Exploring Regulatory Pathways of Digital Therapeutics(DTx)

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MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evalution

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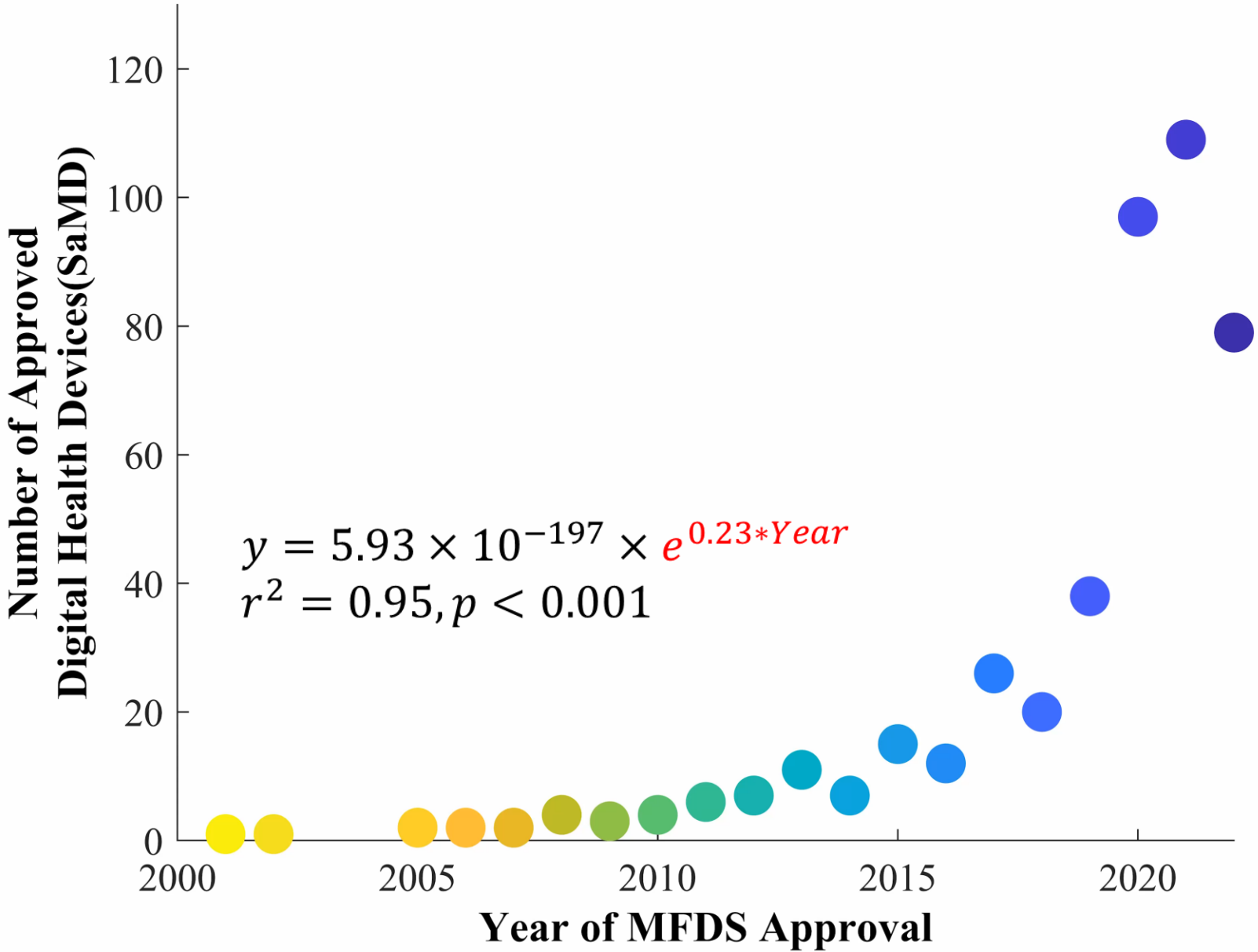

