SPECIAL ARTICLE eISSN 2233-9183
J Korean Acad Child Adolesc Psychiatry 2023;34(4):192-203
https://doi.org/10.5765/jkacap.230044

Check for updates

Analysis of the Status and Future Direction for Digital Therapeutics in Children and Adolescent Psychiatry

Haemi Choi[1*], Bora Kim[1,2*], Insoo Kim[3], Jae-Gu Kang[1], Yoonjae Lee[1], Hyowon Lee[1], and Min-Hyeon Park[1]

[1]Department of Psychiatry, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea
[2]Department of Literature and Art Therapy, Konkuk University, Seoul, Korea
[3]Department of Novel, Chung-Ang University Graduate School of Arts Short Course, Seoul, Korea

Digital therapeutics based on software, such as artificial intelligence, virtual reality, games, and smartphone applications, are in the spotlight as new therapeutic alternatives in child and adolescent psychiatry. It draws attention to overcoming conventional therapeutics' limitations, such as toxicity, cost, and accessibility, and encourages patients to participate in the treatment attractively. The growth potential of the digital therapeutics market for psychiatric disorders in children and adolescents in Korea and abroad has been highlighted. Clinical studies and Food and Drug Administration approvals for digital therapeutics have increased, and cases approved by the Ministry of Food and Drug Safety have emerged in Korea. As seen above, digital transformation in child and adolescent psychiatry will change treatment paradigms significantly. Therefore, as this new field has just begun to emerge, it is necessary to verify the effectiveness and scope of the application of digital therapeutics and consider preparing a compensation system and institutional arrangements. Accordingly, this study analyzed the development trends and application status of digital therapeutics in children and adolescents and presented limitations and development directions from the perspective of application in healthcare. Further, the study is expected to identify the utility and limitations of digital therapeutics for children and adolescents and establish effective application measures.

Keywords: Healthcare; Telemedicine; Mental health; Digital technology; Mobile health.

Received: July 11, 2023 / **Revised:** September 6, 2023 / **Accepted:** September 8, 2023
Address for correspondence: Min-Hyeon Park, Department of Psychiatry, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 1021 Tongil-ro, Eunpyeong-gu, Seoul 03312, Korea
Tel: +82-2-2030-2722, Fax: +82-2-2030-2720, E-mail: neominnie00@hanmail.net
*These authors contributed equally to this work.

INTRODUCTION

Digital therapeutics (DTx), based on digital technology, have begun to attract attention as a third therapeutic option to overcome the limitations of conventional therapeutics, such as toxicity, side effects, manufacturing and purchasing costs, and accessibility [1,2]. In particular, as the non-face-to-face medical system was activated owing to the coronavirus disease 2019 (COVID-19) pandemic, the need for and demand for pharmaceutical and medical services through technology-based approaches, such as telemedicine, have rapidly increased. Moreover, the U.S. Food and Drug Administration (FDA) accelerated the adoption of digital solutions, allowing DTx to temporarily approve psychiatric treatment during the COVID-19 pandemic [3]. Moreover, DTx is expected to play a vital role in future healthcare services, showing direct effects on disease prevention, management, and treatment beyond simple health management (monitoring) [4,5].

DTx refers to evidence-based software products directly applied to patients for disease prevention, management, and treatment based on digital technology [6], forming an axis of non-face-to-face medical care and telemedicine [7]. According to the Ministry of Food and Drug Safety of Republic of Korea (MFDS) licensing system, they are classified as medical devices. Notwithstanding, they can also be considered close to medicine when they provide treatment functions similar to conventional medicines by utilizing software [8]. DTx has the advantages of significantly reducing the time and cost of development compared to conventional therapeutics, performing treatment functions through evidence-based treatment methods such as cognitive behavioral therapy, having less toxicity and side effects, and increasing accessibility to data-based individualized treatment [9]. Moreover, because a variety of digital technologies can converge, including artificial intelligence (AI), big data, virtual reality (VR), augmented reality (AR), metaverse, games, and applications, the scope for developing and utilizing therapeutics is broad.

DTx, which provides continuous and personalized treatment with this attractive approach, is emerging as a new treatment method for psychiatric disorders in children and adolescents. In child and adolescent psychiatry, treatment effectiveness can be substantially improved through behavioral interventions, a field in which existing pharmaceutical companies repeatedly fail to develop novel drugs [10]. Hence, products psychiatric disorders account for most DTx products currently being developed [11,12]. Additionally, since child and adolescent psychiatry often requires long-term treatment and a lot of labor and costs in treatment [7,13], the development and demand for DTx that can be used for an extended period at a relatively low cost is expected to continue [7]. Furthermore, by utilizing the functions of DTx, Personal Health Records, including psychiatric data that are classified as sensitive information under the Personal Information Protection Act and cannot be computerized, can be digitized to easily collect, track, and monitor patient data, thereby overcoming the fragmentation of treatment linkage due to the nature of pediatric psychiatry, which requires various treatment linkages and has the advantage of being able to provide more effective medical services [14,15]. Moreover, modern children and adolescents have high access to digital devices because they are a generation that has grown under the influence of the digital society since infancy. Thus, treatment utilizing attractive digital technologies such as games effectively reduces resistance to treatment among children and adolescents and improves their immersion, thereby enhancing the treatment's sustainability, usefulness, and effectiveness.

Notably, DTx for psychiatric disorders in children and adolescents is being developed. Currently, products released with proven effectiveness in children and adolescents include EndeavorRX (Akili Interactive), ATENTIVmynd (ATENTIV), SparkRx (Limbix), and Canvas Dx (Cognoa). EndeavorRX is a DTx approved by the FDA in 2020 to treat children aged 8 to 12 years with attention deficit hyperactivity disorder (ADHD) through immersive video game experiences on smartphones and tablet devices. Additionally, ATENTIVmynd has been developed to improve attention in ADHD, SparkRx to improve symptoms of adolescent depressive disorder, and Canvas Dx to assist in the early diagnosis of autism spectrum disorder (ASD) are being developed. Furthermore, studies and clinical trial results on DTx for various psychiatric disorders in children and adolescents are continuously accumulated to build a foundation. As digital transformation in child and adolescent psychiatry accelerates, the development of DTx for psychiatric disorders in children and adolescents is expected to begin earnestly, resulting in significant changes in the treatment paradigm. The growth potential of DTx for psychiatric disorders in children and adolescents is substantial, and the scope of application of digital technology is expanding. Thus, it is necessary to verify the effectiveness and scope of the application of therapeutics.

