

Bio & Software toward the Smart Health

What future for Italy?

Digital or Smart? Medicine at the Time of the Bioconvergence and Digital Transformation

Giuseppe Recchia – Vice President, Smith Kline Foundation – Verona, Italy

Disclosure Statement

■ Vice President, Smith Kline Foundation



■ Consultant, *GSK spa*



■ Co-Founder and CEO, *daVinci Digital Therapeutics*



Agenda & Glossary

- Digital Health
- Digital Medicine
- Digital Therapy
- Digital Transformation
- Mobile Health
- Smart Health
- Artificial Intelligence
- Machine Learning
- Internet of Things – IoT
- Decentralized Clinical Trials

Digital Transformation

Digital Transformation In The Music Business:



Alvaro Rebollo Ena

Follow

Mar 24 · 7 min read

What Other Businesses Could Have Learnt From It, And The Convergence (or Not) of Spotify and Netflix



I stepped in the music business in the year 2000. I was really lucky to be able to experience the final days of the majors' golden age: A lot of CDs were sold, massive media campaigns were launched, piracy on the Internet was still inexistent, revenues were not that bad...



1982



1999

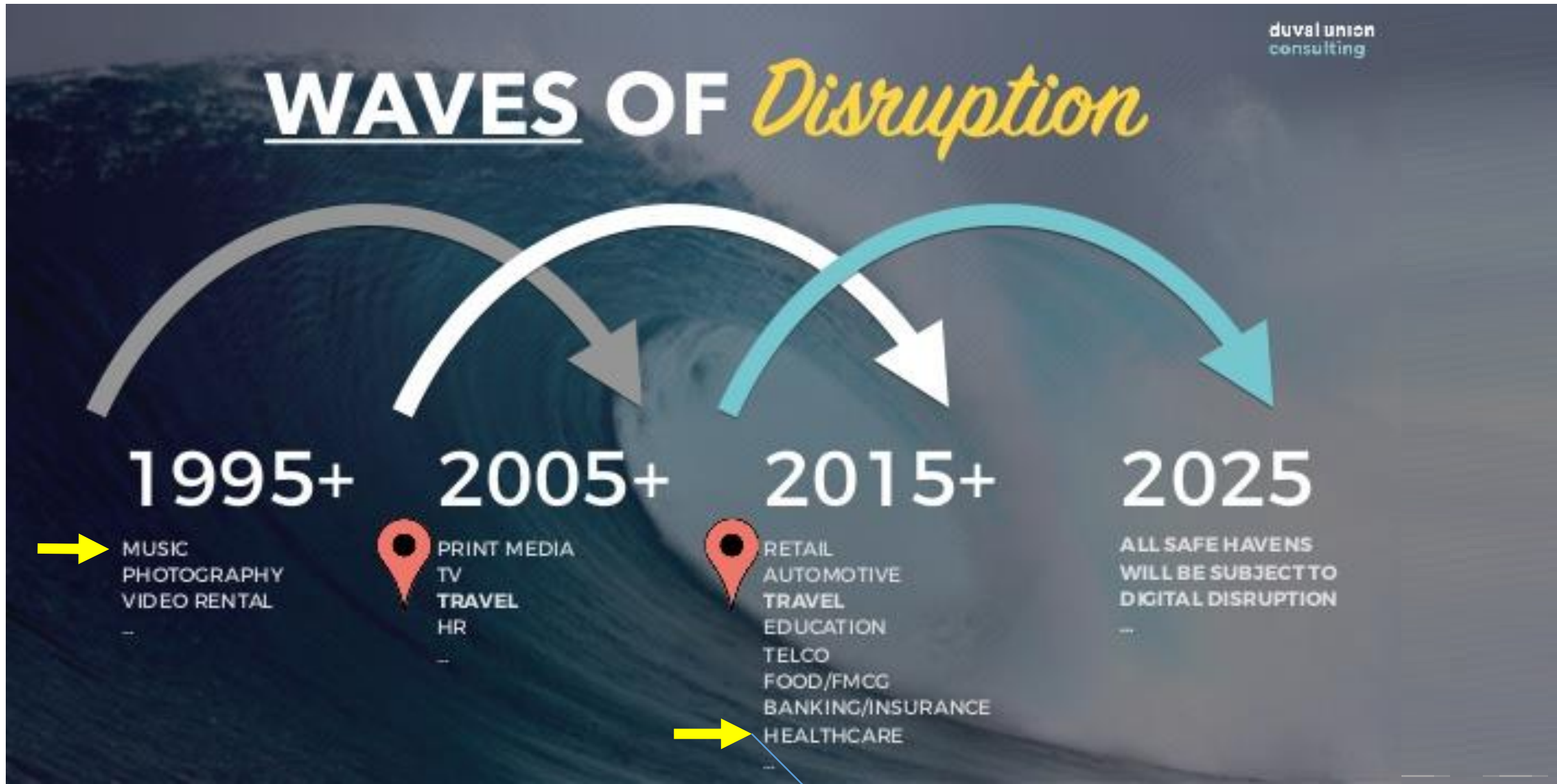


2003

2006



Digital Transformation... It is its turn



It is 2025....



Digital Therapeutics: pharma's threat or opportunity



Paul Simms
Chairman
eyeforpharma



Jim O'Donoghue
President
S3 Connected Health

It is 2025 and digitally delivered therapies are now part of our regular healthcare experience. The smartphone, already our first port of call on health matters, has been elevated to the role of personal health mentor and condition management guide.

Offering us therapies and advice, both consciously and subconsciously, our device acts as our general healthcare concierge too, knowing when we've taken our medicine, showing us ways to optimize our desired lifestyle and determining medication dosages, and inviting us to visit specialists when they detect anomalous data. We are even seeing the emergence of the digital twin, a virtual version of yourself which can 'trial' treatments on your behalf before being adopted in your real body.

And clinicians, in a different role from the past, now rely on the data from your device too. They sanction or suggest technology-enabled patient services offering treatments that in many cases do not involve a chemical or biological intervention, but a digital one.

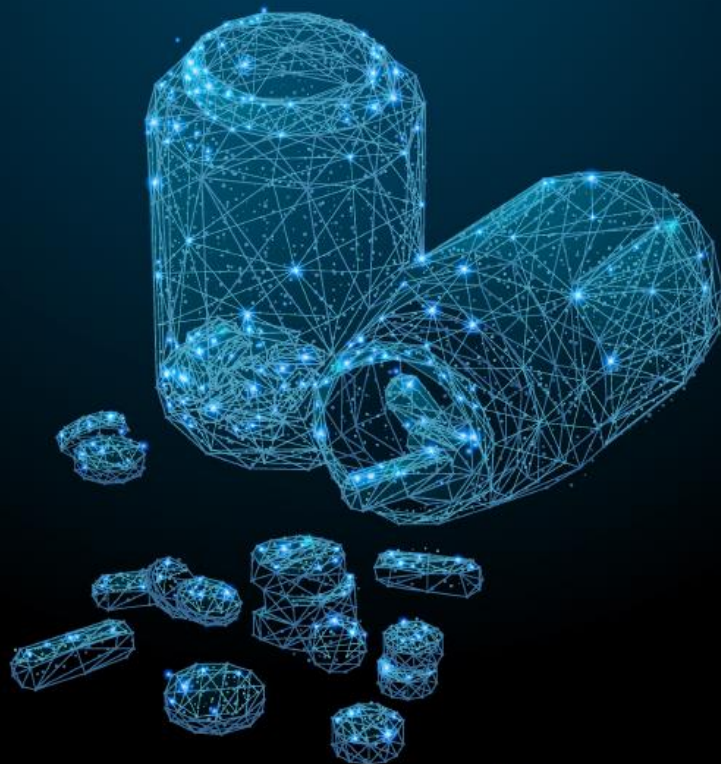
These therapies now routinely generate data in real time for deep-learning AI to interpret, enabling care providers to automate routine aspects of care, for example through alerts and 'bot' consultations, which give patients much of the information they need to stay compliant with their care plans.