Launch of Digital Health Devices Division

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- Ministry of Food and Drug Safety
  - National Institute of Food and Drug Safety
    - Medical Device Evaluation Department
      - High-tech Medical Devices Division
      - In-vitro Diagnostic Devices Division
      - Cardiovascular and Imaging Devices Division
      - Orthopedic and Restorative Devices Division
      - Dental and Gastroenterology Devices Division
      - **Digital Health Devices Division**

Focus On

- ✓ Software as Medical Devices (SaMD)
- ✓ Machine Learning enabled Medical Devices(MLMD)
- ✓ **Digital Therapeutics(DTx)**
- ✓ Medical Devices with VR·AR technology
- ✓ Medical Mobile Applications
- ✓ Ubiquitous Medical Device (Telemedicine & Wireless Medical Device)
- ✓ Cybersecurity

DTx & South Korea

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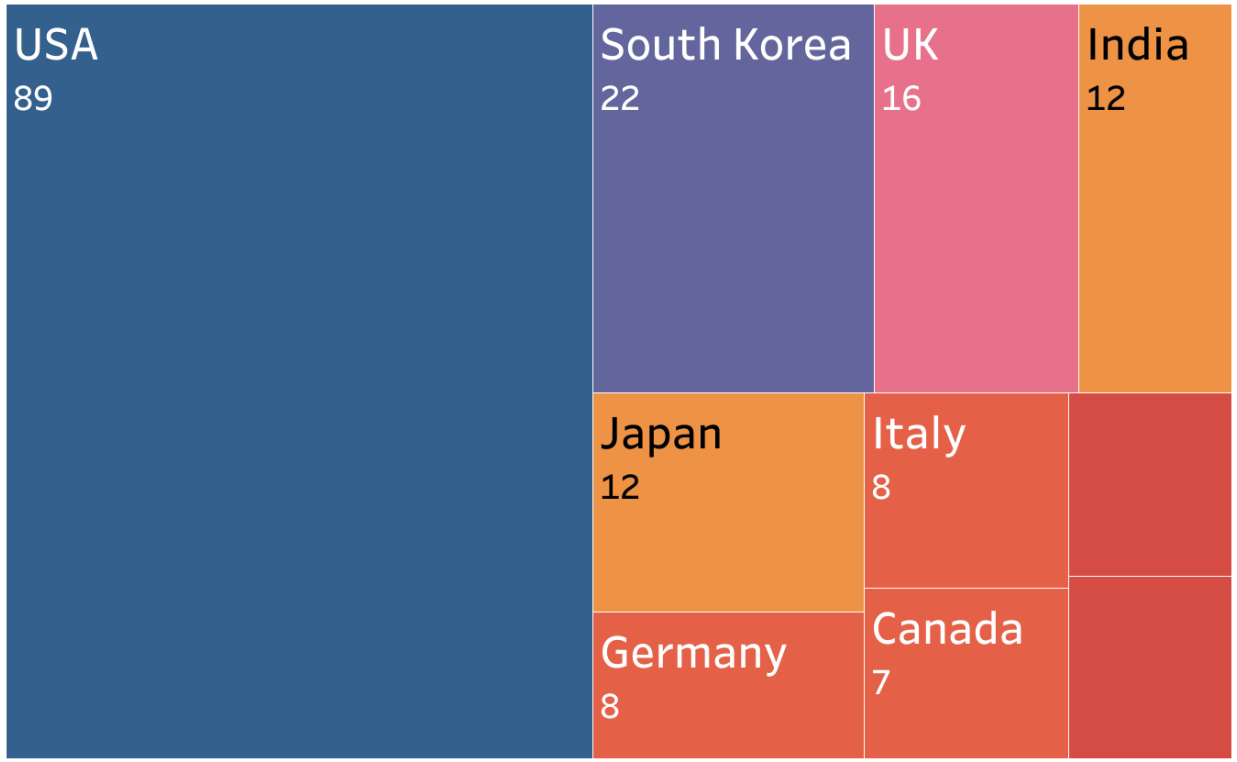
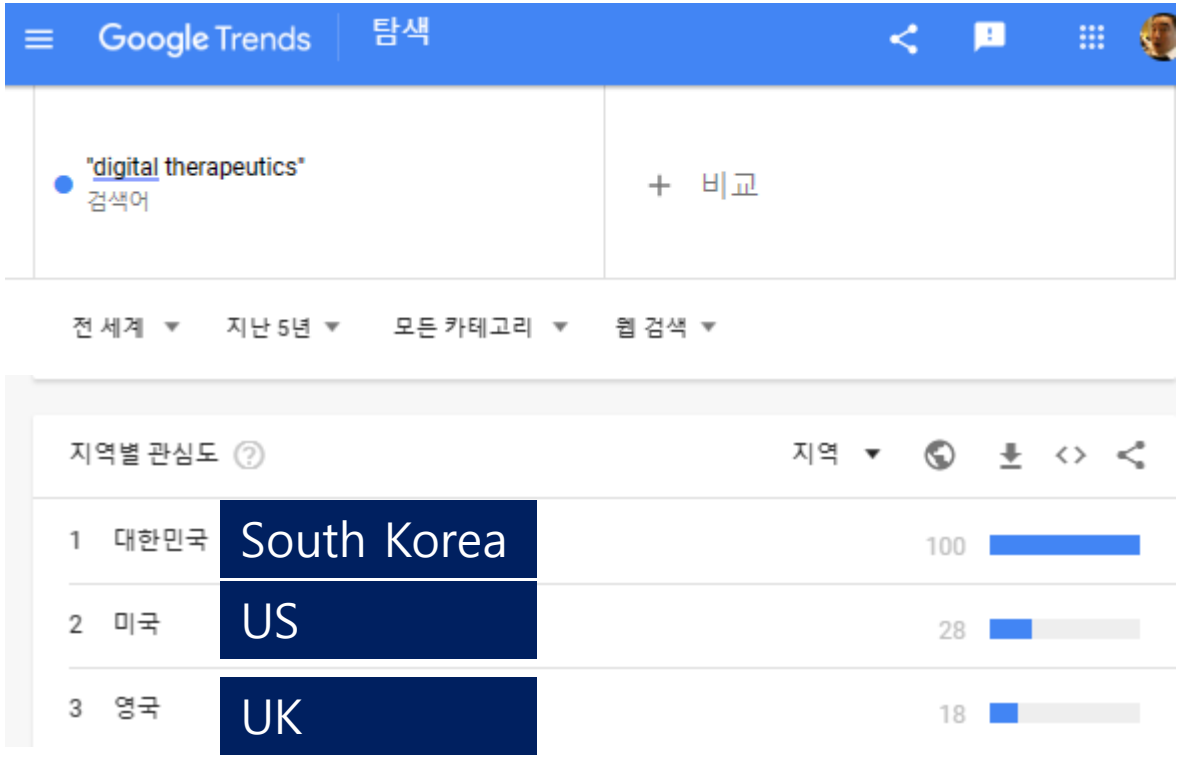
Keen Interests of DTx in South Korea



