 2 diabetes
10	Number's Adventures	Dyscalculia
11	Parkinson Rehab	Parkinson's disease
12	Quicklypro-App	Motor rehabilitation
13	Relab/Bended	Multiple sclerosis
		Parkinson's disease
		Heart attack
14	Remo	Motor rehabilitation (for post-stroke patients)
15	Scrivo Bene	Dysorthografia
16	Turbo Lettura	Dyslexia
17	Volo Bla Bla	Speech disorder (phonological disorder)

Target population size and treatment rate

An analysis aimed at identifying the population of subjects in Italy affected by each of the considered therapeutic areas was conducted. Epidemiological estimates were conducted through literature analysis, preferably from Italian sources.

Two methodological approaches were adopted based on the available sources:

- Searching for disease prevalence. The percentage value of the prevalence was then applied to the Italian population of the year 2023 (59,000,000 individuals according to ISTAT data). In this way, the population of individuals affected by the pathology in Italy was represented.
- Literature search regarding the population affected by the pathology in Italy (in case prevalence data were not available).

Once the number of subjects affected by pathology in Italy was obtained, the target population was estimated, i.e., the population of subjects who could benefit from digital therapy. To conduct a representative analysis, the following scenarios were considered:

1. TARGET POPULATION = 5% of the population affected by pathology
2. TARGET POPULATION = 10% of the population affected by pathology
3. TARGET POPULATION = 20% of the population affected by pathology

Once the target population was defined, general assumptions about the treatment rate were made; the experience that is progressively being acquired on digital therapies has allowed for defining an incremental treatment rate in the 2025-2028 timeline.
The following estimates were then used:

A. ADOPTION RATE YEAR 1 (Y1): 5% of the target population
B. ADOPTION RATE YEAR 2 (Y2): 10% of the target population
C. ADOPTION RATE YEAR 3 (Y3): 15% of the target population

Table 3: Representation of the target population over three years (2025 – 2028) considering scenario no. 1 (target population = 5% of the affected population).

		45.580	91.161	136.741
Therapeutic area	**Population suffering from pathology (Italy)**	**Target population (5%)**	**Target y1**	**Target y2**	**Target y3**
ADHD	1.652.000	82.600	4.130	8.260	12.390
Mild cognitive impairment	836.443	41.822	2.091	4.182	6.273
Depression	2.240.340	112.017	5.601	11.202	16.803
Diabetes type 2	3.363.000	168.150	8.408	16.815	25.223
Discalculia	96.081	4.804	240	480	721
Dyslexia	187.693	9.385	469	938	1.408
Dysortography	101.744	5.087	254	509	763
Speech disorders	590.000	29.500	1.475	2.950	4.425
Stroke	90.000	4.500	225	450	675
Parkinson	112.100	5.605	280	561	841
Heart disease	3.658.000	182.900	9.145	18.290	27.435

Chronic respiratory diseases	688.766	34.438	1.722	3.444	5.166
Motor rehabilitation	4.425.000	221.250	11.063	22.125	33.188
Motor rehabilitation (for post stroke patients)	54.000	2.700	135	270	405
Multiple sclerosis	137.000	6.850	343	685	1.028

Table 4: Representation of the target population over three years (2025 – 2028) considering scenario no. 2 (target population = 10% of the affected population).

		91.161	**182.322**	**273.483**
Therapeutic area	**Target population (10%)**	**Target y1**	**Target y2**	**Target y3**
ADHD	165.200	8.260	16.520	24.780
Mild cognitive impairment	83.644	4.182	8.364	12.547
Depression	224.034	11.202	22.403	33.605
Type 2 diabetes	336.300	16.815	33.630	50.445
Dyscalculia	9.608	480	961	1.441
Dyslexia	18.769	938	1.877	2.815
Dysorthographia	10.174	509	1.017	1.526
Speech disorder	59.000	2.950	5.900	8.850
Stroke	9.000	450	900	1.350
Parkinson's disease	11.210	561	1.121	1.682
Heart Disease	365.800	18.290	36.580	54.870
Chronic respiratory conditions	68.877	3.444	6.888	10.331
Motor rehabilitation	5.400	270	540	810
Motor rehabilitation (for post- stroke patient)	442.500	22.125	44.250	66.375
Multiple sclerosis	13.700	685	1.370	2.055

Table 5: Representation of the target population over three years (2025 – 2028) considering scenario no. 3 (target population = 20% of the affected population).

