



Strategies to Increase Patients' Adherence to Digital Therapeutics for Musculoskeletal Diseases: A Narrative Review

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Digital therapeutics (DTx) are a promising intervention for musculoskeletal diseases. However, real-world adherence remains low despite their established clinical efficacy and safety. This study analyzed the factors influencing patient adherence to DTx from four perspectives—DTx-related characteristics, patient-related factors, medical professional-related factors, and health system-related factors—and proposed an actionable strategic framework for each stakeholder group. A comprehensive literature search of PubMed and Google Scholar (January 2014 to December 2024) identified 45 eligible references on adherence to DTx for musculoskeletal diseases, including systematic reviews, randomized controlled trials, case-control studies, and other relevant publications. Key DTx features that affect adherence include demonstrated efficacy and safety, personalization, user-friendly interface design, gamification, reward systems, feedback mechanisms, and technical reliability. Patient-related factors included demographic characteristics, disease type and severity, and digital health literacy. Factors related to medical professionals included their perception of and preference for DTx as well as patient education and training efforts. Health system-related factors included regulatory frameworks, infrastructure, and accessibility. Based on these findings, we developed a strategic framework illustrating how developers, patients, physicians, and health system-level stakeholders can collaborate to improve adherence. These insights may serve as a valuable resource for promoting the adoption and widespread implementation of DTx.

Key Words: Digital therapeutics, musculoskeletal diseases, adherence

INTRODUCTION

Musculoskeletal diseases encompass a broad range of conditions affecting the bones, joints, muscles, and connective tissues.¹ These diseases often cause pain, reduced physical func-

tion, and consequent disability, thereby lowering quality of life.² According to the 2019 Global Burden of Disease report, low back pain was the leading cause of disability attributed to musculoskeletal disorders, with neck pain, osteoarthritis, gout, and rheumatoid arthritis also serving as major contributing conditions.³ The prevalence of musculoskeletal diseases continues to rise with population aging, and the associated social and economic burden from disability remains a global concern.⁴

Digital therapeutics (DTx) are emerging as innovative treatment options for musculoskeletal diseases.⁵ DTx are defined as software as a medical device that deliver evidence-based therapeutic interventions to prevent, manage, or treat medical conditions.⁶ Musculoskeletal diseases are conventionally treated with medications, physical therapy, injections, and surgical interventions. However, with the advancements of big data analytics, information and communication technology, and artifi-

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cial intelligence, DTx have gained increasing attention as potential alternatives to conventional treatment approaches.

Although DTx share many similarities with traditional pharmaceuticals, they are characterized by their ability to overcome spatial and temporal limitations because they are typically accessed via smartphones, tablets, and head-mounted displays (HMDs). Moreover, DTx enable patients to actively engage in their own treatment and receive care tailored for their specific conditions, thereby facilitating a shift from hospital-based to patient-centered care.⁷ As evidence-based therapeutic options expand through DTx, these interventions are expected to help address unmet medical needs and improve the efficiency of healthcare systems.

Research has been conducted on the development of DTx but also on various stakeholders to successfully integrate DTx into healthcare systems.⁸ However, Pear Therapeutics—a company that developed DTx for treating substance use disorders approved by the U.S. FDA—declared bankruptcy in April 2023.⁹ The bankruptcy was attributed to challenges in securing insurance reimbursement for its marketed products and a low patient fulfillment rate of 51%, which hindered continuous patient engagement.¹⁰ Additionally, among DTx listed in Germany’s DiGA directory, only about 80% of patients who received a prescription actually activated the DTx.^{11,12} Although DTx may overcome certain regulatory barriers, these findings suggest that sustained patient utilization remains a critical issue.

Previous studies have primarily focused on the clinical efficacy of DTx, emphasizing outcomes such as pain relief and functional improvement in musculoskeletal diseases.⁵ However, studies on how patients can use DTx continuously and effectively over time are limited.

Therefore, the present study comprehensively analyzed factors influencing adherence to DTx in patients with musculoskeletal diseases from the perspectives of DTx, patients, medical professionals, and the healthcare system. Additionally, practical strategies are proposed for each stakeholder to enhance their adherence.