Scientific Articles(Web of Science)



Public interests(Google Trends)

(source : Web of science, access date : 1/7/2023)
(search condition : keyword("Digital Therapeutics"), Document Type : Article, Editorial, Review)

(source : Google Trends, access date : 1/7/2023)
(search condition : keyword("Digital Therapeutics"), period : 2018-2023)

Regulatory Status for DTx

DTx Guidances in South Korea

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No.	Title
1	Guidance on Review and Approval of Digital Therapeutics
2	Guidance on Safety, Performance Evaluation, and Clinical Trial Design of Digital Therapeutics for Insomnia Improvement
3	Guidance on Safety, Performance Evaluation, and Clinical Trial Design of Digital Therapeutics for Alcohol Use Disorders Improvement
4	Guidance on Safety, Performance Evaluation, and Clinical Trial Design of Digital Therapeutics for Nicotine Use Disorder Improvement
5	Guidance on Safety, Performance Evaluation, and Clinical Trial Design of Digital Therapeutics for Depressive Disorder Improvement
6	Guidance on Safety, Performance Evaluation, and Clinical Trial Design of Digital Therapeutics for Panic Disorder Improvement

Definition

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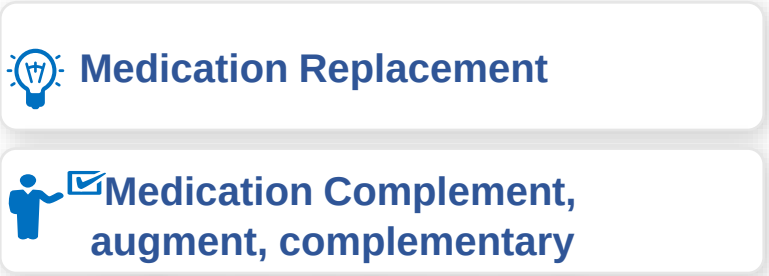
Definition of DTx

Software as a Medical Device (SaMD) that provides **evidence-based therapeutic intervention** to patients for prevention, control, or treatment of medical disorders and/or diseases.
※ The use of a DTx is for “patients” who require therapeutic intervention

Charateristics

- **“Prevention, control” of DTx subject to patients who need treatment intervention**
  - E.g) A product for preventing reoccurrence of heart failure of patients by analyzing·displaying cardiac abnormalities
- **Display specific intended use (indications, efficacy, effectiveness)**
- **Required demonstrating safety·effiocacu ectiveness through clinical trials, supporting lieratures, etc**
- **Enable to be used alone or with other exsiting drugs, medical devices, and therapy**



Decision Criteria for identification of DTx

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(1) Software medical devices

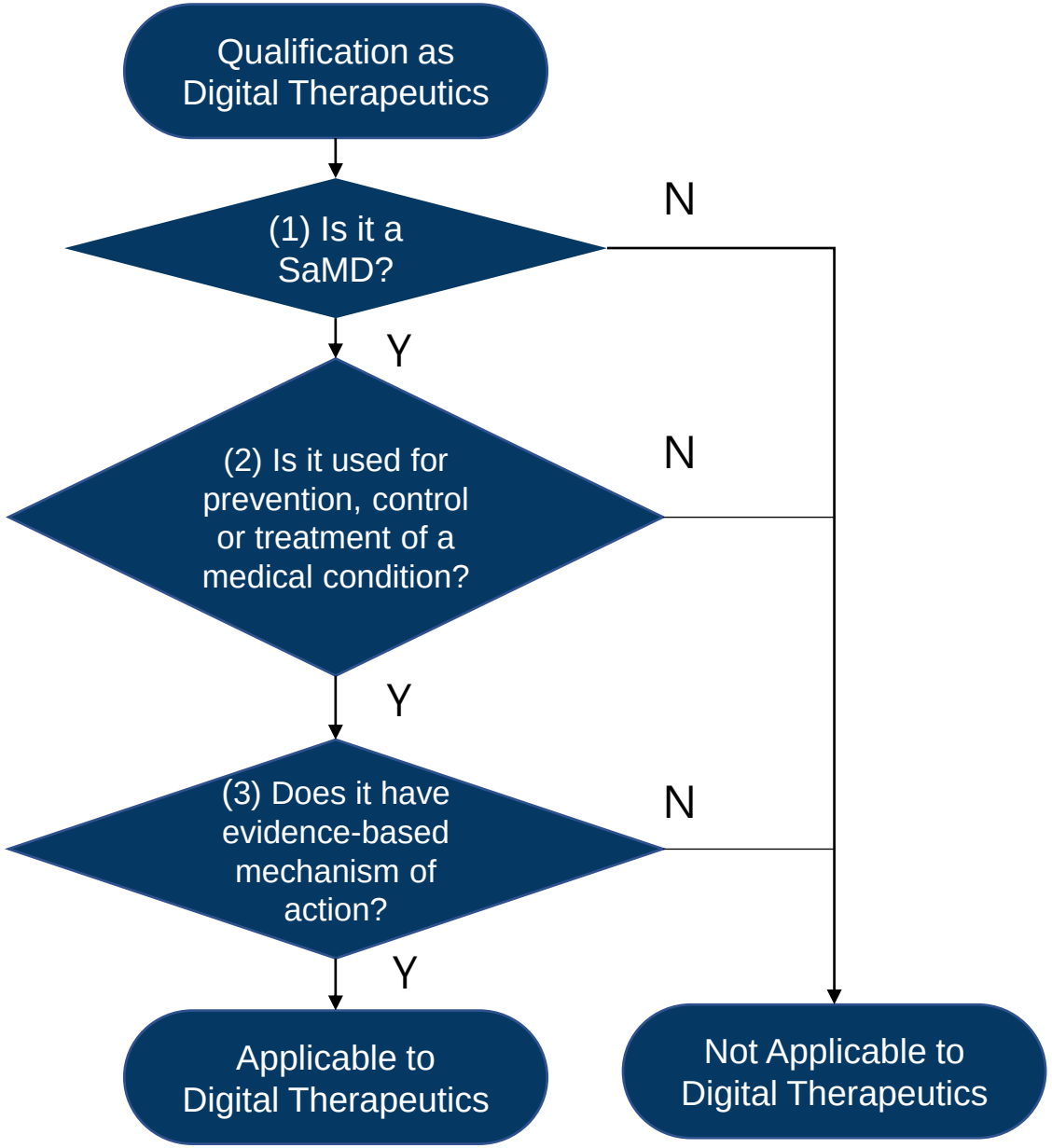
- embedded in PC, mobile products, H/W for general purpose (industrial products) such as HMD

