

Digital therapeutics: Emerging trends in clinical pharmacology

Shubham M. Shende, Ashwini G. Manjrekar, Praful S. Urade, Moni R. Dorlikar and Mahesh A. Hadke

Department of Pharmaceutics, Manvatkar College of Pharmacy, Ghodpeth (MS), India

ABSTRACT

Digital therapeutics (DTx) are software-based interventions intended to prevent, manage, or treat medical disorders and are distinguished from general digital-health tools by a therapeutic claim supported by clinical evidence. Their clinical value is increasingly being explored alongside pharmacotherapy, particularly for medication adherence, behavioral modification, symptom management, and adjunctive treatment. However, DTx should not be equated with mobile health (mHealth), telemedicine, wearable devices, remote patient monitoring, or Artificial Intelligence (AI); these technologies may support a DTx but are not synonymous with it. This narrative review summarizes the evolution, definitions, clinical evidence, regulatory landscape, and emerging applications of DTx with emphasis on clinical pharmacology. Literature was identified from PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, Google Scholar, and SpringerLink, with additional regulatory and product information obtained from official regulatory sources. Particular attention was given to randomized or controlled clinical studies, prescription DTx, medication-related outcomes, and regulatory terminology. Clinical evidence indicates that selected DTx can improve disease-specific outcomes, including abstinence and treatment retention in substance-use disorders, attention outcomes in pediatric attention-deficit/hyperactivity disorder, insomnia severity, depression symptoms as an adjunct to antidepressants, glycemic control, and migraine frequency. Nevertheless, evidence is heterogeneous, long-term effectiveness and engagement remain uncertain for several products, and DTx do not routinely provide pharmacokinetic monitoring or autonomous dose adjustment. Future clinical-pharmacology applications should therefore focus on evidence-based medication adherence support, pharmacogenomics-informed decision support, therapeutic drug monitoring, adverse-drug-reaction surveillance, and integration with interoperable clinical systems while maintaining appropriate human oversight, cybersecurity, and post-market evaluation.

KEYWORDS

Digital therapeutics; Clinical pharmacology; Medication adherence; Precision medicine; Pharmacogenomics; Therapeutic drug monitoring; Pharmacovigilance; Digital health

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Introduction

Rapid advances in AI, mobile computing, cloud infrastructure, connected devices, and health-data analytics are changing how healthcare is delivered and evaluated [1]. Within this broader digital-health ecosystem, DTx have emerged as software interventions designed to deliver a therapeutic intervention for a defined medical condition [2]. Their distinguishing feature is not the use of a smartphone, wearable sensor, AI model, or remote communication alone, but the combination of a therapeutic claim with evidence supporting the intended clinical use [3].

DTx are clinically relevant to pharmacology because many treatment failures are related not only to drug efficacy but also to adherence, inappropriate use, adverse effects, polypharmacy, drug-drug interactions, and variability in treatment response [4]. A DTx may complement pharmacotherapy by reinforcing adherence, delivering behavioral therapy, collecting patient-reported outcomes, supporting symptom monitoring, or facilitating clinician review [5]. These functions can improve the information available for treatment decisions, but they should not be interpreted as equivalent to pharmacokinetic measurement or validated dose individualization unless the specific product has been clinically and regulatorily evaluated for that purpose [6].

A critical distinction is required between DTx and other digital-health technologies. mHealth apps may support wellness, education, self-management, or communication without delivering a validated therapeutic intervention [7]. Telemedicine is a mode of healthcare delivery involving remote interaction with a healthcare professional [8]. Wearables and remote patient monitoring systems primarily collect and transmit physiological or behavioral data [9]. AI tools may perform prediction, classification, or decision support. Any of these

technologies can be incorporated into a DTx ecosystem, but none is intrinsically a DTx [10].

This review therefore focuses on DTx as therapeutic software and examines their clinical evidence and relevance to clinical pharmacology [11]. Particular attention is given to medication adherence, precision medicine, pharmacogenomics, TDM, Adverse Drug Reaction (ADR) surveillance, pharmacovigilance, regulatory status, implementation barriers, and future clinical applications (Figure 1) [12].

