Beyond the Pill: How Digital Therapeutics are Shaping the Future of Pharma

Ana Catarina Cardoso

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Abstract

Title: Beyond the Pill: The Paradigm of Digital Therapeutics in Pharma Industry

Author: Ana Catarina Barroso Cardoso

The pharmaceutical industry faces growing pressure to innovate beyond traditional drug development. Digital Therapeutics (DTx) have emerged as a transformative force, offering software-driven medical interventions that complement or replace pharmacological therapies. This thesis systematically reviewed 23 studies, selected from an initial pool of 186 articles identified using keywords such as "Digital Therapeutics", "Pharmaceutical Industry", and "Healthcare Innovation". The final selection included randomized controlled trials, systematic reviews, and meta-analyses, analyzed using the PICOS framework. This study aims to provide a comprehensive analysis of the challenges and opportunities surrounding DTx adoption.

The results demonstrate that DTx significantly improve patient outcomes. For chronic conditions like diabetes and cardiovascular diseases, DTx enhanced adherence, reduced hospital readmissions, and achieved cost savings. In mental health, DTx fostered engagement and reduced stigma through remote, patient-centered care. Blended care models, integrating DTx with traditional treatments, proved effective in optimizing therapeutic adherence and outcomes.

However, critical challenges remain. Regulatory fragmentation, the need for robust clinical validation, and fragmented reimbursement systems hinder adoption. Nevertheless, pharmaceutical companies are investing in DTx through technology partnerships, AI-driven platforms, and subscription-based models, addressing barriers and scaling solutions effectively.

This thesis underscores the transformative potential of DTx in reshaping healthcare delivery. By overcoming barriers, DTx can enhance accessibility, efficiency, and personalization, offering scalable solutions poised to revolutionize the pharmaceutical industry.

Keywords: Digital Therapeutics, Pharmaceutical Industry, Healthcare, Disruptive Innovation, Digital Health, Pharma Digital Transformation, Technology Acceptance

Resumo

Título: Além da Pílula: O Paradigma da Terapêutica Digital na Indústria Farmacêutica

Autor: Ana Catarina Barroso Cardoso

A indústria farmacêutica enfrenta uma crescente pressão para inovar além do desenvolvimento tradicional de medicamentos. As Terapêuticas Digitais emergiram como uma força transformadora, oferecendo intervenções médicas que podem complementar ou substituir terapias farmacológicas. Esta tese realizou uma revisão sistemática de 23 estudos, selecionados a partir de 186 artigos iniciais, através de palavras-chave como "Terapêuticas Digitais", "Indústria Farmacêutica" e "Inovação em Cuidados de Saúde". A seleção final incluiu ensaios clínicos randomizados, revisões sistemáticas e meta-análises, analisados utilizando o enquadramento PICOS. Este estudo visa fornecer uma análise abrangente dos desafios e oportunidades associados à adoção das DTx.

Os resultados demonstraram que as DTx, para doenças crónicas, como diabetes e doenças cardiovasculares, aumentaram a adesão ao tratamento e reduziram reinternamentos hospitalares e custos. Na saúde mental, promoveram o envolvimento dos pacientes e reduziram o estigma através de cuidados remotos e centrados no paciente. Os modelos de cuidados híbridos, que integram as DTx com tratamentos tradicionais, demonstraram eficácia na otimização da adesão terapêutica e dos resultados clínicos. Contudo, a fragmentação regulatória, a necessidade de validação clínica robusta e os sistemas de reembolso fragmentados dificultam a adoção. Ainda assim, as empresas farmacêuticas estão a investir nas DTx através de parcerias tecnológicas, plataformas impulsionadas por IA e modelos de subscrição, abordando barreiras e escalando soluções de forma eficaz.

Esta tese destaca o potencial transformador das DTx na redefinição da prestação de cuidados de saúde. Ao superar as barreiras, as DTx podem melhorar a acessibilidade, eficiência e personalização, oferecendo soluções escaláveis que prometem revolucionar a indústria farmacêutica.

Palavras-chave: Terapias Digitais, Indústria Farmacêutica, Cuidados de Saúde, Inovação Disruptiva, Saúde Digital, Transformação Digital na Indústria Farmacêutica, Aceitação da Tecnologia

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List of Abbreviations

Artificial Intelligence	AI
Attention Deficit Hyperactivity Disorder	ADHD
Behavioral Intention	BI
Cognitive Behavioral Therapy	CBT
Digital Therapeutics	DTx
Digital Therapeutics Alliance	DTA
European Federation of Pharmaceutical Industries and Associations	EFPIA
Food and Drug Administration	FDA
Machine Learning	ML
Patient Engagement	PE
Perceived Ease of Use	PEOU
Perceived Usefulness	PU
Population, Intervention, Comparison, Outcome, Study Design	PICOS
Preferred Reporting Items for Systematic reviews and Meta-Analyses	PRISMA
Randomized Controlled Trial	RCT
Research and Development	R&D
Systematic Literature Review	SLR
Technology Acceptance Model	TAM
Theory of Reasoned Action	TRA
Unified Theory of Acceptance and Use of Technology	UTAUT

1. Introduction

The pharmaceutical industry has traditionally focused its efforts on developing and commercializing medications. This process is costly, time-consuming, and there is a high-risk of failure with many products never finishing through the pipeline (Raijada et al., 2021; Sverdlov et al., 2018). Despite significant investments, research and development (R&D) productivity in the pharmaceutical sector has declined notably in recent years, prompting growing interest in innovative approaches to enhance healthcare delivery and treatment outcomes (Dang, Arora, & Rane, 2020). One such approach is Digital Therapeutics (DTx), which emerged from the technology sector and is now revolutionizing healthcare (Dang, Dang, & Rane, 2023).

According to the Digital Therapeutics Alliance (DTA), an international non-profit organization dedicated to advancing digital therapeutics in healthcare (https://www.dtxalliance.org), "digital therapeutics (DTx) are 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." These technologies, often delivered via mobile applications, telemedicine platforms, and other digital tools, can be used independently or alongside traditional therapies to improve patient outcomes (Rajendran, Kella, & Narayanasamy, 2024). By incorporating or being synergized with advanced technologies such as artificial intelligence (AI), genomics, robotics, and real-time monitoring, DTx have the potential to transform disease management, particularly for chronic conditions such as diabetes, hypertension, and mental health disorders (Rajendran, Kella, & Narayanasamy, 2024).

Furthermore, these innovations are said to perform better regarding common limitations of pharmaceutical drugs, such as poor medication adherence and insufficient efficacy, offering new pathways to improve patient care (Biskupiak, Ha, Rohaj, & Bulaj, 2024).

This study is particularly relevant as it explores how Digital Therapeutics are reshaping the pharmaceutical industry by driving innovation, improving treatment outcomes, and redefining patient engagement. By investigating the opportunities and challenges of integrating DTx into traditional pharmaceutical business models, this research contributes to academic literature and industry practice. It provides a deeper understanding of DTx's transformative potential and highlights the strategic adaptations required for successful adoption.

1.1. Problem Statement

While Digital Therapeutics offer great potential to improve healthcare, the pharmaceutical industry faces significant challenges in integrating these digital innovations into existing business models. This study seeks to address the following questions: How can Digital Therapeutics (DTx) be effectively utilized by the pharmaceutical industry? Are current business models compatible with this shift toward digital interventions? Should pharmaceutical companies adapt or change their strategies to incorporate DTx into their portfolios? Moreover, do these companies understand how to approach the rapidly evolving field of Digital Therapeutics, and what steps should they take to capitalize on its potential?

By focusing on how DTx are transforming the pharmaceutical industry and the strategic responses required for successful integration, this study aims to provide a comprehensive analysis of the challenges and opportunities surrounding DTx adoption.

1.2. Key Research Questions

To address the problem statement, this research focuses on the following key questions:

- Q1: How are Digital Therapeutics (DTx) reshaping the pharmaceutical industry, particularly in terms of driving innovation in product development, enhancing treatment efficacy, and redefining patient engagement?
- Q2: To what extent can DTx complement or even replace traditional pharmaceutical therapies in the treatment of various medical conditions?

These questions serve as the foundation for investigating the role of DTx as a disruptive force within the pharmaceutical sector, assessing both their potential and the barriers to their widespread adoption.

1.3. Structure

This dissertation is split into six sections. Following the Introduction, the Background chapter explores an overview of the pharmaceutical industry and the emerging field of Digital Therapeutics, discussing their technological advancements, challenges, and theoretical foundations, including disruptive innovation and technology acceptance models.

The Methodology chapter outlines the systematic literature review approach, explaining the data collection, selection process, and analysis methods used in the study. The Results chapter

presents the key findings, offering insights into the role of DTx in driving innovation and improving healthcare outcomes. In the Discussion, these findings are critically analyzed in the context of the research questions, focusing on challenges such as market adoption, stakeholder influence, and reimbursement dynamics. Finally, the Conclusion summarizes the main insights, highlights the study's contributions to the pharmaceutical industry and academia, acknowledges its limitations, and suggests directions for future research.

2. Background

2.1. Pharmaceutical Industry

In the context of economics and management, an industry is typically defined as a group of companies that produce similar products or services and compete within a given or common market. In general, it presents similar consumers, similar technologies, and resources. Understanding this definition is crucial to understand the competitive forces, business strategies, and innovation trends or patterns that characterize a specific economic sector (Porter, 1980).

The pharmaceutical industry, which is responsible for developing, producing, and marketing medicines and therapies that prevent, treat, and even cure diseases, clearly illustrates the characteristics of a very competitive and innovative sector. From large multinational corporations to small biotechnology startups, the pharmaceutical sector plays a vital role in advancing healthcare globally, driving not only medical innovation but also the economy (Grand View Research, n.d.).

In addition, the fact that the industry is labor and capital intensive in terms of research and development (R&D) makes it more relevant in relation to economic development and health care. The scope of the industry's effects can go beyond its economic contributions; it plays a role in the healthcare system on a global level, fighting illnesses, saving lives, and enhancing the lives of many people (Grand View Research, n.d.).

The pharmaceutical industry's structure resembles an iceberg, with large research-driven companies, often referred to as "Big Pharma," dominating the visible portion, while smaller generic manufacturers remain less prominent due to the patent system. This system grants

innovators temporary market exclusivity before allowing generics to enter the market at reduced costs (Bunnage, 2011; Taylor, 2015). Leading industry players include Johnson & Johnson, AbbVie, Novartis, Merck & Co., Roche, and Pfizer (Christel, 2024).

2.1.1. Europe's Pharmaceutical Industry

The European pharmaceutical industry is a critical player on the global stage, characterized by substantial contributions to both economic growth and healthcare advancement (EFPIA, 2024). According to Statista and the European Federation of Pharmaceutical Industries and Associations, the industry in Europe is marked by several key indicators that reflect its scale, innovation, and impact.

Revenue of Leading Pharmaceutical Markets

In 2022, the revenue generated from the European pharmaceutical market was impressive, with Germany at the forefront with a revenue of 52 billion euros, followed by France with almost 41 billion, and Italy with 35 billion (Statista, 2022).

These figures - presented in Annex A - showcase the robust economic impact of the industry across various European countries, driven by the development and commercialization of new medicines and a strong presence in the global market.

Investment in Research and Development (R&D)

A continuous and heavy investment in R&D is vital for maintaining the sector's competitiveness and ensuring the development of cutting-edge medical solutions (EFPIA, 2024). Based on the data in Annex A from EFPIA, Europe has had a constant growth in the funding of the pharmaceutical R&D across the analyzed times: 3.0% (period 2009-2013); up slightly to 3.7% (period 2014-2018); and standing at yet a lot more at 6.7% for (2019-2023).