MATERIALS AND METHODS

Scope

This study defined the concept of adherence to DTx and analyzed the factors influencing adherence by progressively expanding the perspective to include DTx, patients, medical professionals, and the health system. Subsequently, a strategic framework was proposed to enhance patient adherence to DTx.

Data collection

A comprehensive literature search was conducted using PubMed and Google Scholar for articles published between January 2014 and December 2024. The following search string was applied: (“digital therapeutics” OR “DTx”) AND (“adher-

ence” OR “compliance”) AND (“musculoskeletal” OR “musculoskeletal disease” OR “musculoskeletal disorder” OR “musculoskeletal pain”). Systematic reviews, randomized controlled trials, case-control studies, and case reports were included in this review. Additional publications relevant to the scope were identified through manual searching. After removing duplicates, titles and abstracts were screened, and potentially relevant references (n=67) underwent full-text review. References (n=22) were excluded if they were unrelated to the topic, if the full text was unavailable, or if they were published in languages other than English, Korean, or German. Ultimately, 45 studies met the inclusion criteria and were included (Fig. 1).

Ethical considerations

This study was conducted as a literature review of previously published articles and did not involve the collection of new data from human participants, animals, or personal information. Therefore, approval from an Institutional Review Board (IRB) was not required.

RESULTS

Adherence

Definition

The terms “adherence” and “compliance” have often been used interchangeably to describe the extent to which patients follow medical prescriptions. However, an important distinction exists between the two: adherence refers to the patient’s voluntary and active engagement in carrying out the prescribed treatment, whereas compliance implies a more passive act of merely following the physician’s instructions.^{13,14} Given that patients with musculoskeletal diseases are expected to actively

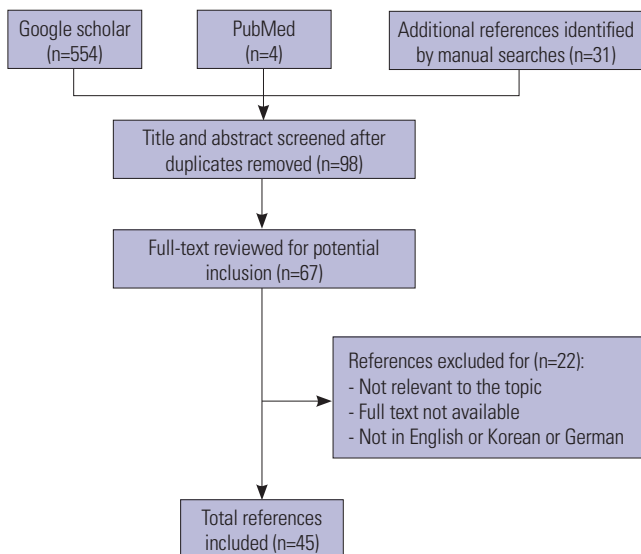


Fig. 1. Flowchart of the reference selection process.

use prescribed DTx, the term “adherence” is more appropriate for describing treatment behavior in this context. Engagement generally refers to the patient’s consistent interaction, whereas retention indicates the duration or continuity of the patient’s involvement in the digital health program.^{15,16} Both terms should be distinguished from adherence.

Methods of measurement and assessment

The methods used to measure adherence can be broadly categorized into direct and indirect approaches. Direct methods involve the analysis of application usage time and log data, whereas indirect methods include patient self-reports, surveys, medical records, patient diaries, and the assessment of clinical efficacy.¹⁷

In DTx designed for insomnia and anxiety disorders, adherence is primarily measured by the completion rate of scheduled therapeutic sessions.¹⁸ Similarly, in rehabilitation programs for musculoskeletal diseases, the completion rate of prescribed exercise repetitions is the most frequently used metric. Parameters such as the number of exercise session attendance, session completion rate, exercise duration, and intensity are commonly assessed. Exercise completion rate refers to the proportion of prescribed individual exercises that patients performed, whereas session completion rate reflects attendance and completion at the session level. Accordingly, a session may be classified as completed even if all prescribed exercises within that session are not fully executed.¹⁹ The most widely accepted criterion for satisfactory adherence is performing at least 80% of the prescribed exercises.¹⁴ Recently, adherence has increasingly been measured using application log data from DTx platforms; however, accurately determining whether patients perform the exercises as prescribed remains a major challenge.

