Digital Therapeutics:
Pharmacy Care Innovation and Implications for Policy

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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)

**Categorizations of the digital health technology ecosystem will continue to evolve. This is a select representation of a broad, diverse ecosystem.*

DIGITAL THERAPEUTICS ALLIANCE

What is a digital therapeutic?

Digital therapeutics (DTx) deliver therapeutic interventions directly to patients using evidence-based, clinically evaluated software to treat, manage, and prevent a broad spectrum of behavioral, mental, and physical diseases and disorders.

Whether DTx products are used independently, in tandem with remote or in-person clinician-delivered therapy, or paired with medications, devices, and other therapies, DTA stands behind rigorous patient-centered core principles, ethical standards, and product development best practices to ensure product integrity, user-centered designs, patient privacy, and validated clinical outcomes.

DIGITAL THERAPEUTICS ALLIANCE

Digital Therapeutic Core Principles

Product Quality Matters.

How do I know that this product is a digital therapeutic?

DTx products must adhere to each of these foundational principles:

1. Prevent, manage, or treat a medical disorder or disease
2. Produce a medical intervention that is driven by software
3. Incorporate design, manufacture, and quality best practices
4. Engage end users in product development and usability processes
5. Incorporate patient privacy and security protections
6. Apply product deployment, management, and maintenance best practices
7. Publish trial results inclusive of clinically meaningful outcomes in peer-reviewed journals
8. Be reviewed and cleared or approved by regulatory bodies as required to support product claims of risk, efficacy, and intended use
9. Make claims appropriate to clinical validation and regulatory status
10. Collect, analyze, and apply real world evidence and/or product performance data

DTA's industry principles, code of ethics, and best practices establish expectations for high quality DTx products.

What diseases do DTx products target?

Blood disorders
- Coagulation disorders, including hemophilia

Neoplasms
- Cancer, side effect management
- Cancer, drug therapy optimization

Endocrine, nutritional, and metabolic diseases
- Diabetes, type 1
- Diabetes, type 2
- Metabolic syndrome
- Obesity
- Pre-diabetes

Mental, behavioral, and cognitive disorders
- Alcohol use disorder
- Attention-deficit/ hyperactivity disorder (ADHD)
- Anxiety
- Autism spectrum disorder
- Depression
- Eating disorders
- ICU delirium
- Opioid use disorder (OUD)
- Pain (acute, chronic)
- Panic disorder, panic attacks
- Post-traumatic stress disorder (PTSD)
- Schizophrenia (positive symptoms)
- Stress-related chronic diseases
- Substance use disorder (SUD)

Nervous system disorders
- Epilepsy
- Insomnia, sleep disorders
- Lupus
- Migraine
- Multiple sclerosis (MS)
- Parkinson's disease (PD)

Circulatory system disorders
- Hypertension
- Stroke

Respiratory system disorders
- Asthma
- Chronic obstructive pulmonary disease (COPD)

Digestive system disorders
- Irritable bowel syndrome (IBS)

Skin and subcutaneous tissue disorders
- Skin disorders

Musculoskeletal system and connective tissue disorders
- Movement disorders
- Orthopedic conditions
- Osteoarthritis

Pregnancy and childbirth
- Post-partum depression

Injury, poisoning, and certain other consequences of external causes
- Traumatic brain injury (TBI)

DIGITAL THERAPEUTICS ALLIANCE

*As of March 2020

DTx Product Categories

Digital therapeutics generally align with one of these categories based on the product's primary purpose:

	Digital Therapeutic to: TREAT A DISEASE	Digital Therapeutic to: MANAGE A DISEASE	Digital Therapeutic to: IMPROVE A HEALTH FUNCTION*
Level of medical claims	Medium to high-risk claims	Medium to high-risk claims	Low to medium-risk claims
Clinical endpoints	Must use clinical endpoints to support product claims	Must use clinical endpoints to support product claims	Must use clinical endpoints to support product claims
Clinical evidence	Clinical trials and ongoing evidence generation required	Clinical trials and ongoing evidence generation required	Clinical trials and ongoing evidence generation required
Regulatory oversight	Third-party validation of efficacy and safety claims by regulatory or equivalent national body	Third-party validation of efficacy and safety claims by regulatory or equivalent national body	Degree of regulatory oversight depends on local regulatory body frameworks
Patient access	Prescription required	Prescription required OR Non-prescription product	Non-prescription product

*Incudes digital therapeutics that prevent a disease

DIGITAL THERAPEUTICS ALLIANCE

Digital Health Center of Excellence

Content current as of:
09/22/2020

Regulated Product(s)
Medical Devices

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.