Such regular increase in the Europe growth graphs shows the dedication of European countries around research and innovation, though the increase is low when compared to global competitors. Nevertheless, Europe is one of the leading players in the pharmaceutical business, thanks to its sophisticated infrastructure, human capital, and much focus on health care systems quality (EFPIA, 2024).

Employment and Economic Contribution

According to EFPIA, the pharmaceutical industry in Europe provides employment to nearly 900,000 people across various European countries, highlighting its role as a major source of specialized employment and underscoring its substantial economic and social impact. Germany led in employment numbers with 123,475 positions, followed closely by France with 95,867, and Italy with 68,600. The United Kingdom and Spain also reported substantial employment with 70,000 and 50,600 positions, respectively (see Annex A).

2.1.2. Current challenges of the Pharmaceutical Industry

The pharmaceutical business model has traditionally revolved around the development, manufacturing, and sale of patented medications. However, this model faces increasing disruption from multiple sources, particularly with the emergence of Digital Therapeutics (DTx). According to IQVIA (2021), the shift toward value-based healthcare is one of the primary drivers of this disruption. Governments, payers, and patients are demanding more cost-effective solutions, creating pressure on pharmaceutical companies to deliver therapies that go beyond traditional drug-based treatments.

Simultaneously, the growth of generic drug manufacturing and biosimilars has intensified competition, eroding profit margins for traditional pharmaceutical companies. Digital Therapeutics further amplify this threat by offering alternative solutions to drug-based therapies, particularly in areas such as mental health, diabetes, and cardiovascular diseases (Nature Digital Medicine, 2019). These developments force pharmaceutical companies to re-evaluate their reliance on blockbuster drugs and explore ways to integrate digital solutions into their portfolios.

Adding to these pressures, the regulatory landscape is evolving to accommodate Digital Therapeutics. Governments in regions such as Europe and the United States are establishing specific regulatory pathways for DTx, like Germany's DiGA model. While these frameworks create opportunities for innovation, they also present challenges. Pharmaceutical companies now need to navigate two sets of regulatory requirements: one for traditional drugs and another for digital therapies (European Medicines Agency, 2023).

Moreover, DTx stand out for being scalable, affordable, and highly personalized (Chung, 2019; Sverdlov et al., 2018; Yang et al., 2020). In a global healthcare environment under increasing

pressure to provide high-quality care at lower costs, DTx are emerging as a compelling alternative to traditional drugs. This growing competition highlights the urgent need for pharmaceutical companies to innovate and integrate digital solutions into their strategies (Ellis, 2016; Nature Digital Medicine, 2019).

2.1.3. Porter's 5 Forces Model

The Porter's 5 Forces model (Porter, 1980) is widely recognized as one of the most applied frameworks for analyzing the competitive dynamics within an industry. This model evaluates competition by analyzing five key forces: the threat of substitution, the threat of new entrants, the bargaining power of buyers, the bargaining power of suppliers, and the intensity of rivalry within the industry (Porter, 1980). In the pharmaceutical sector, these forces interact to create a highly competitive and rivalrous environment (Ellis, 2016).

One of the main drivers of this rivalry is the significant threat of substitution. Generic drugs, which replace branded medications after patent expiration, pose a substantial risk to research-focused pharmaceutical companies (Taylor, 2015). Furthermore, the emergence of digital therapeutics (DTx) intensifies this threat, as they present more affordable and potentially effective alternatives to traditional treatments (Chung, 2019; Sverdlov et al., 2018; Yang et al., 2020).

The threat of new entrants is another critical factor. Although the pharmaceutical industry typically has high entry barriers due to substantial costs associated with research, development, and regulatory approval, technological innovations and the rise of startups specializing in digital health solutions are partially lowering these barriers (Chung, 2019).

Buyer bargaining power also plays a pivotal role, particularly in markets dominated by public healthcare systems or large distributors with significant influence over drug pricing and adoption (Ellis, 2016; Taylor, 2015). On the other hand, supplier bargaining power can vary depending on the availability of critical raw materials and the control over essential patents related to drug production.

In summary, the interaction of these forces shapes the competitive landscape of the pharmaceutical industry, driving both innovation and strategies to mitigate substitution and rivalry risks.

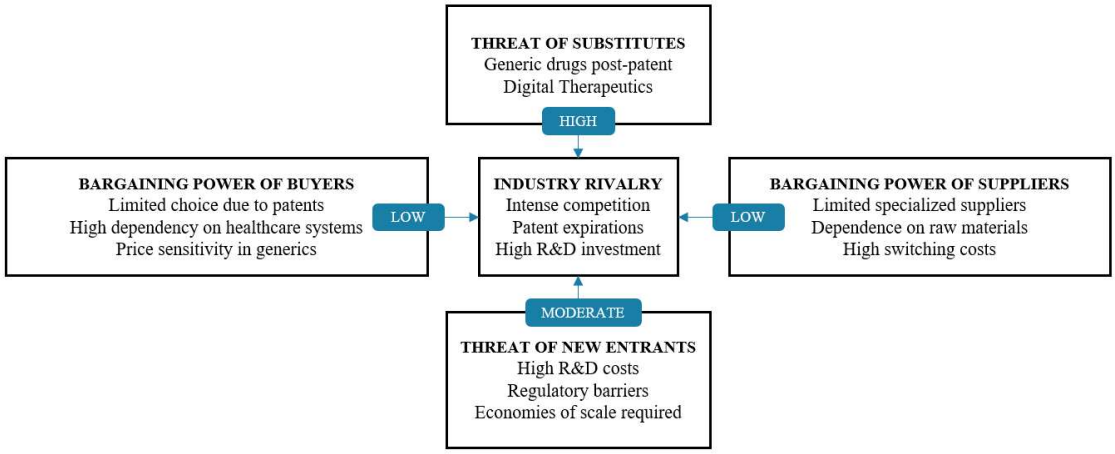

Figure 1 *– Porter's Five Forces Model Applied to the Pharmaceutical Industry (Porter, 1980; Taylor, 2015; Ellis, 2016; Chung, 2019; Sverdlov et al., 2018; Whiteside, 2022; Yang et al., 2020).*

2.2. Digital Therapeutics: A Disruptive Innovation

Innovation is a cornerstone of economic and business theory, driving growth, competitive advantage, and market transformation. Schumpeter (1934) defines innovation as the introduction of new or improved ideas, products, or services that transform industries, often through resource reallocation and technological advancements. In healthcare, innovation manifests in three primary forms: product innovation, such as the creation of new therapies; process innovation, which enhances manufacturing or delivery processes; and business model innovation, which reshapes how value is delivered to consumers (Porter, 1985; Chesbrough, 2003). These innovations are particularly relevant in the pharmaceutical sector, where research and development (R&D) is pivotal for addressing complex health challenges and improving patient outcomes (Grand View Research, n.d.).

Recently, Digital Therapeutics (DTx) have emerged as a transformative innovation, representing a disruptive force in healthcare (Christensen, 1997; Deloitte, 2023). DTx are evidence-based, software-driven medical interventions designed to treat, manage, or prevent diseases, offering a promising adjunct or alternative to conventional therapies. Delivered via digital platforms such as mobile applications and telemedicine, DTx bridge the gap between technology and clinical care, enabling personalized and real-time interventions (Rajendran, Kella, & Narayanasamy, 2024).

According to DTA, within the broader digital health landscape, there are three distinct categories of technologies, – Digital Health, Digital Medicine, and Digital Therapeutics - each representing a different level of intervention:

Digital Health: is an umbrella term referring to the use of digital technologies to improve health and well-being. This category includes a wide range of tools, from health-monitoring apps to wearable devices such as smartwatches and sensors that track physical conditions. While digital health technologies provide valuable support for health management and prevention, they are not specifically designed to deliver therapeutic interventions.

Digital Medicine: is a subset of digital health, focusing on technologies that integrate with traditional medical practices. It involves using connected devices, apps, and platforms to enhance existing medical care by improving patient monitoring, treatment personalization, and data collection. Digital medicine serves to augment traditional treatments and healthcare practices rather than replace them.

Digital Therapeutics: is the most specialized and innovative category. DTx are digital interventions that directly treat, manage, or prevent specific diseases. These therapies are evidence-based and undergo rigorous clinical trials to establish their efficacy and safety. They can be used either independently or alongside traditional medications to enhance patient outcomes. It is divided in three key subcategories based on their primary function:

- Treat a disease: Directly target specific medical conditions, such as diabetes, cardiovascular diseases, and mental health disorders. These interventions require clinical evidence to demonstrate therapeutic effectiveness and often need regulatory approval and prescriptions.
- Manage a disease: Focus on chronic disease management by improving treatment adherence, symptom monitoring, and ongoing care. Examples include hypertension management apps or respiratory condition monitoring tools.
- Improve a health function: Enhance health-related functions like cognition, motor skills, or emotional well-being. These therapies do not treat specific diseases but improve overall patient functionality, as seen in neuroplasticity and cognitive rehabilitation applications.

A visual representation of these categories is presented in Table 1 bellow.

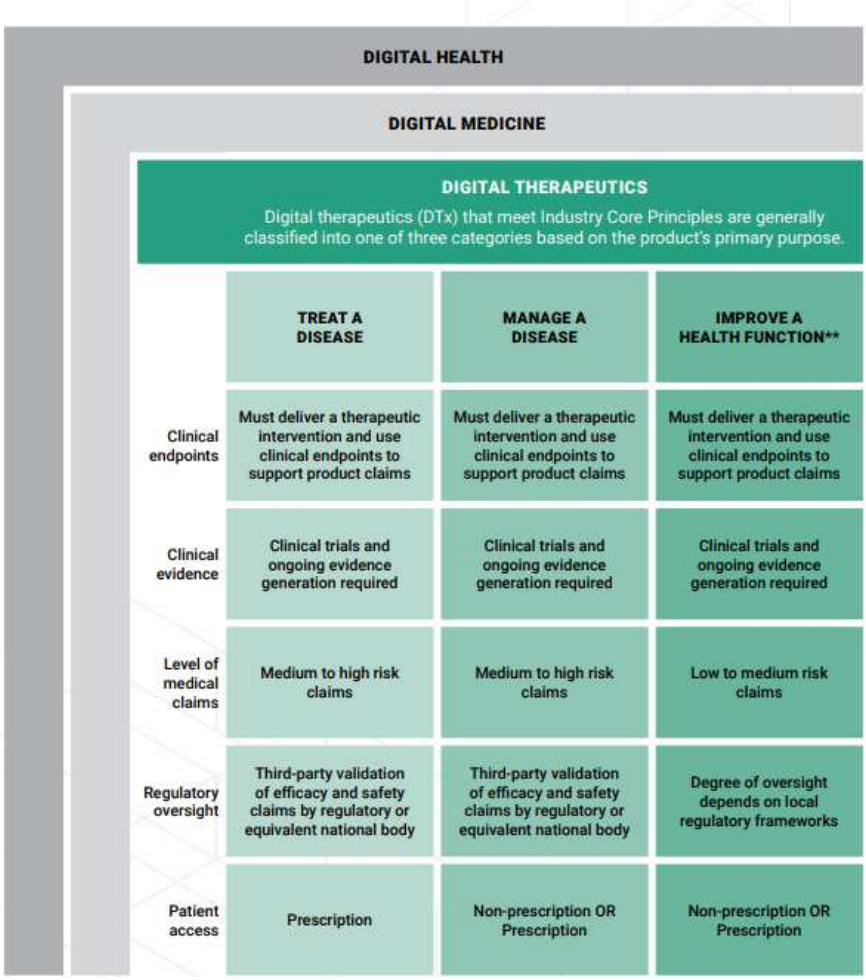

Table 1 *- DTx Product Categorization (DTA, 2024; available at https://dtxalliance.org/understanding-dtx/)*

To illustrate how the main pharmaceutical companies are integrating Digital Therapeutics (DTx) into their strategies, a table, available in Appendix A, presents concrete examples of partnerships, developed therapies, and their respective impacts. Companies such as Sanofi, Novartis, Pfizer, and Eli Lilly are collaborating with digital health startups and platforms to offer innovative solutions across various therapeutic areas, including mental health, dermatology, and oncology (FDA, 2017; Fierce Pharma, n.d.; Happify Health, n.d.; Sidekick Health, n.d.).

