



HBD Think Tank East 2023
December 14th 2023

Social Implementation of Digital Therapeutics for smoking cessation and hypertension

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St. Luke's International Hospital

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COI Disclosure

Name of Presenter: ©Tomoyuki Tanigawa

Companies, etc. in a relation of conflict of interest requiring disclosure by the lead presenter or co-presenter(s) in relation to the contents of the presentation:

- | | |
|--|--------------|
| ① Advisor/Employee : | CureApp, Inc |
| ② Stock ownership/capital gain : | CureApp, Inc |
| ③ Patent royalties : | None |
| ④ Honoraria : | None |
| ⑤ Writing fees : | None |
| ⑥ Grants for commissioned/joint research : | None |
| ⑦ Scholarship grants : | None |
| ⑧ Endowed chair : | None |
| ⑨ Gifts or other forms of compensation : | None |

Today's topic

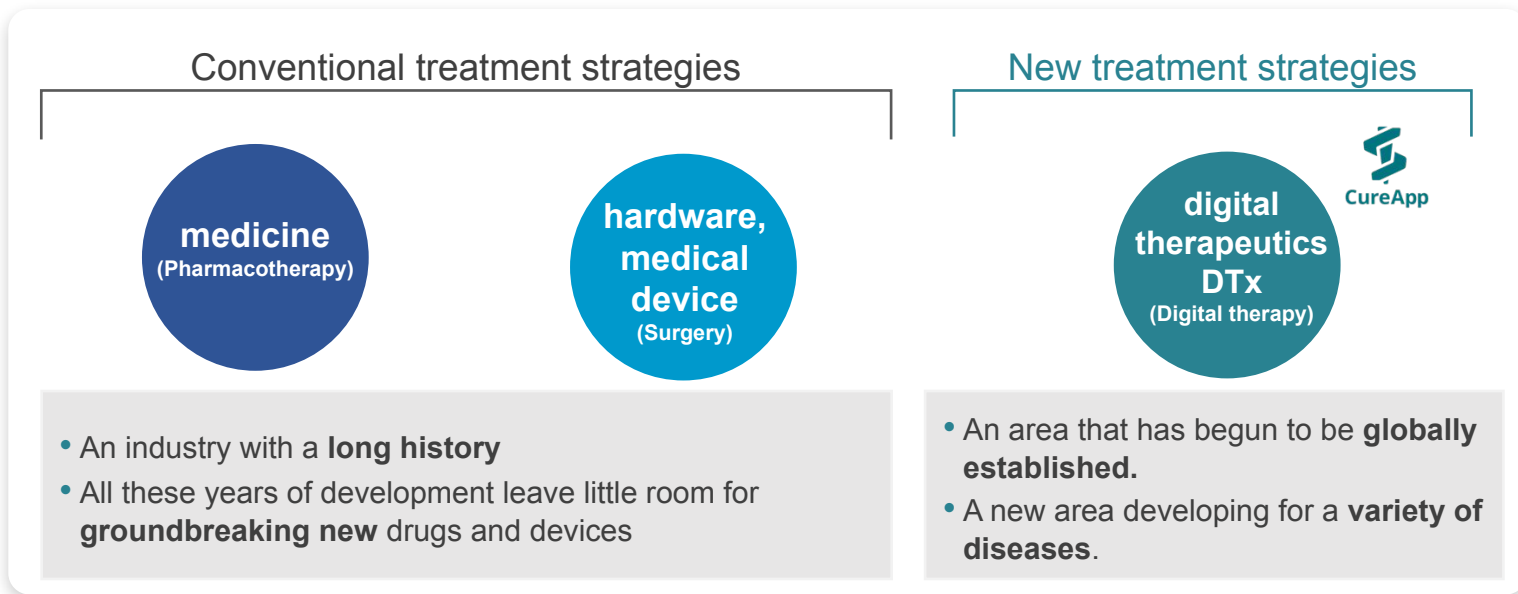
- DTx as a Therapeutic SaMD
- Representing DTx Examples in Japan
 - CureApp SC for smoking cessation
 - CureApp HT for hypertension