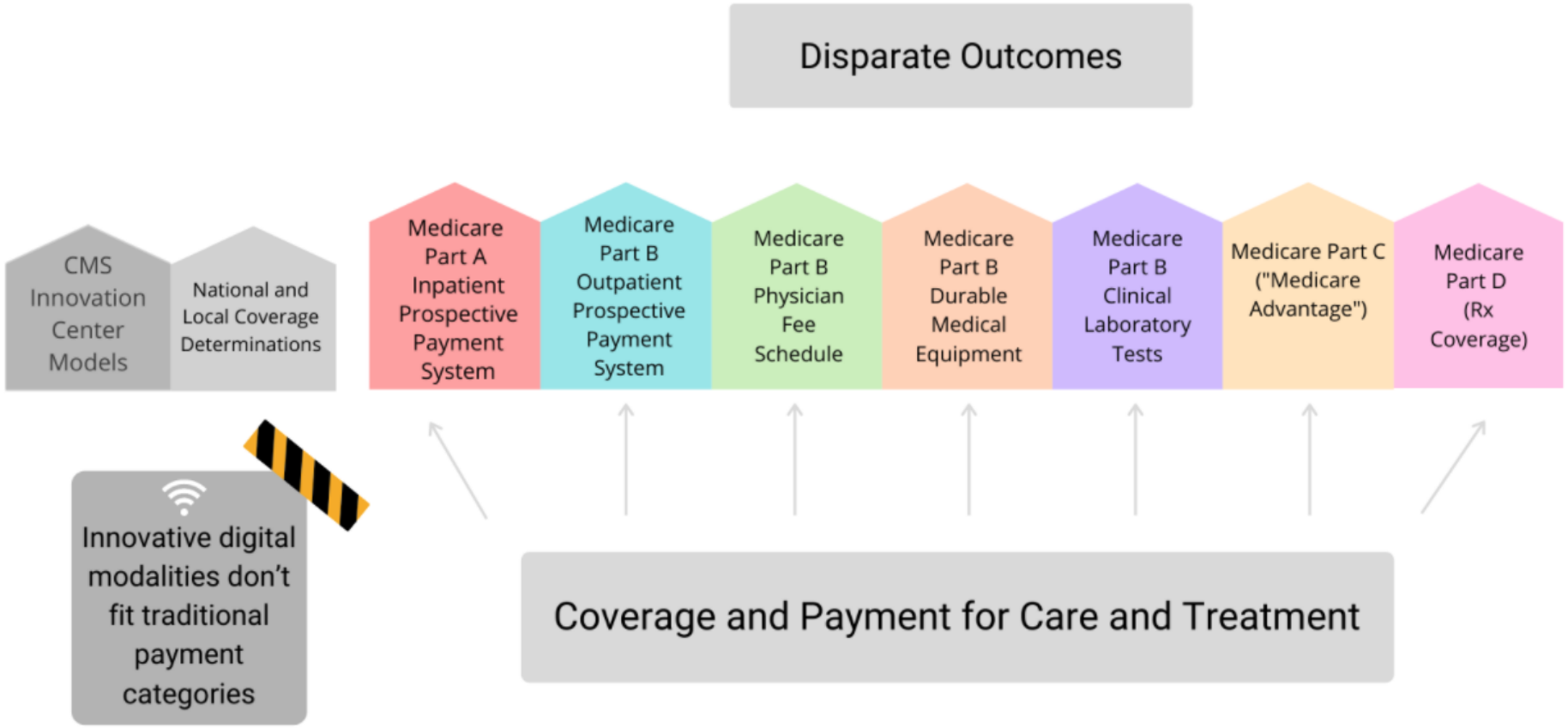
FDA’s Emergency Use Authorization

“In the context of the COVID-19 public health emergency, the use of digital health technologies, including software as a medical device or other digital therapeutics solutions, may improve mental health and well-being of patients with psychiatric conditions during periods of shelter-in-place, isolation, and quarantine. In addition, the use of such technologies has the potential to facilitate “social distancing” by reducing patient contact with, and proximity to, health care providers, and can ease the burden on hospitals, other health care facilities, and health care professionals that are experiencing increased demand due to the COVID-19 public health emergency.”