Digital technologies act as a force multiplier for clinicians at all levels from consultants to nurses, who are now able to focus their time on the patients in most need and with the most complex ailments. Where necessary, the AI alerts a clinician to the need to intervene and assists them in making rapid decisions on the best and most appropriate course of action.

Meanwhile, payers rely on the rich real-world dataset that is now generated from these technologies and are used as an integral part of outcome based contracting without adding excessive burden to health systems. Digital therapeutics (DTx) are now a core part of the payer's arsenal of care delivery tools, having in many cases proven their worth in driving better care alongside analog medicines or, where they replace chemical alternatives, they do so often at a far lower cost. DTx revenues have ballooned as payers and HTAs see the value of recommending and prescribing them outright.

And in general, we now have a more proactive, voluntary health system where citizens actively prevent rather than simply manage their exposure to chronic diseases, moving the dial on population health at a global level whilst driving down costs. Healthcare systems under ever-increasing pressure from ageing populations can now do more with less. Patients are enjoying more quality years of wellness than they would have expected a decade before.

Welcome



It is 2025...

- ... and **digitally delivered therapies and home testing** are now part of our regular healthcare experience.
- The **smartphone** has been elevated to the role of personal health mentor and condition management guide.
- Offering us **therapies, diagnosis and advice**, consciously and subconsciously, our device acts as our general healthcare concierge too, knowing when we've taken our medicine, showing us ways to optimize our desired lifestyle and determining medication dosages, and inviting us to visit specialists when they detect anomalous **laboratory** data.

It is 2025....

- **Clinicians**, in a different role from the past, now rely on the **data** from your device too for their decisions.
- They sanction or suggest technology-enabled patient services offering treatments that in many cases do not involve a chemical or biological intervention, but a digital one.
- These **therapies** now routinely generate **data** in real time for deep learning to interpret, enabling care providers to automate routine aspects of care, for example through alerts and 'bot' consultations, which give patients much of the information they need to stay compliant with their care plans.

It is 2025...

- **Smartphone, the hub of diagnosis**, is capable of performing routine laboratories (with suitable hardware additions), generating **real time, real world** biosensor data of most physiologic metrics, doing a substantial part of the physical examination, with a virtual medical assistant to process these multi-layered medical data for each individual.
- Where necessary, the **Artificial Intelligence** alerts a clinician to the need to intervene and assists them in making rapid decisions on the best and most appropriate course of action.
- **Payers** rely on the rich **real-world dataset** that is now generated from these technologies and are used as an integral part of outcome based contracting

Digital Transformation in Healthcare

Digital health is a cultural transformation of traditional healthcare

- Roles
- Ways of Working
- Organization
- Sites

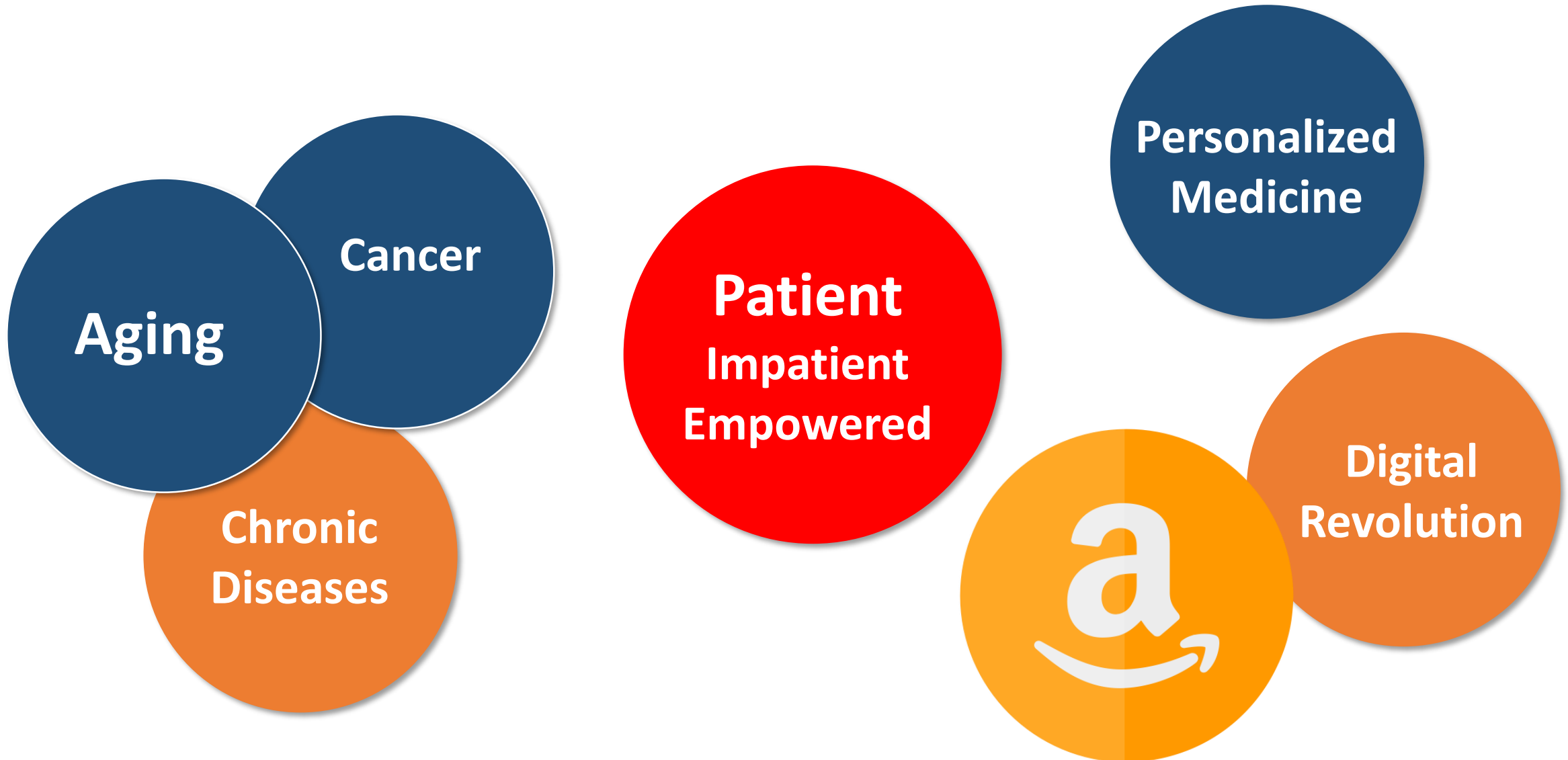


Traditional healthcare



Collaborative healthcare

The Journey to 2025 – Driving Forces ...