Today's topic

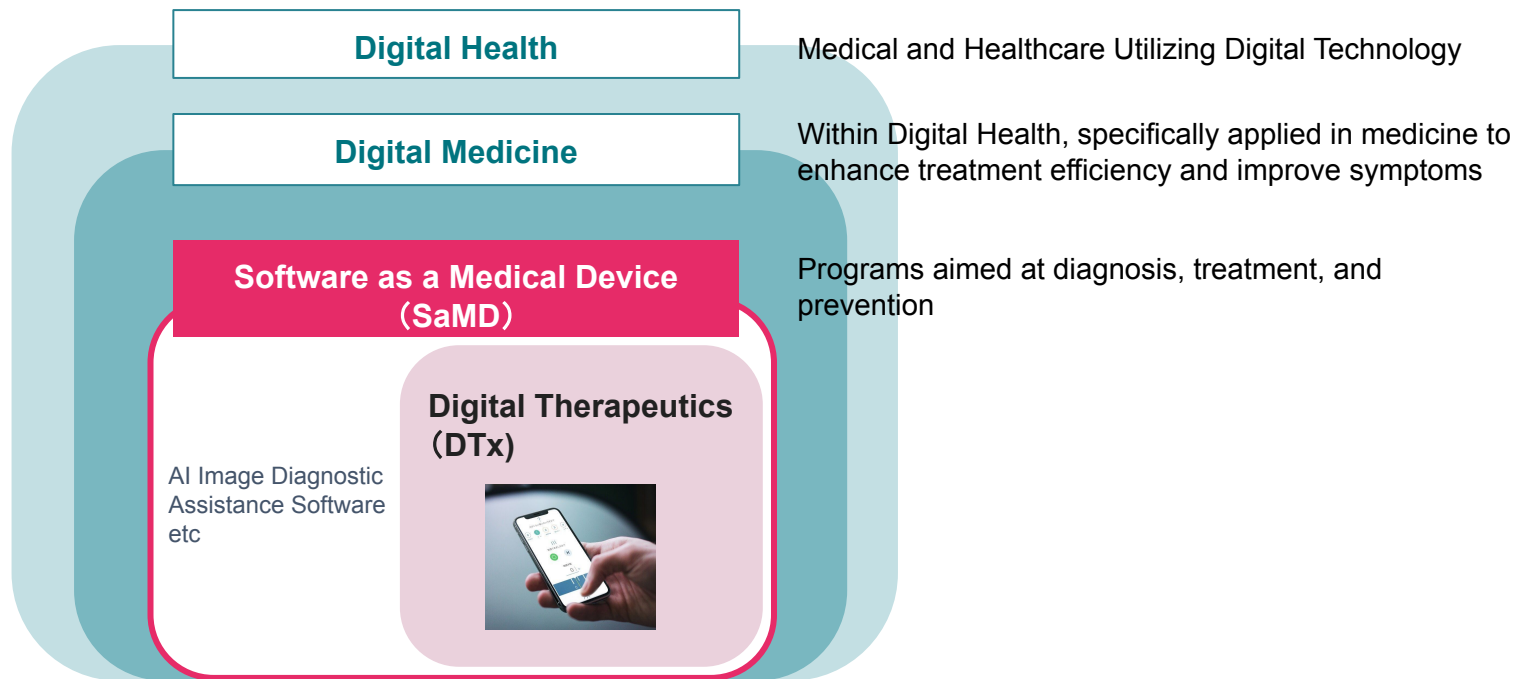
- **DTx as a Therapeutic SaMD**
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Digital therapeutics(DTx), a new treatment strategy

With the revision of the Pharmaceutical Affairs Law in 2014, a new treatment strategy called "Digital Therapeutics, DTx" is beginning to emerge next to medicine and hardware medical devices.



DTx as a Therapeutic SaMD



What is "Treatment with App"?

Medical institution
(Doctor, staff)



Intervention by medical staff is difficult.
"Treatment gap"



- Prescription

First Visit

- Install and register

Between hospital visits

- Record treatment progress, physical condition, etc.
- Receive treatment guidance automatically

follow-up visit

- Being promoted the practice and retention of behavior change

Patients



Three differences from “healthcare apps”

DTx are referred to as digital therapies in academic societies and are the "latest medical treatments".

DTx is...

providing the clinically support based on **medical evidences**

禁煙治療のための標準手順書
第8版

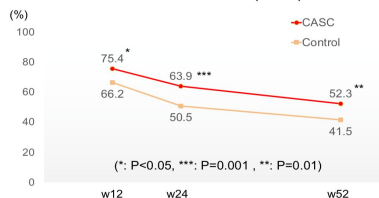
本手順書は、2009年4月に初版、改訂第7版(2012年4月)と第8版(2015年4月)を改訂し、改訂第8版として改訂された。改訂第8版(2015年4月)において、改訂第8版の最終版として改訂された。

2015年 4版

日本禁煙学会
日本呼吸学会
日本循環学会
日本神経学会

obtained **regulatory approval** and **reimbursement** through pivotal clinical trials

• Continuous abstinence rate (CAR) from Week 9



一般的なヘルスケアアプリ

開発
リリース

CureAppの治療アプリ*

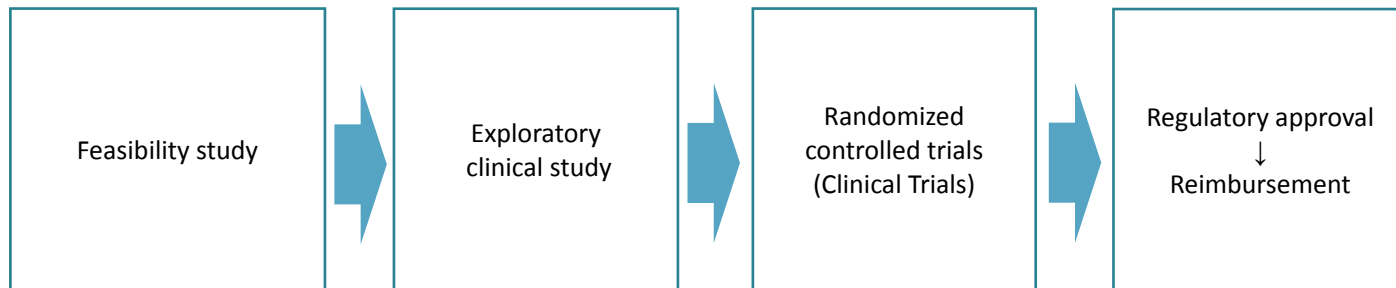
開発
介入試験(1~2年)
治験(1~2年)
医学的エビデンスの取得
薬事認証
リリース
市販後調査