-U.S. Food and Drug Administration (source)

DIGITAL THERAPEUTICS ALLIANCE

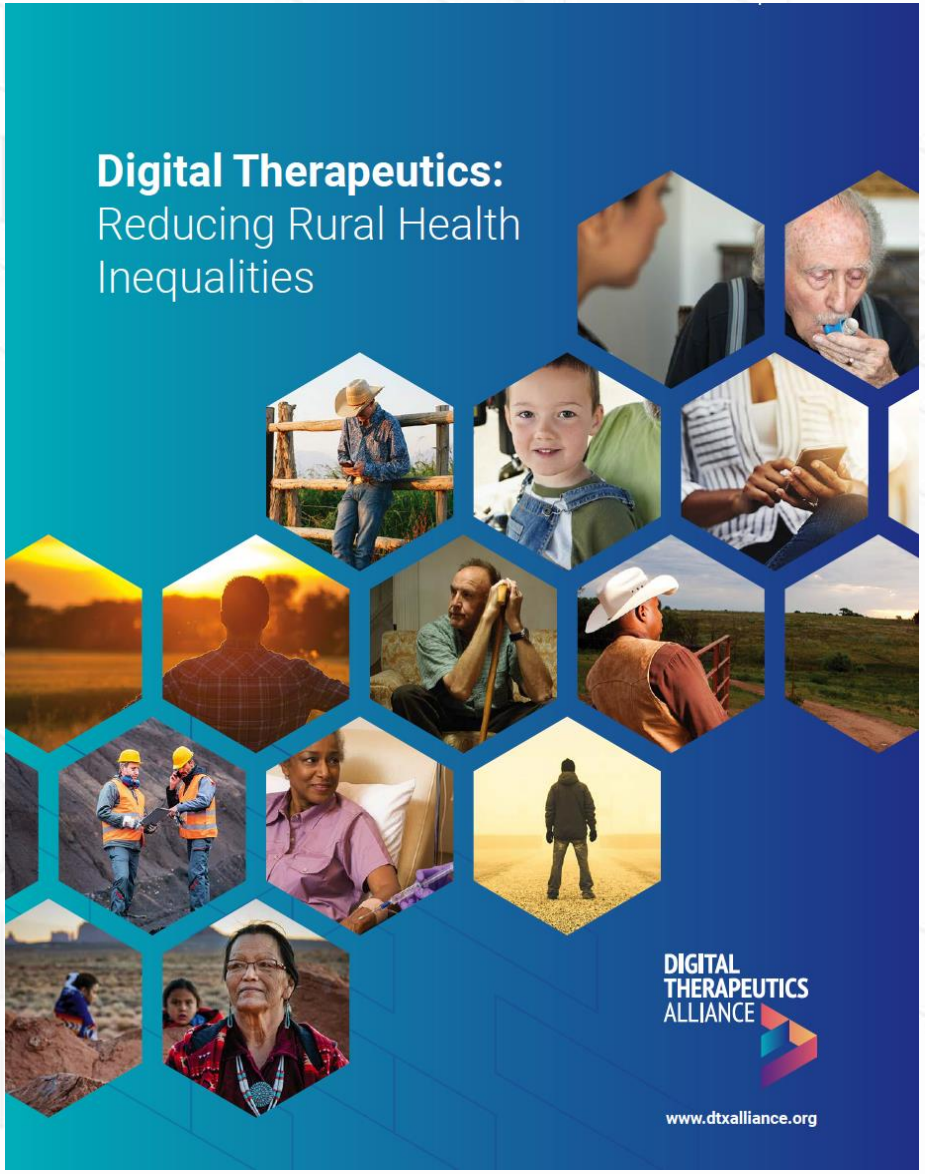
Medicare Benefit Categories



https://www.healthaffairs.org/do/10.1377/hblog20201021.783035/full/

DIGITAL THERAPEUTICS ALLIANCE

DTA Paper: Rural & Underserved Communities



Download at https://dtxalliance.org/wp-content/uploads/2021/01/DTA_Rural-Health_r13_110220.pdf

DTx Value Assessment & Integration Guide

Draft Table of Contents:*

*Content subject to change prior to launch

How do we differentiate between different digital health products?

