



Challenges in Quantifying the Value of Digital Therapeutics: New Challenges to Bridge the Efficacy- Effectiveness Divide

Conflicts of Interest

- Jason Shafrin, PhD is an employee of the Center for Healthcare Economics and Policy within FTI Consulting, a consulting firm which includes health care and life sciences clients
- Megan Coder, PharmD, MBA is the Vice President of Global Policy for the Digital Therapeutics Alliance, a 501(c)(6) non-profit trade association of industry leaders and stakeholders engaged in the evidence-driven advancement of digital therapeutics
- Wayne Burton, MD is a healthcare consultant, with health care and life sciences clients
- Stephen Schueller, PhD declares no conflicts of interest.

Panelists

Jason Shafrin, PhD

Moderator

Senior Managing Director,
Center for Healthcare Economics and Policy
FTI Consulting



Megan Coder, PharmD, MBA

Panelist

Vice President of Global Policy
Digital Therapeutics Alliance



Stephen M Schueller, PhD

Panelists

Associate Professor of Psychological Science
School of Social Ecology
University of California, Irvine



Wayne N Burton, MD

Panelist

Former Global Corporate Medical Director
American Express
Hinsdale, IL USA



What are digital therapeutics?

Digital
Health

Digital
Medicine

Digital
Therapeutics

	Digital Health	Digital Medicine	Digital Therapeutic
Definition	Technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes; capture, store or transmit health data; and/or support life science and clinical operations	Evidence-based software and/or hardware products that measure and/or intervene in the service of human health	Products that deliver evidence-based therapeutic interventions to prevent, manage, or treat a medical disorder or disease
Clinical Evidence	Not required	Required	Required
Regulatory oversight	Not a medical device Often a consumer product	Oversight varies. Could be medical devices, or a tool to develop other drugs or devices	Reviewed by regulatory bodies regarding claims of safety, efficacy and intended use
Example categories	• Lifestyle apps • Fitness trackers • Electronic health records • E-prescribing • Telehealth • Length of stay monitoring tools	• Electronically measured patient reported outcomes • Medication adherence tools • Sensors that measure patient vital signs and physiological data • Ingestible sensors	• Medical intervention to improve health and treat a disease

Numerous digital therapeutics have already arrived on the market

Many digital therapeutics are used to treat mental health conditions, substance abuse and pain, but also include treatments for heart failure and diabetes

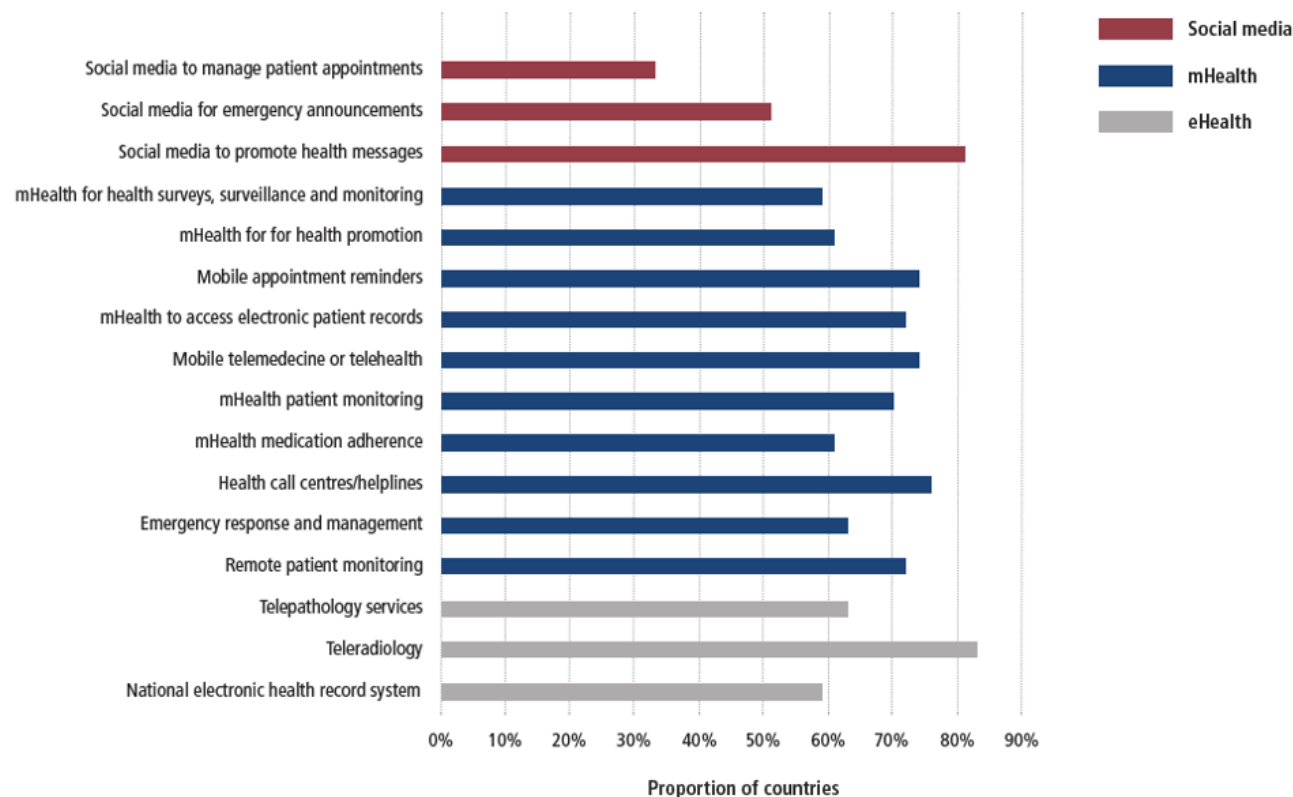
Table 1. Sampling the Digital Therapeutics Pipeline.