(2) Applicable scope

- Targeted diseases : International Classification of Diseases (ICD), Korea Standard Classification of Diseases (KCD)

(3) Types of clinical evidence (optional)

- Clinical Practice Guidelines (CPGs) recognized by Korea Academy of Medical Sciences
- Clinical articles posted on peer-reviewed Journal
- Documents for pilot study & investigator's clinical study



Major Essential Technical Documents for Approval of DTx

「Enforcement Regulations of the Medical Device Act」Article 9. Review of Technical Document

MoA Clinical Principles for DTx	• Clinical Practice Guideline(CPG) • Peer-Reviewed Journal • Pilot Clinical Trials Report
Software V&V Cybersecurity	• Software V & V • Cybersecurity Checklist & Risk Management Document
Clinical Trials	• Prospective Clinical Study ※ MFDS may recommend manufacturers to submit RWE of approved DTx if necessary

Considerations for Review & Approval of DTx

✓ RCT Documents

Should submit documents ensured clinical efficacy of a product through a prospective clinical study

✓ Pilot Study

Pilot study may be considered by conducting pilot study, if it is determined to difficult to calculate the sample size statistically even though there are materials such as literatures, etc on similar products when designing of clinical trials. In addition, supporting documents(grounds) may be prepared through pilot study, if there isn’t any ground on MoA for treatment of corresponding diseases.

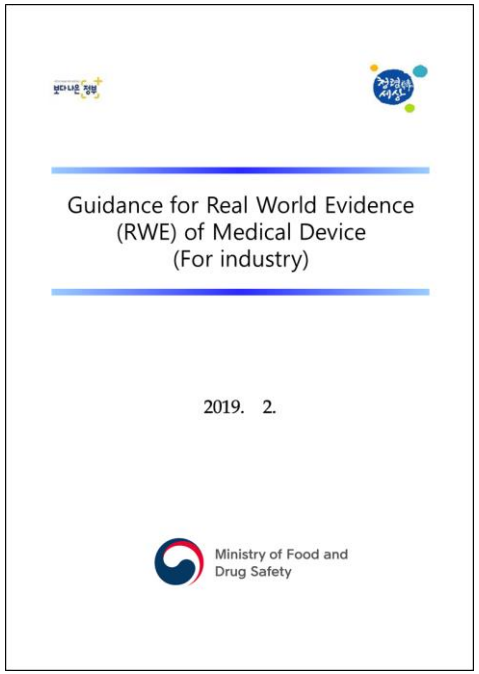
Considerations for Review & Approval of DTx

✓ Real World Evidence

To monitor the potential benefits and risks of digital therapeutics after obtaining approval, documents on real world evidence collected and analyzed from real world data in post-market may be required, if necessary.