The biggest challenge to health and healthcare...

Chronic Diseases!

Leading causes of disability, 1990 and 2017

Global all-age YLDs

1990 rank

1 Low back pain

2 Headache disorders**

3 Dietary iron deficiency

4 Depressive disorders

5 COPD

6 Age-related hearing loss

9 Diabetes

2017 rank

1 Low back pain

2 Headache disorders**

3 Depressive disorders

4 Diabetes

5 Age-related hearing loss

6 COPD†

7 Dietary iron deficiency

Communicable, maternal, neonatal, and nutritional diseases

Non-communicable diseases

**Headache disorders mainly include migraine.

†Chronic obstructive pulmonary disease

Drugs are not enough!

- Support
- Education
- Monitoring
- Adherence



we need something more...

Patients - What do they want?

- Take control of their health
- Empowerment
- De-centralization
- Home Testing for Chronic Diseases



Patient



CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

**CTTI Recommendations:
Decentralized Clinical Trials**

September 2018

What do patients want?



Patient

Theme 2

Empowered patients – access to data, more control

While digitally supported healthcare professionals will play an important role in changing the way that healthcare is delivered, understanding **how technology can have a positive impact on the patient experience** is just as significant.

The general population is looking for information and more control over almost all aspects of their lives. Giving an individual access to their own health data makes them more likely to engage with it in a way that will improve the quality of care they receive and their overall healthcare experience.

What do patients want?



Patient

Diagnose Yourself, Anywhere

At rHEALTH®, we develop technologies that fundamentally change how people access analytical and diagnostic information*.

Combining portable diagnostic and monitoring capabilities will enable delivery of better and more timely health information. From this, we can begin to shift away from existing standards of curative medicine to future predictive, preemptive, and personalized medicine.

*rHEALTH devices are limited by FDA regulation for research or investigational purposes only.

What do Patients prefer?



Patient

At-Home Health Testing

imaware™ provides awareness of life-altering diseases to empower patients to engage in personalized healthcare



New Players in healthcare...

Amazon has explored getting into consumer health diagnostics — testing for disease at home

PUBLISHED FRI, DEC 14 2018 • 3:54 PM EST | UPDATED FRI, DEC 14 2018 • 4:10 PM EST



Christina Farr
@CHRISSYFARR



Eugene Kim
@EUGENEKIM222

SHARE



KEY POINTS

- Amazon looked at buying a start-up developing at-home health tests called Confer Health, but talks broke down a few months ago.
- As recently as this summer, it had a team dedicated to diagnostics within its moonshots group “Grand Challenge.” It is unknown whether the group is still active.
- A move into the home health-testing space would be a signal of Amazon’s ambitions to remake the entire health care supply chain, and could compete with testing giants Quest and LabCorp.



Patient



New Players in healthcare...

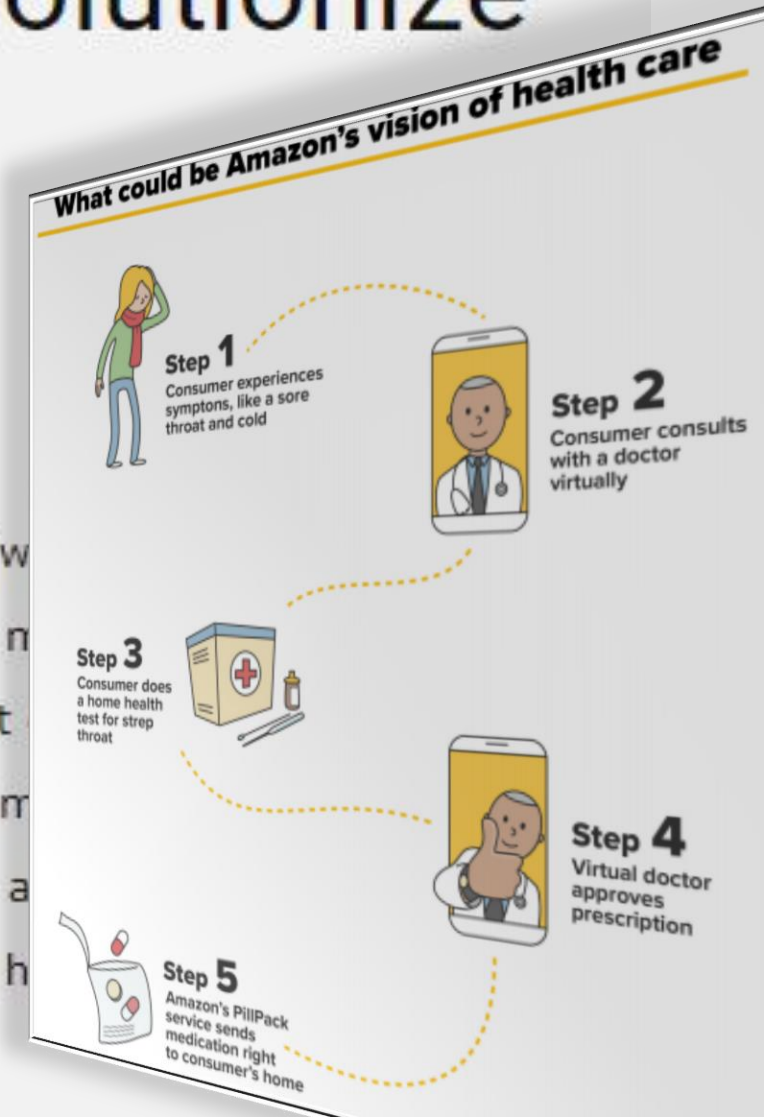
Amazon, Google, Apple To Revolutionize Consumer Health Tech

August 20, 2019



rising cost of healthcare...

With the proliferation of hardware and software, it's only a matter of time before devices turn into sensors that can provide data to practitioners to continuously monitor health. For a very long time, the U.S. has been a leader in those in the healthcare field, but...