Company	Product	Indication(s)	Status	Commercial partner	Investment partner
Pear Therapeutics	reSET	Substance use disorder ^{25,26}	Marketed	Sandoz ²⁷	Novartis
	reSET-O	Opioid use disorder ²⁸	Marketed	Sandoz ^a	
	Somryst	Chronic insomnia ²⁹	Marketed		
	Pear-004	Schizophrenia	Marketed ^b Pivotal		
	Pear-006	Multiple sclerosis	Discovery	Novartis ³⁰	
	Unspecified	Gastrointestinal conditions	Discovery	Ironwood Pharmaceuticals ³¹	
Welldoc	Bluestar	Type I diabetes, Type II diabetes ³²	Marketed	Astellas ³³	
Akili Interactive	Endeavor	ADHD ³⁴	Marketed	Shionogi ³⁵	Amgen, Merck
	AKL-T02	Autism spectrum disorder ³⁶	Pilot		
	AKL-T03	Major depressive disorder	Pilot		
Nightware	Nightware	Post-traumatic stress disorder	Marketed		
Click Therapeutics	CT-152	Major depressive disorder	Pivotal	Otsuka ³⁷	Sanofi, Hikma
Cognoa	Autism Diagnostic	Autism spectrum disorder	Pivotal	EVERSANA	
	Autism Therapeutic	Autism spectrum disorder ³⁸	Feasibility		
Biofourmis	BiovitalsHF V1	Heart failure	Marketed	Novartis ³⁹	
	BiovitalsHF V2	Heart failure ⁴⁰	Pivotal		
	BF140	Pain ⁴¹	Pilot	Chugai ⁴²	
Propeller Health	Propeller	Asthma ⁴³ , chronic obstructive pulmonary disease ⁴⁴	Marketed	AstraZeneca ⁴⁵ , GlaxoSmithKline, Novartis, Orion, Boehringer Ingelheim	
AppliedVR	EaseVRx	Chronic pain ⁴⁶	Efficacy		
	RelieVRx	Acute postoperative pain ⁴⁷	Efficacy		
	AnxietyVRx	Generalized anxiety	Discovery		
Happify Health	Happify	Multiple sclerosis-associated depression and anxiety	Discovery	Sanofi ⁴⁸	

Prior to COVID-19, digital health tools were already in use by a majority of European countries

“While some of the digital health tools used were novel (in particular contact-tracing apps), much of the underpinning technology that has been used during the pandemic already existed. At the system level, most actions to support the use of digital health tools during the pandemic have concerned the relaxation of limiting mechanisms, in particular the opening up of financing and reimbursement for these services where that was not already the case, and increased direct investment in digital health tools and the infrastructure to support them.”

Figure 2: The level of uptake of digital health prior to the pandemic varied by type of application



But what about digital therapeutics?



Megan Coder, PharmD, MBA

Digital Therapeutics Alliance

ISPOR Europe 2021

Products across the digital health ecosystem serve different, but complementary purposes. Depending on each product's intended use and risk, it is subject to increasing degrees of clinical evaluation, regulatory oversight, and real-world data requirements.

DIGITAL HEALTH TECHNOLOGIES*



Enterprise SYSTEMS & SUPPORT

Platforms for healthcare systems, clinics, and other enterprise settings

- Clinical administration and management tools
- Predictive analytics
- Clinical trial management



Clinician SERVICES & SUPPORT

Platforms primarily for clinicians and clinical support staff

- Health Information Technology
- Electronic medical record and prescribing systems
- Point of care and workflow enhancement tools
- Telehealth platforms



Patient-facing WELLNESS & SUPPORT

Products that capture, store, or transmit health data

- Lifestyle and wellness apps
- Activity and fitness trackers
- Medication reminder apps
- Wearables and sensors (*non-clinical grade*)
- Consumer health information



Patient-facing DIAGNOSTIC & MONITORING

Products used to diagnose, guide diagnoses, or actively monitor patients

- Digital diagnostics
- Digital biomarkers
- Remote patient monitoring tools
- Wearables and biometric sensors (*clinical grade*)
- Medication ingestible sensors
- Connected drug delivery devices