For more information, please refer to the MFDS guidance* about Real World Evidence.

* Publication Date : 2019



Clinical Trials Trends

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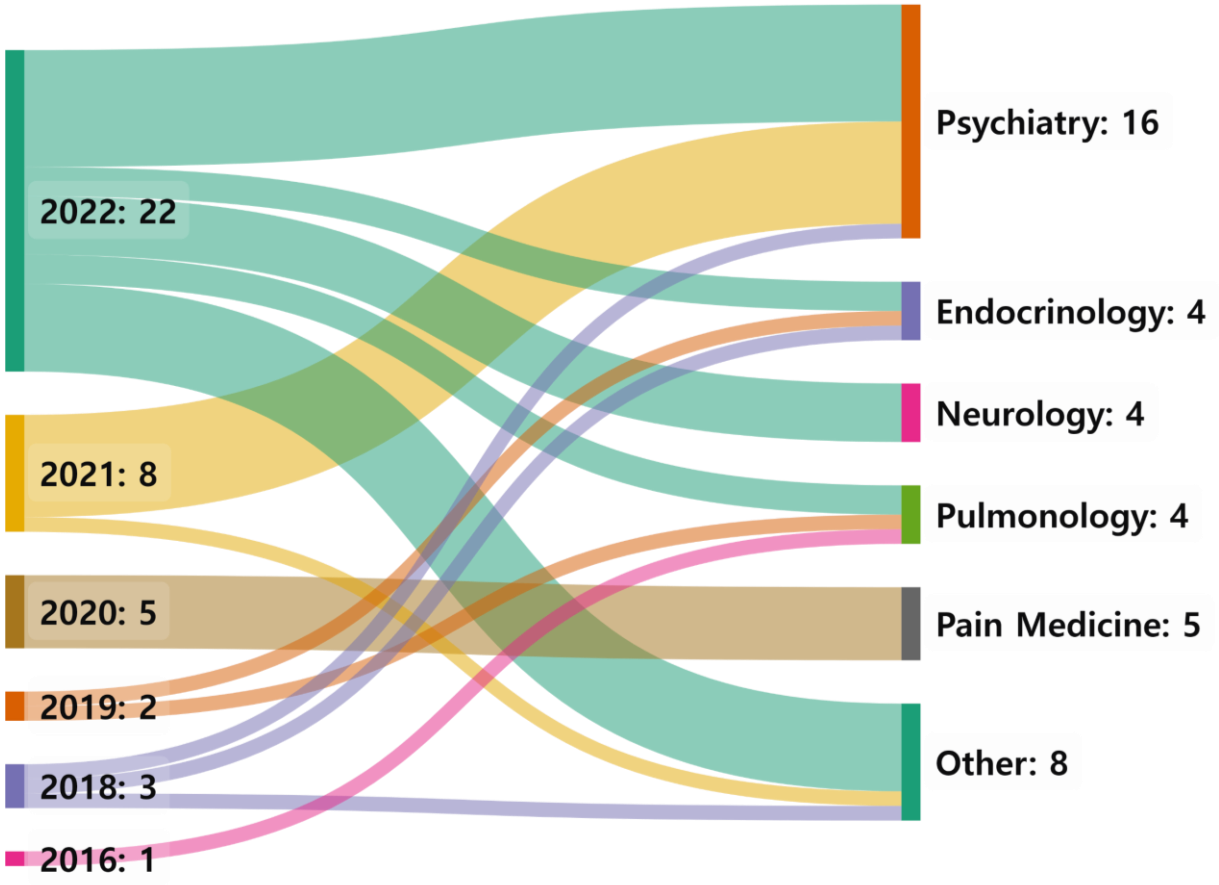
Open database(clinicaltrials.gov)