DIGITAL HEALTH

use of Digital Technologies to
(1) support and deliver
healthcare (2) improve health
and well-being of people



1

SMART HEALTH

Digital Health Technologies

Digital Medicine

DIGITAL HEALTH

DIGITAL
MEDICINE

- measure
- intervention

Digital Health
Technologies
based on

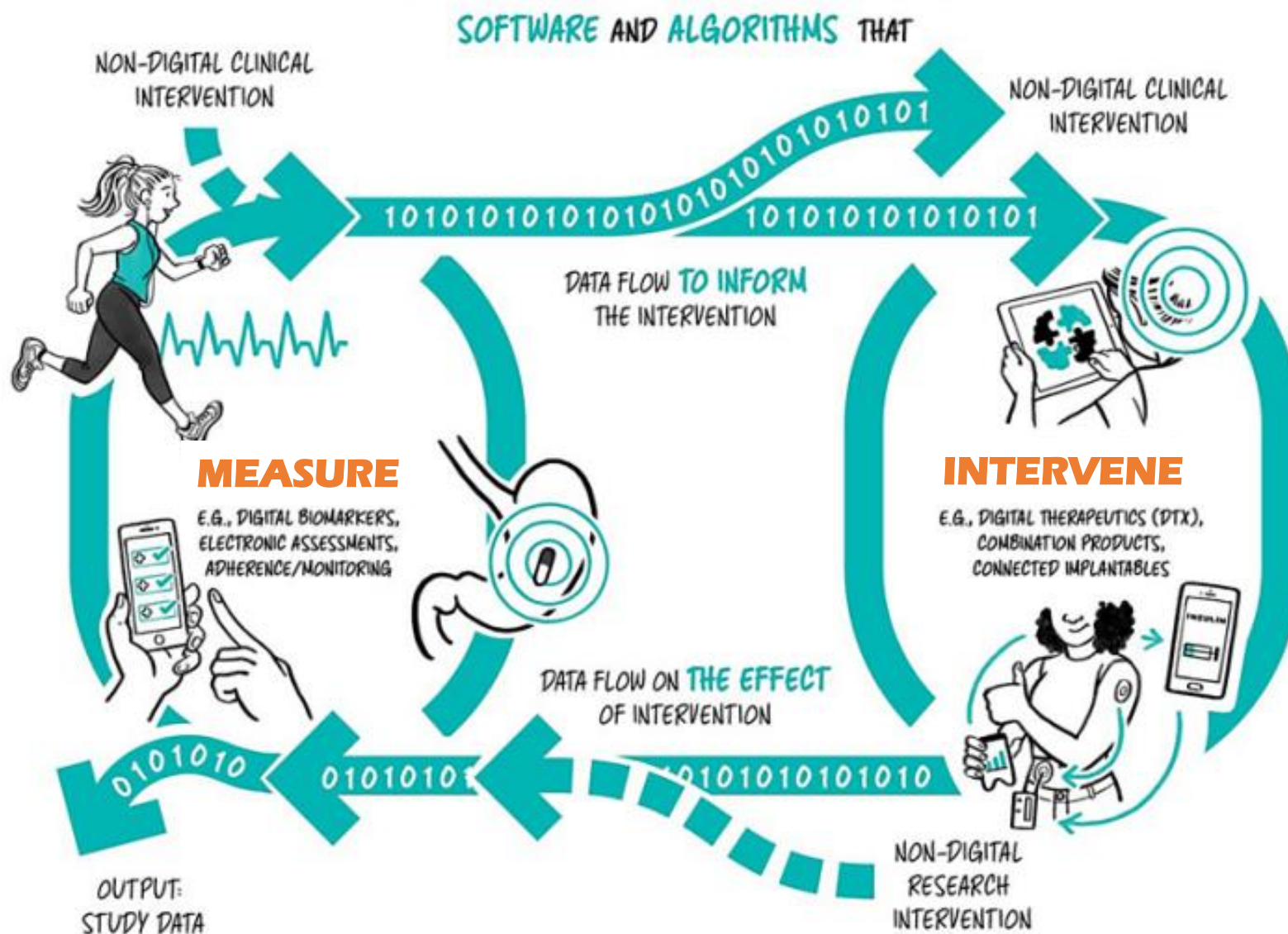
EVIDENCE



2

Digital Medicine Technologies

Digital Medicine



Digital Health Tools

- measurement
- intervention

to optimize

- healthcare processes
- health outcomes

based on

- scientific evidence

Mobile Devices and Health

Ida Sim, M.D., Ph.D.

From the Division of General Internal Medicine, University of California, San Francisco, San Francisco. Address reprint requests to Dr. Sim at the University of California, San Francisco, 1545 Divisadero St., Suite 308, San Francisco, CA 94143-0320, or at ida.sim@ucsf.edu.

N Engl J Med 2019;381:956-68.

DOI: 10.1056/NEJMr1806949

Copyright © 2019 Massachusetts Medical Society.

MOBILE HEALTH — THE APPLICATION OF SENSORS, MOBILE APPS, SOCIAL media, and location-tracking technology to obtain data pertinent to wellness and disease diagnosis, prevention, and management — makes it theoretically possible to monitor and intervene whenever and wherever acute and chronic medical conditions occur. With 81% of North American adults owning a smartphone,¹ this frontier could be reached in the foreseeable future in the United States and is particularly relevant to the management of chronic diseases. More than 40% of U.S. adults have two or more chronic conditions² and chronic conditions now account for 71% of all U.S. health care spending,³ so the promise of mobile health is especially attractive.

Mobile health is at the swirling confluence of remote sensing, consumer-facing personal technologies, and artificial intelligence (AI). Data from smartphone applica-

Digital Therapy

DIGITAL HEALTH

DIGITAL
MEDICINE

DTx

Digital Health
Technologies
based on

EVIDENCE



DIGITAL
THERAPEUTICS

Digital Therapy Technologies

3

What are Digital Therapeutics?



Marketed

- a. Deprexis (EU 2009)
- b. Reset (FDA 2017)
- c. Reset-O (FDA 2017)
- d. Zemy (EU 2017)
- e. Oleena (FDA 2019)



Late Development

- a. AKL-T01 (FDA expected 2019)
- b. Somryst (FDA expected 2020?)
- c. CureApp Smoking Cessation (2020?)