Patient-facing THERAPEUTIC INTERVENTIONS

Products that deliver medical interventions and therapies

- **Digital therapeutics**
 - » Clinical interventions delivered directly to patients via software to treat, manage, or prevent a disease or disorder
- Non-DTx medical devices (e.g., insulin pump, artificial pancreas, pacemaker, CPAP)

DTx Value Assessment & Integration Guide

VERSION: 1.0



GUIDE UNDER DEVELOPMENT

DTx Value Assessment & Integration Guide

Contents

Guide Introduction	4
HCDM Feedback Process	5
Industry Overview: Digital Health & Therapeutic Landscape	6
DTx Product Evaluation: General Requirements & Intended Use	12
Step 1: DTx product assessment overview	13
Step 2: DTx product technical considerations	16
Step 3: DTx product appropriateness and usability	17
DTx Product Evaluation: Regulatory & Security	18
Step 4: Regulatory oversight	19
Step 5: Product security best practices	20
Step 6: Product data privacy and governance	21
DTx Product Evaluation: Clinical Impact, Safety & Effectiveness	22
Step 7: DTx product evaluation types	23
Step 8: Assessing clinical trial evidence	24
Step 9: Types of real-world data (RWD) generated by DTx products	25
Step 10: Utilizing DTx-generated real-world data (RWD)	26
Step 11: Development & impact of real-world evidence (RWE)	27
DTx Product Evaluation: Economic Assessment	29
Step 12: Preparing for a DTx economic analysis	30
Step 13: Undertaking a formal economic analysis	31
Step 14: Key considerations for a DTx economic impact evaluation	32
Step 15: Factors that affect DTx therapy economic impact	33
Implementing Digital Therapeutics in Practice	35
Step 16: DTx product implementation and engagement	36
Step 17: Appropriateness of post-market implementation studies	39
Step 18: Clinical team engagement	40
Step 19: DTx product authorization and distribution	41
Step 20: Ensuring quality data sets	42
Step 21: Access to DTx product outcome	43

Step 7: DTx product evaluation types

Digital therapeutics undergo a multiple evaluations throughout the product life cycle. These clinical and economic studies are used in the evaluation of product safety, effectiveness, real-world utilization, implementation, value assessment, and therapy optimization. In general:

- **Regulatory oversight:** *Clinical pre-market evaluations* are often required to secure regulatory clearance and/or CE marking through notified bodies.
- **Coverage and reimbursement:** *Clinical trials, real-world data, and economic evaluations* are often required for initial and ongoing payor assessments.
- **Clinical Practice:** *RCTs and real-world data* are used to determine direct patient care, clinician decision making, and ongoing product innovation decisions.
- **Clinical Guidelines:** *RCTs and clinical trials* are used for inclusion of DTx products into clinical guidelines.

Check all that apply

This overview provides the types of studies that a DTx product may have undergone. It is important for HCDMs to conduct a thorough review of study design and outcomes.

Experimental/Interventional studies

- ☐ Randomized Controlled Trial (RCT)
- ☐ *Other controlled trials:* Non-randomized controlled trial, self-controlled study, crossover study
- ☐ *Non-controlled studies:* Prospective single arm trial, open label trial, head-to-head comparative trial
- ☐ Other: _____

Observational studies

- ☐ *Descriptive:* Case report, case series, cross-sectional (descriptive or prevalence)
- ☐ *Analytical:* Cross-sectional survey, case-control, cohort (prospective or historical)
- ☐ Other: _____

Real-world outcomes

Real-world data generation [Steps 9 & 10]

- ☐ Product performance and technical outputs
- ☐ Clinical and end user engagement and satisfaction measures
- ☐ Other: _____

Real-world evidence [Step 11]

- ☐ Pragmatic clinical trial to conduct randomized trials with real-world elements
- ☐ Real-world evidence (RWE) as a retrospective or prospective observational study
- ☐ Other: _____

Economic evaluation

- ☐ Budget impact analysis
- ☐ Cost-benefit analysis
- ☐ Cost-effectiveness analysis
- ☐ Cost-utility analysis
- ☐ Cost-minimization analysis
- ☐ Other: _____

Systematic review

- ☐ Meta analysis
- ☐ Other: _____

DTx Regulatory Pathways

- IMDRF Software as a Medical Device framework
- United States – Food and Drug Administration
 - 510(k) and De Novo pathways
 - Pre-certification pilot
 - Digital Health Center of Excellence
- Europe – CE Marking through qualified Notified Bodies
 - In-country registration
- United Kingdom – UKCA Mark through MHRA
- South Korea – new regulatory pathway as of Fall 2020

cellence

Digital Health Center of Excellence

[Subscribe to Email Updates](#) [Share](#) [Tweet](#) [LinkedIn](#) [Email](#) [Print](#)