			182.322	364.643	546.965
Therapeutic area	**Population suffering from pathology (italy)**	**Target population (20%)**	**Target y1**	**Target y2**	**Target y3**
ADHD	1.652.000	330.400	16.520	33.040	49.560
Mild cognitive impairment	836.443	167.289	8.364	16.729	25.093
Depression	2.240.340	448.068	22.403	44.807	67.210
Diabetes type 2	3.363.000	672.600	33.630	67.260	100.890
Discalculia	96.081	19.216	961	1.922	2.882
Dyslexia	187.693	37.539	1.877	3.754	5.631
Dysortography	101.744	20.349	1.017	2.035	3.052
Speech disorders	590.000	118.000	5.900	11.800	17.700
Stroke	90.000	18.000	900	1.800	2.700
Parkinson	112.100	22.420	1.121	2.242	3.363
Heart disease	3.658.000	731.600	36.580	73.160	109.740
Chronic respiratory diseases	688.766	137.753	6.888	13.775	20.663
Motor rehabilitation	54.000	10.800	540	1.080	1.620
Motor rehabilitation (for post stroke patients)	4.425.000	885.000	44.250	88.500	132.750
Multiple slerosis	137.000	27.400	1.370	2.740	4.110

Price of digital therapeutics (DTx)

The price of DTx was estimated based on the value of digital health technologies (DiGA) currently reimbursed on the permanent list in Germany (for details refer to chapter 4.2 – analysis of DiGA prices). Two potential scenarios were considered:

A. DTx price 100€

B. DTx price 200€

Sensitivity analysis

Subsequently, six possible scenarios derived from the combination of the considered variables were analyzed, thus defining four possible scenarios represented in figure 1.
The following tables report the cost estimates for the different scenarios.

Table 6: Cost estimation considering a target population of 5% of the affected population and a DTx price per technology of €100.

Target population 5% DTx price 100€	Year 1	Year 2	Year 3
Tot (€)	**4.558.042**	**9.116.084**	**13.674.125**
ADHD	413.000	826.000	1.239.000
Mild cognitive impairment	209.111	418.222	627.332
Depression	560.085	1.120.170	1.680.255
Diabetes type 2	840.750	1.681.500	2.522.250
Dyscalculia	24.020	48.041	72.061
Dyslexia	46.923	93.847	140.770
Dysortography	25.436	50.872	76.308
Speech disorders	147.500	295.000	442.500
Stroke	22.500	45.000	67.500
Parkinson	28.025	56.050	84.075
Heart disease	914.500	1.829.000	2.743.500
Chronic respiratory diseases	172.192	344.383	516.575
Motor rehabilitation	13.500	27.000	40.500
Motor rehabilitation (for post stroke patients)	1.106.250	2.212.500	3.318.750
Multiple slerosis	34.250	68.500	102.750

Table 7: Cost estimation considering a target population of 5% of the affected population and a cost per technology of €200.