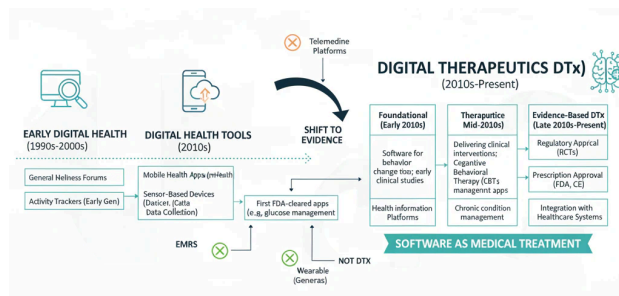


Figure 1. Evolution of DTx [11,12].

Literature Search and Review Methodology

A narrative literature review was undertaken to identify evidence relevant to DTx and their role in clinical pharmacology. PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, Google Scholar, and SpringerLink were searched for publications available from January 2010 through August 2026, with earlier seminal

*Correspondence: Mr. Shubham M. Shende, Department of Pharmaceutics, Manvatkar College of Pharmacy, Ghodpeth (MS), India, e-mail: sshende35@gmail.com

publications retained when necessary to describe the development of DTx. Search terms were combined using Boolean operators and included: (“digital therapeutics” OR “digital therapeutic” OR “prescription digital therapeutic” OR “software-based therapy”) AND (“clinical pharmacology” OR “medication adherence” OR “precision dosing” OR “pharmacogenomics” OR “therapeutic drug monitoring” OR “adverse drug reaction” OR “pharmacovigilance”) as well as disease-specific terms such as diabetes, insomnia, depression, substance-use disorder, ADHD, and migraine.

Priority was given to randomized controlled trials, controlled clinical studies, systematic reviews, regulatory documents, and peer-reviewed clinical evidence concerning named DTx products. Studies describing general mHealth, telemedicine, wearables, remote monitoring, or AI without a therapeutic DTx component were used only when needed to clarify conceptual boundaries. Product and regulatory claims were cross-checked against official FDA records where available. Publications without sufficient information to establish the intervention, population, comparator, or clinically relevant outcome were not used to support efficacy claims. Because this was a narrative review rather than a systematic review or meta-analysis, no formal risk-of-bias scoring or quantitative pooling was undertaken.

Definition and Scope of Digital Therapeutics

Digital Therapeutics Alliance describes DTx as evidence-based therapeutic interventions delivered through high-quality software programs to prevent, manage, or treat a medical disorder or disease [13]. In practice, a DTx is characterized by a defined therapeutic purpose, a software-delivered intervention, and clinical evidence appropriate to the intended use [14]. Regulatory classification varies by jurisdiction and by the product’s intended use and claims; therefore, not every DTx has the same regulatory pathway or prescription requirement [15].

DTx may use cognitive behavioral therapy, behavioral activation, structured education, adherence support, symptom-management programs, or other clinically defined interventions [16]. AI and machine learning may be used for personalization or adaptation, but they are not mandatory components [17]. Likewise, continuous monitoring is not a universal requirement. Some DTx are delivered as fixed-duration programs with scheduled exercises and patient-reported outcomes rather than continuous physiological sensing (Figure 2) [18].

Table 1. Distinguishing DTx from other digital-health technologies.

Technology	Primary function	Relationship to DTx	Typical example	Reference
DTx	Software-delivered therapeutic intervention for a defined disorder	Core intervention; requires evidence appropriate to intended therapeutic claims	Prescription CBT-I or behavioral therapy software	[19-21]
mHealth apps	Health, wellness, education, self-management, tracking	May support a DTx but most mHealth apps are not DTx	Medication reminder or fitness app	[22-24]
Telemedicine	Remote delivery of professional healthcare services	Delivery channel; not itself a DTx	Video consultation	[25-27]
Wearables	Measurement of physiological/behavioral parameters	May supply data to a DTx; not inherently therapeutic	Smartwatch, ECG patch	[28,29]
Remote patient monitoring	Collection/transmission of patient data for clinical review	May complement DTx; primary function is monitoring	Home BP or glucose monitoring	[30,31]
AI-based health tools	Prediction, classification, recommendation, or decision support	May be embedded in a DTx or operate independently	Clinical prediction or decision-support model	[32,33]