Digital Therapeutic Landscape

- Digital health ecosystem product overview
- Digital therapeutic definition and core principles
- DTx product types
- DTx industry code of ethics

How do we identify high quality digital therapeutics?

DTx Product Assessment: Safety, Efficacy, Intended Use

- DTx product assessment and evaluation
- Clinical & economic evidence expectations
- DTx product evaluation types
- Assessing clinical trial evidence
- DTx product technical considerations
- Product appropriateness and usability
- DTx products on the market

What types of data do digital therapeutics generate?

DTx Product Clinical Evaluation: Product Ongoing Effectiveness & Economic Impact

- Interpreting real-world data (RWD)
- Real-world data (RWD) types generated by DTx products
- Developing targeted real-world evidence (RWE)
- Assessing and applying real-world evidence (RWE)
- Health Economic and Outcomes Research (HEOR)

How do we evaluate the economic impact of digital therapeutics?

Economic Assessment

- How DTx products address payor needs
- Factors that affect DTx therapy economic impact
- DTx economic impact evaluation framework*
- DTx economic impact evaluation considerations

How do we deliver digital therapeutics to patients?

Implementing Digital Therapeutics

- DTx implementation and engagement*
- Appropriateness of implementation studies
- Ensuring quality data sets

How do we implement and optimize DTx products in clinical practice?

Clinical Practice Considerations

- DTx product benefits for patients and caregivers
- DTx product benefits for clinicians and health systems
- Product authorization and distribution
- Clinician team engagement
- Access to product outcomes

How to we assess DTx product compliance with applicable regulations?

Compliance Assessment: Regulatory, Data, and IP Considerations

- Regulatory oversight
- Region-specific regulatory pathway considerations
- Product security best practices
- Product data integrity, quality, and governance
- Intellectual property considerations

DTx Product Case Studies

Conclusion and look at the horizon

Susan A. Cantrell, RPh, CAE

Chief Executive Officer

AMCP

AMCP

Optimizing medicine.
Improving lives.

Mission

To improve patient health by ensuring access to high-quality, cost-effective medications and other therapies.

AMCP

PARTNERSHIP FORUM

No. 3 — 2019

Digital Therapeutics: What are They and Where Do They Fit in Pharmacy and Medical Benefits?

Digital Therapeutics (DTx)

What are they and where do they fit into pharmacy and medical benefits?

Forum Objectives

- Describe digital therapeutics (DTx) and how managed care organizations evaluate their value.
- Identify where digital therapeutics fit in within a coverage benefit.
- Outline evidentiary standards needed for coverage of digital therapeutics.
- Outline how payers/managed care organizations may leverage digital therapeutics for value-based care and patient engagement.

Characteristics of DTx

- Software that delivers a clinical mechanism-of-action, either alone or in combination with other standard-of-care treatments, to improve outcomes
- As with other treatments (e.g., small molecule drugs, biologics, devices), stakeholders expect
  - Appropriate clinical evidence of safety and efficacy
  - Good manufacturing practices

Solutions Along the Patient Journey





Focus areas to improve care along the patient journey				
Outpatient • Moving PCP visits to virtual modalities • Reducing price dispersion • Care avoidance from personal health/self-diagnostic tools	**Inpatient** • Reduction of re-admissions • Reducing price dispersion • Reducing expensive ER visits	**Prescription** medication • Reducing price dispersion	Home **health** • Reducing unit cost of home care through virtualization and tele-health	**New** modalities • Increase in revenue from virtual visits • Percent of value created captured by digital solutions (assumed 10%)
Opportunity for digital therapeutics				
• Self-service • Remote patient engagement	• Financial transparency through better tracking of outcomes	• Clinical transparency into use and adherence	• Quantified self wellness • Treatment adherence • Health monitoring and coaching • Social connectivity • Wearables	• Virtual access tools • Remote care

Evidence Requirements

- Varies based on medical claim or function
- Should align with standards for clinical evidence
- Evidence of safety and efficacy based on
  - Standardized endpoints for the disease area
  - Appropriate patient population
  - Clinical trials conducted using good clinical practices
- Clinical evidence must be evaluated by appropriate health authorities and receive market authorization with a regulatory label
- Ongoing data to support modifications/improvements to product follow GMPs