The emergence of DTx, alongside the development of artificial intelligence (AI) and machine learning (ML), is rapidly transforming the healthcare landscape. AI and ML are enhancing the personalization of treatments and improving patient engagement, both of which are essential for the success of digital therapeutics. These technologies enable more precise disease management, bridging the gap between traditional therapies and digital solutions (FDA, 2021).

By integrating innovative approaches, DTx disrupt traditional pharmaceutical business models, making healthcare delivery more personalized and efficient. This highlights the growing need to explore and understand the evolving relationship between digital and traditional therapeutic approaches, as DTx continue to reshape healthcare delivery (Deloitte, 2020).

2.2.1. Theoretical Frameworks: Adoption and Engagement

As Digital Therapeutics (DTx) gain prominence in the healthcare sector, understanding the factors influencing their adoption is critical for their success. Research aimed at explaining the acceptance and subsequent use of new technologies has become increasingly significant in recent decades, especially within the field of information systems (Rondan-Cataluña et al., 2015). Over the years, three primary theories and models of technology acceptance have been developed: the Theory of Reasoned Action (TRA), the Technology Acceptance Model (TAM), and the Unified Theory of Acceptance and Use of Technology (UTAUT) (Rondan-Cataluña et al., 2015).

Theory of Reasoned Action (TRA)

Introduced by Fishbein and Ajzen (1975), TRA explores individuals' conscious behaviors, proposing that specific actions are determined by behavioral intention (BI). BI is influenced by attitudes (A) and subjective norms (SN) related to the behavior (Fishbein & Ajzen, 1975). As a general model, TRA is not confined to specific behaviors or technologies, enabling its application across various fields of research.

Technology Acceptance Model (TAM)

Derived from TRA, TAM was developed by Davis (1986) to model the acceptance of information systems and identify the key determinants of technology acceptance. Two primary factors are highlighted in TAM: Perceived Usefulness (PU) and Perceived Ease of Use (PEOU). The model has been widely recognized as a robust framework for predicting user acceptance (Rondan-Cataluña et al., 2015).

In the context of DTx, TAM implies that healthcare professionals and patients must perceive tangible benefits, such as improved clinical outcomes and more efficient care processes. Moreover, the tools must be intuitive and easy to use. Positive perceptions of PU and PEOU

significantly enhance behavioral intention and actual adoption (Davis, 1986; Venkatesh & Davis, 2000).

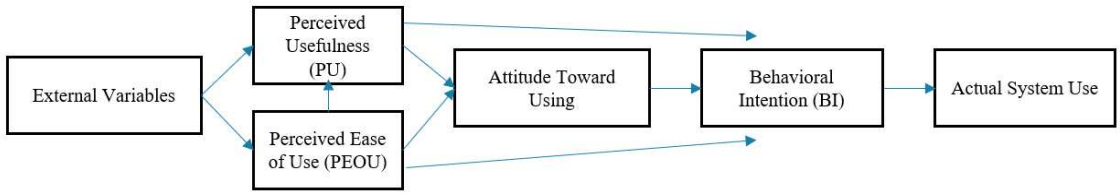

Figure 2 *- Technology Acceptance Model (Davis, 1986)*

TAM Extensions: TAM2 and TAM3

Venkatesh and Davis (2000) expanded the original TAM by introducing additional precursors to PU, such as social influence processes and cognitive instrumental processes, including job relevance. TAM3 (Venkatesh & Bala, 2008) further refined the model by focusing on factors influencing PEOU, such as computer self-efficacy and perceived enjoyment. These factors are particularly relevant in the context of user experience with digital technologies. For DTx, this evolution is crucial, as digital therapies need to seamlessly integrate into the daily routines of both patients and healthcare providers.

Unified Theory of Acceptance and Use of Technology (UTAUT)

Building on previous models, Venkatesh et al. (2003) synthesized key elements from TRA, TAM, and other popular models to develop UTAUT. This theory identifies four primary factors influencing technology acceptance: performance expectancy, effort expectancy, social influence, and facilitating conditions. UTAUT2, an evolution of the original model, incorporates hedonic motivation, price value, and habit as additional determinants of BI, making it particularly applicable to consumer technologies (Venkatesh et al., 2012).

In conclusion, these theories and models provide a robust theoretical foundation for analyzing how individuals, including patients and healthcare professionals, accept new technologies such as DTx. By integrating attitudes, social norms, perceived usefulness, perceived ease of use, and other behavioral and contextual factors, they offer valuable insights into the intentions and behaviors underlying technology adoption.

2.3. A Unified Perspective on Patient Engagement and Treatment Efficacy

Patient engagement is a central factor in determining the success and effectiveness of Digital Therapeutics. It extends beyond adherence to treatment protocols to include active, ongoing participation, where patients play a proactive role in their care through real-time feedback and personalized interventions. This continuous interaction not only fosters a sense of empowerment but also significantly enhances treatment efficacy, particularly in the management of chronic and long-term conditions.

Patient Engagement (PE) refers to the meaningful and collaborative involvement of patients in clinical decision-making, treatment monitoring, and health outcome evaluations. As noted by Auwal et al. (2023), engaged patients do not merely follow treatment plans; they help shape them. By sharing their preferences, experiences, and needs, patients ensure that treatments are better aligned to their realities. This collaboration bridges gaps in healthcare delivery, improves adherence, and drives measurable improvements in therapeutic outcomes.

For instance, in chronic disease management, DTx platforms that monitor glucose levels for diabetic patients provide tailored, real-time recommendations based on their lifestyle and behavior. Similarly, in mental health treatments, digital platforms delivering Cognitive Behavioral Therapy (CBT) offer adaptive interventions that adjust content and feedback in response to patient progress. These personalized tools empower patients, fostering a stronger sense of ownership and control over their health. This, in turn, promotes greater commitment to treatment plans and translates into tangible improvements in health outcomes (Auwal et al., 2023).

Furthermore, patient feedback plays a critical role in refining digital therapeutic interventions, creating a continuous cycle of improvement. DTx platforms can leverage real-time data to dynamically adjust therapies, ensuring they remain responsive to each patient's evolving needs. For example, in mental health care, real-time insights allow platforms to fine-tune therapy delivery, keeping the treatment relevant and engaging. This adaptability not only enhances clinical efficacy but also builds trust, satisfaction, and long-term engagement.

In summary, patient engagement serves as a foundational element in the success of Digital Therapeutics, transforming the patient experience into an interactive, personalized process. By actively involving patients in their own care, DTx optimize treatment efficacy, improve

adherence, and contribute to a more patient-centered healthcare model. This shift toward collaborative care highlights the transformative potential of DTx in creating effective, adaptive, and sustainable healthcare solutions.

2.4. Proposed Model: Relationship between Efficacy and Impact

An initial focus on studying the effectiveness of Digital Therapeutics (DTx) was driven by the need to establish a solid and reliable foundation for any subsequent analysis regarding the impact of these technologies on the pharmaceutical industry. The validation of effectiveness is a crucial step, as without evidence that DTx provide real clinical benefits, it would be premature to examine their potential clinical impact or the effects they could have on the market.

Once the effectiveness of DTx have been validated, it becomes possible to explore their potential to generate clinical impact by assessing how these digital therapies can complement or substitute conventional treatments, improve adherence, and enhance therapeutic outcomes. Patient interaction and engagement are key elements at this stage, as the success of these technologies hinges on their acceptance and continued use by patients.

Following clinical validation and patient engagement, the next step is to consider the acceptance of these innovations by the pharmaceutical industry. This aspect not only involves the adoption by healthcare professionals and patients, but also how DTx can integrate into the industry's portfolio, influence the development of new products and business models, and affect commercial strategies within the sector.

Finally, the proposed model to be used in this dissertation provides a comprehensive framework to understand not only the incremental benefits of DTx but also their role as a transformative force within the pharmaceutical industry, capable of driving long-term, systemic change. Figure 3 presents a simplified representation of the model.

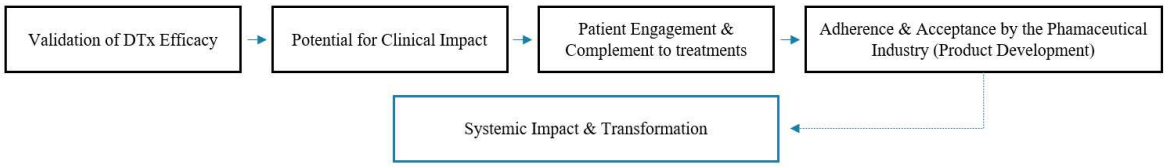

Figure 3 *– Proposed Model for Assessing the Impact of DTx. (own illustration)*

3. Methodology

3.1. Research Design

This master's thesis employs a Systematic Literature Review (SLR) as its primary methodological framework. The SLR was chosen for its ability to systematically consolidate and analyze existing evidence on the efficacy of Digital Therapeutics (DTx), specifically focusing on key areas such as patient engagement and product development, while also comparing these digital interventions with traditional pharmaceutical treatments.

3.2. Literature Search Strategy and Data Collection Process

The literature search was conducted between September and December 2024, employing PubMed, ProQuest, and Google Scholar as the primary databases. These databases were chosen for their accessibility and extensive coverage of peer-reviewed articles and studies, ensuring a comprehensive exploration of academic work related to the integration of Digital Therapeutics in the pharmaceutical industry.

In alignment with the PRISMA protocol (Preferred Reporting Items for Systematic reviews and Meta-Analyses), the search strategy was meticulously designed to ensure a structured and thorough identification of relevant studies, providing transparency throughout the entire process.

The first stage, Identification, involved searching databases using predefined selection criteria. This stage was guided by a combination of keywords that reflected the primary dimensions of the research focus, ensuring that the search was both comprehensive and targeted. The core keywords included "*Digital Therapeutics*", "*Pharmaceutical Industry*", "*Healthcare Innovation*", "*Digital Health*", "*Pharma Digital Transformation*", and "*Therapeutic Interventions*".

To refine the results and ensure relevance, keyword combinations such as "*Digital Therapeutics*" AND "*Pharmaceutical*", "*Digital Therapeutics*" AND "*Healthcare Innovation*", and "*Digital Therapeutics*" AND "*Pharma*" AND "*Patient Care*" were employed. Additionally, we filtered the search to focus specifically on peer-reviewed academic journals, review or systematic review articles, clinical trials, meta-analysis and randomized controlled trials (RCT). This strategy was designed to capture the most relevant literature while excluding studies that fell outside the scope of this review, focusing exclusively on articles written in English.

In the Selection phase, duplicate articles were removed, followed by a review of titles and abstracts to exclude irrelevant studies. This process yielded an initial set of 186 articles. After eliminating 144 irrelevant or duplicate articles, 42 articles remained, meeting the criteria for level 2 screening. These were subjected to a full-text review in the subsequent Eligibility phase, where each article was evaluated against the inclusion criteria to determine its relevance to the research questions, resulting in 23 full-text articles.

3.3. Data Analysis Methods

The final stage, Inclusion, involved the selection of the most relevant studies that met all predefined criteria. After a careful review of the full texts, the articles that did not align closely with the research objectives were excluded, resulting in a consolidated set of 23 articles. From these 23, 5 were randomized controlled trials (RCTs) and/or meta-analyses, offering high-quality empirical evidence on the clinical effects of digital therapeutics (DTx), while the remaining eighteen included narrative reviews, practical applications, and systematic reviews. This final selection ensures a balance between empirical data and broader theoretical insights, covering a comprehensive spectrum of research in digital therapeutics.