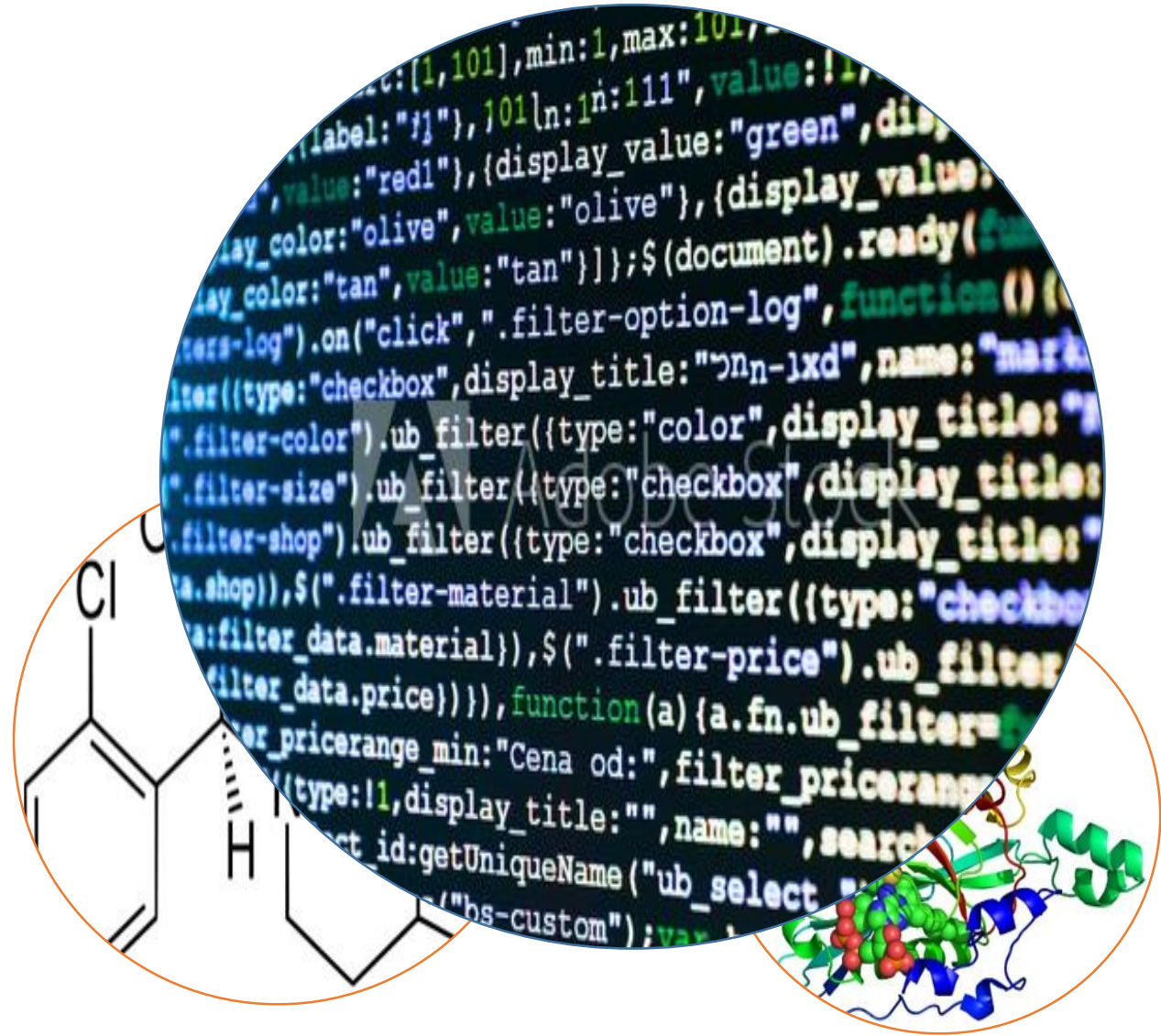
Early Development

- a. MDD daVinci Digital Therapeutics
- b. Obesity daVinci Digital Therapeutics

What are Digital Therapeutics?



- therapeutic interventions
- **Active Ingredient**
- developed through RCTs
- approved by regulatory bodies
- subject to HTA assessment
- reimbursed by NHS / insurance
- prescribed by a Physician



How is the Active Ingredient prepared?

Clinical Expertise

- Specialists, Academia

Software Expertise

Experience

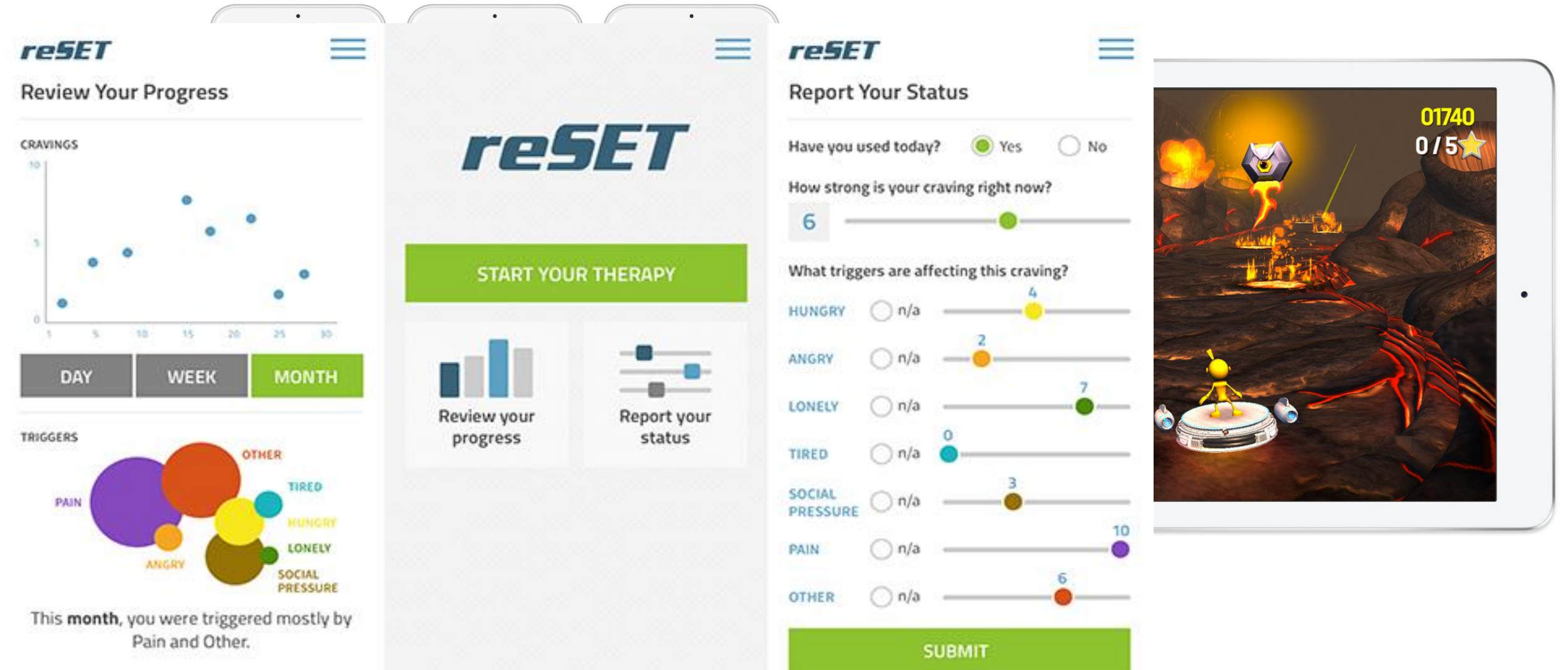
- Patients, Caregivers
- GPs

UX / UI Expertise



Artificial Intelligence

Algorithms must take the «form» of ...



mApps, Games, Sensors....

How do Digital Therapeutics work?



