2021 LIFE SCIENCES BOOTCAMP SERIES

DIGITAL HEALTH INSIGHTS

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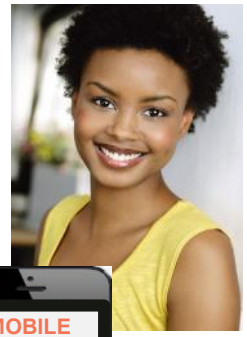
McDermott Will & Emery

AGENDA

- Survey of Digital Health Landscape
  - The Connected Patient and Digital Health Ecosystem
  - Telehealth Care Delivery Models
  - Remote Patient Monitoring
  - Emerging Virtual Care Models
- Data as an Asset
  - Data Sources & Goals
  - Developing Your Data Strategy
  - Use Cases
  - Artificial Intelligence
- FDA and its approach to Digital Health
  - FDA Regulatory Priorities
  - Use Cases
  - FDA Guidance

NEW PARADIGM FOR HEALTHCARE: THE “CONNECTED” PATIENT

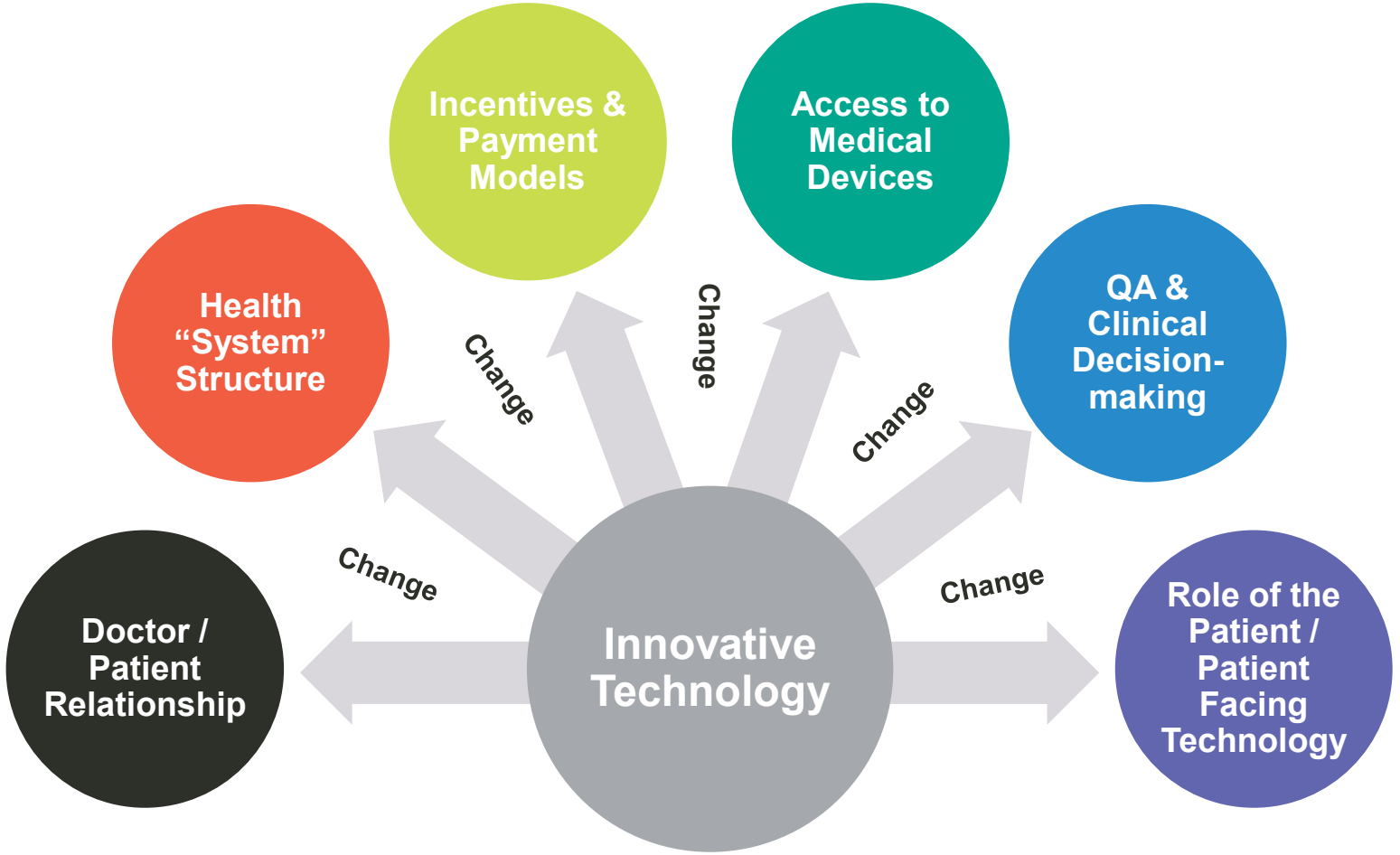


WEARABLES

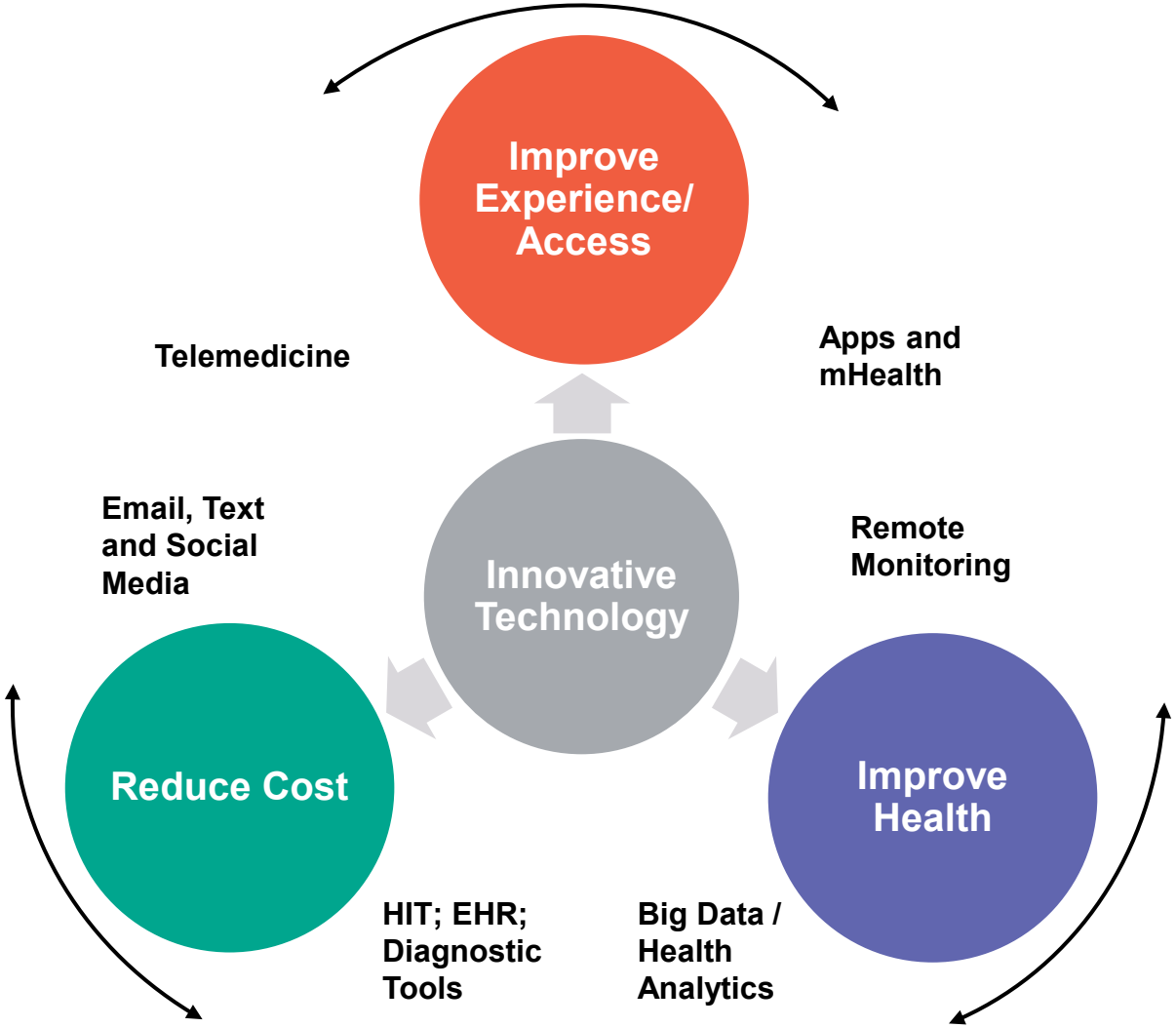
Consumer/Patient