Empowering digital health stakeholders to advance health care

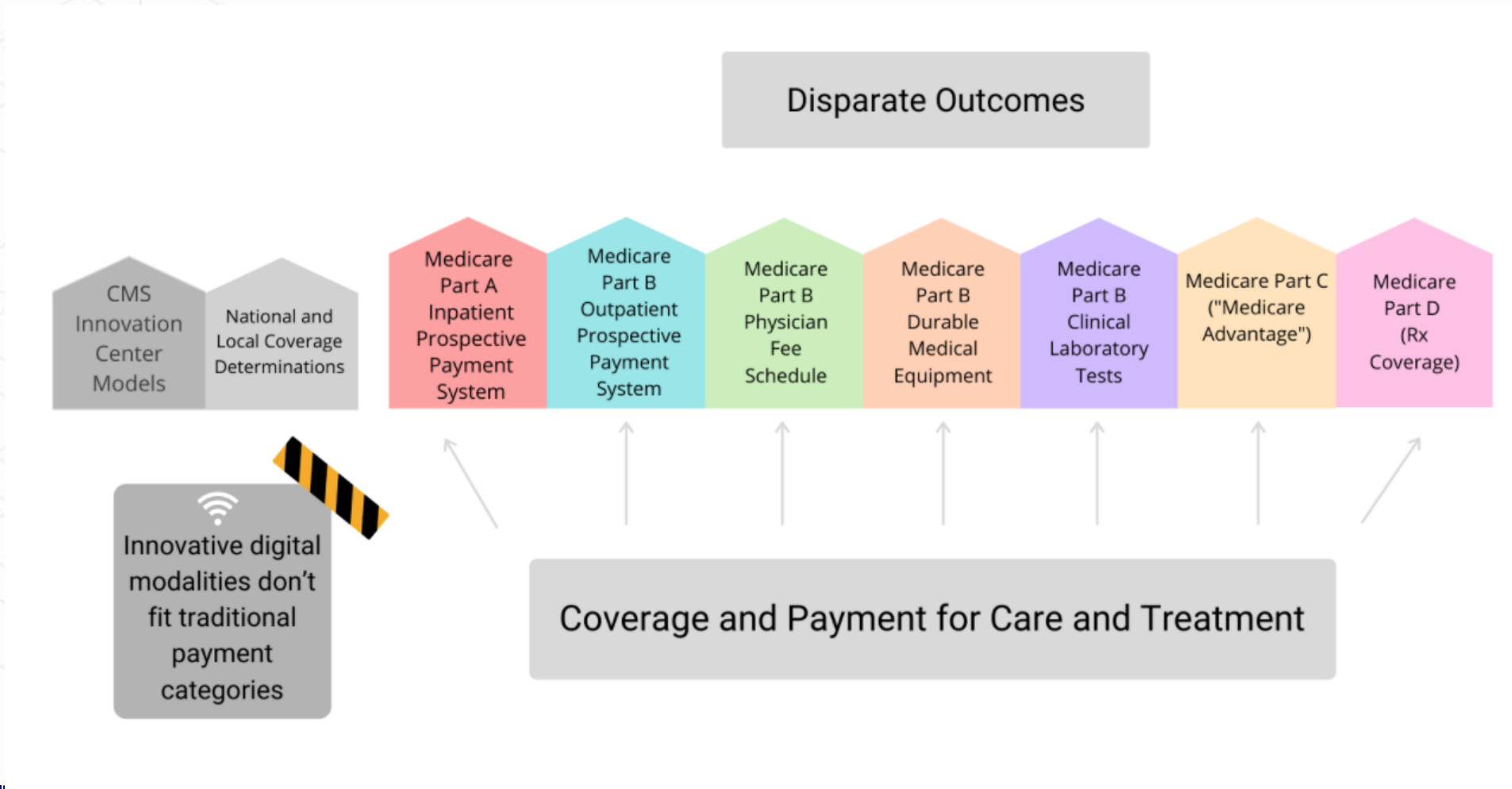


Our goal: Empower stakeholders to advance health care by fostering responsible and high-quality digital health innovation.