To ensure a consistent evaluation of the objectives, scope, and findings across the literature, data extraction and analysis were conducted using the PICOS framework (Population, Intervention, Comparison, Outcome, and Study Design). Relevant details, including study results, were systematically recorded and analyzed to maintain methodological rigor and coherence.

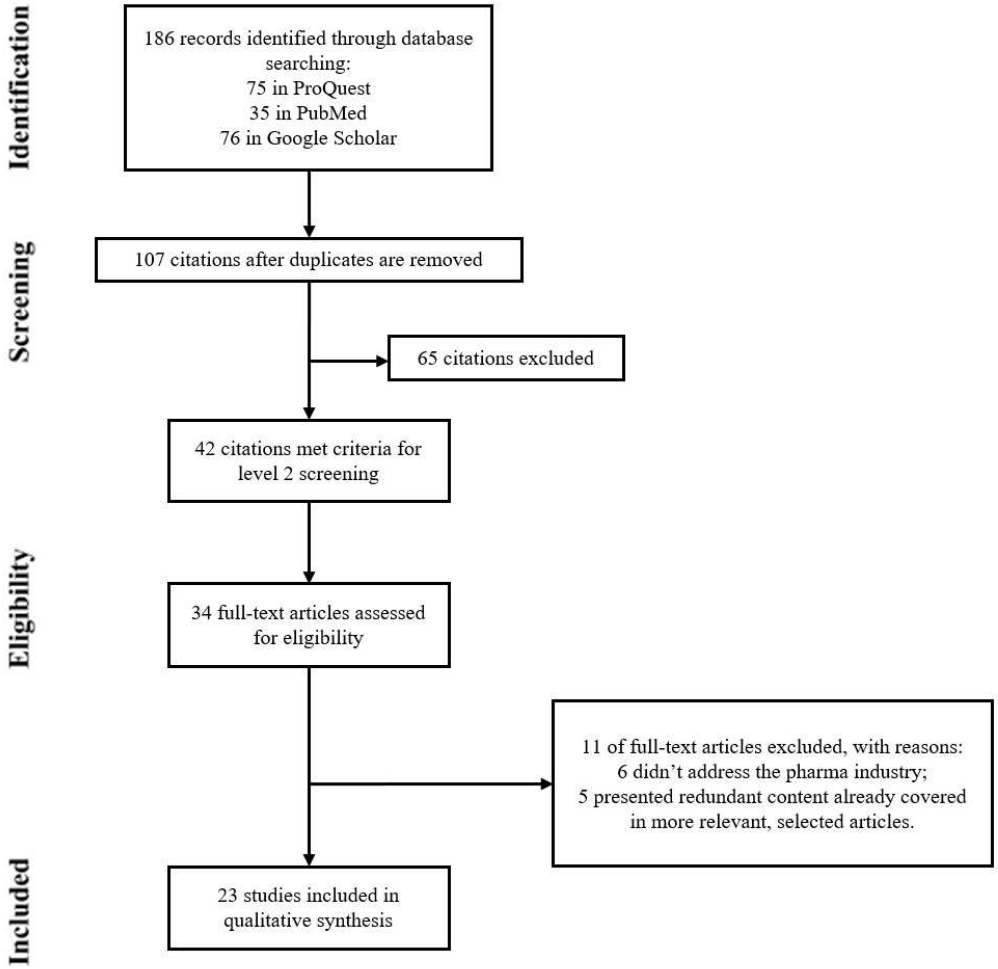

Figure 4 *- PRISMA Flow Diagram (own illustration)*

4. Results

4.1. Key Findings Overview

This systematic literature review synthesized findings from 23 selected articles, all analyzed using the PICOS framework. The framework allowed for a structured assessment of populations studied, types of interventions, comparative approaches, and measured outcomes. The primary results can be summarized as follows:

Population: A diverse range of populations was included, covering conditions such as neurological disorders (e.g., Parkinson's disease), mental health issues (e.g., depression and alcohol dependence), chronic diseases (e.g., heart failure), and others. Studies focused on specific demographics such as children, adults, and older patients to understand how DTx interventions vary across groups.

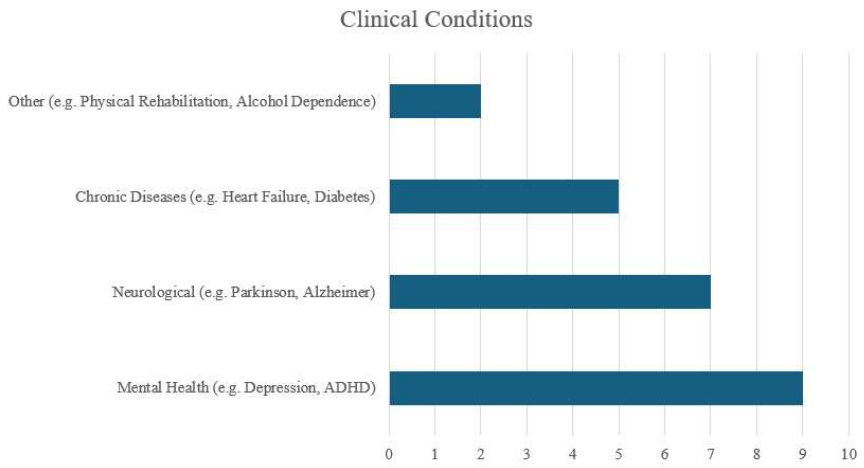

***Figure 5** - Distribution of clinical conditions across selected articles (own illustration)*

Interventions: The interventions reviewed encompassed various digital therapeutics (DTx) modalities, including smartphone apps, virtual reality (VR) therapies, game-based digital therapeutics, and blended care models. Smartphone apps primarily facilitated real-time monitoring of patients' health metrics and provided motivational support to enhance adherence to treatment plans. Virtual reality-based therapies offered immersive experiences that created therapeutic environments for patients, particularly in physical rehabilitation contexts. Game-based digital therapeutics were designed to deliver immediate feedback, promoting engagement and interaction, especially in populations such as children with attention-deficit hyperactivity disorder (ADHD). Blended care models integrated digital solutions with in-person healthcare, allowing for personalized treatment approaches tailored to individual patient needs. Many DTx

interventions offered features like real-time monitoring, feedback mechanisms, motivational support, and patient-centered care, highlighting the varied formats through which DTx are delivered.

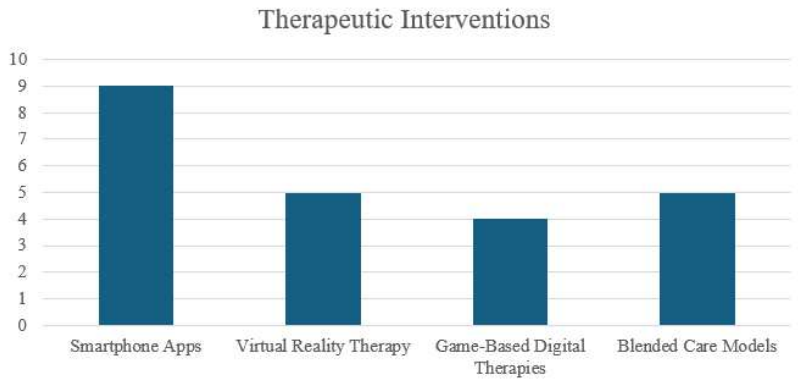

Figure 6 *- Distribution of Therapeutic Interventions across selected articles (own illustration)*

Comparison: Comparative outcomes often contrasted DTx with traditional pharmaceutical treatments or conventional care to assess how digital approaches influence adherence, symptom reduction, quality of life, and other health metrics.

Outcome: Overall, DTx interventions demonstrated promising outcomes, including improved patient engagement and adherence and symptom management, particularly when used to complement traditional treatments. For chronic conditions, the combination of DTx and conventional care showed an increase in patient adherence, while DTx alone provided alternative management for mental health and behavioral issues.

Study Design: Of the selected studies, five were Randomized Controlled Trials (RCTs) or meta-analyses (providing high empirical rigor) and eighteen were narrative or systematic reviews offering theoretical insights. Most studies demonstrated clear methodologies, with randomization, blinding, and intention-to-treat analysis noted in RCTs. However, limitations such as sample size variability, heterogeneity in intervention types, and short follow-up periods were commonly identified.

This comprehensive synthesis of DTx literature highlights the transformative potential of DTx in enhancing pharmaceutical practices, improving patient engagement, and reshaping healthcare delivery, especially when combined with traditional interventions. The findings also underscore the need for further research on long-term efficacy and the standardization of assessment metrics to improve comparability across studies.

The detailed characterization of each selected article, as organized using the PICOS framework, are summarized in tables and presented in Appendix B.

4.2. Structured Analysis of Results

The following analysis is structured according to the Proposed Model previously outlined in Figure 4. This framework offers a clear organization for evaluating the findings and establishing connections across the selected studies, covering aspects from the validation of DTx efficacy, patient engagement, their role as a complement to traditional treatments, acceptance by the pharmaceutical industry, to their broader systemic impact on the pharmaceutical sector.

4.2.1. Efficacy of Digital Therapeutics

The selected studies highlight the substantial effectiveness of Digital Therapeutics (DTx) across a broad spectrum of clinical conditions. Their primary benefits have been observed in improving treatment adherence and managing chronic conditions. The integration of digital solutions with traditional therapeutic approaches has proven particularly impactful, often yielding significant improvements in patient outcomes. These therapies not only support treatment protocols but also enhance the effectiveness of conventional methods, thereby amplifying overall clinical success (Biskupiak, Ha, Rohaj, & Bulaj, 2024; Rajendran et al., 2024).

Furthermore, DTx play a pivotal role in accelerating drug development. As noted by Wang et al. (2023), the real-time collection of patient data during clinical trials enhances precision, reduces costs, and expedites approval processes, significantly advancing the development of therapies for complex conditions such as neurological and cardiovascular diseases (Wang, Lee, & Shin, 2023).

In the field of neurological diseases, DTx have shown remarkable promise in managing conditions like Parkinson's disease. The ability to personalize digital interventions through continuous patient monitoring and dynamic treatment plan adjustments has been vital for optimizing clinical outcomes. This approach facilitates a deeper understanding of disease progression, ensuring interventions are tailored to patients' evolving needs (Ellis & Earhart, 2021; Rajendran et al., 2024).

Similarly, for chronic conditions such as heart failure, DTx have been instrumental in reducing hospital readmissions and enhancing patient recovery. Digital cardiac rehabilitation programs, for instance, provide continuous support and monitoring throughout the recovery process. These programs not only complement pharmacological treatments but also improve clinical outcomes and alleviate the burden on healthcare systems (Biskupiak, Ha, Rohaj, & Bulaj, 2024; Zhang et al., 2022).

4.2.2. Enhancing Patient Engagement & Supporting Treatment Adherence

DTx have had a transformative impact on patient engagement by offering innovative ways to improve adherence to prescribed treatment regimens. Their ability to deliver personalized, real-time interventions has been a cornerstone of their success. These interventions not only address patients' immediate needs but also ensure continuous, adaptive care, making it easier for patients to stay committed to their therapeutic plans (Dang, Arora, & Rane, 2020; Forbes et al., 2023).

One of the most significant advantages of DTx lies in their capacity for personalization. According to Khirasaria et al. (2020), tailoring treatment to individual preferences and schedules makes the experience more relevant and effective, fostering better adherence and reducing frustration with standardized therapies. Additionally, the inherent flexibility of DTx allows patients to follow therapeutic protocols at their own pace, further encouraging sustained engagement (Khirasaria et al., 2020), Milne-Ives et al., 2020).