- Wearable Biometric and Behavioral Data tracking (Medication reminders, BP, Heartrate, etc.)
- Communication with HCP
- Control and Monitoring of Auxiliary Medical Devices

DIGITAL HEALTH ECOSYSTEM IS CHANGING TRADITIONAL HEALTHCARE PARADIGMS

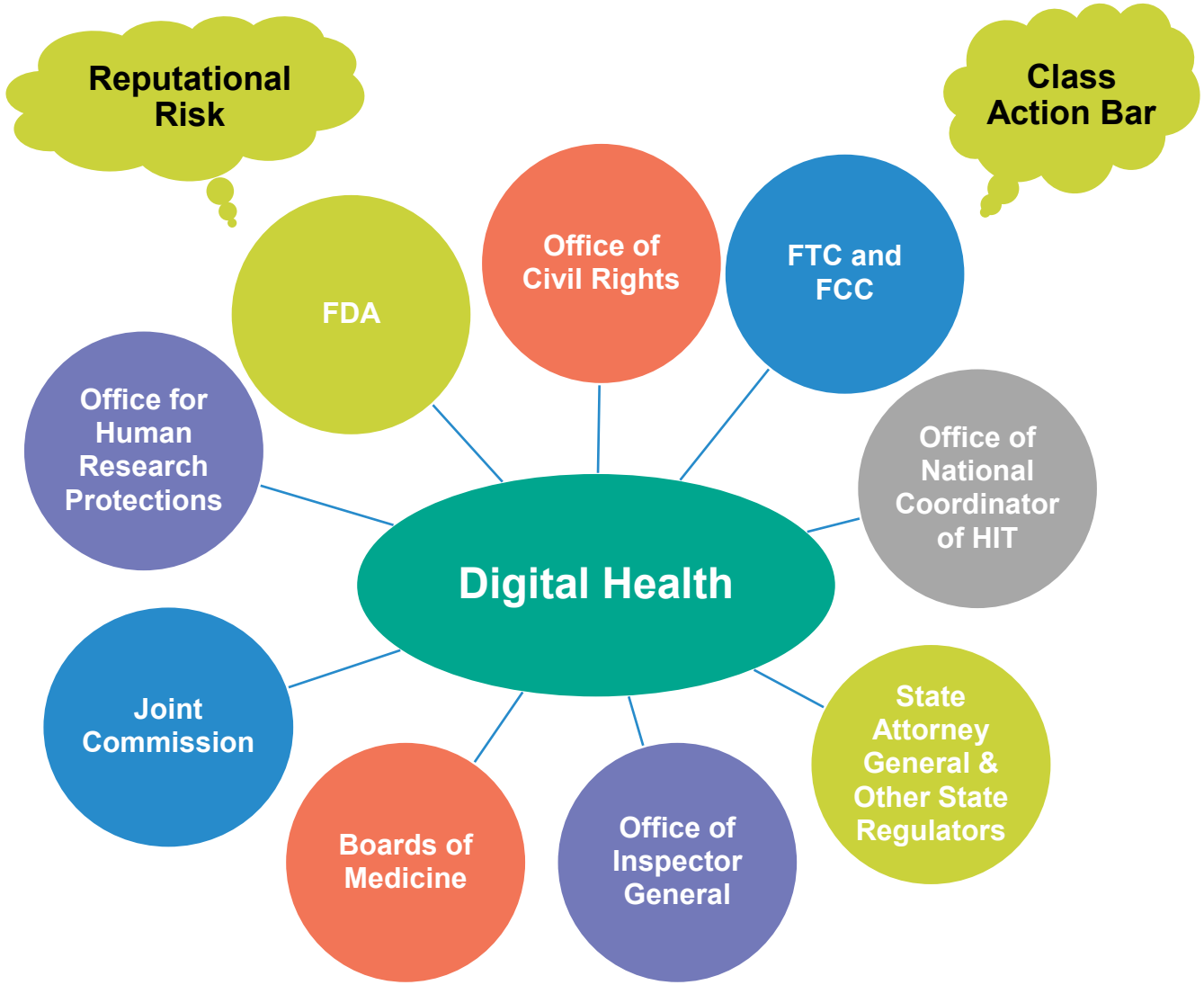


…AND HELPING TO ACHIEVE THE TRIPLE AIM



DIGITAL HEALTH – THE PERFECT STORM OF OPPORTUNITY AND RISK

- Opportunities
  - Advancing Patient Engagement in Care
  - Connecting HCPs to Underserved Patient Populations
  - Harnessing Data and Analytics to Improve Care
  - Innovative Collaborations & Partnerships
- Risks
  - Many Regulators with Divergent Priorities
  - Product Safety and Effectiveness
  - General Privacy and Security
  - Financial Relationships & Pricing
  - Slow Market Adoption