Adherence to DTx for musculoskeletal diseases

Because real-world data (RWD) on adherence to DTx for musculoskeletal diseases remain limited, most available evidence has been derived from clinical studies. Among patients with osteoarthritis who performed smartphone-based exercises, the mean adherence rate was 86.3% at 3 months and 84.1% at 12 months.²⁰ Another study involving patients with osteoarthritis prescribed smartphone-based exercises reported mean adherence rates of 82.7% at 3 weeks and 85.4% at 6 weeks.²¹ Similarly, among patients who performed smartphone-based exercises following flexor tendon repair, the mean adherence rate was 93.2% at 6 weeks.²² Notably, the methods used to assess adherence differed across studies. In the first study, adherence was defined as the percentage of completed activities, including exercises, text or video lessons, and quizzes, on the lesson materials. In contrast, in the second and third studies, adherence was assessed as the percentage of exercises completed out of the total number of prescribed exercises.

Analysis of factors influencing adherence to DTx in musculoskeletal diseases

This section analyzes the factors influencing adherence, initially focusing on the characteristics of DTx and subsequently expanding the scope to encompass patient-, medical professional-, and health system-related factors. The World Health Organization (WHO) has emphasized that adherence is influenced by various factors, including patient-, condition-, therapy-, health system-related, and socioeconomic factors, and that a multidisciplinary approach is required.²³ To achieve the intended therapeutic effects of DTx, adherence is essential, and major stakeholders such as patients, healthcare professionals, and system-level actors must work together.²⁴ Based on the multidimensional approach model proposed by the WHO and recent DTx research, four main domains were identified: 1) DTx-related factors, 2) patient-related factors, 3) medical professional-related factors, and 4) health system-related factors. The factors within each domain were described according to those most frequently reported and emphasized in the reviewed literature.^{8,24}

DTx

Efficacy and safety

Efficacy and safety are considered crucial factors for increasing adherence to DTx.²⁵ The initial development of DTx primarily focused on digitizing existing clinical practice guidelines to establish therapeutic efficacy. For instance, in the management of insomnia, cognitive behavioral therapy (CBT) is recommended over pharmacotherapy, making insomnia DTx a representative example of digitizing a first-line intervention.²⁶ In contrast, for musculoskeletal diseases, such as low back pain and osteoarthritis, exercise therapy combined with pharmacological management constitutes the first-line treatment approach.²⁷⁻²⁹ Therefore, demonstrating the efficacy of DTx for musculoskeletal diseases in the real world may be relatively more challenging, as it requires accounting for the effects of concurrent pharmacological treatments.

DTx are noninvasive interventions and are therefore generally not associated with serious adverse effects. However, because DTx are delivered through hardware such as smartphones, tablets, and HMDs, users may experience eye strain, headaches, and dizziness.³⁰ Therefore, minimizing these adverse effects should remain a primary consideration for the future development of DTx.

Personalization

Delivering individualized treatments tailored to the condition of patients with musculoskeletal diseases is crucial, as symptoms can vary depending on the patient’s baseline health status and disease progression, even among individuals with the same diagnosis.² Moreover, personalized treatment enhances patients’ perception that they are receiving care tailored to their

specific condition, which can improve their awareness of treatment efficacy and promote the sustained use of DTx.³¹

Easy-to-use design

Adherence to DTx can be improved when patients can easily understand and operate these devices. According to a 2023 survey by the Health Insurance Review & Assessment Service (HIRA) in Korea, public awareness of DTx was remarkably low, at only 19.5% (293/1500; n=1500).³² Given this low awareness and the fact that most patients are first-time users of DTx—the software should be designed to be intuitive, user-friendly, and easy to operate. A well-designed interface facilitates rapid adaptation and reduces discomfort, thereby minimizing unnecessary fatigue during treatment.

Gamification

Gamification is most commonly defined as the application of game design elements in non-game contexts.³³ Various game mechanisms, such as feedback, rewards, and social interactions, have been incorporated into digital health applications.³³ Accordingly, gamification elements, such as providing visual or auditory feedback based on the patient's exercise posture or offering rewards upon the completion of exercise sessions, can be integrated into DTx for musculoskeletal diseases.³⁴

The primary advantage of gamification lies in its ability to enhance user engagement with DTx, thereby encouraging sustained patient participation in treatment.³³ By incorporating gamification elements, repetitive exercise-based interventions can be transformed into enjoyable experiences.³⁵ Furthermore, feedback and rewards serve as powerful motivational drivers during the treatment process.