Therefore, this study aimed to analyze the development trends and application status of DTx in child and adolescent psychiatry in Korea and abroad. Further, it aimed to present the limitations, development directions, and future tasks of DTx from the perspective of application in healthcare. This study is expected to identify the utility and limitations of DTx in child and adolescent psychiatry and establish effective application measures for DTx in the future.

DEVELOPMENT TRENDS OF DTx IN CHILD AND ADOLESCENT PSYCHIATRY

The Digital Therapeutics Alliance (DTA), launched in 2017, is a nonprofit trade association of industries that developed DTx in 17 countries, including the United States and Europe. Approximately 100 companies participated, including global pharmaceutical companies such as Novartis and Otsuka and companies specializing in DTx, such as Akili Interactive, Big Health, Cognoa, Limbix, and Pear Therapeutics [16]. Furthermore, 13 Korean companies, including AIMMED, MiNDCAFE, and WELT (a spin-off company of Samsung), are also members of DTA [16,17]. DTA divides DTx into three categories depending on its main purpose: disease prevention and health function improvement, disease management, and disease treatment (Table 1) [18]. Additionally, DTx is classified into standalone, augmented, and complementary types depending on the kind that affects disease treatment (Table 2) [19]. Table 3 shows representative DTx in the child and adolescent psychiatry fields approved or provisionally approved overseas [20-54].

The most representative example of a standalone DTx is the reSET, developed by Pear Therapeutics in the United States. The reSET, the world's first DTx approved by the FDA in 2017, is an application for treating addiction to various substances and drugs, such as alcohol, marijuana, and cocaine, in adolescents and adults over 18 years old. It is a program prescribed and used for 12 weeks with existing treatment programs that provide cognitive behavioral therapy through various content. These include text and animation when patients install it on their smartphones and enter information about their condition and drug use [20,21]. In addition to the effectiveness of the therapy itself, it also supports patients in completing existing treatment programs better [21]. Pear Therapeutics has also received marketing approval for reSET-O, an addiction treatment application for narcotic analgesics, and Somryst, a therapeutic for insomnia. It has developed a digi-

Table 1. Classification of digital therapeutics by purposes

Classification	Disease prevention and health function improvement	Disease management	Disease treatment
Regulatory oversight	The extent of regulation depends on local regulatory systems	Validation of efficacy and safety claims is conducted by a national regulatory organization or its equivalent	Validation of efficacy and safety claims is conducted by a national regulatory organization or its equivalent
Level of medical claims	Low to medium-risk claims	Medium to high-risk claims	Medium to high-risk claims
Clinical evidence	Clinical trials and ongoing evidence generation are required	Clinical trials and ongoing evidence generation are required	Clinical trials and ongoing evidence generation are required
Patient access	Nonprescription or Prescription	Nonprescription or Prescription	Prescription
Clinical endpoints	Delivering a therapeutic intervention while supporting product claims with clinical endpoints	Delivering a therapeutic intervention while supporting product claims with clinical endpoints	Delivering a therapeutic intervention while supporting product claims with clinical endpoints

Adapted from Digital Therapeutics Alliance [18], under the permission of Digital Therapeutics Alliance

Table 2. Types of digital therapeutics

Type	Content
Standalone	Designed for independent disease treatment, it can be used either as a replacement for conventional medications or in conjunction with other treatments. This type is prevalent in the field mental health, where mobile apps can deliver cognitive behavioral therapy digitally
Augmented	Designed for use alongside prescribed pharmacological interventions to augment their effectiveness, typically supporting the existing treatment of chronic diseases such as diabetes
Complementary	Designed to complement existing treatments and improve the self-management of health conditions alongside therapeutic medications. This type is prevalent in managing behavioral patterns and lifestyles related to obesity, hypertension, and other important disease factors

The content has been summarized from S3 Connected Health [19]

tal application of cognitive behavioral therapy to treat psychiatric disorders in adolescents and adults [22,23]. Another representative standalone DTx for children and adolescents is SparkRx. SparkRx is a DTx that provides cognitive behavioral therapy to children and adolescents aged 13–22 years with depressive symptoms. Although SparkRx has not been licensed or approved by the FDA, it has received emergency use authorization per the FDA's enforcement policy for DTx to treat psychiatric disorders during the public health emergency called COVID-19. It can be used free of charge without a prescription [24,25]. A treatment program combining cognitive behavioral therapy and behavioral activation protocols was provided for five weeks, and a significant reduction in depressive symptoms was reported in a clinical trial [26].

In addition to smartphone applications, standalone therapeutics provide highly immersive cognitive behavioral therapy in various forms, such as games and VR or AR, for pediatric and adolescent patients. For example, Akili Interactive's EndeavorRx, approved by the FDA in 2020, was the first game to be used as a therapeutic agent for ADHD. EndeavorRx showed improvements in spatial working memory in both children and adolescents with ADHD and typical development aged 8–12 years, indicating that the more severe the ADHD symptoms, the greater the degree of improvement [27,28]. It has been reported that the activity of midline frontal theta, a brain wave related to attention and cognitive control ability, increases while playing the game and is associated with decreased inattention symptoms [29]. In addition to EndeaverRx, game-type DTx for children and adolescents, such as ATENTIVmynd, REThink, MindLight, Mightier, and RECOGNeyes, are either under development or have been developed [32-36]. However, to recognize the effectiveness of game-type therapeutics, the transfer effect should be evaluated and compared before and after the intervention [37-39]. The transfer effect can be determined by improving cognitive functions other than the trained cognitive function and the sustainability of the treatment effect after the end of training [39]. Currently, transfer effects are classified into two distinct categories, namely, near transfer effects and far transfer effects. In particular, when only cog-

Table 3. Representative digital therapeutics in children adolescent psychiatry approved or provisionally approved abroad