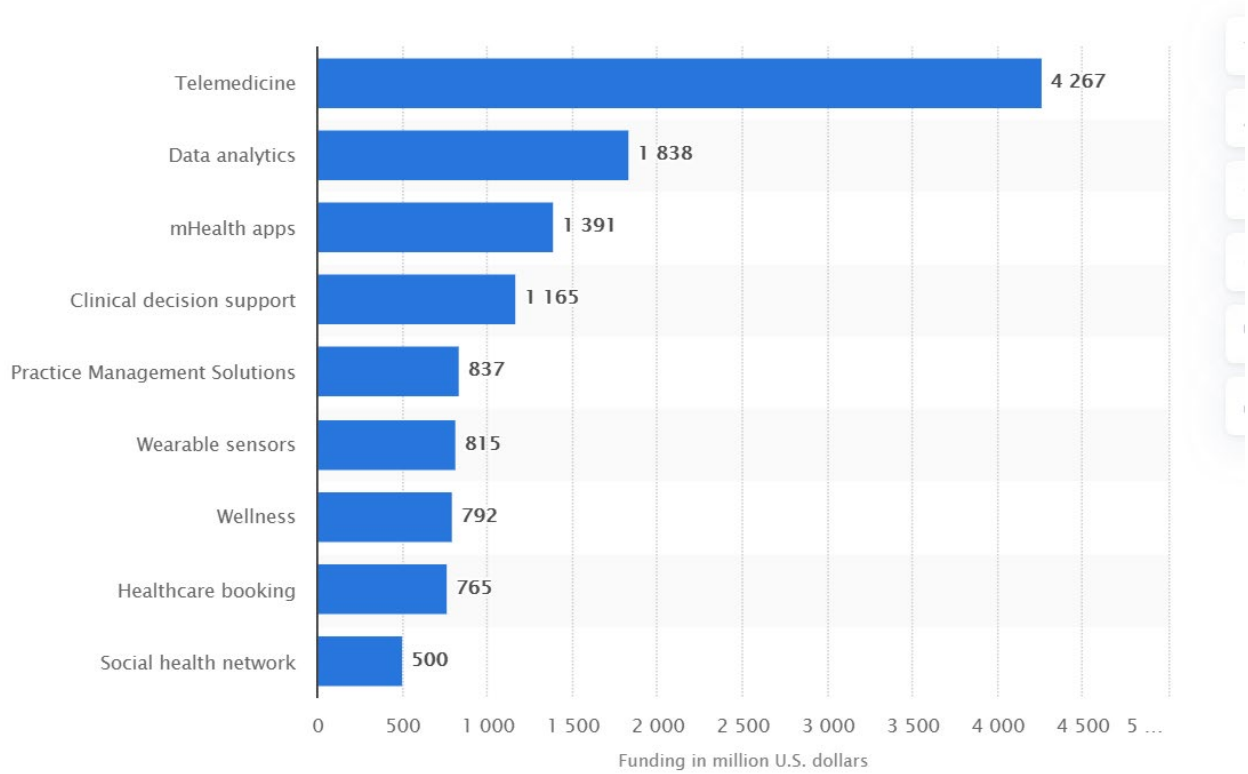


DIGITAL HEALTH – BY THE NUMBERS

Worldwide Digital Health Market to Hit $504.4 Billion by 2025, with > 50% concentrated in North America

- In 2020, digital health deals and overall funding increased significantly. The year saw a **28% increase in M&A** from 2019.
- Venture funding **up 66%** with a **record $14.8 billion** raised in 2020
- Total corporate funding for digital health - including VC, debt, and public market financing - **reached $21.6 billion in 2020**

Top funded DH categories worldwide in 2020 (USD)



Source: , Rock Health, Mercom Capital Group, Inc.

EMERGING VIRTUAL CARE MODELS – NOTABLE DEALS AND COLLABORATIONS

BD Scanwell	**Becton Dickinson and Scanwell Health** | Collaboration to create an at-home rapid test for SARS-CoV-2 using a BD antigen test and the Scanwell Health mobile app.
Cigna MDLIVE	**Cigna and MDLIVE |** Evernorth, Cigna's Health Services Business, acquires MDLIVE, providing Evernorth with a platform that expands Evernorth's capabilities to deliver a more affordable, convenient and connected patient care experience.
omada PHYSERA	**Omada Health and Physera |** Omada buys Physera for $30M, adding virtual musculoskeletal care to Omada Health's services.
ginger Blackstone	**Blackstone and Ginger** | Ginger received $100 Million Series E financing from Blackstone to bring value-based mental healthcare to millions of employees and health plan members
TriNetX The Carlyle Group	**Carlyle and TriNetx** | Carlyle's investment in TriNetx accelerates development of new clinical research capabilities for healthcare organizations and life sciences customers

BENCHMARKING: PHARMA DIGITAL HEALTH ENVIRONMENT

Lilly Names HealthVoyager as Winner of Digital Health Innovation Challenge for Inflammatory Bowel Disease (IBD)

December 2, 2019

Download PDF

INDIANAPOLIS, Dec. 2, 2019 /PRNewswire/ -- Eli Lilly and Company's (NYSE: LLY) first digital health open innovation challenge, "Transforming IBD Care: Better Disease Monitoring, Management, and Care for People with Inflammatory Bowel Disease," has concluded, with HealthVoyager, an application developed by Boston Children's Hospital and Klick Health, being named the winner. The idea leverages a highly customizable software platform for doctors to create a personalized and immersive educational experience for patients living with inflammatory bowel disease (IBD). At Lilly's headquarters in Indianapolis, five finalists presented their digital health solutions aimed at transforming IBD care, during which an expert panel of judges evaluated each idea's impact, novelty, technical feasibility and ability to address long-term needs of people with IBD.

STARTUPS, HEALTH TECH

If Big Pharma is from Mars and digital health startups from Venus, PharmStars wants to play Cupid

Digital health startups and pharma industry players sometimes don't speak the same language, and the culture gap has led to failures in the past. A new accelerator focused on helping digital health companies engage better with pharma hopes to flip the script.

Digital health, digital therapeutics, digital medicines – what's in a name?

Elise Reuter, 1/21/20 (MedCity News)

Marrying science with consumer tech

In the long run, for these companies to survive, they must have two things: solid clinical evidence and a good understanding of what patients need.

Andrew Hedin, a principal with Menlo Park-based Bessemer Venture Partners, said he often sees companies with one of two backgrounds. Some have strong clinical experience and take a biotech-like approach to research. Others come from a consumer technology background, building tools that are appealing to patients, but with little scientific backing.

"I believe both are doomed to fail. You need to marry both expertises," he said in a phone interview. "A digital therapeutic won't be effective unless a patient consistently engages with that product."

Digital Health Investments: from spray and pray to strategic

It's no secret that pharma have been increasingly investing in digital health solutions. According to our findings, since 2014, the top 10 pharma companies have contributed to 129 digital health investments and 8 acquisitions of digital health companies, accounting for over 13% of their shared investment activity during that period. While we identified investment activity in 8 of the 10 pharma companies, only 2 (Roche and Merck) have doubled down on their investments, and converted them into acquisitions in the digital health space.

While the total number of investments appear to be decreasing, the amount of capital being invested is increasing, with the exception of 2017 which was offset by the mammoth GRAIL investment of $1.2B. Is this a sign of investors knowing better what they're looking for instead of adopting a spray and pray approach? We think so.