Target population 5% DTx price 200€	Year 1	Year 2	Year 3
Tot (€)	**9.116.084**	**18.232.167**	**27.348.251**
ADHD	826.000	1.652.000	2.478.000
Mild cognitive impairment	418.222	836.443	1.254.665
Depression	1.120.170	2.240.340	3.360.510
Diabetes type 2	1.681.500	3.363.000	5.044.500
Dyscalculia	48.041	96.081	144.122
Dyslexia	93.847	187.693	281.540
Dysortography	50.872	101.744	152.616
Speech disorders	295.000	590.000	885.000
Stroke	45.000	90.000	135.000
Parkinson	56.050	112.100	168.150
Heart disease	1.829.000	3.658.000	5.487.000
Chronic respiratory diseases	344.383	688.766	1.033.149
Motor rehabilitation	27.000	54.000	81.000
Motor rehabilitation (for post stroke patients)	2.212.500	4.425.000	6.637.500
Multiple sclerosis	68.500	137.000	205.500

Table 8: Cost estimation considering a target population of 10% of the affected population and a cost per technology of €100.

Target population 10% DTx price 100€	Year 1	Year 2	Year 3
Tot (€)	**9.116.084**	**18.232.167**	**27.348.251**
ADHD	826.000	1.652.000	2.478.000
Mild cognitive impairment	418.222	836.443	1.254.665
Depression	1.120.170	2.240.340	3.360.510
Diabetes type 2	1.681.500	3.363.000	5.044.500
Dyscalculia	48.041	96.081	144.122
Dyslexia	93.847	187.693	281.540
Dysortography	50.872	101.744	152.616
Speech disorders	295.000	590.000	885.000
Stroke	45.000	90.000	135.000
Parkinson's disease	56.050	112.100	168.150
Heart disease	1.829.000	3.658.000	5.487.000
Chronic respiratory diseases	344.383	688.766	1.033.149
Motor rehabilitation	27.000	54.000	81.000
Motor rehabilitation (for post stroke patients)	2.212.500	4.425.000	6.637.500
Multiple sclerosis	68.500	137.000	205.500

Table 9: Cost estimation considering a target population of 10% of the affected population and a cost per technology of €200.

Target population 10% DTx price 200€	Year 1	Year 2	Year 3
Tot (€)	**18.232.167**	**36.464.334**	**54.696.481**
ADHD	1.652.000	3.304.000	4.956.000
Mild cognitive impairment	836.443	1.672.886	2.509.329
Depression	2.240.340	4.480.680	6.721.000
Diabetes type 2	3.363.000	6.726.000	10.089.000
Dyscalculia	96.081	192.162	288.243
Dyslexia	187.693	375.386	563.079
Dysortography	101.744	203.488	305.232
Speech disorders	590.000	1.180.000	1.770.000
Stroke	90.000	180.000	270.000
Parkinson's disease	112.100	224.200	336.300
Heart disease	3.658.000	7.316.000	10.974.000
Chronic respiratory diseases	688.766	1.377.532	2.066.298
Motor rehabilitation	54.000	108.000	162.000
Motor rehabilitation (for post stroke patients)	4.425.000	8.850.000	13.275.000
Multiple sclerosis	137.000	274.000	411.000

Table 10: Cost Estimate Considering a Target Population Equal to 20% of the Population Affected by the Disease and a Cost per Technology of €100

Target population 20% DTx price 100€	Year 1	Year 2	Year 3
Tot (€)	**18.232.167**	**36.464.334**	**54.696.481**
ADHD	1.652.000	3.304.000	4.956.000
Mild cognitive impairment	836.443	1.672.886	2.509.329
Depression	2.240.340	4.480.680	6.721.000
Diabetes type 2	3.363.000	6.726.000	10.089.000
Dyscalculia	96.081	192.162	288.243
Dyslexia	187.693	375.386	563.079
Dysortography	101.744	203.488	305.232
Speech disorders	590.000	1.180.000	1.770.000
Stroke	90.000	180.000	270.000
Parkinson's disease	112.100	224.200	336.300
Heart disease	3.658.000	7.316.000	10.974.000
Chronic respiratory diseases	688.766	1.377.532	2.066.298
Motor rehabilitation	54.000	108.000	162.000
Motor rehabilitation (for post stroke patients)	4.425.000	8.850.000	13.275.000
Multiple sclerosis	137.000	274.000	411.000

Table 11: Cost estimation considering a target population of 20% of the affected population and a cost per technology of €200.