prescribed by a doctor

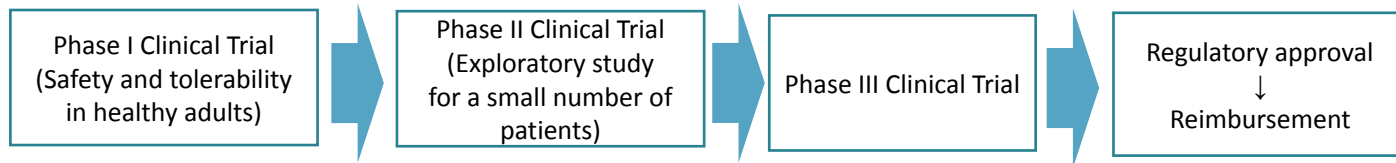


Process for regulatory approval and insurance reimbursement of DTx

<How DTx Reaches Patients>



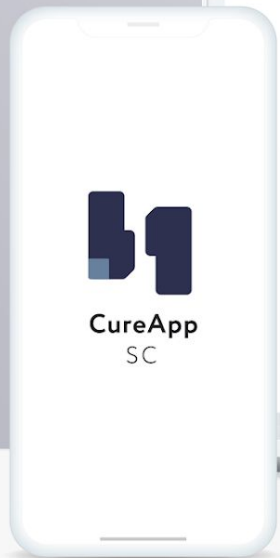
<Drug approval process>



Today's topic

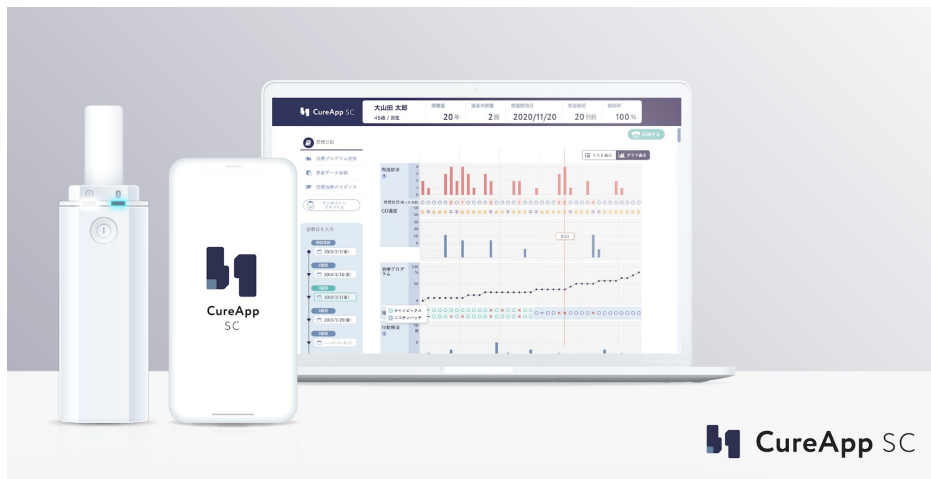
- DTx as a Therapeutic SaMD
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for Smoking Cessation



DTx for smoking cessation

CureApp SC(Smoking Cessation) is a DTx designed to aid patients who receive standardized outpatient smoking cessation treatment program in Japan.



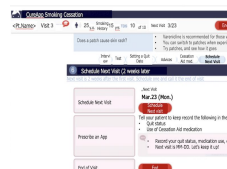
App for patients

Personalized guidance based on a patient's therapy status and condition



CO checker

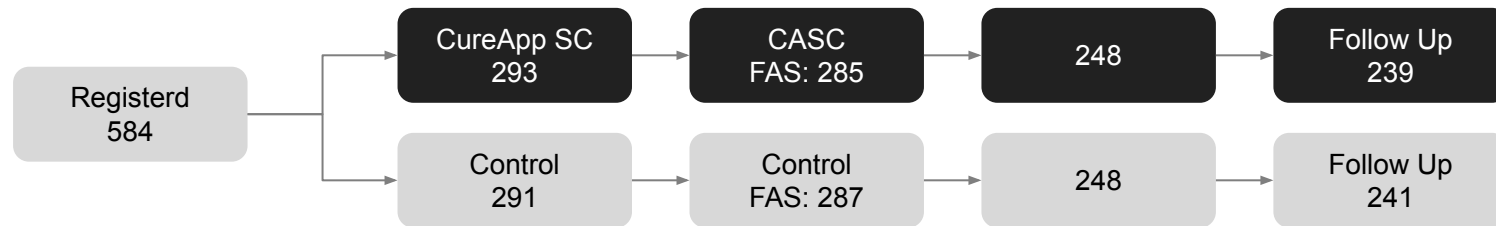
Accurately measure the concentration of carbon monoxide in their breath **at home**