MERCK

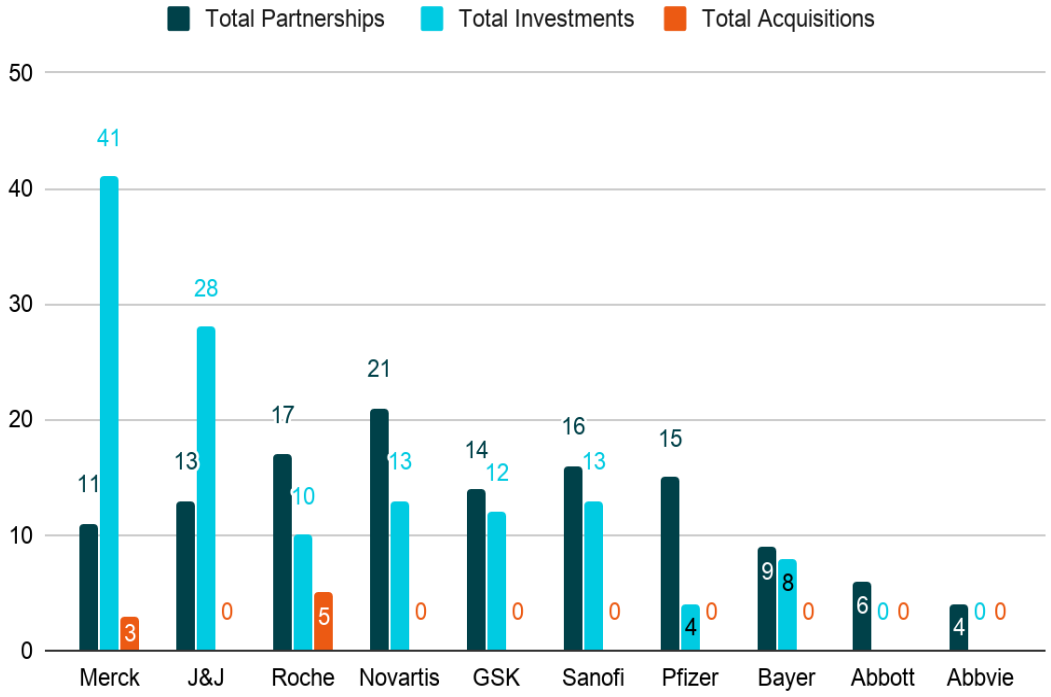
Media > News releases > News Release

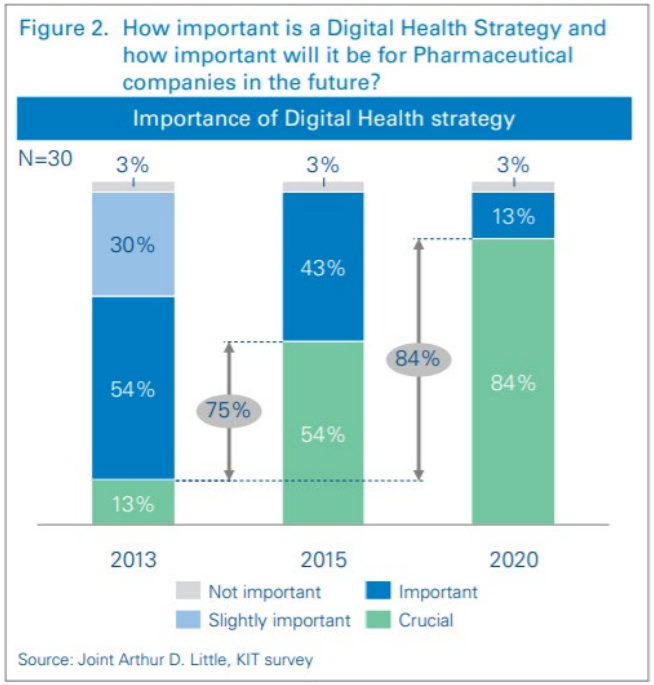
Healthy Interactions and Merck Announce Launch of Digital Health Platform Designed to Enhance Patient Engagement in Diabetes Management

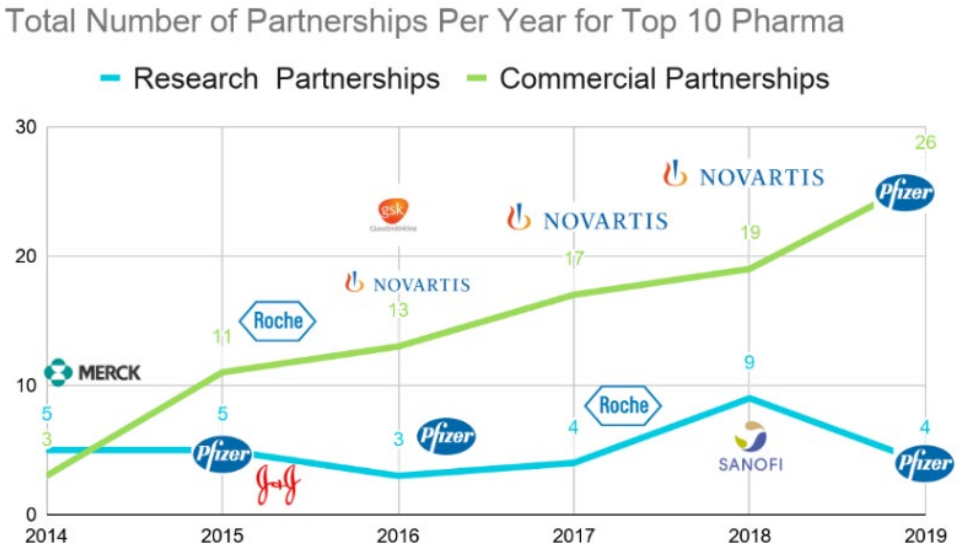
AstraZeneca Announces Collaboration with Massachusetts General Hospital to Accelerate Digital Health Solutions

Heart failure and asthma studies will pilot a new digital health platform to help improve outcomes for patients with chronic diseases

BENCHMARKING: DIGITAL HEALTH INVESTMENT LANDSCAPE FOR PHARMA/BIOTECH





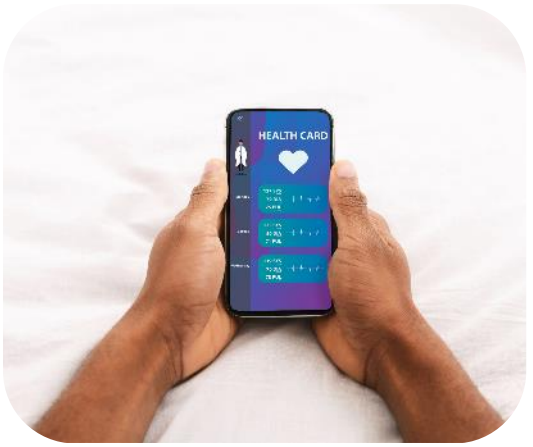


Source: https://www.healthxl.com/blog/measuring-digital-health-maturity-review-of-top-10-pharma-activity-over-the-last-5-years