Device	Applicant	Target disease	Features	Target age	FDA approval
reSET [20,21]	Pear Therapeutics	Substance use disorder (except opioid)	A mobile application designed to address addiction and dependency issues related to stimulants, alcohol, cannabis, and cocaine. A 12-week (90 days) CBT program prescribed for use in conjunction with an existing therapy program. Its goal is to increase abstinence from substances and improve retention in outpatient therapy. This is the first FDA-cleared DTx for disease treatment	18 years and older	September 14, 2017
reSET-O [22]	Pear Therapeutics	Opioid use disorder	A mobile application designed for treating addiction and dependency on opioids. A 12-week (84 days) CBT program prescribed and used as an adjunct outpatient treatment alongside transmucosal buprenorphine and contingency management. Its aim is to enhance retention in outpatient treatment using buprenorphine	18 years and older	December 10, 2018
Somryst [23]	Pear Therapeutics	Chronic insomnia	A mobile application designed to enhance sleep quality. A 9-week CBT program available by prescription only. It comprises six treatment modules focused on CBT concepts, including sleep restriction and consolidation, stimulus control, and cognitive reconstruction. It leads to significant and enduring improvements in insomnia symptoms. It serves as a complement to current therapy	22 years and older	March 26, 2020
SparkRx [24-26]	Limbix	Depression	A mobile application designed to alleviate depression symptoms. It provides a neurobehavioral intervention (CBT–behavioral activation) as an adjunct treatment for depression symptoms. This intervention spans five levels, aiding users in understanding depression and acquiring coping skills to manage their symptoms	13–22 yrs	Not cleared or approved (under the FDA's enforcement policy, a prescription is not required)
EndeavorRx [27-29]	Akili Interactive	ADHD	An action video game designed to improve attention function in children primarily diagnosed with inattentive or combined-type ADHD. It digitally assesses sustained and selective attention and provides a treatment program that challenges a child's attention control during gameplay. This requires concentration and the ability to multitask. It represents the first and the only FDA-authorized prescription treatment for children with ADHD delivered through a video game	8–12 yrs	June 15, 2020
AKL-T02 [30]	Akili Interactive	ASD	An action video game designed to address cognitive dysfunction, attention-related functions, and associated symptoms in children with ASD. This game has been adapted for use with ASD, incorporating specific and simultaneous sensory and motor stimuli to those found in EndeavorRx. It has demonstrated high acceptability and engagement as a treatment, along with improvements in attention-related measures	9–13 yrs	Not cleared or approved

Table 3. Representative digital therapeutics in children adolescent psychiatry approved or provisionally approved abroad (continued)

Device	Applicant	Target disease	Features	Target age	FDA approval
AKL-T03 [31]	Akili Interactive	MDD	A video game aimed at enhancing cognitive function in patients with MDD when used in conjunction with antidepressant medication. It utilizes a multitasking interface, presenting two simultaneous tasks that players must complete. It is specifically designed to offer interference management training with a flexible and personalized level of difficulty, achieved through the application of proprietary algorithms similar to those used in EndeavorRx. It has shown significant improvements in sustained attention	22–55 yrs	Not cleared or approved
ATENTIVmynd [32]	ATENTIV	ADHD	A brain-computer interface therapy combines a headband with mounted dry EEG sensors and a tablet-based game. This consists of a series of virtual world adventures spanning 4 to 8 weeks. During the game, patients face multiple challenges aimed at teaching cognitive skills related to attention and impulse inhibition. The therapy has led to a sustained and significant reduction in the primary symptoms of ADHD, along with a significant improvement in academic performance	6–12 yrs	Not cleared or approved
REThink [33]	Babes-Bolyai University	Emotion regulation	An application designed for tablets, adapted as a prevention tool for children and adolescents to acquire emotion regulation skills. Its purpose is to build psychological resilience by teaching healthy strategies to cope with dysfunctional negative emotions. This is based on the principles of Rational-Emotive Behavior Therapy and Education intervention	10–16 yrs	Not cleared or approved
MindLight [34]	Play Nice Institute	Anxiety and depression	A game that employs three evidence-based strategies to reduce anxiety in children and adolescents. These strategies include neurofeedback training, exposure training, and attention bias modification. The game offers 8–12 weeks of CBT in as little as 5.5 hours of gameplay, with real-time relaxation states measured by the EEG headset	10–16 yrs	Not cleared or approved
Mightier [35]	Boston Children's Hospital and Harvard Medical School	Emotion regulation	A game application designed to facilitate the learning emotional regulation and the practice of calming skills. Users wear a heart rate sensor while playing games. This game demands relaxation while engaging executive functions to complete short reaction tasks, expanding the typical biofeedback paradigm. The program is grounded in CBT, aiming to reduce the need for psychiatric medication and assist in developing emotional control	6–14 yrs	Not cleared or approved
RECOGNeyes [36]	University of Nottingham	ADHD	A computer game played using the eyes as the game controller. The interactive game incorporates eye-tracking technology, which appears to enhance the visual attention system	8–15 yrs	Not cleared or approved

Table 3. Representative digital therapeutics in children adolescent psychiatry approved or provisionally approved abroad (continued)

Device	Applicant	Target disease	Features	Target age	FDA approval
Abilify MyCite [42]	Otsuka Pharmaceutical Co. and Proteus Digital Health	Schizophrenia	A prescription smart pill equipped with built-in technology. The aripiprazole tablets, embedded with sensors, send signals to a wearable Bluetooth patch that connects to a smartphone, enabling the viewing of daily data. This can be used for the treatment of schizophrenia, the acute treatment of manic and mixed episodes associated with bipolar I disorder and an add-on treatment for depression	24 years and older	November 13, 2017
Feel Therapeutics solution [12,43,44]	Feel Therapeutics	MDD, GAD	A remote mental health support program designed to improve emotional awareness and self-regulating skills. This program deploys the Feel Emotion Sensor, Feel Mobile App, and Feel Mental Health Biomarkers platform. It combines evidence-based approaches, including CBT, with psychophysiological data, specifically focusing on emotion-related information from the autonomic nervous system	18 years and older	Not cleared or approved
Canvas Dx [45,46]	Cognoa	ASD	A diagnostic solution designed to assist healthcare providers to diagnose or rule out autism in children. It collects parent or caregiver questionnaires, videos of the child's interactions, and clinician questionnaires, and then provides clinical judgements through algorithm evaluation. This marks the first FDA-approved digital therapeutics for children with ASD	18–72 months	July 2, 2021
EarliPoint Evaluation [47]	EarliTec	ASD	Utilizing the significant of looking behavior as an indicator of neurodevelopmental vulnerability. It tracks and evaluates children's gaze while they watch videos, comparing it to typical behavior. It offers caregivers and healthcare providers information regarding potential developmental vulnerabilities to aid in the diagnosis and assessment of ASD	16–30 months	June 10, 2022
Sleepio [48]	Big Health	Insomnia	A mobile and web-based digital sleep improvement program, clinically proven to relaxation and enhance sleep quality. Comprising six sessions, each averaging 20 minutes, the program can be completed in weeks, alongside a daily sleep diary that takes under 5 minutes to complete. This program helps reduce the need for GP appointments and prescription costs by offering immediate access to CBT for insomnia in situations where face to face CBT is unavailable. It does not replace the care of a medical provider or the patient's prescribed medication	18 years and older	Not cleared or approved (USA: under the FDA's enforcement policy, a prescription is not required; UK: Class I CE mark)
Daylight [49]	Big Health	GAD	A mobile and web-based digital anxiety management program, based on CBT. It only requires 10 minutes per day. By offering instance access to CBT for insomnia in cases where in-person CBT is not available, it helps reduce the need for GP appointments and prescription costs. It is not a substitute for the care of a medical provider or the patient's prescribed medication	18 years and older	Not cleared or approved (USA: under the FDA's enforcement policy, a prescription is not required; UK: Class I CE mark)