Web-based PC app for physicians

Greater insight into the patient's response to treatments **between** clinic visits

Evidence for CureApp SC: Phase III Clinical Trial Design

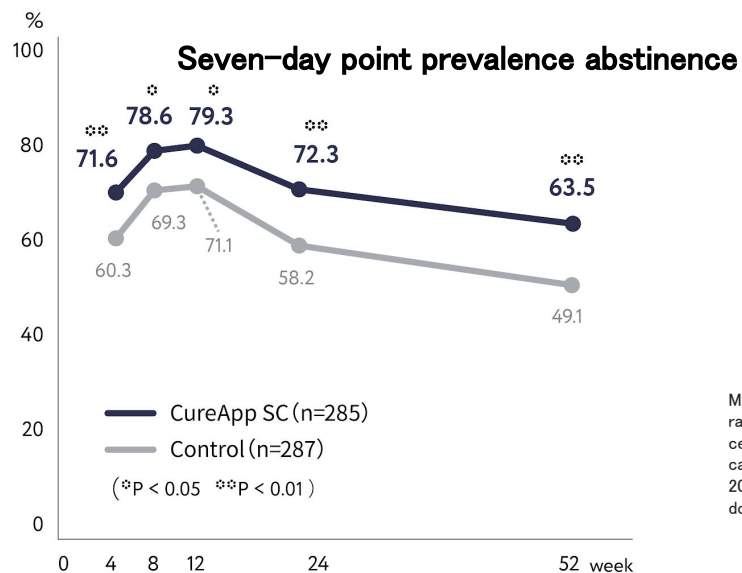
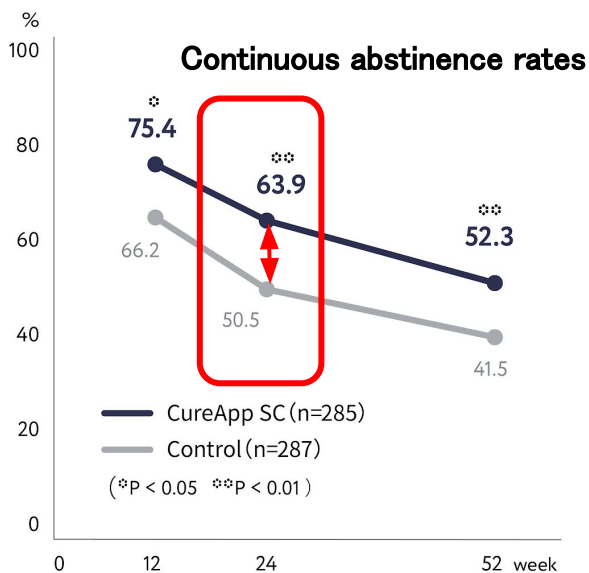


Objective	To examine the efficacy of this product in combination with standard smoking cessation treatment program for nicotine-dependent patients compared to sham application.
Design	Multicenter, randomized, two-arm, controlled intervention trial
Facilities and cases	31 medical institutions in Japan, 584 cases registered
Selection criteria	<p>Patients who meet all of the following criteria 1) to 5)</p> <ol style="list-style-type: none"> 1) Patients diagnosed with nicotine dependence with a TDS score of 5 or higher 2) Patients with a Brinkmann Index (number of cigarettes smoked per day x number of years smoked) of 200 or more 3) Patients who wish to quit smoking immediately. 4) Patients who have given written consent to undergo smoking cessation treatment 5) Patients using a smartphone (OS: Android 5.0 or higher, iPhone 8.0 or higher)
Primary endpoint	Percentage of smokers who have quit smoking for 9-24 weeks

Masaki K, Tateno H, Nomura A, et al. A randomized controlled trial of a smoking cessation smartphone application with a carbon monoxide checker. NPJ Digit Med. 2020;3:35. Published 2020 Mar 12. doi:10.1038/s41746-020-0243-5

Clinical evidence: Results of phase III clinical trials

- Demonstrated statistically significant differences in the primary endpoint (continuous abstinence rate (CAR) from weeks 9 to 24)
- Continued treatment effect was observed 52 weeks after treatment initiation, after completion of the application use period (24 weeks)
- No adverse events related to the use of the product were observed



Masaki K, Tateno H, Nomura A, et al. A randomized controlled trial of a smoking cessation smartphone application with a carbon monoxide checker. NPJ Digit Med. 2020;3:35. Published 2020 Mar 12. doi:10.1038/s41746-020-0243-5

Regulatory approval and insurance reimbursement for CureApp SC

2018.12



Clinical Trial Completed

2020.8



Regulatory approval

2020.12.1



Insurance reimbursement

○ 保険償還価格

販売名	償還価格	類似機能区分	外国平均価格との比	費用対効果評価への該当性
CureApp SC ニコチン依存症治療アプリ及びCOチェッカー	特定保険医療材料としては設定せず、新規技術料にて評価する。			