The boundaries are functional rather than technological. A smartphone application can be a DTx, an mHealth tool, or both only if

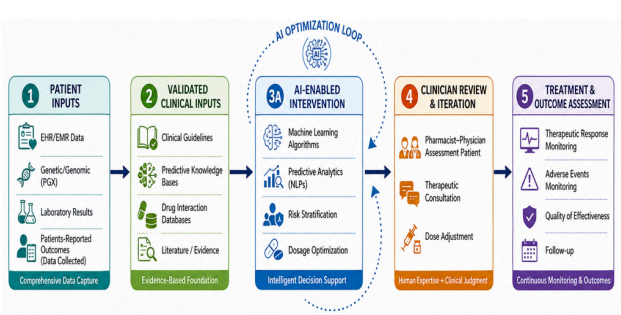


Figure 2. AI-enabled personalized care[17,18].

Distinguishing DTx from Other Digital-Health Technologies

Digital therapeutics (DTx) are a distinct category of digital-health interventions that deliver evidence-based therapeutic interventions through software to prevent, manage, or treat a medical disorder. Unlike digital-health technologies that primarily support healthcare delivery, information access, communication, monitoring, or administrative functions, DTx are intended to produce a measurable clinical or behavioral outcome and are generally supported by clinical evidence. The distinction among DTx, mobile health (mHealth), telemedicine, wearable technologies, and digital health applications is important because these terms are often used interchangeably despite differences in their intended purpose, clinical role, and evidentiary requirements (Table 1).

its intended claims and evidence meet the relevant therapeutic definition. Similarly, a DTx can use wearables, telemedicine, or AI

without those components becoming the defining feature of the DTx (Figure 3) [34].

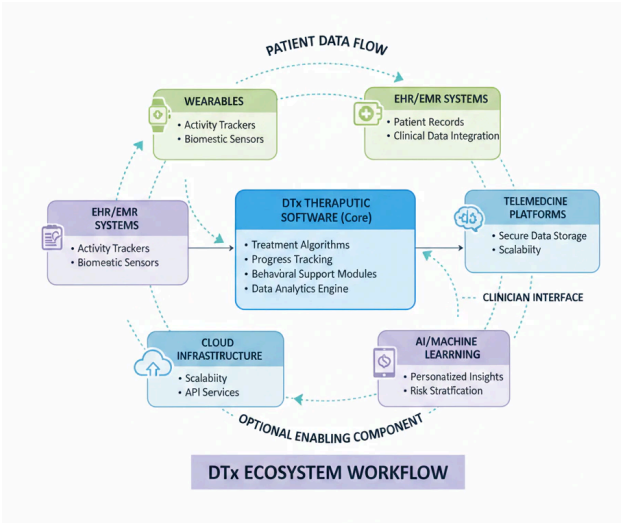


Figure 3. DTx ecosystem [34].

Evolution of Digital Therapeutics

The development of DTx occurred within the broader evolution of digital health. Early electronic medical records and computerized healthcare systems primarily digitized documentation and information exchange[35]. The subsequent expansion of smartphones enabled patient-facing applications for tracking, education, and communication [36]. Wearable sensors and connected devices later increased the availability of patient-generated physiological and behavioral data. The emergence of software-based therapeutic interventions and their clinical evaluation marked a more specific transition toward DTx [37].

Regulatory milestones also contributed to the field. In the United States, reSET received De Novo authorization in 2017 as a computerized behavioral therapy device, establishing a regulatory pathway for a new type of therapeutic software [38]. Subsequent products, including reSET-O, Somryst, EndeavorRx, BT-001/AspyreRx, Rejoyn, and CT-132, entered different FDA device pathways [39]. The COVID-19 pandemic accelerated digital healthcare adoption, but telemedicine and remote monitoring should not be presented as synonymous with DTx [40,41]. Current development increasingly explores adaptive software, digital biomarkers, interoperability, and data-driven personalization, although these capabilities vary considerably among products [42].