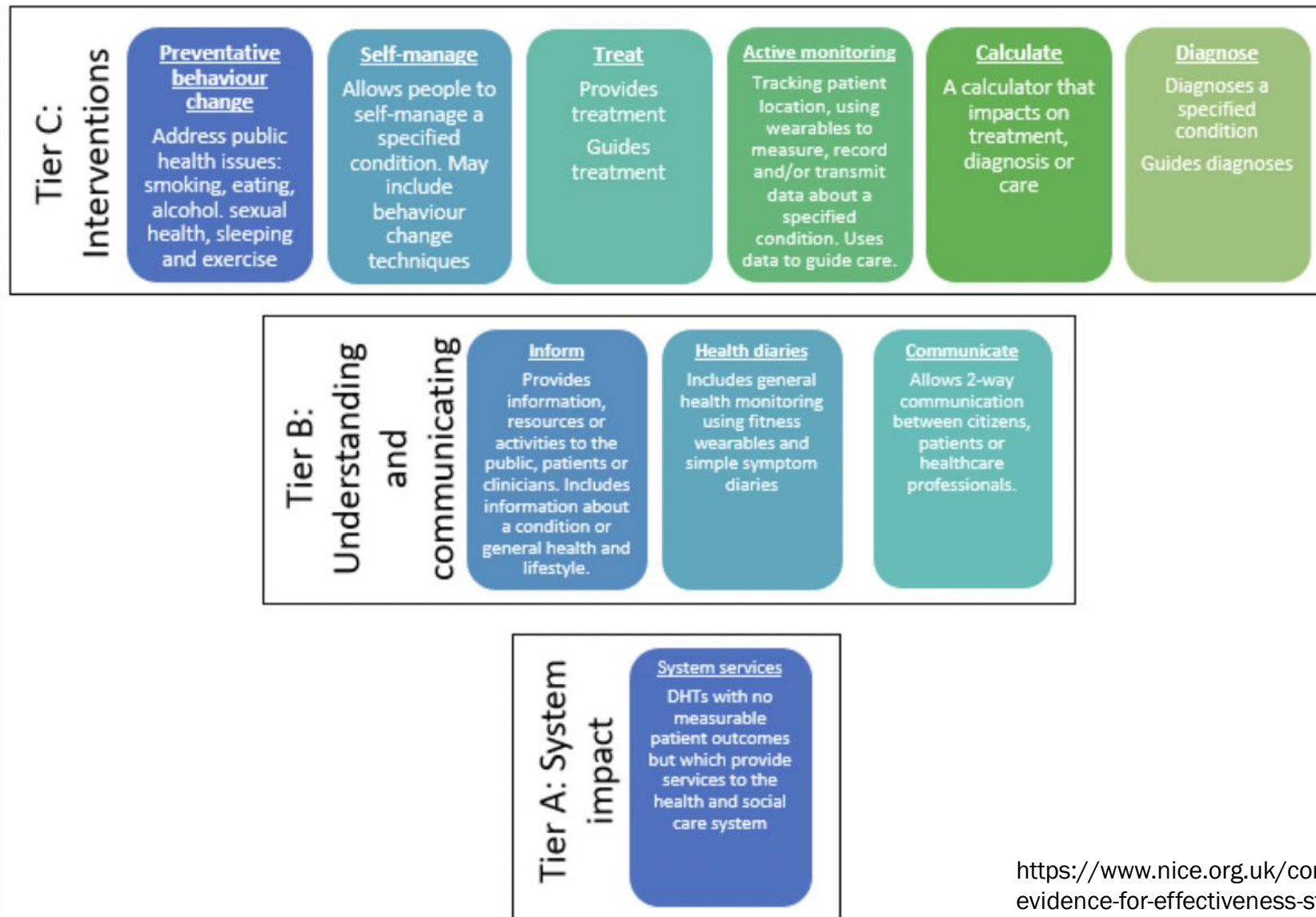
Our objectives: The Digital Health Center of Excellence aims to:

- **Connect and build partnerships** to accelerate digital health advancements.