○ 準用技術料

C110-2 在宅振戦等刺激装置治療指導管理料 注2 導入期加算	140点
C167 疼痛等管理用送信器加算	600点 4回分

Material from Central Social Insurance Medical Council
(<https://www.mhlw.go.jp/content/12404000/000693018.pdf>)

Total cost of CureApp SC was set at **¥25,400 (approx \$188)** for 6-month use, including app purchases and subscription fees.

for Hypertension

 CureApp HT

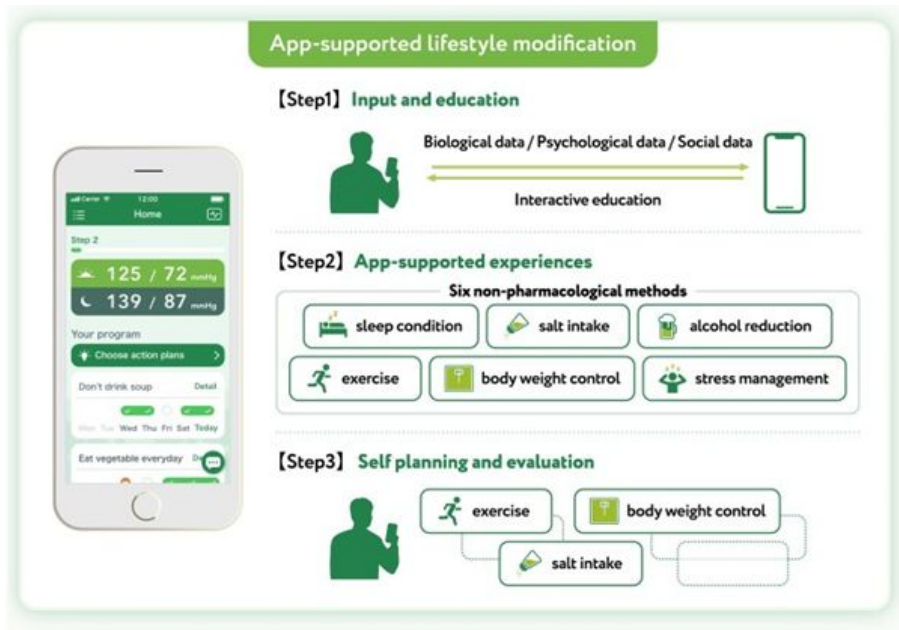
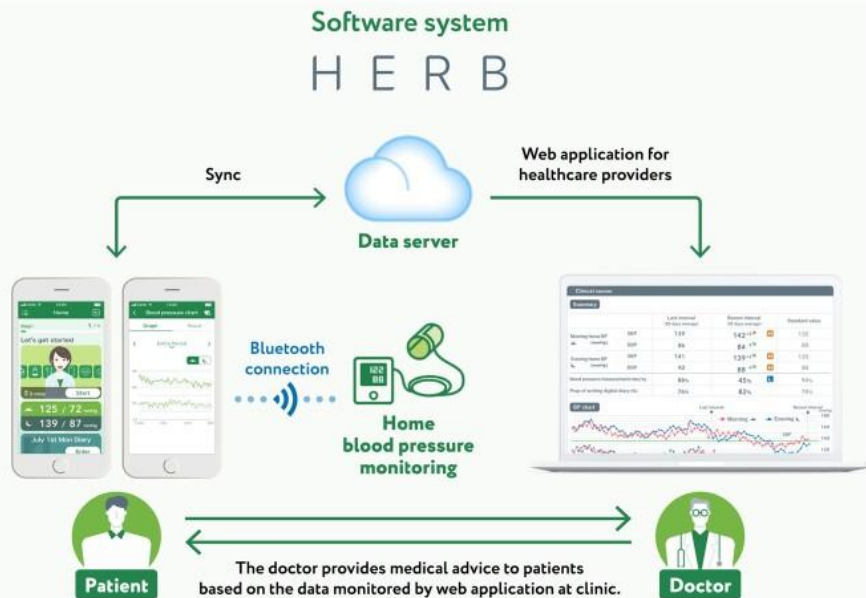
Digital Therapeutic Application for Hypertension