Table 2. Clinical evidence of digital therapeutics.

DTx/ prod uct	Indicati on	Study design/evidence	Key outcome	Clinical-pharmacology relevance	Ref ere nce
reSE T	Substan ce-use disorder	Randomized controlled evidence; adjunct to outpatient treatment	Higher abstinence and treatment retention than treatment as usual in a secondary analysis of 399 non-ODU participants (40.3% vs 17.6% abstinence; retention 76.2% vs 63.2%)	Behavioral support and treatment retention; not a replacement for pharmacotherapy	[47, 48] for
reSE T-O	Opioid- use disorder	24-week randomized trial published 2026	MOUD retention was 70.8% with app + usual care vs 51.9% with usual care; difference did not reach conventional statistical significance (P=0.053); study was underpowered	Potential medication evidence inconclusive	support for [49, 50] retention; remains

Components and Clinical Workflow of a DTx Ecosystem

A DTx ecosystem may contain a patient-facing software interface, therapeutic content, behavioral modules, clinician dashboards, data-integration services, and optional connected sensors. Electronic health record integration can improve continuity of care, while wearable or remote-monitoring data can provide additional information when clinically validated and necessary for the product. Cloud infrastructure may support secure storage and processing. These are enabling components rather than mandatory elements of every DTx [43].

A clinically appropriate workflow begins with identification of the therapeutic indication and patient eligibility. The software then delivers the specified intervention, records relevant outcomes, and may provide feedback or prompts. When the product is designed for clinician involvement, clinically meaningful information is reviewed and incorporated into care. Outcome assessment should use validated clinical endpoints appropriate to the indication. Importantly, software-generated recommendations should not automatically be described as autonomous prescribing or dose adjustment unless such functions have been specifically validated and authorized [44].

Clinical Evidence of Digital Therapeutics

The clinical evidence base is heterogeneous. Some DTx have randomized controlled evidence demonstrating improvement in disease-specific outcomes, whereas others have mainly feasibility, single-arm, or real-world studies. The magnitude and durability of benefit also vary, and engagement can substantially influence effectiveness [45]. Accordingly, DTx should be evaluated using the same critical principles applied to other clinical interventions: appropriate comparator, clinically meaningful endpoint, population representativeness, duration of follow-up, adverse-event assessment, adherence to the intervention, and generalizability[Table 2] [46].

The table illustrates why regulatory status and clinical efficacy should not be conflated. FDA device authorization or clearance establishes that a device met the applicable regulatory standard for its intended use; it does not imply that every possible clinical benefit has been established. Similarly, a statistically significant endpoint in one trial does not establish long-term cost savings, reduced hospitalization, or superiority over pharmacotherapy unless those outcomes were directly studied.

Table 2 (continued)

DTx/product	Indication	Study design/evidence	Key outcome	Clinical-pharmacology relevance	Reference
Somryst	Chronic insomnia	FDA-cleared prescription CBT-I; controlled and real-world evidence	Real-world study reported a 37.2% mean reduction in ISI score after 9 weeks; longer-term outcomes require continued evaluation	Adjunctive non-drug treatment; may reduce symptom burden without adding drug exposure	[51, 52]
EndeavorRx	Attention impairment in pediatric ADHD	Randomized controlled pivotal study; later FDA 510(k) expansion	Improved objective attention measures; clinical effects should be interpreted alongside standard ADHD treatment	Non-drug adjunct; does not replace medication when medication is clinically indicated	[53, 54]
BT-001/A spyre Rx	Type 2 diabetes	FDA De Novo; randomized pivotal/BRIGHT evidence	Evidence supports HbA1c improvement, while broader long-term effectiveness and generalizability remain under study	Behavioral adjunct to standard diabetes therapy; not a substitute for glucose-lowering drugs	[55, 56]
Rejoyn (CT-152)	MDD symptoms adjunctive to antidepressants	Phase 3 randomized, sham-controlled trial (n=386)	Reduced depression symptom severity versus sham; remission difference was not statistically significant	Directly complements pharmacotherapy; demonstrates an adjunctive model rather than drug replacement	[57, 58]
CT-132	Episodic migraine prevention	Phase 3 double-blind randomized controlled trial; FDA De Novo 2025	Treatment difference in monthly migraine days -0.90 days vs sham at 12 weeks; secondary outcomes also improved	Adjunctive behavioral therapy alongside pharmacotherapy	[59, 60]
NightWare	Nightmares associated with PTSD-related sleep disturbance	FDA De Novo device; clinical evidence remains more limited than for some established DTx	Designed to reduce sleep disruption by detecting and modifying smartwatch-based signals; further comparative evidence is needed	Illustrates sensor-enabled therapy; not a medication-management system	[61, 62]