Table 3. Representative digital therapeutics in children adolescent psychiatry approved or provisionally approved abroad (continued)

Device	Applicant	Target disease	Features	Target age	FDA approval
Deprexis [50]	GAIA	Depression	An internet-based software platform accessible 24/7 on any device, designed to enhance depression symptoms when used as an adjunctive therapy. It offers a 12-week program with CBT-based support. The platform employs AI to facilitate interaction with a therapist and provide personalized feedback and strategies for managing depressive symptoms	18 years and older	Not cleared or approved (USA: under the FDA's enforcement policy, a prescription is not required; Germany & Switzerland: Class I CE mark)
FreeSpira [51]	Palo Alto Health Sciences	PTSD, panic disorder, panic attack	A digital panic attack program incorporated proprietary sensors, physiological feedback displays, and coaching to synchronize breathing and normalize CO_2 and respiratory rates over a 28-day course. It aims to reduce symptoms and emergency medical care needs. Patients receive training from clinicians or Freespira coaches and follow a home-based protocol with two 17-minute breathing sessions daily for one month, including four weekly virtual coaching sessions	22 years and older	August 23, 2018
Nightware [52]	Nightware	PTSD	A prescription digital therapeutic system designed to reduce sleep disturbances related to nightmare disorder or nightmares stemming from PTSD. When a nightmare is detected, the device delivers brief vibrations to interrupt the nightmare without fully waking the patient. It is the first FDA-cleared prescription DTx designed to enhance sleep	22 years and older	November 6, 2020
Vorvida [53]	GAIA	Alcohol abuse	A web-based software program spanning 180 days, accessible 24/7 on any device. It utilizes AI to interact with a therapist, providing personalized feedback and strategies for managing drinking behaviors. The program has shown a significant reduction in average daily alcohol consumption at 3 and 6 months	18 years and older	Not cleared or approved (under the FDA's enforcement policy, a prescription is not required)
PEAR-004 [54]	Pear Therapeutics	Schizophrenia	A mobile application-based program designed to improve the symptoms and functioning of individuals with schizophrenia. It deploys a combination of social skills training, CBT for psychosis, and helping in the management of drug treatment	18 years and older	Not cleared or approved (under the FDA's enforcement policy, a prescription is not required)

ADHD, attention deficit hyperactivity disorder; AI, artificial intelligence; ASD, autism spectrum disorder; CBT, cognitive behavioral therapy; CO_2, carbon dioxide; DTx, digital therapeutics; EEG, electroencephalography; FDA, Food and Drug Administration; GAD, generalized anxiety disorder; GP, general practitioner; MDD, major depressive disorder; PTSD, post-traumatic stress disorder

nitive functions similar to the directly trained cognitive functions are improved, and as a far transfer effect, cognitive functions that are not closely related are improved [39]. To date, no reported cases of the far-transfer effect exceed the near-transfer effect in game-type DTx [40,41]. As such, there is insufficient evidence to report transfer effects to improvements in cognitive functions other than those trained or whether the effectiveness of DTx is maintained long-term after training is completed.

An example of an augmented DTx is the Abilify MyCite of Otsuka. It is a method of recording and managing whether and when to take a drug by inserting a sensor into Abilify (Apriqizole), a therapeutic for schizophrenia [42]. This system manages a patient's medication status by sharing it with the patient, parents or caregivers, and physicians. Moreover, the Feel Therapeutics solution of Feel Therapeutics, classified as an augmented type of medication management, is a DTx managing stress using biomarkers [12]. Data was obtained via a wearable band with an integrated sensor measuring heart rate, mood, sleep, and cognitive function. Based on the data, the mobile application connected to the band provides personalized coaching and biological indicators to assist users in improving their emotional stability [43,44].

Finally, a representative example of a complementary DTx is Canvas Dx, developed by Cognoa. Canvas Dx was the first DTx for children with ASD approved by the FDA in 2021 and was developed utilizing AI technology to assist in diagnosing ASD in children aged 18–72 months at risk of developmental delay [45,46]. It collects parent or caregiver questionnaires, videos of the child interacting, and clinician questionnaires, and provides diagnostic results for clinical judgment through algorithm evaluation [46]. Additionally, following Canvas Dx, the EarliPoint Evaluation of EarliTec, an ASD diagnosis-assisted DTx, was approved by the FDA in 2022. EarliPoint Evaluation tracks and assesses the gaze of children aged 16-30 months while they watch videos, comparing their behavior to typical patterns. This is based on the significance of looking behavior as an essential indicator of neurodevelopmental vulnerability. This informs parents, caregivers, and healthcare service providers about potential developmental vulnerabilities [47]. DTx has the advantage of preventing delayed diagnosis and improving prognosis by intervening during the critical period, as ASD is a disorder for which early diagnosis and intervention are crucial.

As mentioned above, the development of DTx in psychiatry, including child and adolescent psychiatric disorders, is highly active and rapidly increasing, especially in the United States and Europe. In addition to the positive evaluation of the effectiveness and marketability of DTx, support policies for DTx are being expanded in Korea, accelerating the research and development of DTx in psychiatry. The MFDS approved the AIMMED Somzz as the first DTx in Korea in 2023. Somzz is a DTx that implements cognitive behavioral therapy techniques in mobile applications to improve insomnia symptoms. This application is designed for patients with chronic insomnia, and its core principle is to improve the patient's insomnia symptoms through a doctor's prescription. It achieves this by providing sleep habit education, implementing behavioral interventions, and delivering real-time feedback through the Somzz application for 6–9 weeks [55]. In a clinical trial, a significant improvement was found in insomnia severity before and after using the Somzz app. The results of the safety and effectiveness evaluation of the innovative medical technology of cognitive behavioral therapy for patients with chronic insomnia using the therapeutic have been revised and announced. Thus making temporary non-reimbursable prescriptions possible for three years from June 1, 2023 [56]. Following Somzz, WELT-I obtained approval from the MFDS as the second DTx for insomnia in Korea. WELT-I is also a DTx that implements cognitive behavioral therapy for insomnia into a mobile application, which improves insomnia symptoms by providing sleep restriction therapy, sleep hygiene education, cognitive restructuring, and relaxation therapy for eight weeks depending on sleep patterns when an insomnia patient installs WLET-I prescribed by a doctor [57].