CureApp HT

高血圧治療補助アプリ™



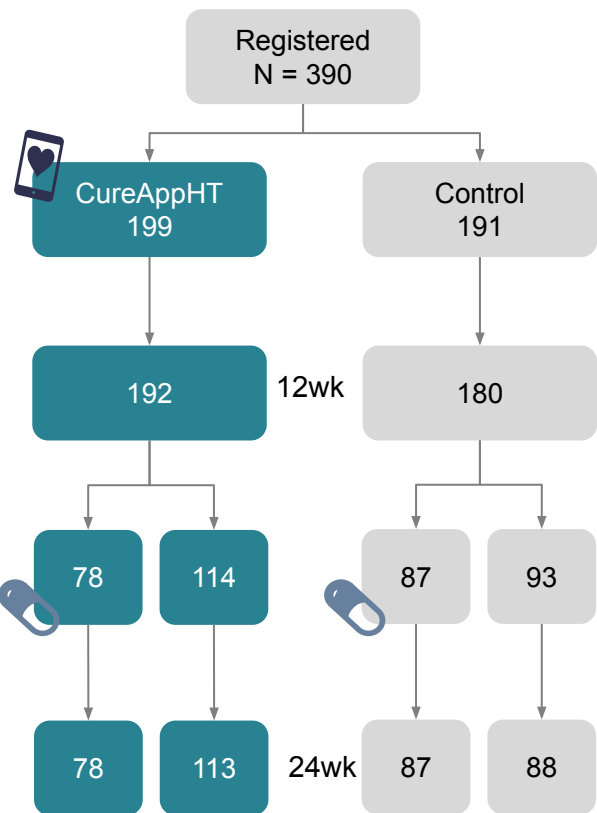
DTx for Hypertension



Efficacy of a digital therapeutics system in the management of essential hypertension: the HERB-DH1 pivotal trial
 Kazuomi Kario, Akihiro Nomura, Noriko Harada, Ayako Okura, Kiyose Nakagawa, Tomoyuki Tanigawa, Eisuke Hida
 European Heart Journal, 2021

Evidence for CureApp HT: Phase III Clinical Trial Design

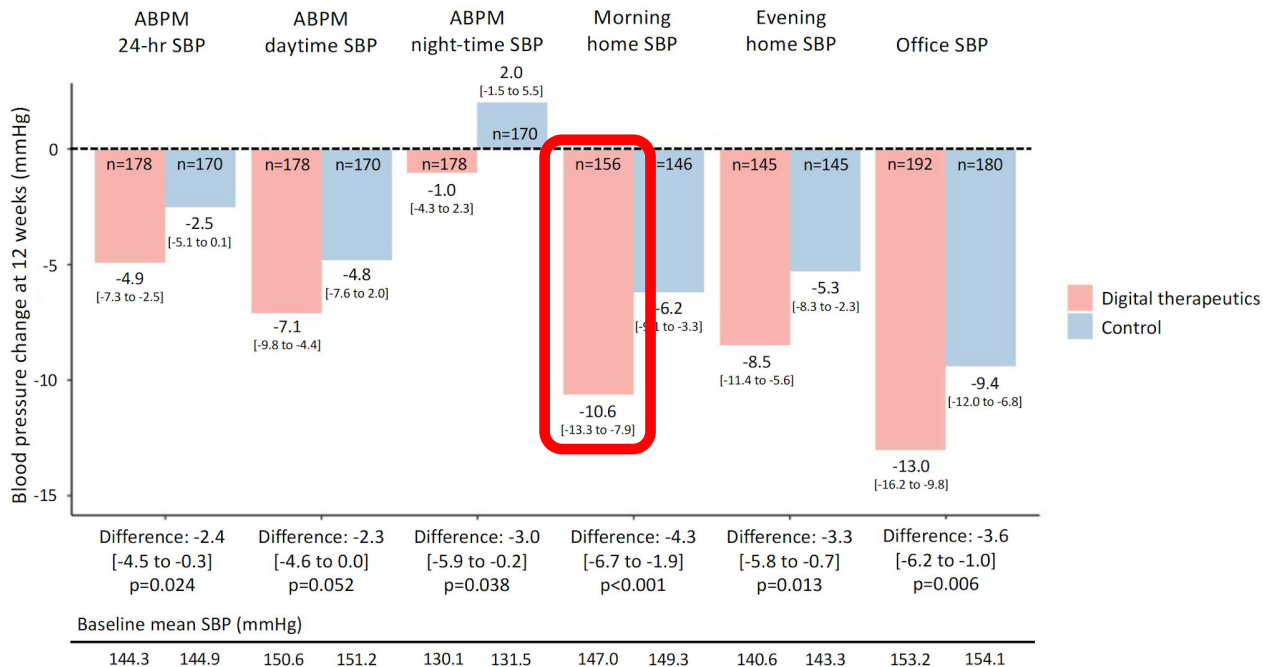
The results of the trial was published in the EHJ 2021.



Objective	To examine the efficacy of digital therapeutics in patients with hypertension not receiving antihypertensive medication.
Design	Randomized, open-label, parallel-group, multicenter (Phase III)
Number of cases	390 cases registered
Selection criteria	<p>Patients who meet all of the following criteria are eligible</p> <ol style="list-style-type: none"> (1) 20 years of age or older and less than 65 years of age (2) Essential hypertension with Grade I or II hypertension (office systolic blood pressure 140-179 mmHg and/or diastolic blood pressure 90-109 mmHg) (3) Mean 24-hour blood pressure by ABPM performed during the screening period is greater than or equal to 130 mmHg systolic (4) Patients who have not been treated with antihypertensive drugs (including those who have not been treated with antihypertensive drugs for at least 3 months at the time of obtaining consent) (5) Smartphone (with iOS or Android) is available and carried on a daily basis (6) Willing to perform ABPM during the screening period and at 12 and 24 weeks after enrollment (7) The investigator or subinvestigator determines that lifestyle guidance without antihypertensive treatment for approximately 12 weeks after enrollment is appropriate.
Primary endpoint	Mean change from baseline to 12 weeks in 24-hour systolic BP measured by ambulatory BP monitoring

Primary Endpoints of Phase III Clinical Trial

Changes from baseline to 12 weeks in 24h, daytime, and nighttime systolic blood pressure based on ambulatory blood pressure monitoring, morning and evening home systolic blood pressure, and office systolic blood pressure.