Payer Evaluations

- Value determination
- Patient acceptance
- RWE, PROs
- AMCP Format for Formulary Submissions

Payer Evaluations

- Understanding value when making coverage decisions. Taking steps to validate products, support reimbursement and widespread adoption
  - Address gaps in care
  - Patient acceptance of the DTx, patient reported outcomes
  - Real-world evidence
  - Logistical issues
- NICE Evidence Standards Framework for Digital Health Technologies is made up of:
  - Effectiveness standards
  - Economic impact standards
- PBMs are further along in establishing digital formularies

https://www.nice.org.uk/about/what-we-do/our-programmes/evidence-standards-framework-for-digital-health-technologies

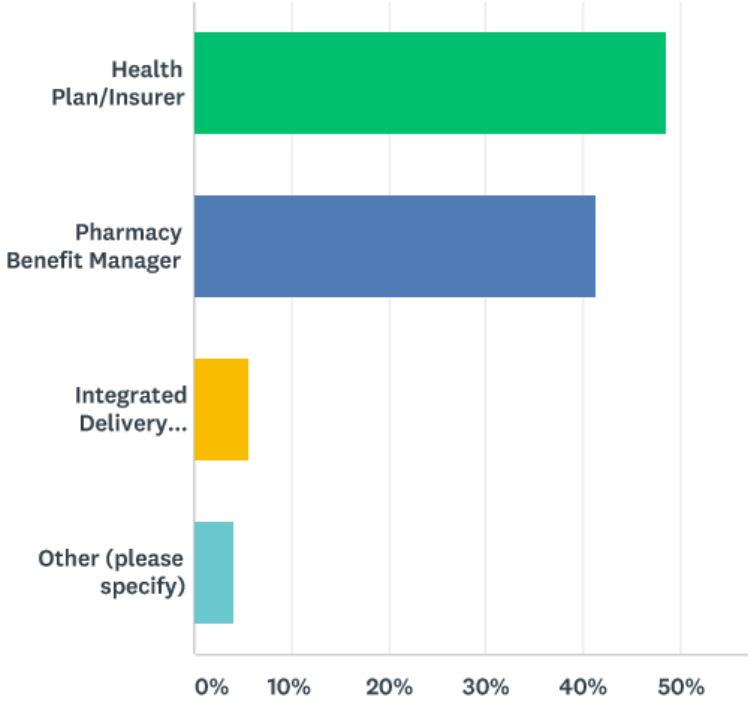
Shyra Bias, PharmD Candidate, 2021, Assessing Barriers to Inclusion of Digital Therapeutics on Formulary: A Cross-Sectional Study Across Health Plans, PBMs, and IDNs. Poster presented at AMCP Nexus 2019

Survey Results: Assessing Barriers to Inclusion of Digital Therapeutics on Formulary

A Cross-Sectional Study Across Health Plans, PBMs, and IDNs

Q1 What is your organization type?

Answered: 70 Skipped: 0



What type of evidence would be required for the decision-making process of DTx?

ANSWER CHOICES	RESPONSES	
Disease state classification provided along with tier guidance	41.43%	29
Real world evidence/observational studies	78.57%	55
Randomized controlled trials	64.29%	45
Relevance to current care pathways	68.57%	48
Detailed adverse events/side effect profile	30.00%	21
Information on drug/DTx interactions	25.71%	18
Return on investment (ROI) evaluation	80.00%	56
FDA approval	45.71%	32
Other (please specify)	5.71%	4
Total Respondents: 70		

A multiple choice, mixed qualitative-quantitative web-based survey (8/15/19 to 9/3/19)

Shyra Bias, PharmD Candidate, 2021, Assessing Barriers to Inclusion of Digital Therapeutics on Formulary: A Cross-Sectional Study Across Health Plans, PBMs, and IDNs.
Poster presented at AMCP Nexus 2019

Strategies for Integrating DTx in Health Care

- ✓ Incorporate into clinical guidelines
- ✓ Incorporate into step therapy
- ✓ Incorporate into value-based contracts
- ✓ Use of standard pharmacy product identifiers to allow for coding within pharmacy benefit systems.