CONSIDERATIONS: TAKEAWAYS FROM DIGITAL HEALTH IN PHARMA

Pharma, tech companies and start-ups all in the digital space

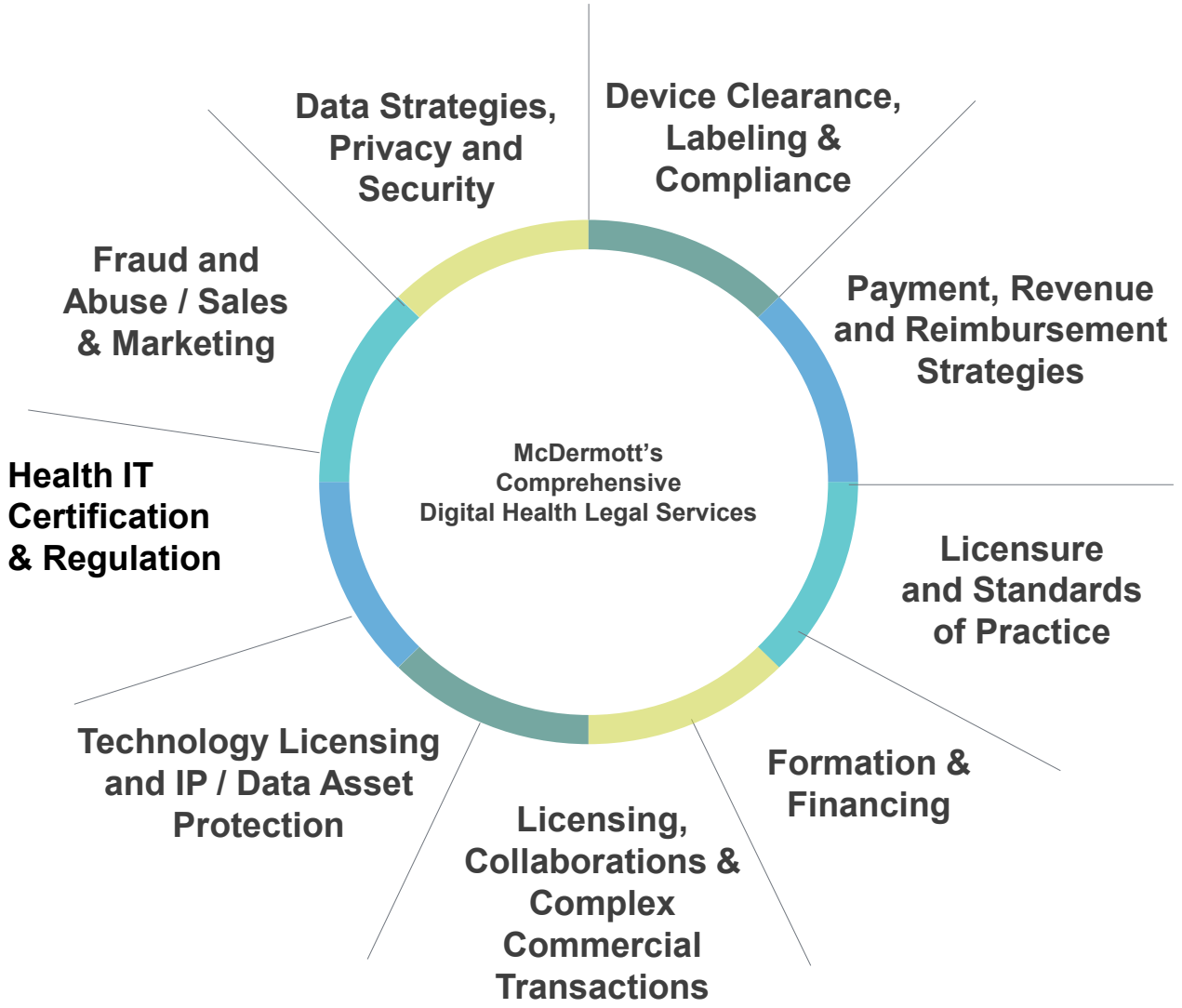
Large investments made by pharma in digital health



Bridging the Gap: clinical expertise vs. consumer tech expertise

Increased exploration, but no proven single “best practice” approach

OVERVIEW OF COMMON REGULATORY ISSUES TO ENTER THE US DIGITAL HEALTH MARKET



TELEHEALTH CARE DELIVERY MODELS

Clinician to Clinician

- Second opinion programs
- eICU; eED
- Virtual conferencing

Provider to Patient

- Remote patient monitoring and chronic care management
- Virtual specialty care / primary care models

Consumer-Driven

- Direct to consumer telehealth platforms
- Mobile apps

TELEHEALTH CARE DELIVERY MODELS

Traditional Modalities of Telehealth Delivery

- Secure videoconferencing, store-and-forward, remote patient monitoring

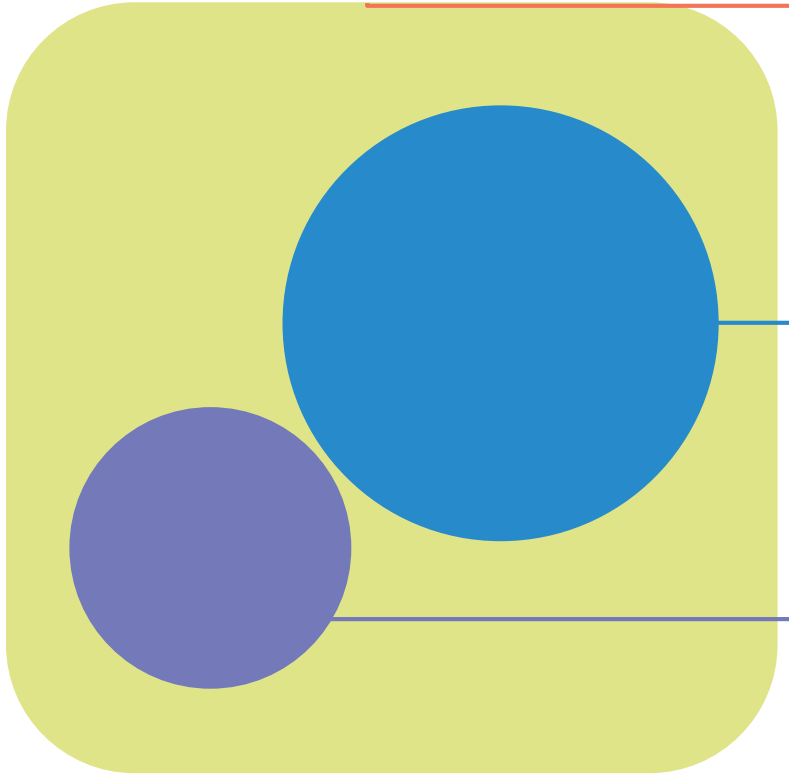
Growth of Innovative Solutions

- Dynamic questionnaires
- Interactive chat
- Artificial intelligence

Key Takeaways

- Increasingly sophisticated non-traditional technologies are changing care delivery
- Regulatory landscape is not necessarily keeping pace with innovative solutions
- COVID-19 flexibilities have significantly (and in some cases, permanently) changed the regulatory and reimbursement landscape

WHY DEFINITIONS MATTER IN THE CONTEXT OF TELEHEALTH



State and Accrediting Body Definition of Telehealth and Virtual Care Services

Colloquially, telehealth refers to any application of technology to furnish healthcare services, monitor patients (e.g., RPM), or to facilitate clinician to clinician communication. States broadly define to capture activities within its rules.