Beyond improving engagement, DTx have also shown great potential in reducing the stigma associated with mental health conditions, such as depression and substance dependence. By enabling patients to receive treatment in the privacy and comfort of their homes, these therapies help overcome societal barriers to care, allowing patients to feel more comfortable seeking and adhering to treatment. As highlighted by Forbes et al. (2023), this approach not only reduces stigma but also empowers patients by providing tools to monitor their progress and adjust behaviors based on real-time feedback, fostering a sense of control and ownership over their treatment journey (Dang, Arora, & Rane, 2020; Forbes et al., 2023).

Moreover, the personalization and engagement offered by DTx significantly enhance treatment adherence. Patients, empowered by these tools, have more control over their therapies, increasing the likelihood of sticking to treatment protocols. This is particularly crucial in managing chronic diseases and mental health conditions, where continuous monitoring and timely interventions are essential to prevent more severe complications and improve long-term

clinical outcomes. The ability to adjust treatment based on personalized feedback further strengthens the patient's commitment to their treatment plan (Dang, Arora, & Rane, 2020; Forbes et al., 2023).

Finally, DTx also facilitates communication and consequently, the relationship between patients and healthcare providers. The ability to monitor progress and communicate in real time allows for immediate adjustments to treatment plans based on data collected through digital platforms. This responsiveness has been critical in ensuring patients receive optimal care. Wang et al. (2023) emphasize that the continuous nature of DTx builds trust between patients and providers, as concerns are addressed promptly and comprehensively (Wang, Lee, & Shin, 2023).

4.2.3. DTx as a Complement to Conventional Treatments

The literature revealed that Digital Therapeutics (DTx) have proven to be an effective alternative, although complementary to traditional pharmacological treatments. The findings indicate that, while DTx do not entirely replace pharmacological therapies, they significantly expand the existing therapeutic options, particularly in the treatment of chronic diseases and mental health conditions. Analysis of digital interventions, such as cardiac rehabilitation programs, demonstrated a notable reduction in hospitalizations and costs by providing continuous and individualized patient monitoring (Appel et al., 2024).

When combined with traditional therapies, DTx showed effectiveness in enhancing treatment adherence and improving healthcare efficiency. The implementation of these solutions in remote patient monitoring resulted in more consistent and personalized support, easing the burden on conventional healthcare systems (Appel et al., 2024). However, the impact of DTx was found to vary considerably depending on factors such as internet access and technical support, issues often overlooked in economic analyses (Armeni et al., 2024).

The integration of DTx into traditional healthcare systems emerged as a significant barrier, limiting the application of these treatments to controlled environments and hindering their expansion into daily clinical practice (Raijada et al., 2021). While some literature discussions suggest the potential for complete substitution of pharmacological therapies by DTx, robust clinical evidence and long-term studies are still lacking to support this approach (He et al., 2023). The use of DTx for mental health conditions, such as depression and substance dependence, showed promising results, but the evidence remains insufficient to justify a full replacement of conventional therapies (Miao et al., 2024).

Furthermore, the lack of global standards for certification and independent validation was identified as a concern regarding the safety and reliability of DTx (Watson et al., 2023). The study also observed that DTx have the potential to significantly improve the quality of life for patients with conditions such as heart failure and Parkinson's disease, where constant monitoring is crucial for achieving positive clinical outcomes (Appel et al., 2024).

4.2.4. Adherence & Acceptance by Pharmaceutical Industry

According to the systematic review, the pharmaceutical industry is gradually recognizing the potential of digital therapeutics (DTx) as an innovative component of healthcare, particularly for their capacity to enhance patient engagement, adherence, and clinical outcomes. This aligns with the perspective of Sverdlov et al. (2018), who emphasize that DTx can complement traditional pharmaceutical treatments by providing personalized and continuous care that supports better health outcomes. Rajendran et al. (2024) further highlight the growing interest within the pharmaceutical sector in adopting DTx, driven by their potential to address quality and adherence challenges in chronic disease management.

Despite this growing interest, the adoption of DTx within the pharmaceutical sector has been cautious. As noted by Sverdlov et al. (2018), one of the primary barriers is the lack of universally accepted standards for clinical validation, which complicates regulatory approval. Rajendran et al. (2024) also underscore the fragmented regulatory landscape as a key challenge, with differences across jurisdictions hindering the global adoption of DTx. For example, Germany has introduced a regulatory pathway to streamline market access for DTx products, but similar frameworks have yet to be widely adopted elsewhere, leaving pharmaceutical companies to navigate a complex and inconsistent approval process.

These regulatory and validation challenges have limited the scale of pharmaceutical industry involvement in DTx, but optimism persists. As Sverdlov et al. (2018) argue, increasing clinical evidence supporting DTx efficacy and the standardization of regulatory frameworks are expected to drive broader integration of these technologies into pharmaceutical treatment models. Similarly, Rajendran et al. (2024) highlight the potential for DTx to complement traditional treatments by offering innovative solutions that enhance patient outcomes, encouraging pharmaceutical companies to invest in and collaborate on the development of these therapies.

Looking forward, both Sverdlov et al. (2018) and Rajendran et al. (2024) suggest that DTx are likely to play a transformative role in healthcare. The continued development of regulatory pathways and robust clinical evidence will be critical in shaping the adoption of DTx and ensuring their integration into pharmaceutical industry practices. With their ability to deliver personalized and efficient care, DTx are poised to complement existing pharmaceutical solutions and redefine treatment paradigms in chronic disease management and beyond.

4.2.5. *Impact of Digital Therapeutics on the Pharmaceutical Industry*

Digital Therapeutics have already begun to reshape the pharmaceutical industry in several ways, particularly in terms of drug development strategies and the interaction between pharmaceutical companies and patients (Sverdlov et al., 2018; Khirasaria et al., 2020). This section highlights key areas where DTx have made an impact, drawing on information from both the previously selected articles and relevant reports to provide a clearer understanding of the topic.

Innovation in Drug Development

DTx have enabled pharmaceutical companies to pursue innovative approaches to drug development. In particular, they have provided new opportunities for personalization, allowing treatments to be adapted to individual patient needs. Digital platforms also facilitate faster and more efficient clinical trials, as patient data can be collected in real time and analyzed continuously. This shift toward digital solutions is helping pharmaceutical companies improve the speed and accuracy of their product development processes, ultimately leading to better-targeted therapies (Abbadessa et al., 2022; Biskupiak, Ha, Rohaj, & Bulaj, 2024; Rajendran et al., 2024; Sverdlov et al., 2018; Khirasaria et al., 2020).

The integration of artificial intelligence (AI) and predictive analytics has further enhanced the drug development process. AI-powered tools streamline clinical trial design, patient recruitment, and data monitoring, reducing both the time and cost associated with new drug approvals (Pharmaceutical Technology, 2024a).

Competition and Market Access

The rise of DTx has reshaped the competitive landscape in the pharmaceutical sector, introducing new market dynamics. Companies must now contend not only with traditional

industry players but also with digital health providers, driving them to integrate DTx into their product portfolios to meet the growing demand for personalized digital care solutions. New opportunities in remote patient monitoring and personalized treatments are driving companies to adopt innovative models like subscriptions, software licensing, and pay-per-use agreements, diversifying revenue streams (Biskupiak, Ha, Rohaj, & Bulaj, 2024; Rajendran et al, 2024; Sverdlov et al., 2018).

By enhancing patient engagement through personalized care, DTx integration intensifies market competition. Companies that fail to navigate regulatory challenges or adopt emerging technologies risk losing their competitive edge to more agile entrants (FDA, 2024; MedDevice, n.d.).

Ultimately, DTx are transforming drug development, market competition, and healthcare delivery, presenting significant opportunities while also posing regulatory, economic, and operational challenges that require strategic adaptation from industry stakeholders.

Shifting Care Models

The advent of DTx is contributing to a broader shift in the healthcare landscape, where the emphasis is moving from hospital-based care to continuous, remote care. This shift challenges pharmaceutical companies to rethink their traditional models of distribution and patient engagement. In this new paradigm, pharmaceutical companies must consider how to best deliver care in a digital-first world, where the focus is on ongoing monitoring and treatment personalization. As such, DTx are playing a pivotal role in redefining the future of healthcare, offering new possibilities for the management of chronic conditions and the enhancement of patient outcomes (Biskupiak, Ha, Rohaj, & Bulaj, 2024; Rajendran et al., 2024; Sverdlov et al., 2018). In this context, remote monitoring tools support personalized, continuous care, improving patient outcomes while reducing healthcare costs through fewer hospitalizations and emergency visits (Appel et al., 2024).

Operational Cost Reduction and Workforce Transformation

The adoption of DTx has significantly reduced operational costs through automation and data-driven decision-making. Digitalization of clinical trials lowers patient recruitment and monitoring expenses, while predictive analytics accelerate the identification of effective treatments, reducing research time and costs (Pharmaceutical Technology, 2024b).

Additionally, remote patient monitoring in long-term treatments has the potential to cut costs related to hospitalizations and frequent consultations (Appel et al., 2024).

This digital shift also transforms the pharmaceutical workforce. As demand for expertise in AI, data analytics, and cybersecurity rises, traditional roles are shrinking, while new positions in technological innovation are emerging. Research and development teams must integrate these technologies, requiring substantial reskilling efforts to adapt to the evolving industry (Pharmaphorum, 2024). Consequently, while some functions may decline, new opportunities in software design, cybersecurity, and big data analysis are growing, essential for the success of digital therapies (KPMG, 2023).

Investments and Innovation

Rising investments in DTx have accelerated technological advancements and the development of new therapies. Pharmaceutical companies are increasingly funding initiatives involving AI, big data analytics, and digital monitoring platforms. These investments are expected to improve treatment adherence and long-term healthcare outcomes, thus enhancing patient experiences and lowering healthcare costs (McKinsey & Company, 2023a; McKinsey & Company, 2023c).

Revenue Models and Pricing Strategies

The digitalization of healthcare has transformed revenue models within the pharmaceutical industry. Traditional revenue streams based on drug sales have expanded to include subscription services, licensing agreements, and pay-for-performance models. This transition necessitates new pricing strategies that reflect the unique value propositions of digital therapies, balancing innovation with affordability (KPMG, 2023; McKinsey & Company, 2023b; McKinsey & Company, 2023c).

Regulatory and Economic Challenges

Despite their potential, the widespread adoption of DTx faces regulatory and economic hurdles. Regulatory frameworks for digital therapies remain fragmented across countries, creating market entry barriers. Standardizing approval processes and establishing clear reimbursement policies are critical for fostering global adoption (FDA, 2024; Recchia, G., & Gussoni, G., 2023).

The evolving nature of DTx pricing and reimbursement models presents further challenges. Without well-defined policies, healthcare providers and insurers may hesitate to adopt these therapies, slowing market growth (LSVP, n.d.).

5. Discussion

5.1. Non-Exhaustive List of DTx Applications

To better understand the practical applications of DTx across various medical areas, Table 1 provides a non-exhaustive list categorizing their uses by specialty, condition, and intervention phase. This table highlights how DTx improve clinical outcomes and their potential to complement or replace traditional therapies.