AMCP/ACHP Consumer Survey
Growing use of Digital Apps

11% percent of respondents said they had used a smartphone app to manage their health

32% were open to using the modality, which includes prescribed digital therapeutics

ACHP AMCP Consumer Survey, conducted by Leede Research, May 2020 Findings

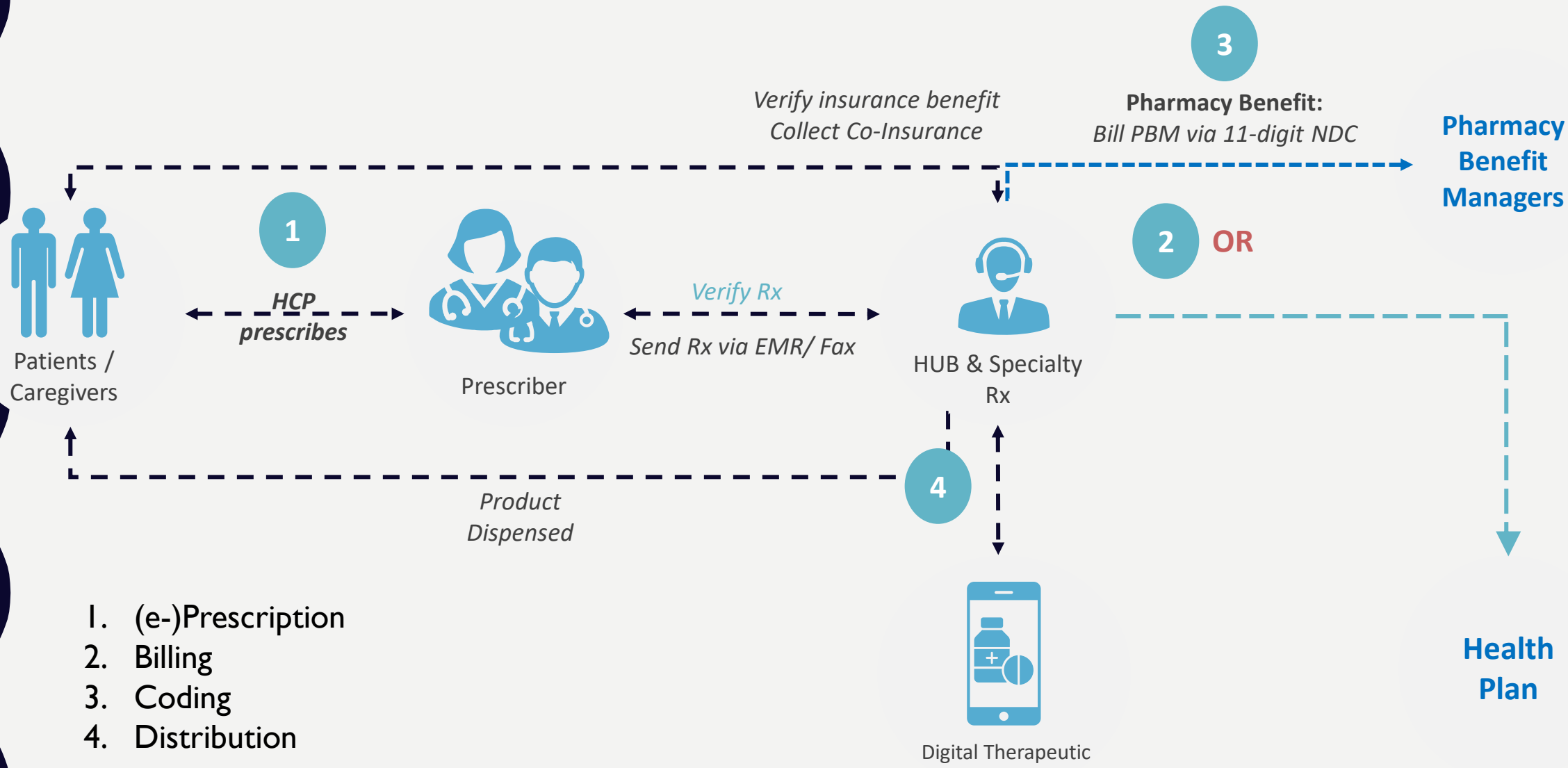
Laura Topor
President
Granada Health, Inc.