In addition to Somzz and WELT-I, which can be classified as representative standalone DTx utilizing cognitive behavioral therapy techniques in Korea, clinical trials of DTx in psychiatry for children, adolescents, and adults are in progress. These preparations encompass various stages, including game-based improvement of attention deficits in pediatric patients with ADHD and ameliorating depression in patients with depressive disorder using VR or AR technology (Table 4) [58]. Most DTx currently in clinical trials with official approval in Korea are cognitive therapy software. Further, their scope of use is expanding, including the improvement of alcohol addiction disorder, nicotine addiction, improvement of symptoms of mild cognitive impairment, and attention function in ADHD.

Cognitive behavioral therapy mechanisms are widely used in psychiatry in Korea and abroad, especially in developing DTx for psychiatric disorders in children and adolescents. In clinical practice guidelines, cognitive behavioral therapy is recommended as the primary treatment. In addition, it has the advantage of treating various diseases and symptoms by delivering clinically proven cognitive behavioral therapy techniques through digital methods, such as applications and games, resulting in high accessibility and scalability. Moreover, the effectiveness of online-based cognitive behavioral therapy in improving depressive disorders and anxiety dis-

Table 4. Digital therapeutics in child and adolescent psychiatry approved clinical trials from MFDS*

Device	Applicant	Target disease	Clinical trial phase	MFDS approval
Minds.NAVI	MINDsAI	MDD	Pivotal study	November 3, 2021
CHEEU.Forest	MINDsAI	MDD	Pivotal study	December 23, 2021
Anxeilax	HAII	GAD	Confirmatory clinical study	December 30, 2021
D-kit/EF1	DoBrain	Mild intellectual disorder, borderline intellectual functioning	Pivotal study	October 20, 2022
ALCO-THERA	Medimind	Alcohol abuse	Confirmatory clinical study	October 20, 2022
OMNFIT DTx MDD	Omni C&S	MDD	Confirmatory clinical study	November 29, 2022
Neuro-World	WOORI SOFT	ADHD	Pivotal study	December 1, 2022
AttnKare-D	Hippo T&C	ADHD	Confirmatory clinical study	January 6, 2023
No official name (CBT-based)	WELT	Eating disorder	Confirmatory clinical study	January 17, 2023
NDTx-01	Neudive	ASD or SCD	Pivotal study	February 22, 2023
No official name (metaverse-based)	DoBrain	High-functioning ASD	Pivotal study	March 23, 2023
NICO-THERA	Medimind	Nicotin abuse	Confirmatory clinical study	April 10, 2023
BlueKare-T	Hippo T&C	Depression	Confirmatory clinical study	June 8, 2023

*these cases are referenced from data retrieved between 2021 Sep 1 and 2023 Jul 7 from MFDS [58]. ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; CBT, cognitive behavioral therapy; GAD, generalized anxiety disorder; MDD, major depressive disorder; MFDS, Ministry of Food and Drug Safety of Republic of Korea; SCD, social communication disorder

orders in children and adolescents has been proven. Accordingly, to date, DTx for children and adolescents has mainly been developed focusing on cognitive behavioral therapy for depression, anxiety, obsessive-compulsive disorder, disruptive behavior disorder, drug abuse, eating disorders, and body image problems. However, there is insufficient evidence on the long-term effects of DTx, and the mechanism of this effect is often not elucidated, even when the treatment effects are identified. Hence, studies have been performed to elucidate treatment mechanisms and are continuously being conducted to overcome the limitations of DTx. For example, ATENTIVmynd used resting-state functional magnetic resonance imaging to measure the brain network before and after treatment. As a result, it was suggested that one treatment mechanism could improve the inattention symptom and internalizing problems in children with ADHD by reorganizing the salience network associated with focusing attention on essential stimuli [59]. Furthermore, brain maturation can be promoted by reorganizing brain networks. However, this study also has limitations because the sample size was small, and long-term follow-up is required [59]. Despite these limitations, DTx is likely to be used as a treatment tool in the future because the study results are encouraging for preventing and treating psychiatric disorders in children and adolescents.

DEVELOPMENT DIRECTIONS OF DTx

DTx in child and adolescent psychiatric disorders not only has excellent accessibility but also has the obvious advantages of low cost, low risk, and overcoming the fragmentation of child psychiatric treatment linkage. Thus, it is expected to grow in the future while overcoming physical limitations, such as medical location, time, and human resource availability. However, because we are currently in a transitional period in which rapidly developing digital technology is permeating the medical community, the direction in which digital technology will be accepted and regulated is crucial. As this new field has just begun to emerge, it is clear that there are various areas of controversy and matters to consider.

First, because objective proof of effectiveness is insufficient, there is an urgent need to verify its additional effectiveness. For instance, game-type DTx needs to be confirmed for transferability (transfer effect, persistence of treatment, and spread of effects to adjacent functions) in addition to short-term effectiveness indicators. Additionally, as a new field has recently emerged, there is still insufficient evidence on whether the effectiveness of DTx is maintained in the long term. Further, the possibility of long-term side effects from using digital technologies, such as audiovisual and electrical stimulation, should be considered. In particular, DTx is also used to rehabilitate cranial nerve disorders such as Alzheimer's disease, Parkinson's disease, and stroke and can induce brain neuroplasticity. Therefore, it is necessary to examine how DTx affects brain development and maturation. Moreover, DTx emphasizes personalized treatment. However, it is difficult to exclude the influence of confounding effects owing to in-

dividual characteristics that can affect treatment, even though it is challenging to differentiate and classify patients using digital technology. Therefore, high-quality, real-world evidence, clinical verification, and follow-up evaluations are required.