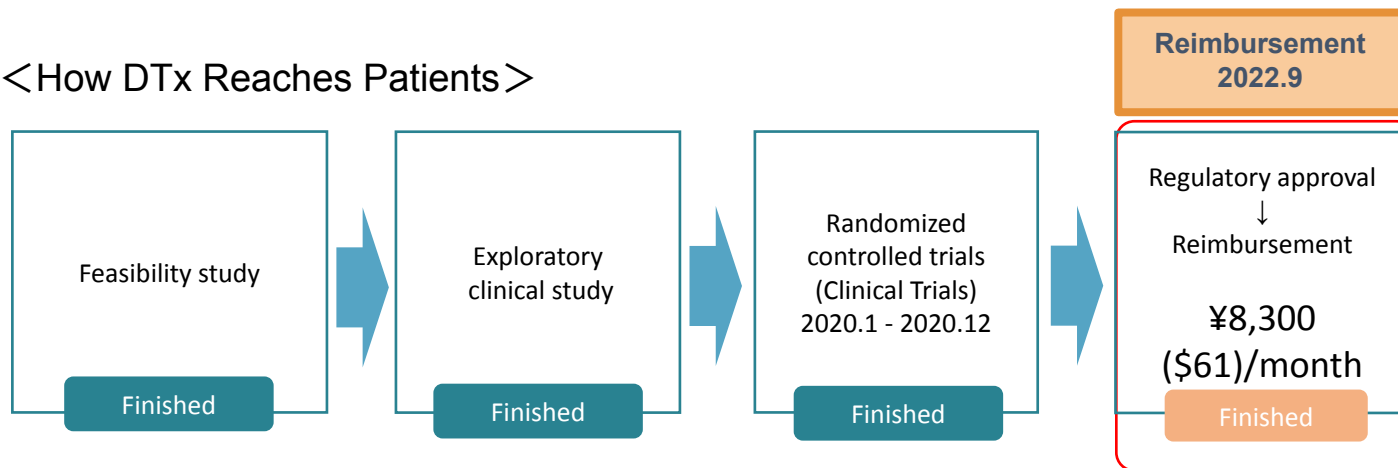


Primary endpoint:

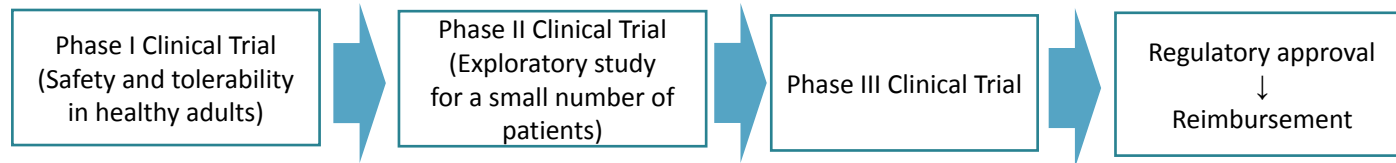
Between-group differences in 24h ambulatory SBPs at 12 weeks were -2.4 (95% confidence interval -4.5 to -0.3)

Process for regulatory approval and insurance reimbursement of CureApp HT

<How DTx Reaches Patients>



<Drug approval process>



*引用Digital therapeutics for essential hypertension using a smartphone application: A randomized, open-label, multicenter pilot study (<https://onlinelibrary.wiley.com/doi/10.1111/jch.14191>)

Model structure for evaluating cost-effectiveness of CureApp HT

Input

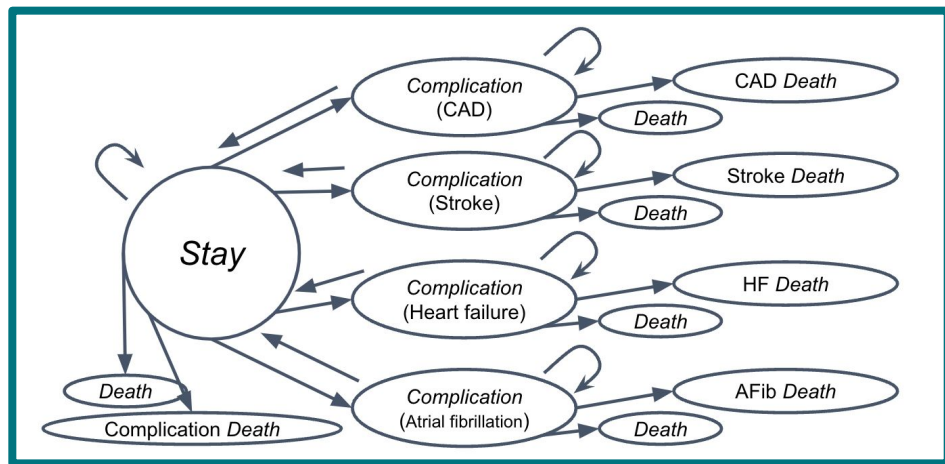
- Age
- Baseline SBP
- Annual BP increase
- Annual mortality rates by complications
- Annual incidence rates of each complication among hypertension patients
- Annual costs
- Health utilities
- Discount rates