MC DIGITAL THERAPEUTICS TASK GROUP

- The MC Digital Therapeutics (DTx) Task Group will evaluate and identify the existing NCPDP or external standards that will fully or partially support DTx participant data exchange and propose changes to existing standards or alternatively develop new standards to support DTx requirements. Through the task group work, electronic data exchange between DTx trading partners and patient access to digital therapeutics will be supported.

DTx QUESTIONS TO NCPDP

1. Can you e-prescribe?
2. Can DTx be billed like a drug or medical device?
3. How do you code a DTx?
4. How are DTx products provided to pharmacies or patients? What is the "Product"?



1. (e-)Prescription
2. Billing
3. Coding
4. Distribution

EXISTING NCPDP STANDARDS REVIEWED/UNDER REVIEW

• Billing Unit Standard	• Product Identifiers Standard
• SCRIPT Transactions	• Telecommunication Standard Transactions
• Formulary and Benefit Standard (F&B)	• Real-Time Prescription Benefit (RTPB)
• Specialty Pharmacy Data Reporting Standard	• Benefit Integration Standard
• Medical Rebate Data Submission Standard	• Manufacturer Rebate Standard

BILLING UNIT STANDARD

- Common billing units are "each" (EA), milliliter (mL) or gram (GM)
- Digital Therapeutics organizations should bring their product to the NCPDP Billing Unit Task Group to verify the appropriate billing unit for their product based upon its use.
  - The manufacturer should fill our a Quantity Unit Information Communication (QUIC) form to aid in Task Group discussion and adjudication

PRODUCT IDENTIFIERS STANDARD

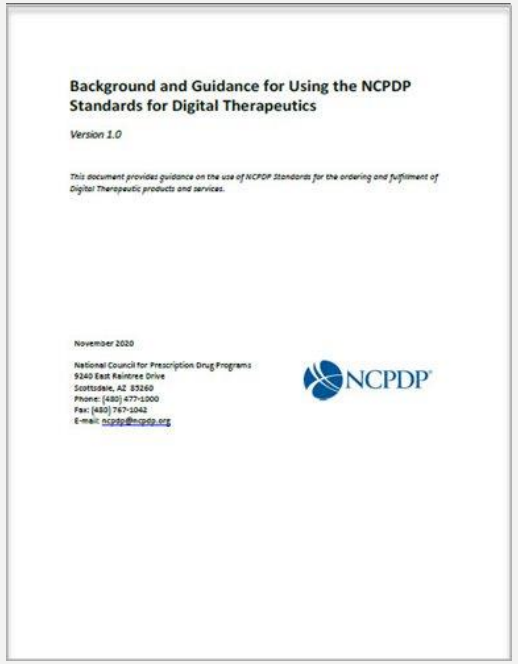
The following product identifiers are accepted for use in NCPDP standards:

NDC	UPC
National Health Related Item Code (NHRIC)	Device Identifier (DI) portion of the UDI
Health Industry Business Communications Council® Code (HIBCC®) (19-digit limit)	Product Identification Numbers (PIN)
Global Trade Identification Number (GTIN)	

NEXT STEPS

- Complete review of existing standards
- Solicitation of use cases that vary from the *Initial Use Case* and determine standards useability
- Update *"Guidance for Using the NCPDP Standards for Digital Therapeutics"* document

https://ncpdp.org/Resources


Background and Guidance for Using the NCPDP Standards for Digital Therapeutics

Version 1.0

This document provides guidance on the use of NCPDP Standards for the ordering and fulfillment of Digital Therapeutic products and services.

November 2020

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NCPDP

FROM AMCP

- ***Descriptions for digital therapeutic:*** To qualify, the product must be a "high-quality digital intervention, making a medical claim, that is driven by software programs to prevent, manage or treat a medical disorder or disease." Digital therapeutics also "require approval and third-party validation of efficacy and safety claims" by a regulatory or equivalent national body, such as the Food and Drug Administration, or a recognized accreditation or health services organization.
- ***Coverage decision standards:*** Coverage by payers will first include a thorough examination of the safety, efficacy, and usability of a product, along with the therapy's medical claim or function. Products intended to replace a pharmaceutical intervention, for example, may require more evidence for coverage than those intended to monitor a condition.

https://www.amcp.org/Resource-Center/blog/amcp-helping-define-digital-therapeutics-coverage-decisions

Thank You