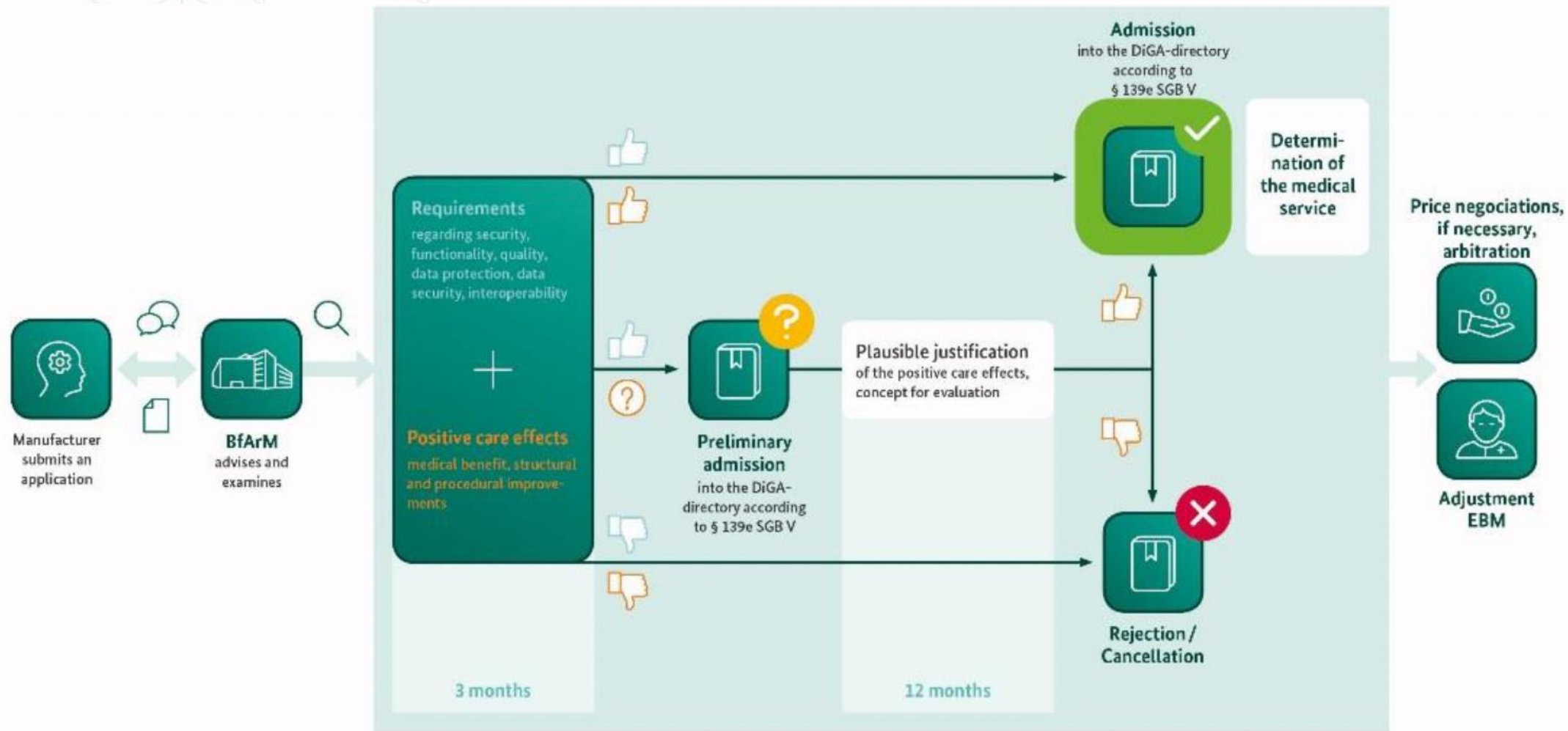
U.S. Medicare Benefit Categories



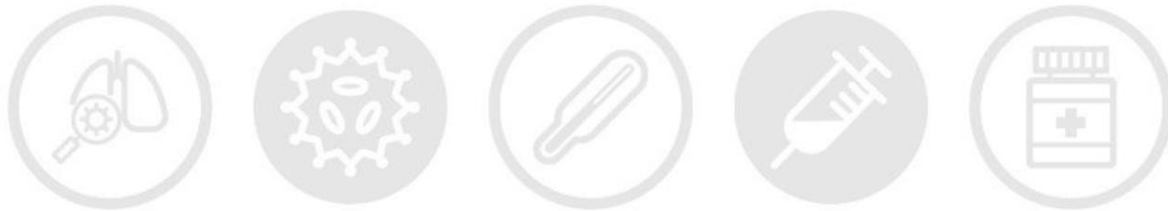
United Kingdom: NICE



Germany: BfArM



South Korea Guidelines



Guideline on Review and Approval of Digital Therapeutics(For Industry)



November 2020

**DIGITAL
THERAPEUTICS
ALLIANCE**

3. Definitions

A. Digital Therapeutics (DTx)

Software as a Medical Device (SaMD) that provides evidence-based therapeutic intervention to patients for prevention, control, or treatment of medical disabilities and/or diseases

※ The use of digital therapeutics is for “patients“ who” require therapeutic intervention

B. Software as a Medical Device (SaMD)

Medical device that does not require actual hardware, has appropriate functionalities for medical purposes, and consists solely of software in its own individual form.



Ministry of Food and Drug Safety
Medical Device Evaluation Department



Stephen Schueller, PhD
University of California, Irvine

ISPOR Europe 2021

Academic
and Clinician:
Digital
Therapies
ISPOR 2021

- Stephen Schueller, PhD
 - Associate Professor of Psychological Science & Informatics, University of California, Irvine
 - Executive Director of One Mind PsyberGuide: onemindpsyberguide.org
 - Licensed Clinical Psychologist and Mental Health Services Research
- 

Banbury Forum Recommendations

Banbury Forum Consensus Statement on the Path Forward for Digital Mental Health Treatment