Reward

Rewards are recognized as one of the most effective strategies for inducing behavioral changes.³⁶ In DTx, reward systems typically employ extrinsic incentives, such as badges, points, or level-ups to encourage target behaviors.³⁷ These mechanisms reinforce positive patient behavior and can contribute to improved treatment adherence.³⁸

Short-term rewards provide immediate incentives during or immediately after exercise sessions, thereby enhancing motivation and a sense of accomplishment, which reinforce desired behaviors. Long-term rewards are granted for achieving specific goals or maintaining high engagement levels over a designated period, which motivates patients to sustain their participation in the treatment.³⁹ A donation-based model in which donations are made upon reaching certain exercise goals has also been shown to enhance adherence to mobile app-based exercises.⁴⁰

Feedback system

A feedback system involves analyzing patient behavior and providing information that guides patients toward achieving

improved outcomes. Several DTx techniques for musculoskeletal diseases use pose estimation technology to monitor exercise postures in real time and deliver visual or auditory feedback.^{41,42} This approach helps correct improper postures or movements, thereby maximizing therapeutic effectiveness.

Furthermore, interventions such as alarms have been reported to be effective in improving medication adherence.⁴³ Timely pop-up notifications on smartphones can prompt patients to engage in exercise, thereby promoting sustained participation in physical activity.

Technical problem

Because most DTx are delivered through smartphones or tablets, a stable internet connection is essential. Unstable connectivity can disrupt data transmission and prevent patients from receiving real-time feedback during exercise sessions.

Ensuring security and privacy is fundamental to DTx implementation because protecting personal data is essential for earning patient trust and promoting broader adoption. Inadequate security may expose vulnerabilities, including data breaches, which undermine confidence in both technology and healthcare systems, thereby hindering clinical integration. To mitigate these risks, DTx should incorporate robust encryption, implement strong authentication, and adhere to stringent data-protection regulations.⁴⁴

Patients

Demographic characteristics

To improve patient adherence to DTx, it is essential to consider patients' demographic characteristics. Previous studies have identified demographic factors as key patient-related variables influencing DTx adoption.⁸ This is because patient age, education level, and socioeconomic status are closely associated with patients' attitudes and responses to treatment interventions, as well as with their ability to use digital devices.⁴⁵ In particular, younger individuals with higher health literacy, education, and income tend to adopt DTx more readily.⁸ Because factors such as age and socioeconomic status are difficult to modify, healthcare providers should evaluate whether patients are capable of effectively utilizing DTx when prescribing it.

Types and severity of diseases

Treatment of musculoskeletal conditions varies substantially depending on whether the condition is acute or chronic and on the rate of disease progression. Therefore, DTx should be prescribed according to both disease type and severity. Because DTx for musculoskeletal diseases is primarily designed around exercise therapy, it is typically more suitable for chronic conditions with gradual progression rather than acute illnesses.⁴⁶

Adherence may also vary according to the disease severity. Patients with mild symptoms may demonstrate lower adherence due to relatively minimal pain and reduced motivation for

treatment. Conversely, patients with severe symptoms may experience intense pain and physical limitations which can hinder their ability to use DTx effectively.

Digital health literacy

Digital literacy refers to the ability to understand digital technologies and efficiently search for, evaluate, and utilize information using these technologies.⁴⁷ Digital health literacy extends the concept of digital literacy to the health domain, encompassing the ability to find, comprehend, and assess health information from electronic sources or digital environments and apply this information to address health-related issues.⁴⁸ As DTx are designed based on digital technologies, patients' ability to understand and use these digital tools serves as a critical factor in determining adherence.⁴⁹ In fact, higher levels of digital health literacy have been reported to be associated with an increased likelihood of adopting DTx.⁸