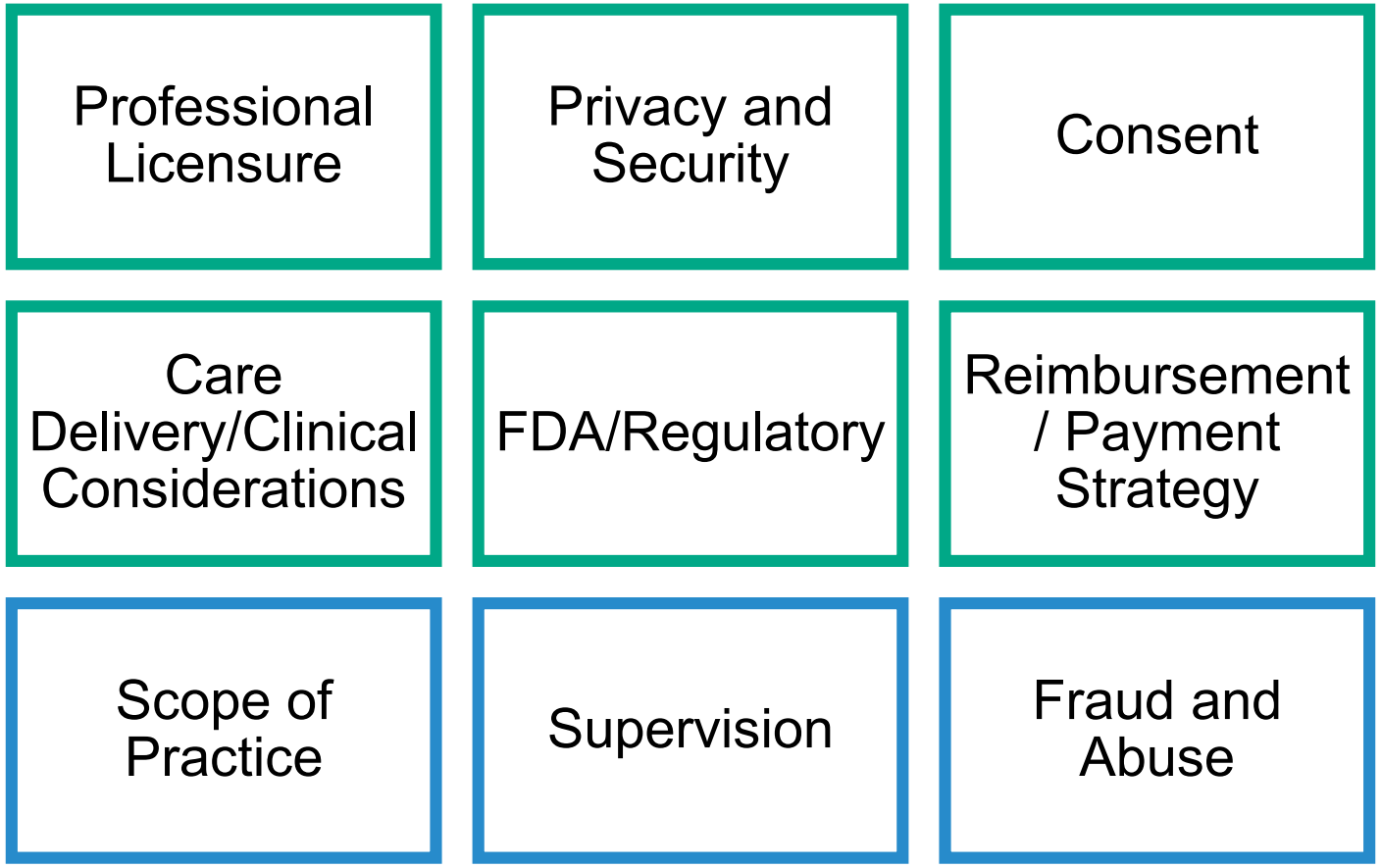
Health Plan Definition of Telehealth Services

For example, Medicare defines telehealth as the use of electronic information and telecommunications technologies to support long-distance clinical health care, patient and professional health-related education, public health and health information

Health Plan Definition of Virtual Care Services

Virtual care services are not telehealth services, and include remote patient monitoring, chronic care management, virtual check-ins and e-visits; virtual care services are not subject to the same requirements and limitations as telehealth services

EVOLVING LEGAL AND REGULATORY RULES IMPACT MODELS



PAYMENT FOR CARE MANAGEMENT AND CARE COORDINATION SERVICES

In recent years, the Centers for Medicare and Medicaid Services (CMS) has established codes to improve payment for care management and care coordination. The codes include a spectrum of services that involve direct patient care, non-face-to-face services, a single encounter, monthly services and services for variety of services provided by the billing practitioner or clinical staff.

Care Plan Oversight (G0181, G0182)	**ESRD Monthly Services** (90951-90970)	**Transitional Care Management (TCM)** (99495, 99496)	**Chronic Care Management (CCM)** (99439, 99487, 99489, 99490, 99491)
Advance Care Planning (99497, 99498)	**Behavioral Health Integration** (99484, 99492, 99493, 99494, G2214)	**Cognitive Impairment Assessment and Care Planning** (99483)	**Prolonged Evaluation & Management (E/M) Without Direct Patient Contact** (99358, 99359)
Prolonged Office/Outpatient E/M Visit (G2212)	**Remote Physiologic Monitoring Treatment Management Services** (99457, 99458)	**Interprofessional Consultation** (99446, 99447, 99448, 99449, 99451, 99452)	**Principal Care Management** (G2064, G2065)

RPM AND CCM MECHANICS

- **Remote patient monitoring**, AKA "**remote physiological monitoring**" uses digital technologies (devices) to collect medical and other forms of health data from individuals in one location and electronically transmit that information securely to healthcare providers in a different location for assessment and recommendations.
- **Chronic care management** also use technology to provide non-face-to-face care management coordination services for certain Medicare beneficiaries having multiple — two or more — chronic conditions.
- Per CMS, RPM and CCM ≠ telehealth services, but rather a new set of services

AMA RPM AND CCM CPT CODES

- 99453
- 99454
- 99091
- 99457
- 99458

- 99490
- 99439
- 99491
- 99487
- 99489

EMERGING VIRTUAL CARE MODELS

- Virtual + In-Person Hybrid = Healthcare of the Future
- Accessibility + Ease of Use > In-Person, Manual Solutions
- Emerging virtual care models driven by four trends
  - reduced burden of care delivery
  - coverage and payment parity for telehealth and RPM
  - enhanced focus on data sharing and privacy
  - expansion of digital care into new healthcare sectors
- Growing use of chatbots for intake, care initiation, triage and follow-up
- Various emerging and new regulatory risks that require evaluation and planning

DATA AS AN ASSET

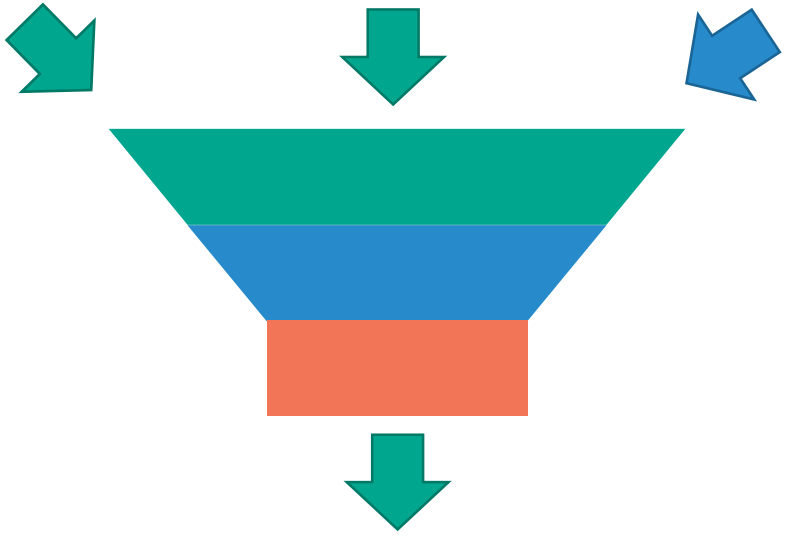
DATA SOURCES AND GOALS

CLINICAL / INSTITUTIONAL DATA

- Clinical Workflows
- Testing Labs
- Claims Data
- EHR
- Clinical Research Data
- Medical Imaging
- Quality Metrics