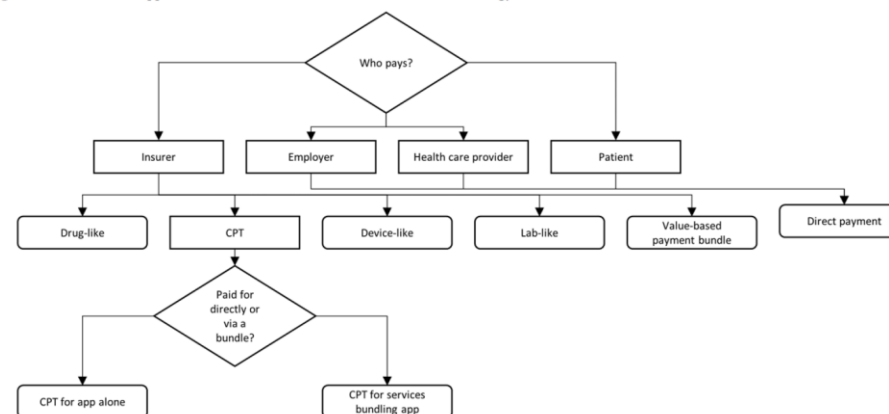
David C. Mohr, Ph.D., Francisca Azocar, Ph.D., Andrew Bertagnolli, Ph.D., Tanzeem Choudhury, Ph.D., Paul Chrisp, Ph.D., Richard Frank, Ph.D., Henry Harbin, M.D., Trina Histon, Ph.D., Debra Kaysen, Ph.D., Camille Nebeker, Ed.D., M.S., Derek Richards, Ph.D., Stephen M. Schueller, Ph.D., Nickolai Titov, Ph.D., John Torous, M.D., Patricia A. Areán, Ph.D., on behalf of the Banbury Forum on Digital Mental Health

1. Guided digital mental health intervention should be frontline interventions for depression, anxiety, and posttraumatic stress disorder
2. Digital mental health interventions should be reimbursable
3. An evidence standards framework should be created to support digital formularies and decision making

The Challenges with Reimbursement Today

- App reimbursement is highly variable today
 - Some apps are reimbursed different ways when working with different payers
 - Some apps use different CPT codes with different payers
- Prescription-based reimbursement is problematic, as social workers cannot prescribe
- Current CPT codes are ill-suited to handling reimbursements for many types of apps, as they are typically tied to provider time

Figure 1. Channels for app reimbursement. CPT: Current Procedural Terminology.



Code	Definition [3]	Context in which use of code was observed
99495	Transitional Care Management Services, with the following required elements: communication (direct contact, telephone, and electronic) with the patient and/or caregiver within 2 business days of discharge. Medical decision making of at least moderate complexity during the service period. Face-to-face visit, within 14 calendar days of discharge	Not observed
99499	Unlisted evaluation and management service	Not observed
A9999	Miscellaneous Durable Medical Equipment (DME) supply or accessory, not otherwise specified	Treatment for substance use disorder (unclear if in active use)
E1399	Durable medical equipment, miscellaneous	Treatment for substance use disorder
G0444	Annual depression screening, 15 min	Medicaid depression initiative
G8431	Screening for depression is documented as being positive, and a follow-up plan is documented	Medicaid depression initiative
G8510	Screening for depression is documented as negative, a follow-up plan is not required	Medicaid depression initiative
H0047	Alcohol and/or other drug abuse services, not otherwise specified	Treatment for substance use disorder (vendor had difficulty obtaining payment from payers using this code)
T1505	Electronic medication compliance management device, includes all components and accessories, not otherwise classified	Treatment for substance use disorder

Examples of app reimbursement strategies

How we evaluate

We review apps against rating criteria developed by experts in the field. Some of those criteria are:

How likely is it that this app will work for me?



Credibility

We look at the research supporting the technology and the credibility of the development process.

What happens the data I enter into this app?



Transparency

We review privacy policies to see if key pieces of information about what happens with entered data are addressed.



User Experience

We explore how fun, functional, easy-to-use, engaging, and interesting the technology is.



Professional Reviews

A professional in a relevant field downloads and uses the technology and writes a narrative review, highlighting pros & cons and some recommendations for use.

How likely is it that I will actually use this app?

What do the professionals say?

[Learn More About Our Criteria](#)



Wayne Burton, MD

Former Chief Medical Officer, American Express

ISPOR Europe 2021

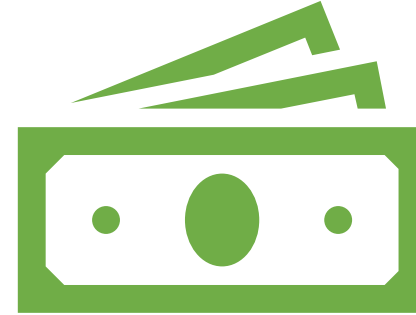
Payer
Perspectives:
Digital
Therapies
ISPOR 2021

- Wayne N. Burton, MD, FACP, FACOEM
 - Former, Chief Medical Officer,
American Express
 - Adjunct Professor, Environmental and
Occupational Sciences, University of
Illinois (Chicago)
- 

Payer Framework for Determining Value



Patient Access/ Experience



Total Cost of
Care (Indirect &
Direct)