Target population 20% DTx price 200€	Year 1	Year 2	Year 3
Tot (€)	**36.464.334**	**72.928.668**	**109.392.962**
ADHD	3.304.000	6.608.000	9.912.000
Mild cognitive impairment	1.672.886	3.345.772	5.018.658
Depression	4.480.680	8.961.360	13.442.000
Diabetes type 2	6.726.000	13.452.000	20.178.000
Dyscalculia	192.162	384.324	576.486
Dyslexia	375.386	750.772	1.126.158
Dysortography	203.488	406.976	610.464
Speech disorders	1.180.000	2.360.000	3.540.000
Stroke	180.000	360.000	540.000
Parkinson's disease	224.200	448.400	672.600
Heart disease	7.316.000	14.632.000	21.948.000
Chronic respiratory diseases	1.377.532	2.755.064	4.132.596
Motor rehabilitation	108.000	216.000	324.000
Motor rehabilitation (for post stroke patients)	8.850.000	17.700.000	26.550.000
Multiple sclerosis	274.000	548.000	822.000

CONCLUSIONS

The proposed model provides a forecast of the expenditure for digital therapies (DTx) charged to the National Health Service (SSN) for the period 2025 – 2028. The budget impact analysis considers several hypothesized scenarios using variables such as:

A. percentage of target population

B. price of DTx

The goal of the budget impact is to evaluate at what price the reimbursement for DTx would be sustainable and to estimate the size of a fund dedicated to these innovative technologies.
Below is a summary of the analyses conducted (table 7).

Table 12: Cost estimation considering a price for DTx of €100 and treatment rate as a variable.

Variable: % Target population DTx price: 100€	Year 1	Year 2	Year 3
5%	4.558.042	9.116.084	13.674.125
10%	9.116.084	18.232.167	27.348.251
20%	18.232.167	36.464.334	54.696.481

Table 13: Cost estimation considering a price for DTx of €100 and treatment rate as a variable.

Variable: % Target population DTx price: 200€	Year 1	Year 2	Year 3
5%	9.116.084	18.232.167	27.348.251
10%	18.232.167	36.464.334	54.696.481
20%	36.464.334	72.928.668	109.392.962

The most reliable scenario considers a target population value of 10% with a price per DTx of €200, which would result in a cost of €18.2 million in year 1, €36.4 million in year 2, and about €54 million in year 3 for the National Health Service.

11. CONCLUSION

The DTx Monitoring Report represents a crucial step toward integrating digital health technologies into the Italian National Health Service (SSN). The report provides a detailed overview of key developments and trends, outlining both the opportunities and challenges associated with digital therapeutics (DTx) and patient-managed digital medical devices (pDMD).

The analysis highlights the urgent need for a clear and consistent regulatory framework to facilitate the adoption and reimbursement of digital technologies, following virtuous examples like Germany and the United Kingdom. In Italy, interest in DTx is steadily growing, with an increasing number of innovative startups and companies developing technologies with high clinical potential.

The report also emphasizes the need to further promote research and scientific evidence to support the clinical efficacy and safety of digital therapeutics. The data collected demonstrates that DTx can significantly improve chronic disease management, reduce healthcare costs, and increase patient access to care. However, it is essential that policymakers and stakeholders work synergistically to implement appropriate policies that support the development of these technologies and facilitate their integration into traditional care pathways.

The operational proposals outlined in the report, particularly the accreditation model based on the experience of the Emilia-Romagna region, offer a concrete path for introducing and adopting DTx in the Italian healthcare context.

In conclusion, the digitization of healthcare and the growing use of digital therapeutics represent not only an opportunity to improve the quality of care but also a fundamental step toward a more sustainable, innovative, and patient-centered healthcare system. It will be crucial to keep a strong focus on the regulatory and operational development of these technologies to ensure their widespread and inclusive adoption, in line with the future healthcare needs of our country.