Clinical Applications Across Therapeutic Areas

DTx have been investigated across mental health, substance-use disorders, metabolic disease, sleep disorders, neurological conditions, pain, and other chronic diseases. Their common clinical role is usually adjunctive: they provide a structured behavioral or cognitive intervention, reinforce self-management, collect patient-reported information, or support treatment engagement. In diabetes, for example, a DTx may deliver cognitive behavioral interventions and self-management support, while glucose monitoring and medication titration remain part of conventional clinical care unless a specific validated system has been authorized for more advanced functions [63].

In mental health, digital CBT and related interventions have demonstrated clinically relevant effects for selected conditions. Rejoyn provides an example of a prescription DTx specifically authorized as an adjunct to antidepressant therapy for adults with major depressive disorder symptoms. In insomnia, Somryst provides a structured digital CBT-I program. In substance-use disorders, reSET and reSET-O illustrate the potential role of software-based behavioral therapy alongside outpatient treatment and medication for opioid-use disorder. These examples support the view that DTx can complement pharmacotherapy rather than simply duplicate it [64].

In neurological and pain conditions, digital interventions may provide rehabilitation, behavioral treatment, symptom tracking, or disease-specific training. CT-132 represents a recent example in migraine prevention, where a phase 3 randomized trial showed a modest but statistically significant additional reduction in monthly migraine days compared with sham. The clinical significance of such effects should be interpreted in the context of baseline disease burden, concomitant medication, patient preference, adherence, and durability [65].

Role of Digital Therapeutics in Clinical Pharmacology

Medication adherence

Medication adherence is one of the most clinically plausible interfaces between DTx and pharmacotherapy. Software can provide reminders, structured education, behavioral reinforcement, self-reporting, and clinician-facing adherence information. However, a reminder function alone does not establish a DTx. The strongest evidence should demonstrate that the therapeutic software improves a clinically relevant adherence measure and, ideally, downstream outcomes such as disease control or treatment retention (Figure 4) [66].

Precision medicine and pharmacogenomics

DTx may provide a digital environment for integrating pharmacogenomic results, patient characteristics, laboratory values, comorbidities, and treatment response into clinical decision support. Such integration could help clinicians apply established pharmacogenomic guidelines when selecting or adjusting medicines. Nevertheless, AI-based prediction should not be described as a substitute for validated pharmacogenomic evidence. A DTx should use clinically validated gene-drug relationships and transparent decision rules where these are required, with appropriate clinician oversight [67].

Therapeutic drug monitoring and precision dosing

TDM is a promising but technically demanding area. A true TDM-enabled digital workflow requires reliable drug concentration measurements, appropriate pharmacokinetic interpretation, validated models, and a clinically governed dose-adjustment process. DTx can facilitate sample collection, adherence documentation, symptom tracking, laboratory integration, and clinician review, but most current DTx should not be described as performing autonomous TDM or



pharmacokinetic dose optimization. Future systems may combine pharmacokinetic models, laboratory data, and validated decision support to improve precision dosing [68].

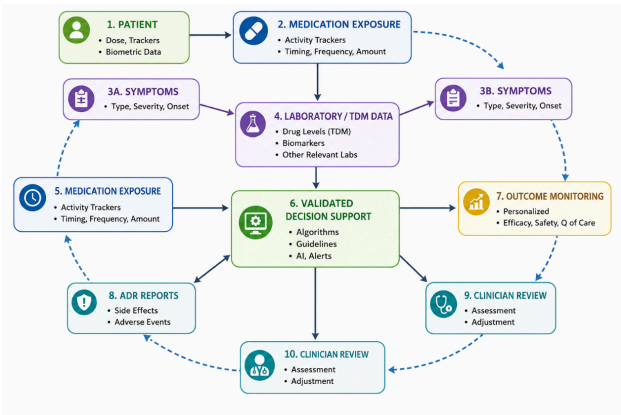


Figure 4. Clinical-pharmacology workflow [66-77].