Clinical Outcomes



Avoidable
Expenditures



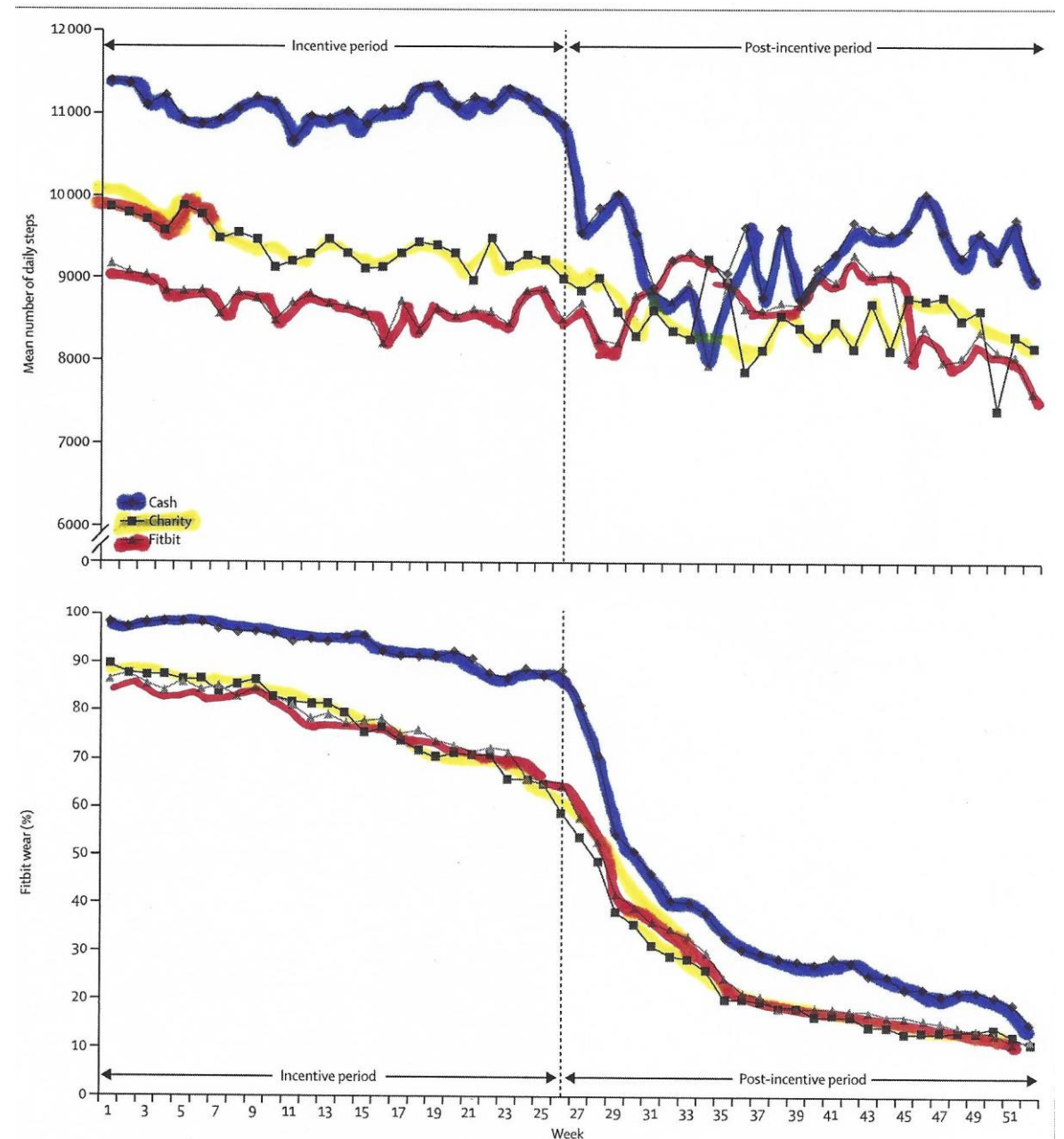
Societal Benefits

There is currently a mosaic of levels of possible evidence for digital therapies:



Randomized Controlled trial of physical activity tracker with and without incentives

- Importance of a randomized trial to evaluate digital therapies
- 1 year study
- Incentive & Post Incentive periods
- Physical activity & health outcomes
- Without an incentive, device use decreased from 90% to 10%
- No improvement in health outcomes (weight, blood pressure, etc.)



Healthcare utilization in opioid use disorder treated with a prescription digital therapeutic

- FDA approved PDA
- Retrospective ≥ 6 month pre/ post medical claims analysis
- Outcomes:
 - *Emergency department visits*
 - *Inpatient hospitalizations*
 - *Total healthcare costs*



Velez et al. Expert Rev Pharmacoeconomics & outcomes research. 2021
Mavicich et al. Cur Med Res & Opinion. 2021



Panel Discussion

ISPOR Europe 2021

Contact Information

Jason Shafrin, PhD

Senior Managing Director,
Center for Healthcare Economics and Policy
FTI Consulting
jason.shafrin@fticonsulting.com



Megan Coder, PharmD, MBA

Vice President of Global Policy
Digital Therapeutics Alliance
mcoder@dtxalliance.org



Stephen M Schueller, PhD

Associate Professor of Psychological Science
School of Social Ecology
University of California, Irvine
s.schueller@uci.edu



Wayne N Burton, MD

Former Global Corporate Medical Director
American Express
Hinsdale, IL USA
wayneburtonmd@comcast.net