PATIENT/ CONSUMER DATA

- CGI/ Wearables/ Mobile Apps
- Public Data



GOALS

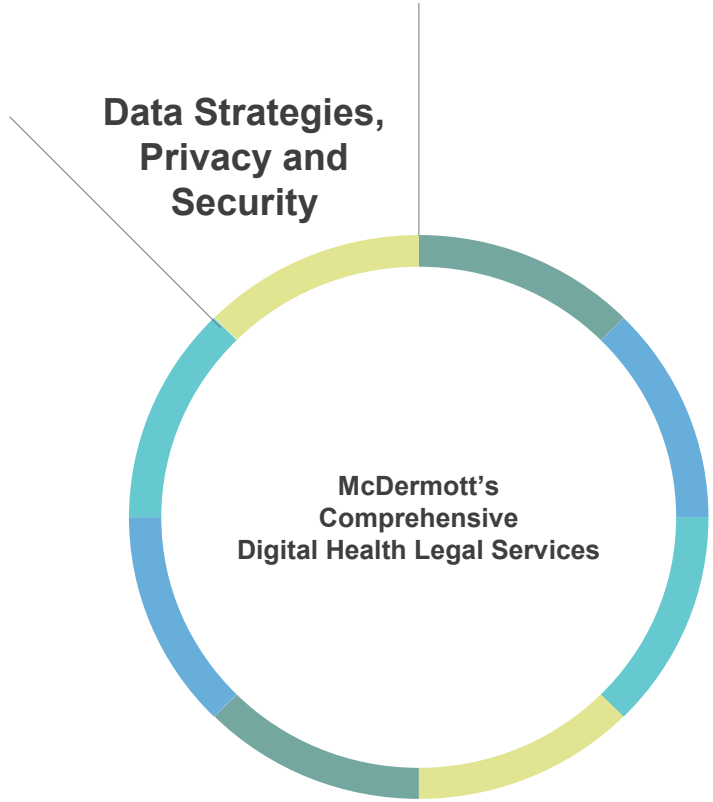
- Workflow Management
- Practice Management
- Risk Analytics
- Diagnostics
- Drug Discovery Engine
- Clinical Decision Support
- Care Management

DEVELOPING A DATA STRATEGY: DEPART WITH YOUR DESTINATION IN MIND

- Anticipate
  - Is it possible that the data may be used for research at a later time?
  - Upfront analysis
  - Enhance flexibility
- Analyze
  - Map out each use/disclosure of PHI and activity

DATA STRATEGIES – A CLOSER LOOK

- Data strategies > privacy and security alone
- Privacy as a competitive advantage
- Know your regulations – which ones apply to you and how you can navigate them strategically
- Data discipline – what data do you need, when and for what activities
- Use versus disclosure – both are regulated
- Deciding to be consumer/patient facing or behind the scenes
- Monetizing data and future use
- De-identification – solution or barrier
- Go on the offensive – how will you build public trust and confidence



DATA STRATEGIES: KEY DATA MAPPING QUESTIONS

Step 1: What data is collected? Identify each known and intended data source

Step 2: From whom is the data being collected? Identify from whom the data is being collected (e.g., CE, consumer, patient, another type)

Step 3: Who is collecting data? Identify data collector and regulatory compliance status (e.g., whether the data or the data collector is regulated)

Step 4: How is data used? Identify intra-enterprise access and use rules, including where and how data is stored, how data is combined or siloed and who has access to stored data.

Step 5: What data is shared and for what purpose? Identify third-party data recipients and providers, including the short- and long-reach contractual or other obligations (if any) associated with information and further dissemination.

Step 6: Why is data collected, used and shared? Identify short and long term business objectives for data to help determine how to map future-state data consistent with business objectives.

DATA STRATEGIES AND ANALYTICS

- Population Health
  - Ingesting Data
    - Deidentification Rights
    - Limited Data Set Rights
    - Data Aggregation Rights

Monetization of Deid Data
(special reqs for LDS: Research, Health Care Ops/Public Health

  - Deidentification Vendors/Statisticians
    - Emerging Trends
      - Outsource entirely
      - Prepare in-house w/external validation
      - Entirely in-house
  - Customer and Consumer Expectation Management

USE CASES

- Adherence/Medication Management
- Medical Necessity
- Patient Engagement
- Early detection and monitoring
- Advanced clinical decision support
- Product-Specific Alerts
- Clinical Trial Recruitment
- Clinical Trial Monitoring

CONSTRUCTIVE DISRUPTION

Not all disruption helps your customers achieve their goals faster

Accept that technology is in continuous development, but . . .

Overlay our thinking about the technology with our current regulations and ethical considerations; and . . .

Our customers – understand their environment, legal obligations, norms and pressures