Adverse drug reaction monitoring and pharmacovigilance

DTx and related digital platforms can facilitate systematic collection of patient-reported symptoms, medication exposure, and treatment outcomes. These data may support earlier identification of potential ADRs and signal generation for pharmacovigilance. However, an alert is not equivalent to a confirmed ADR. Clinical assessment, causality evaluation, and appropriate reporting procedures remain necessary. Integration with electronic health records and standardized terminology could improve the usefulness of longitudinal medication-safety data [69].

Medication safety and polypharmacy

Digital medication-management systems may help patients maintain accurate medication lists, identify potential duplication or interactions, and communicate changes to clinicians. Their clinical-pharmacology value is greatest when they are integrated with validated drug databases and medication reconciliation workflows. Claims of reduced ADRs, hospitalizations, or costs should be limited to outcomes demonstrated in appropriately designed studies [70].

Emerging Technologies Supporting DTx

AI and machine learning can support personalization, prediction, natural-language processing, and adaptive intervention design, but neither technology is required for a DTx. The clinical value of an AI component depends on training data, external validation, calibration, interpretability, monitoring for performance drift, and governance. Generative AI may assist with education or documentation, but generated content requires clinical oversight when used in patient care [71].

Table 4. Products and verified pathways.

Product	FDA verified	pathway/status	Prescription/clinical role	Reference
reSET	De Novo (DEN160018), 2017		Prescription digital therapeutic for substance-use disorder; adjunct to outpatient treatment	[76,77]
reSET-O	510(k) 2018	K173681, cleared	Prescription adjunct for opioid-use disorder treatment; used with standard of care	[78,79]
Somryst	510(k) 2020	K191716, cleared	Prescription digital CBT-I for adults with chronic insomnia	[80,81]

Wearables and digital biomarkers can provide additional information about activity, sleep, heart rhythm, glucose, or other physiological and behavioral variables. Their usefulness depends on measurement validity and the clinical question. Digital twins, virtual reality, chatbots, blockchain, and federated learning are emerging areas, but they should be presented as enabling or adjacent technologies rather than established components of all DTx. The evidence base is particularly heterogeneous for these newer approaches [72].

Regulatory Landscape

Regulatory terminology should reflect the actual pathway and jurisdiction. In the United States, therapeutic software may be regulated as a medical device and may enter the market through De

Novo classification or 510(k) clearance, among other pathways. It is therefore preferable to use terms such as “FDA-cleared,” “FDA-authorized,” or “FDA classified through De Novo,” according to the specific record, rather than the blanket term “FDA-approved.” The term “approval” is appropriate for certain FDA product categories but should not be used indiscriminately for device clearances (Figure 5) [73].

For example, reSET received FDA De Novo authorization in 2017; reSET-O was cleared through 510(k) in 2018; Somryst was cleared through 510(k) in 2020; EndeavorRx received De Novo classification in 2020 and a subsequent 510(k) expansion; BT-001 was classified through De Novo in 2023; Rejoyn was cleared through 510(k) in 2024; and CT-132 received De Novo classification in 2025. These pathways demonstrate that DTx do not have a single universal regulatory route [74].

The European Union uses a medical-device regulatory framework in which software may fall under the Medical Device Regulation (MDR) depending on its intended purpose and classification. “CE-marked” should be used only when a product has actually completed the applicable conformity-assessment process. Regulatory status should therefore be verified for the jurisdiction, product version, intended use, and date of publication. Post-market surveillance, cybersecurity, software lifecycle management, data protection, clinical evaluation, and quality management remain important considerations (Table 4) [75].