Second, DTx has the advantage of overcoming the limitations of accessibility as an axis of telemedicine. However, issues of accessibility and compliance with DTx should be considered. DTx is only effective when it is used. It is more valuable than medication adherence because usage records can be checked electronically. The fulfillment rate can affect product upgrades based on real-world data, real-world evidence, and value-based evaluations derived from the fulfillment rate. Specifically, the real-world fulfillment rate is essential for patients, healthcare professionals, companies, and related organizations, including improving treatment effectiveness and generating corporate profits. However, even in overseas countries where the DTx market is active, there are minor problems in the distribution process of DTx. These include application payment procedures, authentication procedures, and content access, which are difficulties using DTx. Even if children and adolescents are familiar with digital technology, there may be difficulties in accessing DTx themselves if the parents or caregiver assists in use or the actual user is not familiar with digital technology. Moreover, according to the 2022 first-quarter performance data released by Pear Therapeutics, an American DTx company considered a successful case of DTx. The total number of prescriptions for the three developed products (reSET, reSET-O, and Somryst) was more than 9200, and the fulfillment rate was 57% (percentage of completing an application to the end). Although this is a 6% increase compared to the fulfillment rate disclosed in 2021, it is still an insufficient result. Thus, as DTx is a new treatment area, measures to raise user awareness and improve accessibility to DTx within app services should be prepared. Additionally, it is necessary to put efforts such as increasing usability by improving the internal design of the app, continuously managing it, and establishing an educational model.

Third, DTx has been approved in Korea because of the rapid improvement in the approval system by the MFDS. Nevertheless, there are still no management mechanisms for DTx, such as determining treatment prices, calculating physicians' prescribing fees, health insurance applications, and follow-up management. This limits its actual use and market growth. Pear Therapeutics, the first publicly traded DTx company, went bankrupt in 2023 because it failed to provide benefits in the United States national health insurance system. It has been over 5 years since Pear Therapeutics received FDA approval. However, its sales growth has inevitably been slow due to limited application to national or private insurance in the United States and limitations in profit generation. Thus, an innovative compensation system is required at the government level. The Ministry of Health and Welfare recently reported and discussed health insurance application guidelines that would allow DTx patients to receive preliminary benefits. In particular, through an innovative medical technology assessment, track and pay a service fee to physicians who prescribe them at the relevant fee and a usage fee to companies. The bankruptcy of Pear Therapeutics, the first publicly traded DTx company, underscores the importance of promptly addressing various conditions to ensure patients can benefit from innovative treatment technologies. These conditions may include the social consensus required for prescription, the calculation of insurance fees for both prescribers and users, and the designation of control towers.

Finally, regulatory authorities may need to move away from conventional regulatory methods and realistically ease regulations to promptly introduce rapidly changing digital technologies. However, there is a need to acquire more expertise by training experts within the regulatory agencies and have the capabilities and infrastructure to verify DTx effectively. The process of developing DTx is low-cost and low-risk. Hence, if companies without sufficient preparation or expertise use deregulation to create substandard digital therapeutic products indiscriminately, the damage will ultimately fall on patients, resulting in increased distrust of DTx. Furthermore, many companies have attempted to enter the DTx market as a blue ocean. However, this may lead to failure due to various practical limitations. As the wearable device market proliferates and declines, the DTx market may decline quickly.

CONCLUSION

The number of related clinical studies and cases receiving FDA approval in child and adolescent psychiatry increases. Thus, DTx, which treats patients using software such as AI, VR, games, and smartphone applications, is in the spotlight as a novel therapeutic alternative. Children and adolescents with psychiatric disorders often require long-term treatment, which is labor-intensive and expensive. Hence, the demand for DTx will continue to increase because it provides personalized and effective treatment at a relatively low cost. Moreover, unlike medications or injections, DTx opens up significant market opportunities for software development startups because of its scalability, as it can be distributed to millions of people simultaneously. From the perspective of existing pharmaceutical companies, investing in and partnering with DTx companies that require relatively less development time and cost, are less invasive, and can assist or enhance the ef-

fectiveness of existing drugs can be a new business opportunity. As mentioned above, the DTx market's growth potential in psychiatry, including children and adolescents, has been substantially highlighted. Hence, it is predicted that the potential for future growth will be high, and it is possible to be used as an efficient treatment tool. This field has just begun to emerge. It will be necessary to consider the direction to accept and regulate digital technology, such as verifying the effectiveness and scope of the application of therapeutics, innovative compensation systems, and institutional preparation. Accordingly, this study examined the current status of DTx in children and adolescents in Korea and abroad and considered its limitations and development directions from the perspective of its application in healthcare. Based on this study, we believe it can be used to identify the utility and limitations of DTx in child and adolescent psychiatry from the perspective of application in healthcare settings. Further, it can be employed to establish effective application measures for DTx in the rapidly growing digital healthcare technology.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Min-Hyeon Park. Data curation: Haemi Choi, Bora Kim, Insoo Kim, Jae-Gu Kang, Yoonjae Lee, Hyowon Lee. Funding acquisition: Min-Hyeon Park. Investigation: all authors. Project Administration: all authors. Supervision: Min-Hyeon Park. Visualization: Haemi Choi. Writing—original draft: Haemi Choi, Bora Kim. Writing—review & editing: Haemi Choi.

ORCID iDs

Haemi Choi	https://orcid.org/0000-0002-8946-4666
Bora Kim	https://orcid.org/0000-0003-2827-6888
Insoo Kim	https://orcid.org/0000-0002-2087-3066
Jae-Gu Kang	https://orcid.org/0000-0003-1300-8557
Yoonjae Lee	https://orcid.org/0009-0009-1911-5776
Hyowon Lee	https://orcid.org/0009-0005-0809-0228
Min-Hyeon Park	https://orcid.org/0000-0002-1731-1388

Funding Statement

This study was supported by a grant from the Game Science Forum in South Korea and by the Technology Innovation Program (grant PC20ONDI0074; AI [artificial intelligence]-Driven Global PHR [personal health record] Pediatric Developmental Disability Management/Treatment Platform) funded by the Ministry of Trade, Industry, and Energy, Korea. The funders played no role in the study design, data collection and analysis, publication decision, or manuscript preparation.