Combination with a drug

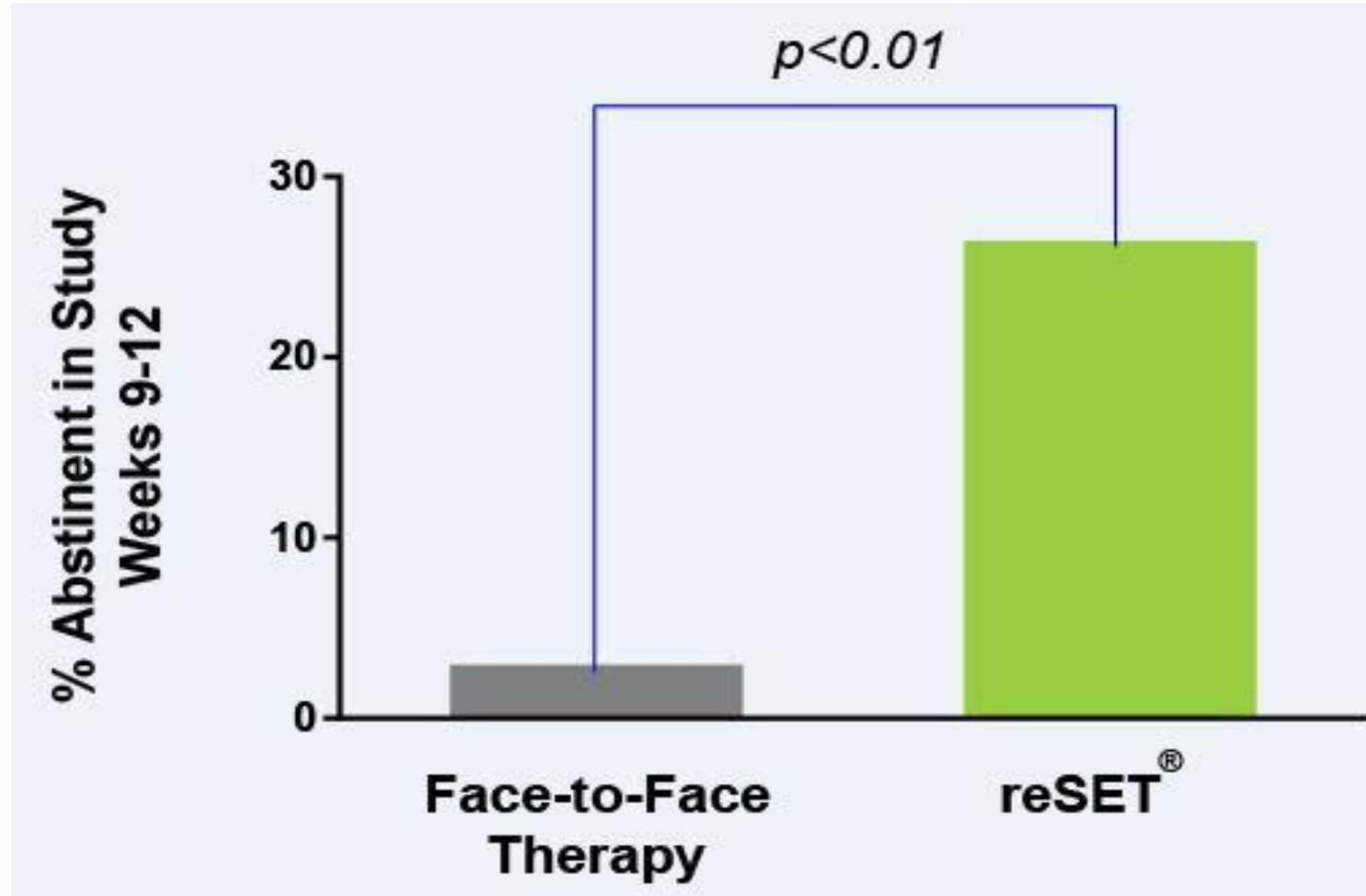
- Monitoring of adherence to therapy
- Drug Dosage Recommendations
- Recommendations on AE management
 - *Diabetes (Voluntis w Roche, Sanofi)*
 - *Oncology (Voluntis w AZ, Roche)*
 - *Asthma / COPD (Propeller w GSK, Novartis, Chiesi; Teva; Adherium w AZ)*

Standalone

- Cognitive Behavioural Therapies – CBTs
- Other therapeutic options
 - *Dependencies (Pear Therapeutics)*
 - *Depression (daVinci Digital Therapeutics)*
 - *ADHD (Akili Interactive)*
 - *Schizophrenia (Pear Therapeutics)*
 - *Obesity (daVinci Digital Therapeutics)*

DTx must improve clinical outcomes by involving and empowering patients in the management of their diseases and therapies

What qualifies software as therapy?



DTx Discovery and Development, 2.9.2019

Therapeutic Intervention

delivered



**Clinician-facing
Web Interface**



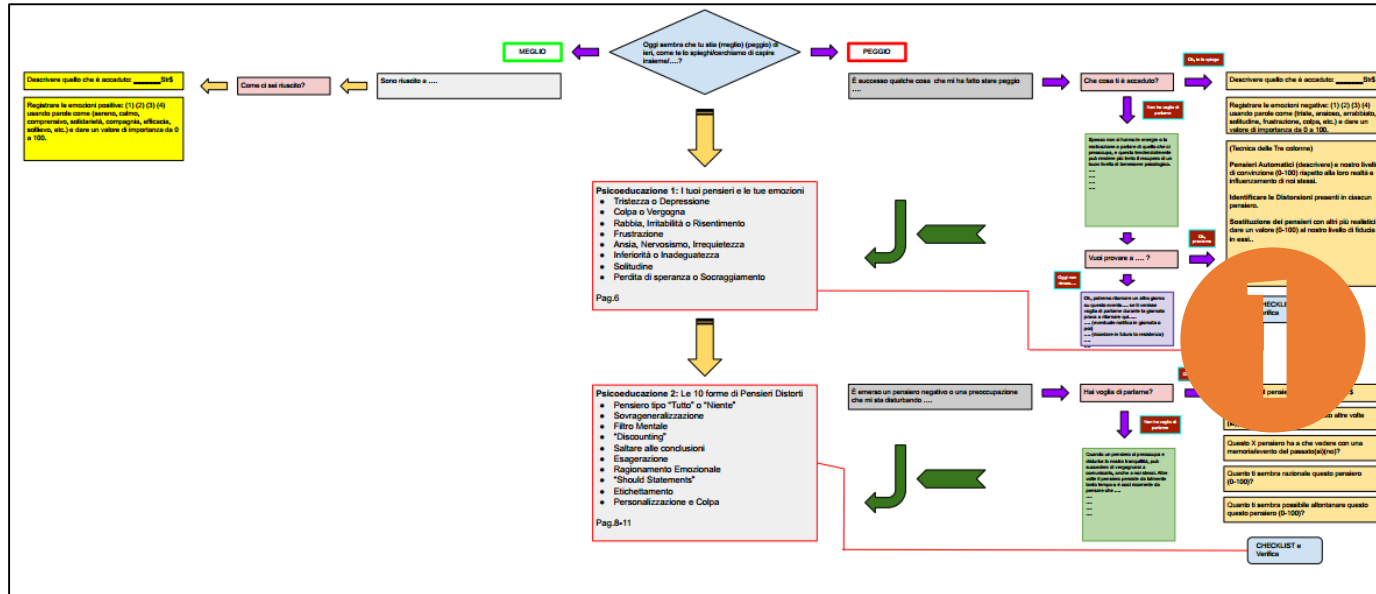
**Patient-facing
Smartphone Application**