Medical professionals

Perception and preference of DTx

Patients tend to trust and follow the recommendations of medical professionals.⁵⁰ However, many medical professionals have expressed concerns about increasing use of digital technology in healthcare. Approximately 46% of outpatient physicians in Germany worry that digitalization could negatively affect the physician–patient relationship.⁵¹ Similarly, in South Korea, only 50.4% (126/250; n=250) of physicians viewed DTx positively, compared with 51.5% (772/1500; n=1500) of the general population who held favorable opinions.³²

Physicians are generally conservative when adopting new treatment options; therefore, it is critical for them to recognize the added value that DTx can provide relative to conventional therapies.⁵² DTx can significantly improve access to treatment, enable patient-centered care, and enhance the overall efficiency of healthcare systems.⁷ According to a study conducted by the HIRA in South Korea, 78.4% (196/250; n=250) of physicians expressed a willingness to use DTx. Those unwilling to adopt these technologies primarily cited the belief that face-to-face treatment is more effective, as well as concerns regarding the efficacy and safety of DTx.³² Given the potential benefits and clinical value of DTx, efforts should be made by medical professionals to improve awareness, trust, and acceptance of these technologies.

Patient education and training

To enhance adherence to musculoskeletal DTx, healthcare providers should thoroughly educate patients about device operation, therapeutic goals, and expected benefits. This is important, because inadequate understanding of device use can lead to incorrect application and reduced adherence. A survey of physicians in South Korea found that patient education regarding the treatment process was identified as the most

needed form of support, receiving the highest response of 25.6% (64/250; n=250).³² These indicate that current education and training systems for patients remain insufficient, highlighting the need for governments and relevant agencies to establish structured educational programs.

Health system

Regulation

Regulation remains the most frequently discussed policy-related issue concerning the integration of DTx into health systems.^{8,53} This prominence arises because DTx must pass through multiple regulatory stages, including clinical trials, medical device approval, and insurance coverage, before being implemented within health systems. Leading countries in digital health, such as the United States, Germany, and South Korea, are promoting the development of the DTx industry by introducing pre-market authorization, followed by a post-market evaluation framework.⁵⁴

These regulations had a significant effect on patient adherence to DTx. For DTx to be widely adopted within healthcare systems, it is essential to enhance access for healthcare providers and patients, thereby improving treatment adherence. In particular, if DTx are covered by the national health insurance, it can significantly reduce the financial burden on patients. In a recent study, 49.2% (738/1500; n=1500) of respondents emphasized the need for DTx reimbursement, with the most common reason being a reduction in the patients' financial burden [33.7% (249/738; n=738)].³² In South Korea, a reimbursement framework for DTx was established in October 2023, and in the United States, the Centers for Medicare & Medicaid Services introduced the Transitional Coverage for Emerging Technologies pathway in July 2023.⁵⁴ As such, a comprehensive and supportive regulatory system, including expedited review processes and reimbursement, is essential for the effective adoption and expansion of DTx.

Infrastructure and accessibility

To enhance patient adherence, it is essential to establish a system that supports the prescription and management of DTx at all healthcare levels, from general hospitals to primary care clinics. Because patients are frequently referred between healthcare institutions, ensuring continuity of DTx access and prescription during these transitions may improve access to treatment and contribute to maintaining patient adherence.⁵⁵

In real-world clinical settings, when physicians prescribe DTx through electronic medical records (EMR), the prescription data must be transmitted to the DTx provider. Conversely, the data generated during the use of DTx must be returned to the EMR. This process must be repeated for each system, particularly in institutions that use multiple DTx products, which causes operational inefficiency. Accordingly, the development and widespread adoption of a unified platform that facilitates