Cost of HERB DTx set at ¥10,000 (\$86.96) / M

Output

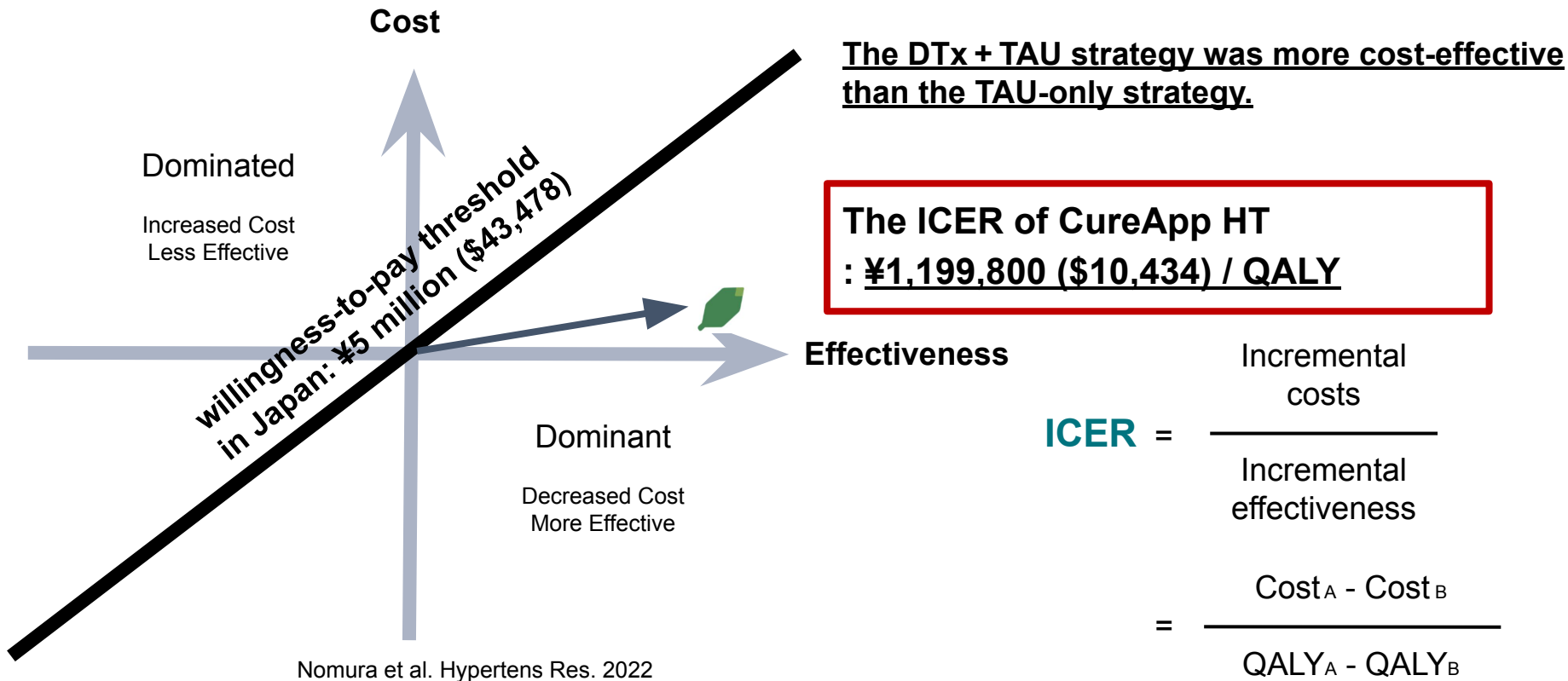
- Quality-Adjusted Life-Years (QALYs)
- Cost

State change in Markov model



Nomura et al. Hypertens Res. 2022

Cost-effectiveness of using prescription DTx in treating hypertension



Conclusions

- Digital Therapeutics are socially significant because they may provide efficacy through "behavior change" approach to diseases that still have poor treatment outcomes.
- Digital Therapeutics, including **CureApp SC for smoking cessation**, the first therapeutic application approved as a medical device in Japan, and **CureApp HT for hypertension**, demonstrated robust evidences and gained regulatory approval, leading to insurance coverage.

Thank you



MISSION

Re-evolving "therapeutics" with software

We strive for the ideal of medical care, a world where all people can receive high-quality treatment without worry. Evolving treatment with the power of technology, we will solve the social issues surrounding healthcare and realize ideal medical care.

VISION

Creating new therapeutic effects through technology

We develop evidence-based medical programs, "Digital Therapeutics (DTx)," for patients who suffer from conditions that conventional treatment methods with drugs or devices were not effective. We aim to deliver the new treatment to as many patients as possible.