1. Digitized T.I.

3. Dashboard - Physician

2. Value-added Services

DTx Discovery – Software Development 1



Active Ingredient

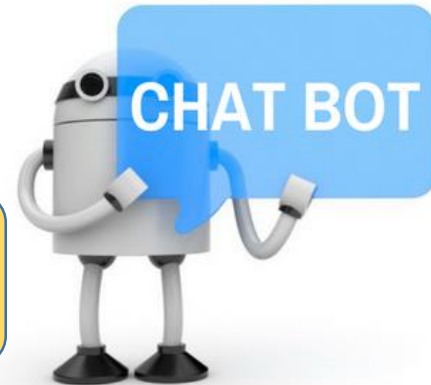
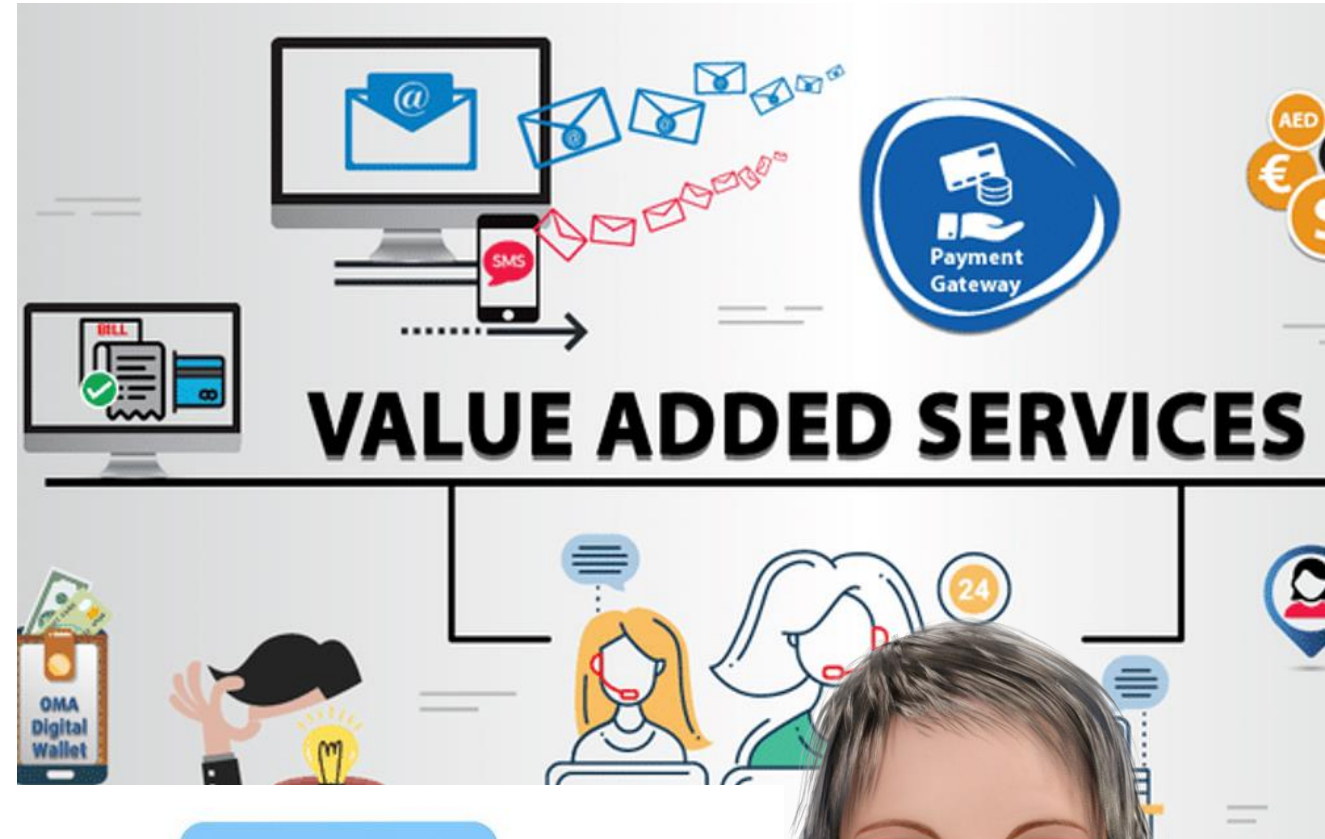
Standards

Utilities



DTx Discovery – Software Development 2

- a. Clinical Record Forms
- b. Connection with Doctor
- c. Connection with Peers
- d. Reminders
- e. Rewarding
- f. Others



Value Added Utilities

DTx Discovery – Software Development 3

a. Data privacy, safety, security

b. User experience/adherence

c. Data integration

Standards

INSIGHTS

World Psychiatry 18:1 - February 2019

Towards a consensus around standards for smartphone apps and digital mental health

Mental disorders impact one in four people worldwide, yet access to care is challenging for those who suffer from them¹. Mental health apps have the potential to address some barriers for the near future, but they must be developed and evaluated by 2020.

Although there are over 10,000 mental health apps commercially available, there are few resources available to help end users (patients, clinicians and health care organizations) to evaluate the quality and suitability of these products. Thus, there is an urgent need for an agreement about appropriate standards and principles for the evaluation of mental health apps.

We reviewed the literature on mental health apps from around the globe, and we seek here to promote consensus on implementing these standards and principles for the evaluation of mental health apps. At a minimum, standards should include consideration of: a) data safety and privacy, b) effectiveness, c) user experience/adherence, d) data integration. Our consensus on the challenges and recommendations in each of these areas is presented below.

Data safety and privacy. Given the climate today regarding the collection, storage, and use of personal data, it is essential to have standards for the collection, storage, and use of health information data². Like with all sensitive health data, smartphones-based sensor data such as global positioning system (GPS), voice, keyboard usage, photos, video and overall phone usage behavior are features that many mental health apps collect, posing significant privacy challenges.

Our recommendations are: a) agreed upon standards for data storage, use and sharing are needed; b) data storage, use and sharing policies must be made transparent to users of the app; c) if data are shared with external partners (e.g., researchers), the partner's storage, use and sharing plans must be shared with the end user; d) the end user must have the option to "opt out" of sharing his/her information; e) any language regarding data storage, use and sharing must be written at a maximum of

6th grade reading level.

Particularly where the aim is to increase reach, engagement and adherence rather than efficacy, A/B testing may be most useful. However, significant changes, such as adding a new principle or substantial changes to that principle, must demonstrate efficacy through the same evaluation pathways as novel therapeutics.

Our recommendations are: a) any new therapeutic principles, which should be identified and defined, must undergo controlled clinical trials to determine their efficacy and effectiveness; b) small changes to an app with an evidence base need not undergo another clinical trial, but any major change requires a re-evaluation of app effectiveness; c) a nosology for mental health apps⁵ and guidelines to match the necessary level of evidence for each app's use cases and risks⁶ should be developed.

User experience/adherence. Users stop using a health app two weeks after download⁷. Clinician end user adherence is influenced by familiarity with technology and app match to the clinician's therapeutic expertise. Lack of adherence is likely a function of app usability, as the input of clinician end users and patients in the development of a mental health app should align with their needs and preferences.

Our recommendations are: a) user-centered/user experience (UX) design methods should be employed when creating an app; this includes involving the intended end user in the development and conducting a workflow analysis to ensure that the app fits the workflow of the intended end user; b) when usability is evaluated, developers should report use statistics to all end users; c) standards concerning best practice in user design research for mental health apps should be articulated.