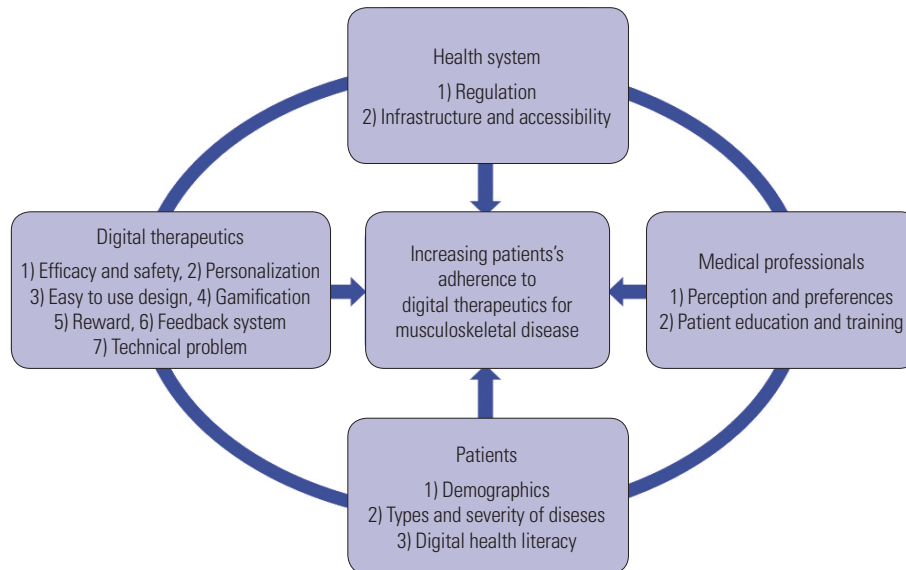


Fig. 2. Framework for strategies to increase patients' adherence to digital therapeutics for musculoskeletal diseases.

smooth integration between EMR and DTx systems is essential to ensure that patients' personal health information is appropriately de-identified and securely protected.

Framework for strategies to increase patient adherence to DTx for musculoskeletal diseases

The factors influencing adherence to DTx are not hierarchical but rather interconnected. Therefore, a strategic framework for improving adherence was developed to encompass the entire process—from the integration of DTx into the health system through physicians' prescriptions for patient utilization (Fig. 2).

From a health system perspective, DTx must first obtain regulatory approval, and the necessary infrastructure should be established to ensure that both medical professionals and patients can easily access these therapies. Subsequently, medical professionals prescribe DTx based on their perceptions and preferences while considering demographic characteristics such as age and type and severity of the disease. At this stage, efforts to enhance physicians' awareness and acceptance of DTx are essential, along with education and training programs aimed at improving patients' digital health literacy to facilitate proper use. In parallel, DTx developers should design their products to improve adherence by carefully considering relevant factors such as efficacy and safety, personalization, user-friendly design, gamification, reward mechanisms, feedback systems, and technical reliability.

DISCUSSION

This study comprehensively reviewed and proposed strategies to enhance adherence to DTx in musculoskeletal diseases. First, the concept of adherence was defined, and methods for its measurement and assessment were summarized. Subse-

quently, strategies to improve adherence were analyzed across four key domains: DTx, patients, medical professionals, and the health system. Furthermore, by presenting an integrating framework that connects these four domains, this study provides a foundation for stakeholders to implement the proposed strategies in real-world clinical practice. The findings are expected to serve as valuable references for promoting the widespread adoption of DTx in clinical practice.

Because RWD on DTx adherence in patients with musculoskeletal diseases remain limited, this review primarily analyzed findings from clinical research. In the reviewed studies, adherence levels were generally high, with rates exceeding 80%.²⁰⁻²² Participants who engaged in digital rehabilitation programs consistently demonstrated higher adherence to exercise therapy than those in the conventional treatment groups. However, adherence reported in clinical trials may have been overestimated due to selection bias during participant recruitment. Additionally, the Hawthorne effect—where participants alter their behavior simply because they are being observed—may have also influenced these results.⁵⁶

In real-world clinical settings, although DTx has been prescribed in several countries, adoption remains limited. In Germany, approximately 374000 prescriptions were recorded over the 3 years up to September 2023, whereas in the United States, the number has been comparatively low.^{57,58} In South Korea, the number of DTx prescriptions appears to be lower than in other countries.⁵⁹ Despite strong evidence supporting the efficacy and safety of DTx in clinical trials, its widespread clinical adoption remains restricted. This limited uptake may be attributed to the small number of medical institutions and professionals prescribing DTx as well as to challenges patients face in maintaining consistent use. Therefore, improving patient adherence is essential for ensuring that DTx becomes a sustainable and effective treatment option, even after regulatory ap-

proval. In this context, an in-depth analysis of the strategies to enhance adherence was conducted.