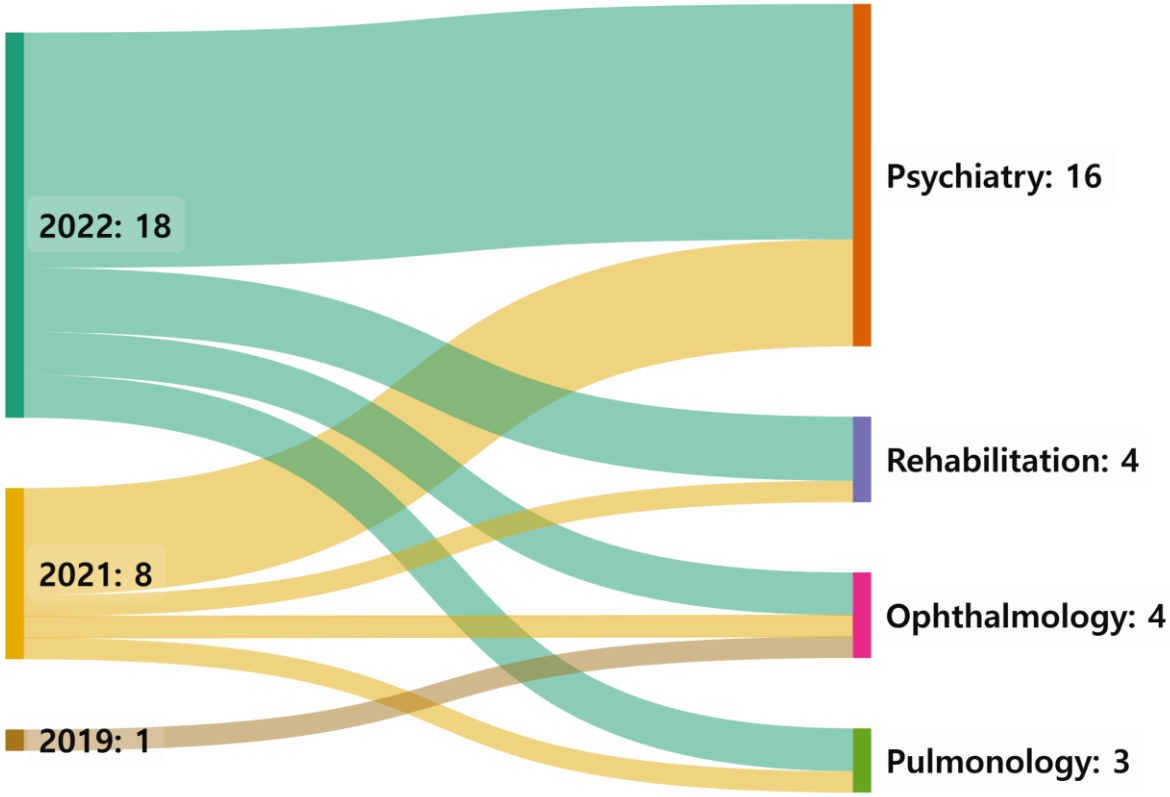


(source : Clinicaltrials.gov, access date : 2/4/2023)

(search condition : keyword("Digital Therapeutics"), period : 2016~2022)

Publish of DTx Guidance(2020)

Open database(https://emed.mfds.go.kr(Korean-only))



(source : https://emed.mfds.go.kr, access date : 2/4/2023)