Data integration. Apps should allow appropriate electronic health record (EHR) integration and sharing of health information with clinicians. One challenge is that EHRs have non-uni-

data storage, use and sharing

Opt out

6th grade reading level

Data audits

involving the intended end user in the development

interoperability with EHR

DTx Pilot Clinical Development



Patient-facing
Smartphone Application

1. Clinical Test - Usability and Acceptability

- ✓ *50 volunteers with / without the disease (Ph1 like)*

2. Pilot Clinical Study to Assess Efficacy and Safety

- ✓ *PoC Study*
- ✓ *50 patients, with mild to moderate depression*
- ✓ *Open, not controlled*
- ✓ *Endpoint : Patient Health Questionnaire-9 (PHQ-9) at day 30 (vs basal)*

Randomized Controlled Clinical Trials

Trial Design

1. Development of a DTx combination with a specific drug (SD) :

$$\text{DTx} + \text{SD} > \text{SD}$$

2. Development of DTx standalone, to be added on Therapy As Usual (TAU):

$$\text{DTx} + \text{TAU} > \text{Digital Placebo} + \text{TAU}$$

Ruoli del Paziente nello sviluppo DTx

1. Utente
2. Tester
3. Informatore
4. Partner



Progettazione Partecipativa

Who pays?



- Patient
- Insurance
- Pharma
- NHS

Digital Therapeutics in the NHS:

The rise of digital therapies
& the evidence that proves
they work

Tuesday, 24 April 2018

#DHLCOLLABORATE

#DigitalHealthLondon

Germany 1.1.2020 - Digitales Versorgungsgesetz – DVG



How do they fit into medical practice?



European Journal of
**Preventive
Cardiology**



Position paper

ESC e-Cardiology Working Group Position Paper: Overcoming challenges in digital health implementation in cardiovascular medicine

European Journal of Preventive
Cardiology

0(00) 1–12

© The European Society of
Cardiology 2019

Article reuse guidelines:

sagepub.com/journals-permissions

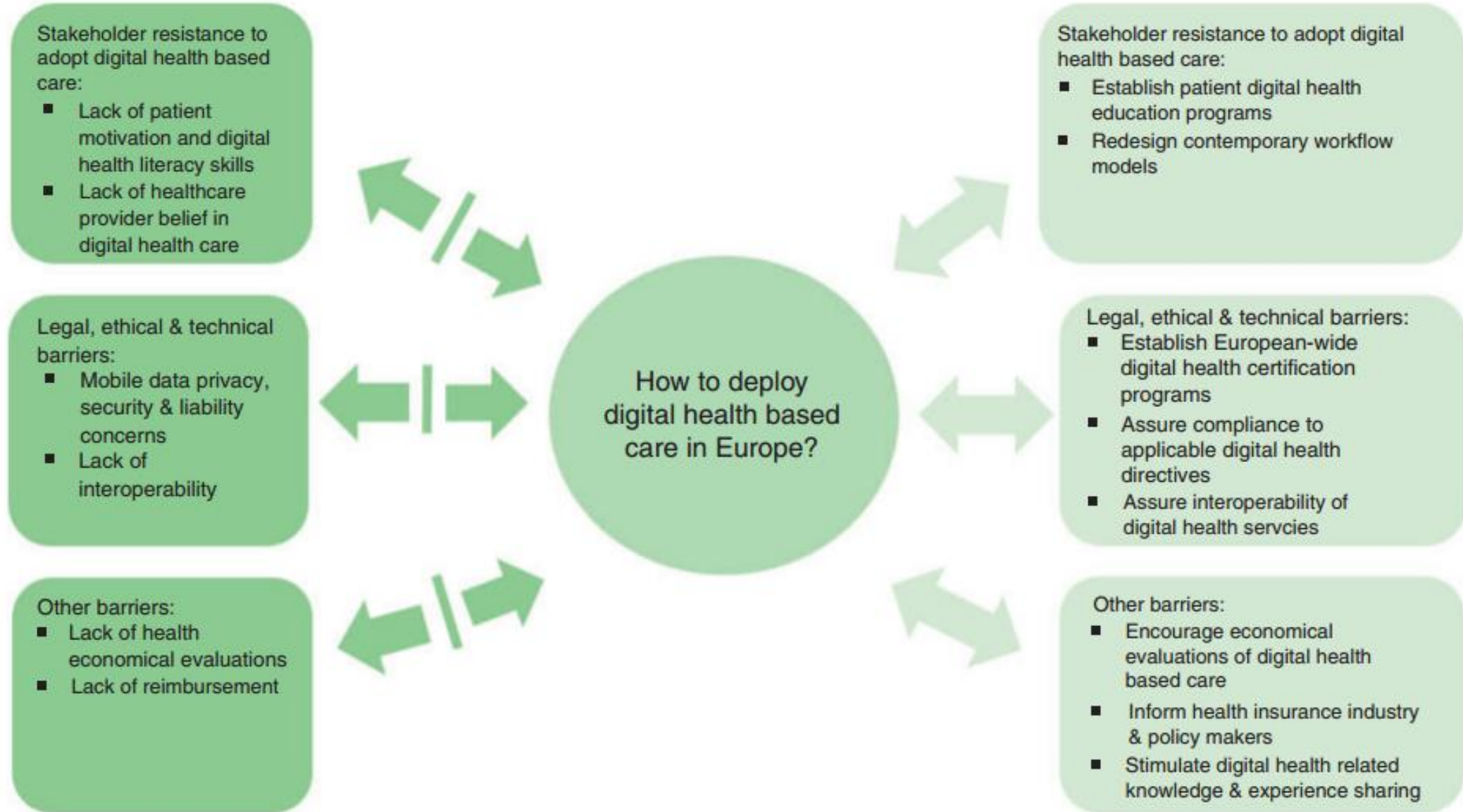
DOI: 10.1177/2047487319832394

journals.sagepub.com/home/ejpc



**Ines Frederix^{1,2,3,4}, Enrico G Caiani^{5,6}, Paul Dendale^{1,3},
Stefan Anker⁷, Jeroen Bax⁸, Alan Böhm^{9,10}, Martin Cowie¹¹,
John Crawford¹², Natasja de Groot¹³, Polychronis Dilaveris¹⁴,
Tina Hansen¹⁵, Friedrich Koehler¹⁶, Goran Krstajić¹⁷,
Ekaterini Lambrinou¹⁸, Patrizio Lancellotti^{19,20}, Pascal Meier²¹,
Lis Neubeck²², Gianfranco Parati²³, Ewa Piotrowicz²⁴,
Marco Tubaro²⁵ and Enno van der Velde⁸**

How do they fit into medical practice?



Main barriers to large-scale deployment

Key measures on how to address these barriers

Digital Therapy Italy #DTxITA

1. To make available to the patient in Italy a new therapeutic modality
2. Creating conditions for Italy to become a reference country for research and production of digital therapies, creating development and work



3 July 2019

- a. Clinical Development and RCTs**
- b. Regulatory Approval
- c. Reimbursement and Business Model**
- d. Introduction into medical practice

Stay tuned ...



@GGRecchia

@fsk_it



Giuseppe Recchia

Fondazione Smith Kline