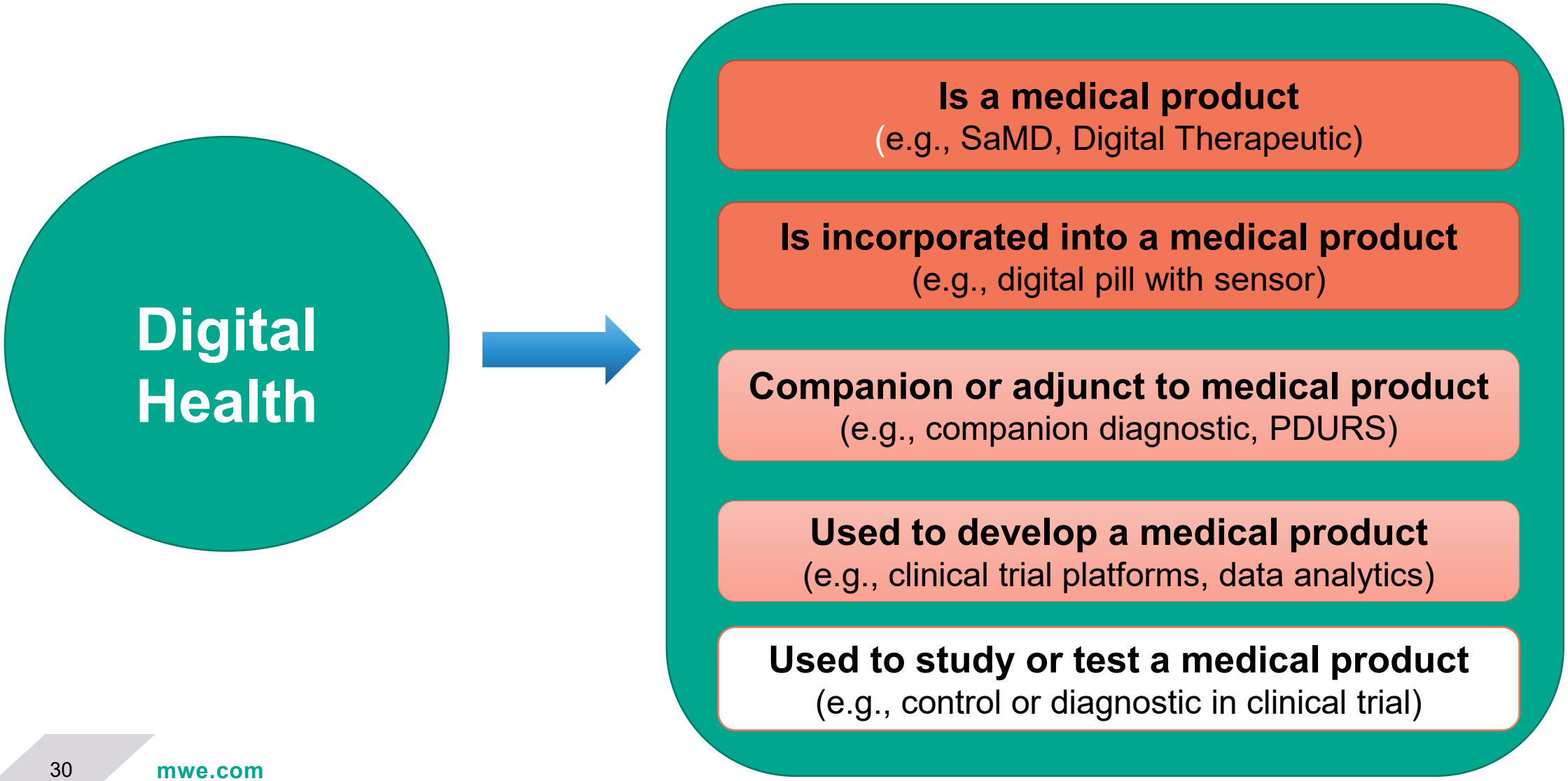
AI CONSIDERATIONS

- Permission to utilize machine learning
  - From customers
  - Consider data subjects
- Bias awareness and testing
  - Careful of the duplication extension loop
- Ultimate use of the algorithm and use of resulting information in RCM context
  - Representations/Warranties of Validity
  - FDA considerations
  - FCA considerations
  - Cut/Paste-Like Risks

FDA'S DIGITAL HEALTH REGULATORY PRIORITIES

1. **Enhancing Patient Access to Quality Products**
   - Breakthrough Device pathway increasingly available for digital health products
   - Digital Health Pre-Certification pathway designed to expedite the premarket review process
2. **Safety and Effectiveness**
   - Interoperability and compatibility of "connected" devices
   - Cybersecurity and Privacy
   - Emphasis on preventing fraudulent "cures" or deception of consumers or healthcare providers
3. **Artificial Intelligence and Machine Learning**
   - New framework for evaluating the safety and effectiveness of AI/ML tools
4. **Shifting Focus to Patient-Generated Health Data (PGHD)**
   - Emphasis on identify and evaluating types of PGHD
   - Assessing appropriate use cases for various types of PGHD
   - Exploring pathways for use of PGHD as valid scientific evidence to support regulatory decisions

USE CASES THAT TRIGGER FDA REGULATIONS



OPPORTUNITIES: DATA USES IN THE FDA FRAMEWORK

Discovery, Research & Development

- Identify potential drug candidates
- Identify patient populations with unmet treatment or diagnostic needs
- Understand clinical processes and work-flows that drive patient outcomes
- Clinical trial planning and design
- Market research

Approval & Launch

- Recruit patients, investigators and clinical trial sites
- Identify co-morbidities or potential contraindications for drug
- Evidence of safety and effectiveness
- Train algorithm for FDA-regulated AI/ML devices

Commercial /Post-market

- Predict, identify, monitor, investigate and report drug safety issues
- Evaluate prescriber habits (e.g., high volume prescribers)
- Review demographic trends for advertising and marketing strategy development

CHALLENGES:
DATA USES IN THE FDA FRAMEWORK

- Laws, rules and norms developed for decades-old product development paradigm
- FDA requirements vary depending on the purpose for which data will be used, who will use it, how it was collected and whether it will be submitted/reported to FDA
  - Analysis is “fact-specific” and “case-by-case”
  - No such thing as “FDA-compliant data” or “Regulatory Grade” data
- Lack of uniform standards for validating the performance, reliability and accuracy of real-world data
- Lack of clear guidance on when certain non-interventional studies will trigger FDA regulation (e.g., when used to train AI or develop digital biomarkers)

OVER-ARCHING REGULATIONS THAT AFFECT DATA

- **Good Clinical Practice ("GCP") Regulations**
  - General requirements for data integrity, prevention of bias and protection of research participants for clinical investigations conducted to support FDA marketing applications (NDA, ANDA, 510(k), PMA, BLA, post-market studies) or records held for inspection by FDA
    - Protection of Human Subjects – 21 CFR Part 50
    - Financial Disclosure by Investigators – 21 CFR Part 54
    - Institutional Review Boards – 21 CFR Part 56
  - Investigational New Drug Application- 21 CFR Part 312 (Part 812 for Devices)
    - General requirements for clinical investigations to support new product approval and review
  - Applications for FDA Approval to Market a New Drug – 21 CFR Part 314 (Part 814 for devices)
    - General requirements for the content and review of product marketing applications, including data submitted to support safety and effectiveness

OVER-ARCHING REGULATIONS THAT AFFECT DATA, CONT'D

- **21 CFR PART 11 (Electronic Records and Electronic Signatures)**
  - Applies to: (1) Records in electronic form created, modified, maintained, archived, retrieved, or transmitted under any FDA records requirement, and (2) Electronic records submitted to FDA
  - Requires:
    - Validation of systems to ensure accuracy, reliability, consistent intended performance
    - Ability to discern invalid or altered records
    - Ready retrieval (including for FDA inspection)
    - Limited access to authorized individuals
    - Validation of source data
    - Audit trails to independently record operator entries and actions that create, modify, or delete records

FDA GUIDANCE

- **Electronic Records**
  - Use of Electronic Health Record Data in Clinical Investigations (July 2018)
  - Electronic Source Data in Clinical Investigations (Sept. 2013)
  - Providing Regulatory Submissions in Electronic Format under Section 745A(a) of the FD&C Act (Dec. 2014)
- **Real World Evidence (RWE) and Real World Data (RWD)**
  - Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics (May 2019)
  - Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Device (Aug. 2017)
- **Artificial Intelligence/Machine Learning**
  - Discussion Paper: Proposed Regulatory Framework for Modification to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)
  - Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan

GENERAL STANDARDS FOR DATA WITHIN THE FDA FRAMEWORK

- Data must be “fit for purpose”
- Data must be sufficient for intended use
- Data collection, aggregation, transfer and analysis must be conducted under appropriate controls and security measures
- Data must allow appropriate “transparency” to evaluate and demonstrate adequacy for purpose, controls, security, etc.
- Data must be traceable and may be auditable (e.g., underlying data, systems, processes or data sets subject to FDA inspection or review)
- Data should be free from biases and evidence of manipulation that affect the integrity of data

USE OF EHR OR OTHER ELECTRONIC SOURCE DATA FOR CLINICAL RESEARCH

- **Interoperability & Integration**
  - Manual transcription may introduce risk of data entry errors unless effective quality control systems are in place
- **Data Standards**
  - Use existing open data standards, when possible
- **Structured and Unstructured Data**
  - FDA encourages exchange of structured data (e.g., demographics, vital signs, laboratory data)
  - Consider the reliability and quality of unstructured data and appropriateness of using it as critical source data, such as study endpoints
- **Validation**
  - Ensure data are transmitted accurately, consistently, and completely with periodic sampling, particularly after software updates

TAKEAWAYS

- Digital health is a key driver for innovation in life sciences
- Regulations and laws vary depending on use cases
- Shift from viewing data as a byproduct of development activities to viewing data as an asset for multiple uses
- Develop “data strategy” over the lifecycle of the product as a part of regulatory strategy for product development
- Data governance should account for FDA requirements and evolving or future use cases