EXECUTIVE SUMMARY

Digital Health Technologies (DHTs) are digital tools and systems designed to support, enhance, or deliver healthcare services. DHTs certified as Medical Devices (MDs) and intended for patient use to monitor, diagnose, prevent, or treat medical conditions fall under the definition of patient-managed Digital Medical Devices (pDMD). Digital Therapeutics (DTx) represent the subset of DHTs specifically intended for treatment. In Europe, pDMD are regulated under the MD Regulation (MDR) and are defined as Software as a Medical Device (SaMDs), not integrated into a hardware MD, projected to be used by an ordinary user, either alone or with assistance of a healthcare professional.

Global clinical trials on DTx. Clinical trials on DTx increased by 54% in 15 months (n=1.888). Mobile applications are the predominant technology investigated (65.4%), followed by web applications (20.1%), virtual reality systems (6.7%), videogames (5.1%), and applications integrated with wearable devices/sensors (2.8%). Psychiatric disorders are the main therapeutic area (52% of trials), with insomnia, depression, and anxiety as the top three conditions addressed. Most clinical trials are conducted in North America (39.4%) and Europe (33.1%), with Germany leading among EU countries (7% of all trials and 20% of European ones). Italy accounts for only 3% of the total (*Submitted to Plos Digital Health*).

EU DTx mapping. **Germany** is the country with the most advanced regulatory framework for Digital Health in Europe. The specific law (DVG) allows clinicians to prescribe certified Digital Health Applications (DiGAs), with a reimbursement by statutory health insurance and a fast-track, evidence-based system. 57 DiGAs are reimbursed in Germany, with 46 on the permanent list and 11 on the temporary list (up to 12 months while gathering evidence). Compared with 2024, when 35 were permanent (+31.4%) and 20 temporary, DiGAs access has increased. Most reimbursed DiGAs target psychiatric disorders.

In the **UK**, Digital Health Technology (DHT) reimbursement depends on local NHS or specific service programs, as there is no specific national law. The Early Value Assessment (EVA), conducted by the National Institute for Health and Care Excellence (NICE) for digital products, provides recommendations to guide local adoption decisions. 27 DTx have been assessed through the EVA process, all targeting psychiatric disorders; 52% received positive recommendations for NHS use during evidence generation, 48% were for research-only use, and none were negatively recommended.

In **France**, the *Prise en Charge Anticipée Numérique* (PECAN) allows temporary reimbursement of DTx up to one year while further evidence is collected. Then, DTx with robust evidence can enter in the List of Products and Services Reimbursable (LPPR). 7 DTx result certified by the Agence du Numérique en Santé (ANS), but none are included in the LPPR.

In **Belgium**, the mHealthBelgium framework regulates digital health applications using a pyramid system: Level 1 (CE marking), Level 2 (reimbursement eligibility), Level 3 light (temporary reimbursement), and Level 3 plus (permanent reimbursement). No DTx are reimbursed; 2 are detected, both at Level 1.

In **Spain**, there is still no dedicated reimbursement pathway for Digital Health Solutions at national level. A preliminary bill for a new Law on Digital Health (*"Ley de Salud Digital"*) is under public consultation.

DiGAs price analysis. The average price of a DiGA is €250.25 (€119.00-618.00) on the permanent and €513.20 (€116.97-2,077.00) on the temporary list. For DiGAs moving from the temporary to the permanent list: 88% had a price reduction, with an average decrease of 48.6% (vs 2024: 91%; average reduction: 47%); 7% had an unchanged price (vs 2024: 3%); and 5% had a price increase (vs 2024: 6%). From 2021 to 2025, DiGAs price reductions when moving from the temporary to permanent list have decreased, peaking at -49% in 2022 and reaching -41% in 2025.

ITA pDMD mapping. 15% of SaMDs commercialised in Italy are pDMDs: 45% with a medical purpose of monitoring (vs 47% in 2024), 41% for therapy (vs 38%), 8% for prevention (vs 9%), and 6% for diagnosis (vs 7%).

ITA DTx mapping. 26 certified DTx are currently commercialized, 11 of which obtained CE marking in 2025. Most are Class I devices (88%), developed by 15 companies, with One Health Vision leading with 10 products (38% of the total).

Budget impact analysis of DTx in Italy. The estimated annual cost of DTx in Italy is approximately €62 million. Musculoskeletal (€15.26 million) and metabolic disorders (€15.51 million) are the areas with the highest potential expenditure.

Italian draft law for DTx and Digital Health Policy Lab proposals. In Italy, DTx are regulated under EU Medical Device Regulation, with a national legislative proposal currently progressing to define their integration into the NHS. A unified bill, combining three previous proposals, outlines definition, evaluation by an ad hoc expert committee, and inclusion in the Essential Levels of Assistance (LEA) based on clinical evidence. Some aspects, such as prescription, dispensing, and measures to ensure equitable access, need to be further defined, as suggested by the Digital Health Policy Lab.

DTx and Artificial Intelligence application in neurodevelopmental disorders. DTx offer personalized, accessible, and continuous support for neurodevelopmental disorders. DTx leverage AI, machine learning algorithms, and real-world data to adapt therapies and monitor progress but require robust clinical validation and standardized methodologies. Challenges include digital inequalities, privacy, ethical concerns, and maintaining the essential human-therapist relationship.

DTx application in mental health. DTx are transforming mental health care by providing accessible, scalable, personalised, and evidence-based interventions for conditions like depression, anxiety, insomnia, and substance use disorders. With around 20,000 mental health apps developed globally and several approved, the mental health sector leads in DTx research, demonstrating significant improvements in symptoms and quality of life. Ensuring privacy, data security, and digital literacy remains essential.

Pharmacological therapy and DHTs combination. The combined use of DHTs and pharmacological treatments improve effectiveness, adherence, personalization, and patient engagement through continuous monitoring, behavioural interventions, and tailored feedback, especially in chronic and mental health conditions. Proper prescription and regulatory alignment are essential to ensure their efficacy and safety.

Data analytics in healthcare: from unsupervised to federated learning. AI-based methods are generally classified into unsupervised and supervised learning: the first explores data structures to reveal patterns and reduce complexity, supporting health data analysis; the second enables classification and regression for prediction tasks. In all cases, data quality, privacy, and the use of federated learning or synthetic data are crucial to ensure reliable and ethical AI applications in healthcare.

Artificial Intelligence as a living component of medical device evolution. Artificial Intelligence (AI) ability to analyse complex clinical data has become a key feature of modern medical devices, especially in Software as a Medical Device (SaMD), which performs medical functions independently of hardware and can learn from real-world data, challenging traditional regulatory models. AI systems demand ethical and clinical accountability. The MDR-AI Act interplay defines Europe new regulatory frontier.

Artificial Intelligence applied to oncology. AI in oncology moves from predictive to foundation models that integrate multimodal clinical, imaging, and genomic data. Generative AI now collaborates with clinicians, supporting complex decision-making. Successful use depends on trust, explainability, and interactive systems. The future lies in continuously learning, agentic AI that enables adaptive, transparent, and patient-centered cancer care.

Economic evaluation of DTx. DTx improve health outcomes and are cost-effective across metabolic, cardiovascular, neurological, rehabilitative, and behavioural conditions. Most evidence comes from the US, Europe, and Asia, with no Italian evaluations identified. Cost-effectiveness is driven by improved adherence, reduced complications, and lower healthcare utilization, with ICERs generally below conventional thresholds.

*The Third Digital Health 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 (DHTs) in the Italian National Health Service.*

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