Medical Area	Condition / Disease	Stages / Phases	DTx Intervention	Clinical Outcomes & Effectiveness	Potential Complementarity or Substitution	References
Neurology	Parkinson's Disease	Early progression phase	Continuous monitoring	Enhanced treatment personalization, improved adherence, and reduced symptom progression	Low – Complementary to pharmacological treatments	Ellis & Earhart (2021); Rajendran et al. (2024)
Neurology	Attention Deficit Hyperactivity Disorder (ADHD)	Mild to moderate cases in school-age children	Game-based digital therapies (mostly for School-age children)	Improved attention span and behavioral control	Moderate – Potential for mild cases	He et al. (2023); Oh et al. (2024)
Mental Health	Depression	Moderate to severe symptoms	Digital Cognitive Behavioral Therapy (CBT)	Reduced symptoms, higher engagement, and improved adherence to treatment	Moderate – Potential in mild to moderate cases	Forbes et al. (2023); Watson et al. (2023
Mental Health	Substance Dependence (Alcohol)	Rehabilitation and relapse prevention phase	Hybrid digital and in-person sessions	Reduced dependency levels and higher engagement in rehabilitation programs	Moderate – Effective as a partial substitute for mild cases	Miyake et al. (2024)
Cardiology	Heart Failure	Post-acute recovery and rehabilitation phase	Digital cardiac rehabilitation	Reduced hospital readmissions, improved recovery rates, and lower healthcare costs	Low – Complementary to clinical care	Appel et al. (2024); Zhang et al. (2022)
Endocrinology	Diabetes	Continuous monitoring in chronic cases	Health monitoring apps	Improved adherence to treatment plans and glycemic control	Low – Assistive but not substitutive	Biskupiak et al. (2024)

Table 2 *- List of DTx applications across selected medical conditions (own illustration)*

5.2. First Research Question

Q1: How are Digital Therapeutics (DTx) reshaping the pharmaceutical industry, particularly in terms of driving innovation in product development, enhancing treatment efficacy, and redefining patient engagement?

DTx emerge as disruptive innovations in the pharmaceutical sector by integrating digital interventions with conventional treatments. However, this transformation faces significant challenges, particularly due to the diversity of technologies employed. The lack of standardization and the scarcity of rigorous clinical validation compromise the reliability of these interventions, limiting their systematic application. Recent studies illustrate this duality: while virtual reality-based digital therapies show promise in treating neurological diseases (Miao et al., 2024), methodological flaws, such as small sample sizes and short observation periods, still limit the conclusions drawn (Zhang et al., 2022).

In the field of therapeutic efficacy, evidence suggests that DTx can improve treatment adherence, particularly in chronic conditions such as diabetes and heart failure (Appel et al.,

2024). However, maintaining long-term engagement remains a significant obstacle. Issues such as digital fatigue and loss of interest are often underestimated, raising questions about whether the observed benefits reflect genuine therapeutic efficacy or a placebo effect arising from the digital experience (Forbes et al., 2023). These uncertainties are exacerbated by the potential influence of conflicts of interest in studies funded by technology developers (Armeni et al., 2024).

Regarding patient engagement, DTx promise greater autonomy and treatment personalization by enabling continuous remote monitoring. However, this approach may generate a paradox: the increased digital interactions may, over time, compromise patient motivation. The lack of consistent human support, particularly in therapies focused on mental health, limits their effectiveness (Forbes et al., 2023). Thus, balancing digital and human elements appears to be essential for the sustainable implementation of these technologies (Miyake et al., 2024).

In summary, DTx presents transformative potential for the pharmaceutical industry by fostering innovation, therapeutic improvement, and enhanced patient engagement. However, their successful integration depends on rigorous clinical validation, strategies to mitigate digital fatigue, and a balanced approach between technology and human support.

5.3. Second Key Research Question

Q2: To what extent can DTx complement or even replace traditional pharmaceutical therapies in the treatment of various medical conditions?

The evolution of Digital Therapeutics (DTx) has challenged the traditional model of the pharmaceutical industry by proposing alternatives and complements for the treatment of various medical conditions. While conventional pharmacological treatments rely on the administration of chemical substances, DTx offers software-based interventions aimed at monitoring and promoting treatment adherence. The results of this investigation indicate that, although DTx do not entirely replace pharmacological therapies, they play a significant role in expanding existing therapeutic options (Appel et al., 2024).

DTx have demonstrated remarkable efficacy when combined with traditional therapies, particularly in the treatment of chronic diseases and mental health conditions. Digital interventions, such as cardiac rehabilitation programs, have proven effective in reducing hospitalizations and costs by providing continuous and individualized monitoring (Appel et al., 2024). The implementation of these solutions improves healthcare efficiency by relieving pressure on conventional systems and enabling closer, more consistent support. However, the

impact of DTx is significantly dependent on contextual factors, such as internet access and technical support, elements that are often overlooked in economic analyses (Armeni et al., 2024). The lack of effective integration with traditional healthcare systems also represents a substantial barrier, limiting the reach of DTx to controlled environments and hindering their expansion into daily clinical practice (Raijada et al., 2021).

Although the possibility of fully replacing pharmacological therapies with DTx is discussed in the literature, this approach still faces significant challenges. Robust clinical evidence and long-term studies are scarce, limiting confidence in the isolated efficacy of DTx for treating complex conditions (He et al., 2023). Applications aimed at mental health, such as those targeting depression and substance dependence, show promising results but remain insufficiently proven to justify full replacement (Miao et al., 2024). Additionally, the lack of global certification standards and independent validation raises concerns about the safety and reliability of these treatments (Watson et al., 2023).

The development of DTx reflects a broader shift in healthcare models, promoting a patient-centered approach focused on remote and continuous care. This evolution requires the pharmaceutical industry to adapt its business models to incorporate these new technologies as valuable complements to conventional therapies. The integration of digital solutions can lead to significant improvements in patients' quality of life, particularly in areas such as heart failure and Parkinson’s disease, where constant monitoring is crucial for positive clinical outcomes (Appel et al., 2024).

In conclusion, DTx represent a promising innovation in healthcare. However, their full integration and potential as substitutes depend on further research, more robust regulation, and overcoming existing technological barriers. Meanwhile, their role as a complement to traditional therapies is widely recognized, offering more personalized, accessible, and patient-centered solutions.

5.4. Addressing the Problem Statement

5.4.1. Optimizing the Integration of Dtx in the Pharmaceutical Industry

The effective integration of Digital Therapeutics into the pharmaceutical industry necessitates a strategic approach that combines clinical rigor, technological partnerships, and operational adaptation. Continuous real-time monitoring for chronic diseases, such as diabetes, highlights

DTx's ability to complement traditional therapies (Appel et al., 2024). However, widespread adoption demands standardized validation processes and evidence-based approaches to build trust among healthcare providers and regulatory bodies.

Cross-sector collaborations with technology companies offer opportunities to leverage expertise in artificial intelligence and digital health. Pilot initiatives, such as digital rehabilitation platforms, demonstrate that scalable solutions are achievable when implemented alongside traditional care systems. To optimize integration, pharmaceutical companies must invest in clinical validation and work closely with healthcare providers to demonstrate the value of DTx across therapeutic areas.

5.4.2. Assessing the Compatibility of Current Business Models with Dtx

Transitioning to Digital Therapeutics requires pharmaceutical companies to rethink traditional business models, which are primarily built around drug development and sales. Unlike physical medications, DTx often rely on subscription-based pricing, software licensing, or value-based models such as pay-for-performance. While these models align with value-based healthcare principles, they present challenges for companies accustomed to revenue structures dependent on drug sales.

Successful examples, such as Sanofi's partnership with Verily for the development of diabetes management platforms, highlight the potential of hybrid approaches that integrate digital tools with pharmacological treatments (Sverdlov et al., 2018). To facilitate this shift, pharmaceutical companies must invest in digital infrastructure, adjust their pricing strategies, and ensure regulatory frameworks evolve to accommodate DTx innovations.

5.4.3. Strategic Transformations for Incorporating DTx

The adoption of Digital Therapeutics requires pharmaceutical companies to undergo organizational transformation. This includes building internal capabilities in digital health, data analytics, and artificial intelligence, as well as fostering a culture that supports innovation. Strategic partnerships with technology firms can accelerate this transformation by bridging knowledge gaps and reducing development timelines.

Pilot programs in mental health and chronic disease management provide practical pathways for testing and scaling DTx solutions. By prioritizing patient-centric strategies and aligning

digital tools with therapeutic goals, pharmaceutical companies can seamlessly integrate Digital Therapeutics into existing care pathways (Rajendran et al., 2024).

5.5. Adoption Challenges: Market, Stakeholders and Reimbursement

An essential aspect of integrating Digital Therapeutics (DTx) into the pharmaceutical industry lies in understanding market dynamics, stakeholder preferences, and economic factors that influence their adoption. These elements significantly shape the success or failure of DTx implementation in healthcare systems.

Market Size and Stakeholder Preferences

The impact of DTx depends on addressing markets where continuous monitoring and adherence support are critical, such as diabetes and heart failure. Studies, like Appel et al. (2024), show that digital cardiac rehabilitation programs reduce hospital readmissions and improve outcomes, positioning DTx as valuable complements to traditional therapies. However, in niche markets with smaller patient populations or limited digital infrastructure, adoption remains challenging (Raijada et al., 2021).

Patient preferences play a defining role. While some embrace technology-driven care, others may resist it without clear, tangible benefits like ease of use and improved outcomes. Physicians, as primary decision-makers, require robust clinical evidence and seamless workflow integration before prescribing DTx (Forbes et al., 2023). Without such validation, healthcare providers may hesitate, even when the technology demonstrates potential.

Reimbursement and Pricing Barriers

Economic considerations, particularly reimbursement frameworks, are critical for widespread DTx adoption. Unlike traditional therapies with established payment models, DTx often operate under subscription-based pricing, pay-for-performance, or software licensing models. Germany's DiGA framework stands out as an example of structured reimbursement enabling market access (Watson et al., 2023). However, globally, fragmented reimbursement pathways and unclear cost-effectiveness hinder adoption (Raijada et al., 2021; Armeni et al., 2024).

For healthcare payers with constrained budgets, the initial costs of DTx may outweigh perceived benefits, despite long-term savings. Without economic studies proving their financial

value, adoption risks remaining limited to pilot programs rather than widespread implementation.

Key Drivers of DTx Adoption

Physicians remain central to DTx adoption, with their decisions influenced by clinical evidence, workflow compatibility, and reimbursement incentives. The absence of large-scale trials validating DTx efficacy contributes to skepticism among providers, particularly in resource-constrained settings (He et al., 2023; Rajendran et al., 2024). Standardized reimbursement remains a missing link, without which physicians may view DTx as an added burden rather than a viable therapeutic tool (Sverdlov et al., 2018).

Patients' willingness to adopt DTx also matters, with older demographics and those with limited digital literacy requiring additional support. Forbes et al. (2023) highlights the importance of balancing innovation with patient-centric design to ensure usability, accessibility, and personalization—key factors for real-world success.

In summary, the successful adoption of DTx depends on aligning stakeholder preferences, addressing economic barriers, and ensuring strong clinical validation. Bridging these gaps through reimbursement frameworks, robust trials, and patient-friendly solutions will be critical to unlocking their full potential in healthcare.

5.6. Implications and Strategic Pathways for DTx Adoption

To address the challenges and opportunities identified in the adoption of Digital Therapeutics (DTx), it is crucial to outline strategic actions and their implications for the pharmaceutical industry. Table 2 provides a structured summary of the key barriers to DTx adoption, along with actionable strategies and their potential impact on the industry. This non-exhaustive list consolidates findings from the research, highlighting areas such as regulatory uncertainty, limited clinical evidence, fragmented reimbursement, technology integration and digital fatigue and adherence. By aligning these strategies with industry priorities, the table serves as a practical guide for stakeholders to navigate the complexities of integrating DTx into pharmaceutical systems while capitalizing on their transformative potential.