The proposed strategic framework emphasizes that the four key domains—DTx itself, patients, medical professionals, and the health system—are not hierarchical but closely interconnected. Therefore, efforts by a single stakeholder are insufficient to enhance adherence. Instead, coordinated collaboration among all stakeholders, including government agencies, medical professionals, and DTx developers, is essential to achieve the successful integration and sustained use of DTx in clinical practice.

Kessel, et al.⁹ mapped factors influencing the uptake of DTx, encompassing the DTx itself, patients, health professionals, the health system, and the regulatory environment. Our study proposed a more in-depth strategic framework specifically focused on enhancing adherence to DTx for musculoskeletal diseases, which represents the major strength of this study. This framework emphasizes that adherence among patients with musculoskeletal diseases is not uniform but may vary according to individual characteristics, disease type, and severity, thereby requiring careful consideration. Furthermore, it highlights DTx-specific features particularly relevant to exercise-based interventions, including gamification, rewards, and feedback systems, which play crucial roles in sustaining patient engagement. Finally, given South Korea's single-payer national health insurance system, this study uniquely integrates the health system and regulatory environment within its framework.

Patient age is considered a primary factor influencing adherence to DTx for musculoskeletal diseases. Older adults tend to have lower levels of digital health literacy, and the type and severity of musculoskeletal conditions vary substantially with age. Previous studies have also identified age as a key determinant of adherence to DTx, showing a clear linear decline as age increases, particularly among individuals aged 75 years and older.^{8,20} While age itself is not modifiable, digital health literacy, which is often affected by age, can be improved through education. Therefore, when prescribing DTx, medical professionals should provide sufficient education and training to compensate for age-related decline in adherence. Additionally, developers should design user interfaces that are intuitive and easy to navigate to minimize the negative impact of age on adherence.

Limitation

This study has certain limitations. First, as a narrative review, it involves inherent methodological constraints such as potential selection bias and limited reproducibility. Second, the study did not analyze the factors influencing adherence based on the RWD generated from the patients' actual use of DTx. Consequently, the analysis primarily relied on evidence from clinical trials and previously published literature. Therefore, the proposed strategies should be applied in real clinical settings with careful consideration. As the prescription and use of DTx continue to expand in clinical practice, the use of RWD

is also expected to increase over time. Future studies should use these data to conduct more comprehensive analyses of adherence-related factors and to develop effective strategies.

Another limitation of this study is that it primarily focused on adherence to exercise-based DTx for musculoskeletal diseases. In DTx-targeting conditions such as fibromyalgia or somatic pain, CBT is often incorporated alongside exercise therapy. Improving adherence to CBT may require different strategies that future studies should consider when developing appropriate approaches.

Finally, among the four domains identified in this study, the medical professionals and health system domains were predominantly based on the context of the Korean healthcare system. Although these findings provide valuable insights, they may not be generalizable to other health systems and cultural environments. Therefore, the applicability of these findings to international settings should be interpreted with caution, and further research across diverse populations and health systems is required.

Conclusion

This study analyzed the strategies to enhance adherence to DTx for musculoskeletal diseases across multiple dimensions. It provides specific recommendations to developers, patients, medical professionals, and health systems to facilitate the effective use of DTx. Because adherence is a critical factor in demonstrating the effectiveness of DTx, sustained collaborations among all stakeholders are essential to support patients in maintaining long-term engagement with these interventions. The findings of this study are expected to serve as valuable references for the adoption and widespread implementation of DTx in clinical practice.

AVAILABILITY OF DATA AND MATERIALS

All data referenced in this review were derived from published literature and publicly accessible sources. No new datasets were generated or analyzed in this study.

AUTHOR CONTRIBUTIONS

Conceptualization: Myeonghwan Bang and Jung Hyun Park. **Data curation:** Myeonghwan Bang. **Investigation:** Myeonghwan Bang. **Methodology:** Myeonghwan Bang and Jung Hyun Park. **Project administration:** Myeonghwan Bang and Jung Hyun Park. **Supervision:** Jung Hyun Park. **Visualization:** Myeonghwan Bang. **Writing—original draft:** Myeonghwan Bang and Jung Hyun Park. **Writing—review & editing:** Myeonghwan Bang and Jung Hyun Park. **Approval of final manuscript:** Myeonghwan Bang and Jung Hyun Park.

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