REFERENCES

1) **Lee YS, Kim YS.** A study on digital therapeutics: cases analysis and suggestion. J Digit Contents Soc 2023;24:303-312.
2) **Ahn SH.** Digital therapeutics trends. Seongnam: Korea Bio Economy brief;2020. p.1-5.
3) **Park BH.** Digital therapeutics developments trends. Seongnam: Bio Economy Brief;2022. p.1-8.
4) **Kim JW, Jang KJ, Hwang EH.** Digital therapeutics. Eumseong: KISTEP Technology Trend Brief;2020. p.1-36.
5) **Park AS, Lee SM.** Current status analysis and development direction of digital therapeutics. Daejeon: ETRI Insight;2020. p.1-63.
6) **Digital Therapeutics Alliance.** DTA: digital therapeutics industry report 2018 [Internet]. Arlington, VA: Digital Therapeutics Alliance [cited 2023 Jul 7]. Available from: https://dtxalliance.org/2018/10/23/dtaindustryreport2018/.
7) **Korean Academy of Child and Adolescent Psychiatry.** Adolescent development and psychiatry. 2nd ed. Paju: Koonja;2021. p.738-753.
8) **National Biotech Policy Research Center.** Digital therapeutics development trends [Internet]. Daejeon: National Biotech Policy Research Center [cited 2023 Jul 7]. Available from: https://www.bio-in.or.kr/board.do?cmd=view&bid=issue&num=291399.
9) **Cho YJ, Kim HS.** Digital therapeutics industry trends and outlook. Daejeon: BioINdustry;2022. p.1-13.
10) **Park JH, Song SJ, Bae MC.** Digital therapeutics technology trends and industry outlook. Daegu: KEIT PD Issue Report;2020. p.76-91.
11) **Sim JY, Shin JY, Han TH, Kim ML, Lee JB.** Establishment of policies for the growth of the digital therapeutics industry based on a stakeholder survey. HIRA Res 2022;2:47-56.
12) **Son JH, Yang SH, Jung IY.** The status and outlook of digital therapeutics [Internet]. Seoul: Korea Insurance Research Institute [cited 2023 Jul 7]. Available from: https://www.kiri.or.kr/report/reportList.do?docId=354589&catId=4.
13) **Suryavanshi MS, Yang Y.** Clinical and economic burden of mental disorders among children with chronic physical conditions, United States, 2008–2013. Prev Chronic Dis 2016;13:E71.
14) **Moon SH.** Eunpyeong St. Mary's Hospital, developed pediatric developmental disability management platform. Medicaltimes 2022 Dec 12.
15) **Park JY, Han MS.** Policy and industry trends on DTx in major countries. Cheongju: Health Industry Brief;2023. p.1-40.
16) **Digital Therapeutics Alliance.** DTA members [Internet]. Arlington, VA: Digital Therapeutics Alliance [cited 2023 Jul 7]. Available from: https://dtxalliance.org/engage/dta-members/.
17) **Korea Medical Devices Industry Association.** KMDIA, signed MOU with Digital Therapeutics Alliance [Internet]. Seoul: Korea Medical Devices Industry Association [cited 2023 Jul 7]. Available from: https://www.kmdia.or.kr/board/board_10V.asp?mode=VIEW&bid=bodo&bidsrl=24&bidssrl=0&intseq=12699.
18) **Digital Therapeutics Alliance.** DTx product categories [Internet]. Arlington, VA: Digital Therapeutics Alliance [cited 2023 Jul 7]. Available from: https://dtxalliance.org/wp-content/uploads/2021/01/DTA_FS_DTx-Product-Categories_010521.pdf.
19) **S3 Connected Health.** Digital therapeutics: pharma's threat or opportunity [Internet]. Dublin: S3 Connected Health [cited 2023 Jul 7]. Available from: https://www.s3connectedhealth.com/resources/white-papers/digital-therapeutics-pharmas-threat-or-opportunity.
20) **Business Wire.** Pear therapeutics announces inclusion of reSET® and reSET-O® on the January 2023 Florida medicaid preferred drug list [Internet]. San Francisco, CA: Business Wire [cited 2023 Jul 7]. Available from: https://www.businesswire.com/news/home/20230118005318/en/Pear-Therapeutics-Announces-Inclusion-of-reSET%C2%AE-and-reSET-O%C2%AE-on-the-January-2023-Florida-Medicaid-Preferred-Drug-List.
21) **U.S. Food and Drug Administration.** De novo classification request