Table 4 (continued)

Product	FDA pathway/status verified	Prescription/clinical role	Reference
EndeavorRx	De Novo DEN200026; 510(k) K231337 for expanded indication	Prescription digital therapeutic for attention impairment in pediatric ADHD	[82,83]
BT-001 / AspyreRx	De Novo DEN220058, 2023	Prescription digital behavioral therapeutic for type 2 diabetes, adjunct to standard care	[84,85]
Rejoyn / CT-152	510(k) K231209, cleared 2024	Prescription adjunct for MDD symptoms in adults on antidepressant medication	[86,87]
CT-132	De Novo DEN240064, granted 2025	Prescription digital therapeutic for episodic migraine prevention	[88,89]
NightWare	De Novo DEN200033, 2020	Digital therapy device intended to reduce sleep disturbance associated with trauma-related nightmares	[90,91]

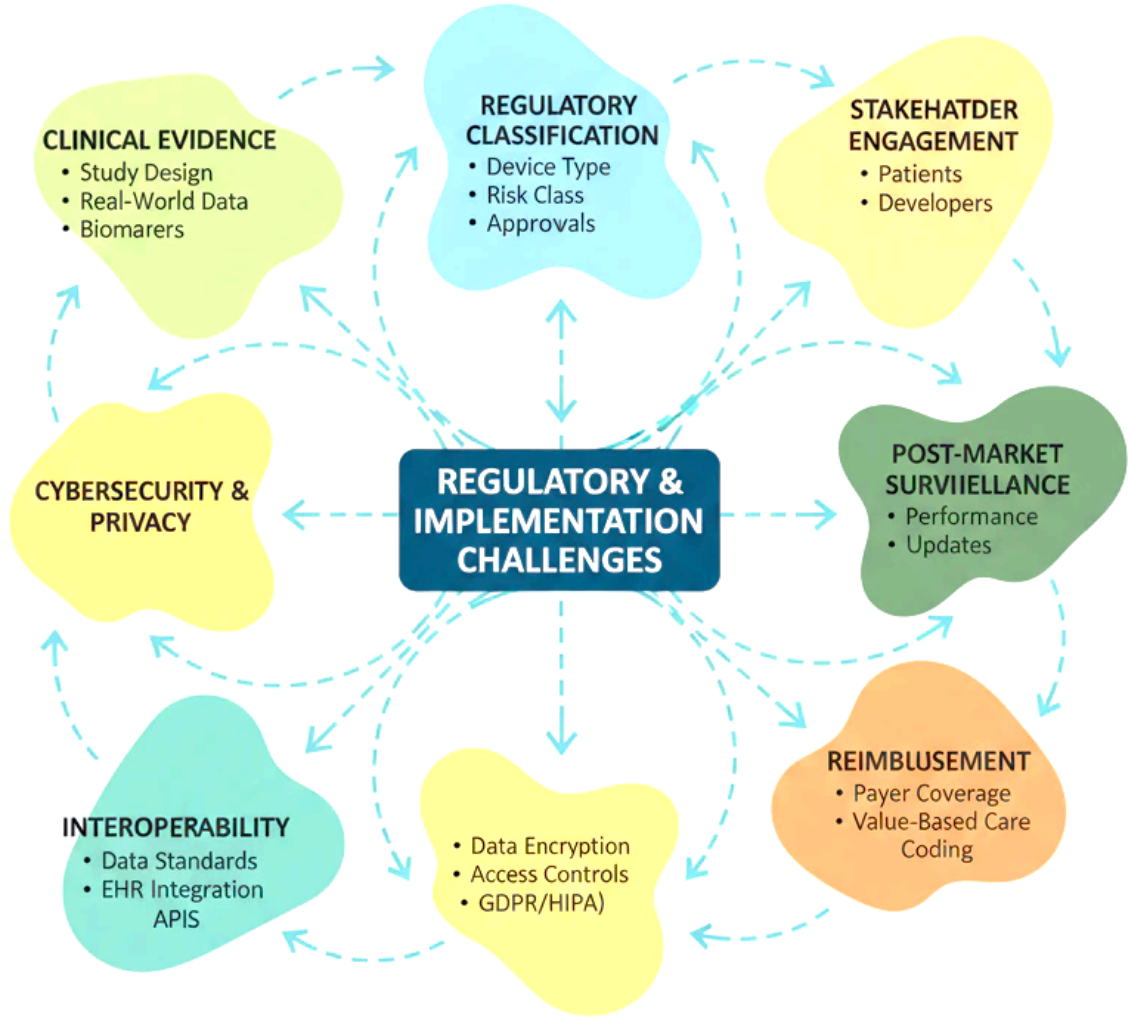


Figure 5. Regulatory and implementation challenges [73-75].