Key Challenge/Aspect	Strategic Action	Implication for the Industry	References
Regulatory Uncertainty	Collaborate with policymakers to establish clear guidelines for DTx approval and reimbursement.	Facilitates integration into healthcare systems while ensuring safety and accommodating rapid technological advancements.	Watson et al. (2023)
Limited Clinical Evidence	Conduct robust, long-term clinical trials that align with pharmacological standards.	Builds trust among regulators, healthcare providers, and patients, enhancing adoption rates.	He et al. (2023)
Fragmented Reimbursement Models	Adopt subscription-based, pay-per-use, or value-based pricing models.	Balances affordability with accessibility, making DTx a viable option for healthcare systems globally.	Rajendran et al. (2024)
Technology Integration	Collaborate with digital health innovators to leverage expertise and accelerate innovation.	Combines technological and clinical knowledge, ensuring faster development and market readiness.	Sverdlov et al. (2018)
Digital Fatigue and Adherence	Create intuitive, user-friendly interfaces that address issues like digital fatigue.	Enhances patient engagement, adherence, and satisfaction, leading to better clinical outcomes.	Forbes et al. (2023)

Table 3 *- Key Challenges and Strategic Pathways for the Adoption of DTx (own illustration)*

5.7. Limitations and Future Research

While this thesis provided a comprehensive analysis of DTx and their impact on the pharmaceutical industry, certain limitations must be acknowledged. Reliance on secondary studies and the still nascent nature of evidence on DTx constrained the scope of definitive conclusions. Furthermore, the fragmentation of regulatory markets and variability in methodologies among analyzed studies hindered result comparisons.

Future research could focus on:

- Analyzing models for integrating DTx into global healthcare systems, considering regional differences in regulation and digital infrastructure.
- Investigating how DTx can improve collaboration between physicians and patients, leveraging technologies such as big data and machine learning to personalize care.
- Exploring best practices for partnerships between pharmaceutical companies and technology startups, including contractual frameworks and co-development strategies.

6. Conclusions

This chapter reflects on the main insights of this study, focusing on the transformative role of Digital Therapeutics in modern healthcare. It outlines their benefits, challenges, and the steps needed to fully unlock their potential in improving global health.

- Revolutionizing Healthcare: DTx enable remote monitoring, real-time support, and personalized care, improving adherence, reducing hospitalizations, and enhancing outcomes. However, their full potential is limited by fragmented regulations and inconsistent validation, making global standards and strong evidence critical for building stakeholder confidence.
- Complementing Traditional Therapies: DTx work effectively alongside traditional therapies, particularly for chronic diseases and mental health conditions, by enhancing engagement and efficacy. Yet, their potential as standalone treatments remains underexplored, highlighting the need for robust, long-term studies to assess their viability in treating complex conditions.
- Adapting Business Models: Integrating DTx requires moving beyond traditional drug-focused revenue models toward innovative frameworks like subscriptions and performance-based payments. Success hinges on investment in digital infrastructure, partnerships with technology firms, and ensuring accessibility for broader, scalable impact.
- Collaborating for Success: Collaboration among pharmaceutical companies, healthcare providers, and technology innovators is essential for scaling solutions. Harmonized regulations and clear reimbursement frameworks are key to overcoming approval barriers and promoting the global adoption of DTx.

In conclusion, digital therapeutics offer transformative solutions to long-standing healthcare challenges, enhancing accessibility, personalization, and efficiency. By addressing regulatory and evidence gaps through collaboration and innovation, DTx can establish themselves as a cornerstone of future healthcare, meeting the evolving needs of global health effectively.

7. References

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8. Appendix

A) Pharmaceutical Companies' Partnerships in DTx

Company	Partnership	Digital Therapy	Impacts
Sanofi	Happify Health	Therapy for Depression and Multiple Sclerosis	Improved emotional management for patients
Novartis	Pear Therapeutics	reSET for Substance Use Disorders	First FDA-approved digital therapy
Pfizer	Sidekick Health	Therapy for Atopic Dermatitis	Improved treatment adherence
Eli Lilly	Sidekick Health	Support for Oncology Patients	Complement to traditional oncology therapies

Source: FDA, 2017; Fierce Pharma, n.d.; Happify Health, n.d.; Sidekick Health, n.d.

AUTHOR, PUBLICATION YEAR	POPULATION (P)	INTERVENTION (I)	COMPARISON (C)	OUTCOME (O)	STUDY DESIGN (S)	RESULTS
Abbadessa G, Brigo F, Clerico M, De Mercanti S, Trojsi F, Tedeschi G, Bonavita S, Lavorgna L, 2022 [1]	Patients with neurological conditions	Digital therapeutic tools (virtual reality, exergames and mobile health apps) for monitoring and treatment of neurological diseases	Traditional rehabilitation methods and standard medical treatments (without digital therapies)	Evaluation of the effects of digital therapeutics on motor, sensory, and cognitive functions in neurological disorders. Improved adherance and symptom monotoring	Narrative review of various digital therapeutic tools and their applications in neurology	Significant improvements in motor control, balance, cognitive functions, and quality of life. Digital therapeutics showed potential to enhance rehabilitation outcomes and patient adherence to therapy
Amyx, M., Phi, N. T. T., Alebouyeh, F., et al., 2024 [2]	Patients using Digital Therapeutics (DTx) across various chronic conditions	Mapping the evidence around digital therapeutics (DTx) for different health conditions	Traditional pharmaceutical therapies and non-digital interventions	Clinical performance of DTx, identifying research gaps, limitations and Impact on patient outcomes, engagement, and treatment adherence	Systematic review of existing evidence, including clinical trials, case studies, and observational studies. Comparisson between different DTx studies	Strong evidence supporting the efficacy of DTx in improving patient outcomes, particularly in chronic disease management, mental health, and patient engagement. The review highlights areas where DTx can complement traditional therapies and where more research is needed
Appel L, Appel E, Kisonas E, Lewis-Fung S, Pardini S, Rosenberg J, Appel J, Smith C, 2024 [3]	Hospitalized patients (aged ≥65 years) diagnosed with dementia	Virtual reality (VR) therapy - watching 360° VR films - to treat behavioral and psychological symtoms of dementia	Patients receiving conventional/traditional care	Quality of life improvement and symptom reduction for dementia patients	Randomized Controlled Trial (RCT) with a strong methodological basis for assessing the efficacy of the intervention	VR intervention significantly reduced symptoms like anxiety and agitation, improving hospitalized dementia patients' quality of life. Participants found the VR experience acceptable and enjoyable.
Armeni, P., Polat, I., De Rossi, L. M., Diaferia, L., Meregalli, S., & Gatti, A.,2024 [5]	General assessment of the use of DTx across diverse conditions	Evaluation of the development, regulatory, and clinical adoption progress of DTx	Traditional therapies and non-digital healthcare interventions	Impact of DTx on therapeutic outcomes, scalability, and patient engagement	Narrative review, combining qualitative and quantitative data from existing studies	The review highlights significant advancements in DTx, with promising results in chronic disease management and mental health, but also face limitations such as regulatory challenges, reimbursement issues, and patient adoption
Biskupiak, Z., Ha, VV., Rohaj, A., & Bulaj, G., 2024 [7]	Patients with chronic diseases (e.g., Alzheimer's, epilepsy, cancer, depression, rheumatoid arthritis)	Digital therapies (DTx) combined with pharmaceuticals	Traditional pharmacotherapy alone (drugs without digital integration)	Improved drug efficacy, increased adherence, reduced side effects, enhanced patient outcomes	Preclinical and clinical studies	Combining DTx with pharmaceuticals show significant improvements in treatment adherence, symptom management, and patient outcomes across multiple chronic conditions. Digital therapeutics enhance drug efficacy, reduce adverse effects, and provide personalized care, improving quality of life and therapy outcomes for patients

Dang, A., Arora, D., & Rane, P, 2020 [11]	Healthcare practitioners and patients with chronic diseases, mental health disorders, and substance addiction	Digital therapeutics (mobile apps, wearable devices, and VR technology) as a supplement to conventional treatments	Traditional/Conventional healthcare approaches	Improved health outcomes, enhanced patient engagement, and better medication adherence	Review Article that summarizes existing literature and evidence on DTx. Analyzes various digital interventions, their applications, regulatory aspects and discusses the potential of DTx to complement/replace conventional treatments	DTx can significantly improve healthcare delivery by providing cost-effective, evidence-based therapeutic interventions. They can complement or replace traditional treatments, especially for chronic and mental health conditions
Ellis T.D. & Earhart G.M., 2021 [18]	Patients with Parkinson's Disease	Digital therapeutic interventions (mobile health platforms, virtual coaches, and digital cognitive-behavioral therapy (CBT)) for managing symptoms in Parkinson's disease	Conventional/Traditional medical treatment and in-person interventions	Evaluation of the effects of digital therapeutics on motor and non-motor symptoms of Parkinson	Narrative review of practical applications and emerging advances in digital therapeutic platforms	Significant improvements in exercise adherence, increased physical activity, weight loss, and enhancements in sleep quality and psychological well-being. Studies indicate potential for improving Parkinson's disease management through personalized digital interventions
Forbes, A., Keleher, M. R., Venditto, M., & DiBiasi, F., 2023 [24]	Patients with depression participating in clinical trials for digital interventions	Assessment of adherence and engagement with digital interventions in clinical trials for depression	Comparison of adherence rates between digital interventions and traditional therapeutic methods	Adherence rates, patient engagement, factors influencing participation, and treatment success	Systematic review of clinical trials on digital interventions for depression	Overall, digital interventions for depression increase engagement and adherence, suggesting they are effective adjunct tools in mental health treatment. However, the study Identifies varying levels of patient adherence with engagement being influenced by factors like ease of use, personalization, and accessibility
He F, Qi Y, Zhou Y, Cao A, Yue X, Fang S, Zheng Y, 2023 [27]	Children and adolescents (aged 4-17) diagnosed with Attention Deficit Hyperactivity Disorder (ADHD)	Digital therapies (e.g., apps, games) targeting ADHD symptoms	Traditional non-digital ADHD therapies	Symptom reduction in ADHD (inattention, impulsive hyperactivity, executive function, and working memory)	Meta-analysis of 31 studies with 2.169 participants	Digital therapies show significant benefits in symptom management, particularly in improving attention spans in children with ADHD
Khirasaria R, Singh V, Batta A, 2020 [28]	Patients with chronic diseases (e.g., diabetes, heart diseases)	Digital therapeutics (DT) including mobile apps, wearable devices, and telemedicine platforms	Traditional/ Conventional treatment approaches	Improved treatment outcomes, reduced healthcare costs, and enhanced patient adherence to healthy behaviors	Review Article: Provides an overview of current research and evidence on DTx. Examines different digital health interventions, their uses, and regulatory considerations and explores how it can enhance or replace conventional treatments	This review identifies that DTx have the potential to modernize healthcare by providing cost-effective, efficient, and accessible treatment options, complementing or replacing conventional treatments, especially for chronic diseases.