Clinical Trials Trends

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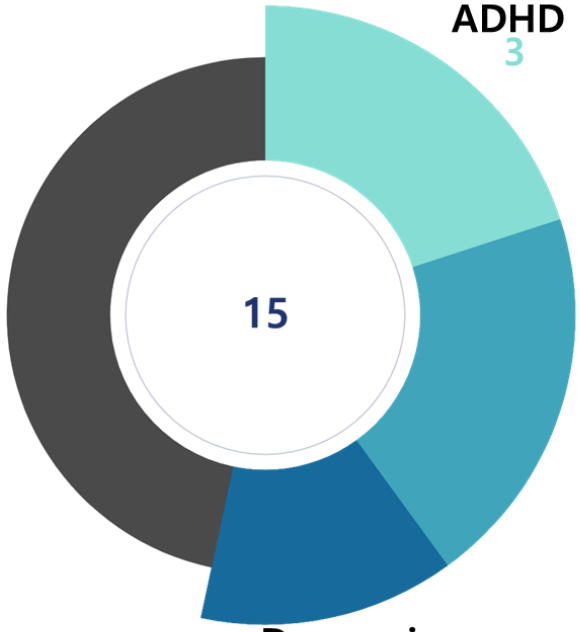
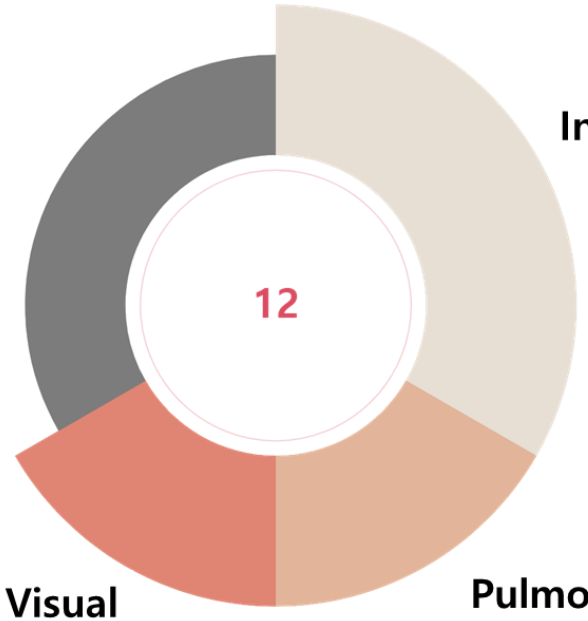
Pilot Clinical Trials



Others
Alcohol Use Disorders
COPD
Developmental Disability
Neglect Syndrome
Nicotine Use Disorder
Vestibular Rehabilitation
Visual Impairment

Pivotal Clinical Trials



Others
Alcohol Use Disorders
Anxiety Disorders
Depressive Disorders
Mild Cognitive Impairment

(source : https://emed.mfds.go.kr/, access date : 1/7/2022)

Challenges

nature reviews psychology

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Cultural Adaptation

Review Article | Published: 26 January 2022

An overview of and recommendations for more accessible digital mental health services

Emily G. Lattie, Colleen Stiles-Shields & Andrea K. Graham

Nature Reviews Psychology **1**, 87–100 (2022) | Cite this article

10k Accesses | **19** Citations | **75** Altmetric | Metrics

To best serve diverse populations of users, DMHIs need to be available in various languages. Adapting evidence-based DMHIs into a new language typically requires cultural adaptations, rather than a straight language translation. For example, in the adaptation of an iCBT programme for Colombian university students,

(source : https://doi.org/10.1038/s44159-021-00003-1)

ADDICTION SSA SOCIETY FOR THE STUDY OF ADDICTION

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REGULATORY OVERSIGHT OF BEHAVIORAL DIGITAL THERAPEUTICS FOR ADDICTION TREATMENT: A COMMENTARY ON KHADJESARI *ET AL.*

Engagement barrier

small portion of the desired population. In psychopharmacology, medicines need to be designed to effectively cross the "brain barrier" and access target neural mechanisms. Likewise, digital therapeutics need to be designed to break the "engagement barrier", that is, be designed according to the cultural norms and individual characteristics of a patient population, which are not always easy and simple to identify. User-centered design research is an

(source : https://doi.org/10.1111/add.15690)

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What principles do we need for DTx development and regulatory harmonization?

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