for reSET [Internet]. Silver Spring, MD: U.S. Food and Drug Administration [cited 2023 Jul 7]. Available from: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160018.pdf.
22) **Christensen DR, Landes RD, Jackson L, Marsch LA, Mancino MJ, Chopra MP, et al.** Adding an internet-delivered treatment to an efficacious treatment package for opioid dependence. J Consult Clin Psychol 2014;82:964-972.
23) **Ritterband LM, Thorndike FP, Ingersoll KS, Lord HR, Gonder-Frederick L, Frederick C, et al.** Effect of a web-based cognitive behavior therapy for insomnia intervention with 1-year follow-up: a randomized clinical trial. JAMA Psychiatry 2017;74:68-75.
24) **Limbix Health, Inc.** SparkRx [Internet]. San Francisco, CA: Limbix [cited 2023 Jul 7]. Available from: https://www.sparkrx.com/patients.
25) **Limbix Health, Inc.** A CBT-based mobile intervention as first line treatment for adolescent depression during COVID-19. Bethesda, MD: ClinicalTrials.gov [cited 2023 Jul 7]. Available from: https://clinicaltrials.gov/ct2/show/NCT04524598.
26) **McCauley E, Gudmundsen G, Schloredt K, Martell C, Rhew I, Hubley S, et al.** The adolescent behavioral activation program: adapting behavioral activation as a treatment for depression in adolescence. J Clin Child Adolesc Psychol 2016;45:291-304.
27) **Kollins SH, Childress A, Heusser AC, Lutz J.** Effectiveness of a digital therapeutic as adjunct to treatment with medication in pediatric ADHD. NPJ Digit Med 2021;4:58.
28) **Davis NO, Bower J, Kollins SH.** Proof-of-concept study of an at-home, engaging, digital intervention for pediatric ADHD. PLoS One 2018;13:e0189749.
29) **Gallen CL, Anguera JA, Gerdes MR, Simon AJ, Cañadas E, Marco EJ.** Enhancing neural markers of attention in children with ADHD using a digital therapeutic. PLoS One 2021;16:e0261981.
30) **U.S. Securities and Exchange Commission.** Form 10-K [Internet]. Washington, DC: U.S. Securities and Exchange Commission [cited 2023 Jul 7]. Available from: https://s201.q4cdn.com/524504872/files/doc_financials/2022/q4/b70a1a5d-b856-42a6-9d89-0ffac61e1f74.pdf.
31) **Keefe RSE, Cañadas E, Farlow D, Etkin A.** Digital intervention for cognitive deficits in major depression: a randomized controlled trial to assess efficacy and safety in adults. Am J Psychiatry 2022;179:482-489.
32) **Lim CG, Lee TS, Guan C, Fung DS, Zhao Y, Teng SS, et al.** A brain-computer interface based attention training program for treating attention deficit hyperactivity disorder. PLoS One 2012;7:e46692.
33) **David OA, Predatu RM, Cardoș RAI.** A pilot study of the REThink online video game applied for coaching emotional understanding in children and adolescents in the therapeutic video game environment: the feeling better resources game. J Evid Based Psychother 2018;18:57-67.
34) **Wijnhoven LA, Creemers DH, Engels RC, Granic I.** The effect of the video game Mindlight on anxiety symptoms in children with an autism spectrum disorder. BMC Psychiatry 2015;15:138.
35) **Mightier.** Mightier main page [Internet]. Boston, MA: Mightier [cited 2023 Jul 7]. Available from: https://www.mightier.com/.
36) **García-Baos A, D'Amelio T, Oliveira I, Collins P, Echevarria C, Zapata LP, et al.** Novel interactive eye-tracking game for training attention in children with attention-deficit/hyperactivity disorder. Prim Care Companion CNS Disord 2019;21:19m02428.
37) **Aldao A, Nolen-Hoeksema S, Schweizer S.** Emotion-regulation strategies across psychopathology: a meta-analytic review. Clin Psychol Rev 2010;30:217-237.
38) **McLaughlin KA, Hatzenbuehler ML, Mennin DS, Nolen-Hoeksema S.** Emotion dysregulation and adolescent psychopathology: a prospective study. Behav Res Ther 2011;49:544-554.
39) **Oei AC, Patterson MD.** Are videogame training gains specific or general? Front Syst Neurosci 2014;8:54.
40) **David OA, Cardoș RAI, Matu S.** Is REThink therapeutic game effective in preventing emotional disorders in children and adolescents? Outcomes of a randomized clinical trial. Eur Child Adolesc Psychiatry 2019;28:111-122.
41) **McDermott AF, Rose M, Norris T, Gordon E.** A novel feed-forward modeling system leads to sustained improvements in attention and academic performance. J Atten Disord 2020;24:1443-1456.
42) **Abilify MyCite.** How the Abilify MyCite® system works [Internet]. Princeton, NJ: Otsuka America Pharmaceutical, Inc. [cited 2023 Jul 7]. Available from: https://www.abilifymycite.com/how-mycite-works.
43) **Feel Therapeutics.** Feel therapeutics main page [Internet]. San Francisco, CA: Feel Therapeutics [cited 2023 Jul 7]. Available from: https://www.feeltherapeutics.com/.
44) **Tsirmpas C, Andrikopoulos D, Fatouros P, Eleftheriou G, Anguera JA, Kontoangelos K, et al.** Feasibility, engagement, and preliminary clinical outcomes of a digital biodata-driven intervention for anxiety and depression. Front Digit Health 2022;4:868970.
45) **Cognoa.** Cognoa main page [Internet]. Palo Alto, CA: Cognoa [cited 2023 Jul 7]. Available from: https://cognoa.com/.
46) **Hackett M.** FDA greenlights Cognoa's tool to detect autism spectrum disorder in kids. MobiHealthNews 2021 Jun 3.
47) **EarliTec Dx, Inc.** Solutions [Internet]. Decatur, GA: EarliTec Dx, Inc [cited 2023 Jul 7]. Available from: https://www.earlitecdx.com/solutions/.
48) **Espie CA, Kyle SD, Williams C, Ong JC, Douglas NJ, Hames P, et al.** A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. Sleep 2012;35:769-781.
49) **Carl JR, Miller CB, Henry AL, Davis ML, Stott R, Smits JAJ, et al.** Efficacy of digital cognitive behavioral therapy for moderate-to-severe symptoms of generalized anxiety disorder: a randomized controlled trial. Depress Anxiety 2020;37:1168-1178.
50) **Twomey C, O'Reilly G, Bültmann O, Meyer B.** Effectiveness of a tailored, integrative Internet intervention (deprexis) for depression: updated meta-analysis. PLoS One 2020;15:e0228100.
51) **Kaplan A, Mannarino AP, Nickell PV.** Evaluating the impact of Freespira on panic disorder patients' health outcomes and healthcare costs within the allegheny health network. Appl Psychophysiol Biofeedback 2020;45:175-181.
52) **Nightware.** Nightware main page [Internet]. Hopkins, MN: Nightware [cited 2023 Jul 7]. Available from: https://nightware.com/.
53) **Zill JM, Christalle E, Meyer B, Härter M, Dirmaier J.** The effectiveness of an internet intervention aimed at reducing alcohol consumption in adults. Dtsch Arztebl Int 2019;116:127-133.
54) **Novartis.** Clinical trial results website [Internet]. Basel: Novartis [cited 2023 Jul 7]. Available from: https://www.novctrd.com/ctrdweb/trialresult/trialresults/pdf?trialResultId=17712.
55) **AIMMED.** Somzz [Internet]. Seoul: AIMMED [cited 2023 Jul 7]. Available from: https://www.aimmed.co.kr/innovation/dtx_pipelines.
56) **Ministry of Health and Welfare.** [Press release][4.20.Thu.The Korea Economic Daily] World's no. 1 cancer diagnostics company also fails to cross government threshold [Internet]. Sejong: Ministry of Health and Welfare [cited 2023 Jul 7]. Available from: https://www.mohw.go.kr/react/al/sal0301vw.jsp?PAR_MENU_ID=04&MENU_ID=0404&page=1&CONT_SEQ=375907.
57) **Choi S.** The second digital therapeutic device is born in Korea···the protagonist is 'WELT'. Medicaltimes 2023 Apr 19.
58) **Ministry of Food and Drug Safety.** Status approved clinical trials [Internet]. Cheongju: Ministry of Food and Drug Safety [cited 2023 Jul 7]. Available from: https://udiportal.mfds.go.kr/msismext/emd/ifm/ctestAprvStatusView.do.
59) **Qian X, Loo BRY, Castellanos FX, Liu S, Koh HL, Poh XWW, et al.** Brain-computer-interface-based intervention re-normalizes brain functional network topology in children with attention deficit/hyperactivity disorder. Transl Psychiatry 2018;8:149.