Kim, HS., 2020 [29]	Patients with various health conditions, including chronic diseases	Digital therapeutics (DTx) using digital devices or software	Traditional/ Conventional treatment approaches	Improved patient outcomes, safety concerns, and regulatory challenges. Highlights potential downsides and risks of DTx over-reliance	Narrative article that discusses the potential benefits and exaggerated claims of digital therapeutics. Analyzes the challenges and concerns related to the clinical effectiveness, safety, and regulatory aspects of DTx	DTx have the potential to improve patient outcomes but face significant challenges in terms of safety, regulatory approval, and patient compliance. They should complement rather than replace conventional treatments
Miao, B. Y., Sushil, M., Xu, A., et al, 2024 [36]	Digital therapeutic clinical trials initiated between 2010 and 2030	DTx interventions in clinical trials using natural language processing	Non-digital clinical trial analysis	Insights into trial characteristics, patient inclusion/exclusion, and trial design challenges	Systematic review using natural language processing	Reveals variability in DTx trial design and outcomes, underscoring the need for standardized methodologies in DTx research
Milne-Ives, M., Lam, C., De Cock, C., Van Velthoven, M. H., & Meinert, E., 2020 [37]	Adults and adolescents using mobile apps for health behavior change and improve lifestyle behaviors	Mobile health apps targeting physical activity, diet, drug use, alcohol use, and mental health	Non-digital behavior change interventions	Improvement in health behaviors, engagement, and health outcomes	Systematic review of existing studies: synthesizes findings from multiple studies, ensuring a robust analysis of existing evidence on mobile health interventions.	The review found that mobile apps significantly improve health behaviors across various domains, including physical activity, diet, substance use, and mental health. Engagement and usability of the apps were crucial for their effectiveness, suggesting that tailored content and feedback enhance user adherence and overall outcomes
Miyake, N., So, R., Kariyama, K. et al, 2024 [38]	Adults with alcohol dependence, consuming >60g/day (men), >40g/day (women)	Smartphone-based app (ALM-002) intervention combined with face-to-face sessions	Conventional care without app support (control group with only face-to-face treatment)	Reduction in alcohol use and dependence symptoms over 12 weeks	Randomized controlled trial (RCT) in which participants were randomly assigned to either a smartphone app intervention with face-to-face support or conventional care	Combined app and face-to-face intervention significantly reduced alcohol dependence, demonstrating app potential as a support in addiction therapy
Netto, A. V., 2020 [39]	Patients receiving healthcare with a combination of physical and digital care (e.g., chronic conditions, elderly care)	Blended care combining physical care and digital therapeutics (DTx)	Traditional face-to-face care - without blended model	Improved patient self-care, enhanced accessibility, and optimization of treatment outcomes	Narrative review of blended care approaches in digital therapeutics	Blended care, integrating face-to-face and digital interventions, improves patient engagement and self-management of chronic conditions. DTx, when combined with traditional care, enhances accessibility and cost-efficiency while maintaining high-quality, evidence-based interventions. This approach has shown promise in expanding access to therapies and reducing the economic burden on healthcare systems.

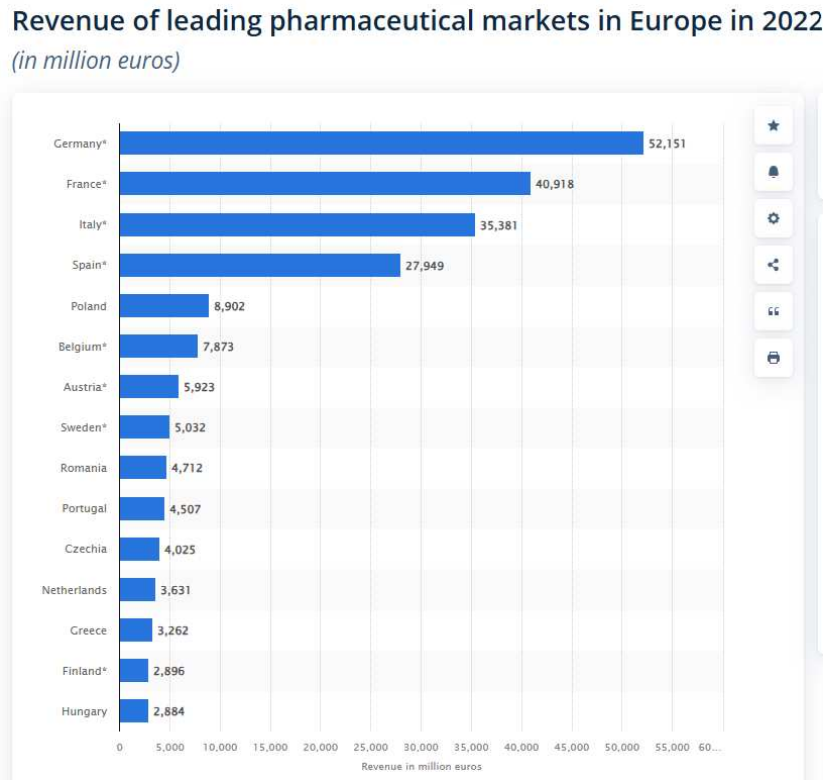
Oh, S., Choi, J., Han, D. H., & Kim, E., 2024 [40]	Children and adolescents diagnosed with Attention Deficit Hyperactivity Disorder (ADHD)	Game-based digital therapeutics (DTx) for symptom management	Traditional pharmaceutical treatments for ADHD	Improvement in ADHD symptoms, particularly inattention and hyperactivity; assessments by parents and teachers	Controlled, Randomized. Systematic review and meta-analysis	Game-based DTx demonstrated moderate to large effects in reducing ADHD symptoms, with significant improvements noted in daily functioning as reported by parents and teachers. These digital interventions serve as effective complements to traditional medication treatments
Raijada, D., Wac, K., Greisen, E., Rantanen, J., & Genina, N., 2023 [46]	Patients requiring personalized drug therapies	Integration of personalized drug delivery systems with digital health solutions	Traditional drug delivery systems	Improved patient adherence, health outcomes, and treatment efficacy	Narrative review discussing various case studies and theoretical models	The integration of personalized drug delivery systems into digital health can enhance treatment outcomes by improving adherence and personalizing patient experiences through data-driven insights
Rajendran, A., Kella, A., & Narayanasamy, D., 2024 [47]	Patients with chronic diseases and psychiatric conditions	Digital therapeutics (including mobile apps, software systems and wearable technology) for prevent and manage diseases. Exploration of DTx integration in pharma industry	Conventional pharma industry practices	Efficacy and safety of digital therapeutics. Enhanced patient adherence, personalized care and improving patient outcomes	Narrative review of current technological advancements and clinical trials	DTx are revolutionizing the pharmaceutical industry by enhancing drug effectiveness and patient adherence. DTx have demonstrated significant improvements in health outcomes, such as weight reduction, improved health behaviors, and enhanced treatment adherence
Seo, Y.-C., Yong, S. Y., Choi, W. W., & Kim, S. H., 2024 [50]	Patients with various chronic and mental conditions (substance abuse, anxiety, musculoskeletal disorders)	Meta-analysis of DTx studies on therapeutic effectiveness applied to multiple health conditions	Control groups receiving traditional treatments or placebo	Evaluation of overall therapeutic effects of DTx	Controlled, Randomized. Meta-analysis of 15 studies with randomized control trials and pre-post designs	DTx demonstrated significant therapeutic effects in conditions like substance abuse and anxiety. Less significant results were observed for musculoskeletal and mental health conditions. Digital therapeutics proved effective in improving health behaviors and reducing adverse effects
Wang, C., Lee, C., & Shin, H., 2023 [58]	Patients with chronic conditions (e.g., diabetes, ADHD, substance use disorders, neurological conditions)	Digital therapeutics (DTx) for the prevention, management, and treatment of chronic and neurological diseases	Non-digital therapeutic development approaches	Insights into definitions, clinical applications, regulatory challenges, and commercialization of DTx	Narrative review and analysis of clinical trials and regulatory frameworks	This review highlights the increasing commercialization of digital therapeutics and identifies potential benefits of it in chronic and neuropsychiatric conditions, with improved adherence and lower side effects compared to traditional therapies. However, it also finds gaps in definitions and regulatory frameworks, and emphasizes the importance of collaboration among stakeholders to enhance implementation in clinical practice

Watson, A., Chapman, R., Shafai, G., & Maricich, Y. A., 2023 [59]	FDA regulations on Digital Therapeutics (DTx)	Analysis of the FDA's evolving regulations for prescribed DTx	Previous regulatory frameworks for medical devices and pharmaceuticals	Impact of regulatory updates on the adoption and implementation of DTx	Narrative review based on FDA regulations and related literature	FDA regulations are adapting to keep pace with DTx developments, clarifying approval and reimbursement pathways. Challenges and future regulatory needs are highlighted.
Yan, K., Balijepalli, C., & Druyts, E., 2021 [60]	Policymakers, healthcare providers, and stakeholders in health technology assessment	Evaluation of digital therapeutics within existing HTA frameworks	Traditional health technologies and therapies	Implications for HTA practices, cost-effectiveness, and integration of DTx	Review article analyzing current HTA frameworks and DTx impacts	The authors discuss the need to adapt HTA frameworks to effectively evaluate DTx, emphasizing the importance of incorporating new methodologies to assess cost-effectiveness and real-world effectiveness.
Zhang, X., Luo, Z., Yang, M., Huang, W., & Yu, P., 2023 [61]	Heart failure patients undergoing cardiac rehabilitation	Digital therapeutics-based cardiac rehabilitation interventions	Traditional cardiac rehabilitation methods	Efficacy and safety of DTx in improving cardiac function and patient outcomes	Systematic review of randomized controlled trials (RCTs) and observational studies	DTx-based cardiac rehabilitation shows promise in improving patient outcomes and adherence to rehabilitation programs. However, further research is needed to standardize protocols and assess long-term effects.

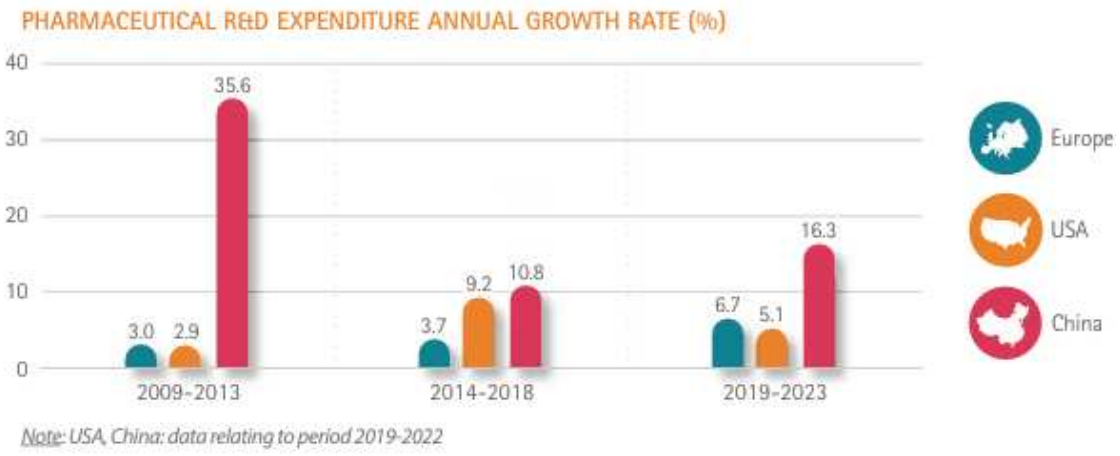
Source: own illustration

9. Annexes

A) Key Indicators of Europe's Pharmaceutical Industry



Source: Statista (2023). Revenue of leading pharmaceutical markets in Europe in 2022. Available at: https://www.statista.com/statistics/458845/european-pharmaceutical-markets-turnover/



Source: EFPIA (2024). Pharmaceutical R&D Expenditure Annual Growth Rate (%). Available at: https://efpia.eu/media/2rxdkn43/the-pharmaceutical-industry-in-figures-2024.pdf

EMPLOYMENT IN THE PHARMACEUTICAL INDUSTRY

EFPIA 2022	Units		Units
Austria	17,915	Latvia	2,681
Belgium	43,501	Lithuania	1,220
Bulgaria	15,750	Malta	1,370
Croatia	6,318	Netherlands	20,000
Cyprus	2,220	Norway	4,500
Czech Rep.	18,000	Poland	30,021
Denmark	39,815	Portugal	8,900
Estonia	380	Romania	33,550
Finland	6,118	Russia	n.a
France	95,867	Slovakia	2,287
Germany	123,475	Slovenia	13,090
Greece	32,637	Spain	50,600
Hungary	34,800	Sweden	15,000
Iceland	900	Switzerland	47,600
Ireland	45,000	Turkey	42,291
Italy	68,600	U.K.	70,000
TOTAL			894,406

Source: EFPIA (2024). The Pharmaceutical Industry: A Key Assest to the European Economy. Available at: https://efpia.eu/media/2rxdkn43/the-pharmaceutical-industry-in-figures-2024.pdf