Advantages and Limitations

Potential advantages include scalability, structured delivery of evidence-based behavioral interventions, improved access, frequent

patient engagement, and the ability to capture patient-generated outcomes. In selected indications, DTx may complement pharmacotherapy and help clinicians understand symptoms and treatment experience between visits. However, these potential

benefits should not be generalized to all products or all health systems [92,93].

Important limitations include digital literacy, unequal access to smartphones and reliable connectivity, disability-related accessibility barriers, language and cultural barriers, variable patient engagement, alert fatigue, interoperability limitations, cybersecurity threats, privacy concerns, algorithmic bias, limited diversity in training and validation datasets, and uncertainty regarding long-term adherence. Reimbursement and workflow integration can also limit adoption. The evidence base may be affected by short follow-up, single-arm designs, self-selection of digitally engaged participants, and attrition. Long-term clinical and economic outcomes therefore require further study [94,95].

Future Perspectives

Future clinical-pharmacology applications should prioritize clinically validated integration rather than technology for its own sake. High-value directions include medication-adherence interventions linked to measurable clinical outcomes; pharmacogenomics-informed decision support; TDM workflows combining laboratory data with validated pharmacokinetic models; digital collection of ADR and medication-safety data; and interoperable integration with electronic health records. Adaptive algorithms may become more useful when their performance can be monitored and their clinical boundaries are clearly defined.

Research should also move toward pragmatic randomized trials, diverse real-world populations, longer follow-up, comparative effectiveness studies, and standardized reporting of engagement and adverse events. Economic evaluation should distinguish theoretical reductions in utilization from demonstrated reductions in hospitalization or cost. Clinician oversight, cybersecurity, equitable access, and post-market monitoring should remain central to implementation.

Conclusion

DTx are an emerging category of therapeutic software with growing clinical evidence across selected medical conditions. Their most immediate relevance to clinical pharmacology is as an adjunct to pharmacotherapy through medication-adherence support, behavioral intervention, symptom monitoring, and structured collection of patient-generated data. Selected products have demonstrated clinically relevant outcomes in randomized or controlled studies, but evidence strength and durability vary substantially. DTx should not be equated with mHealth, telemedicine, wearables, remote monitoring, or AI, and not all DTx use AI or continuous monitoring. Future progress will depend on rigorous clinical evaluation, accurate regulatory classification, interoperable systems, cybersecurity, equitable access, and careful integration with pharmacogenomics, TDM, ADR surveillance, and medication-safety workflows.

Data Availability Statement

The data that support the findings of this study are available within the article and its Supplementary Information. No new data were created or analyzed during the preparation of this review.

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AI Disclosure

The authors state that AI-assisted tools were utilized for language refinement, grammar correction, and improving readability of the manuscript. All scientific content, literature interpretation, critical analysis and final editorial decisions were performed by the authors who take full responsibility for the accuracy and integrity of the manuscript.

Conflict of Interest

The authors declared that there are no known competing financial interests.

Author Contributions

Shubham M. Shende: Conceptualization, Literature Survey, Data Curation, Writing-Original draft, Review & Editing, Visualization, Corresponding author.

Praful Urade: Reviewed literature, edited manuscript, and validation.

Ashwini G. Manjrekar: Literature collection, interpretation of data, manuscript review.

Moni R. Dorlikar: Data collection, reference management, manuscript editing, proofreading

Mahesh A. Hadke: Supervised study, critically revised the manuscript, and finally approved the version to be published.

Ethics Declaration

This article is a review of previously published literature and does not involve human participants, animals or personally identifiable information. Hence, ethical approval and informed consent were not required for this study.

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