Progetto "Terapie Digitali per l'Italia" #DTxITA

Terapie Digitali
Sviluppo e Sperimentazione Clinica

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How "digital therapeutics" differ from traditional health and wellness apps

nature

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The emerging world of digital therapeutics

The treatment of many physical and mental-health conditions is going digital

JoS JOURNAL OF STROKE

http://j-stroke.org/

| This Article | Aims and Scope | Instructions for Authors | e-Submission |

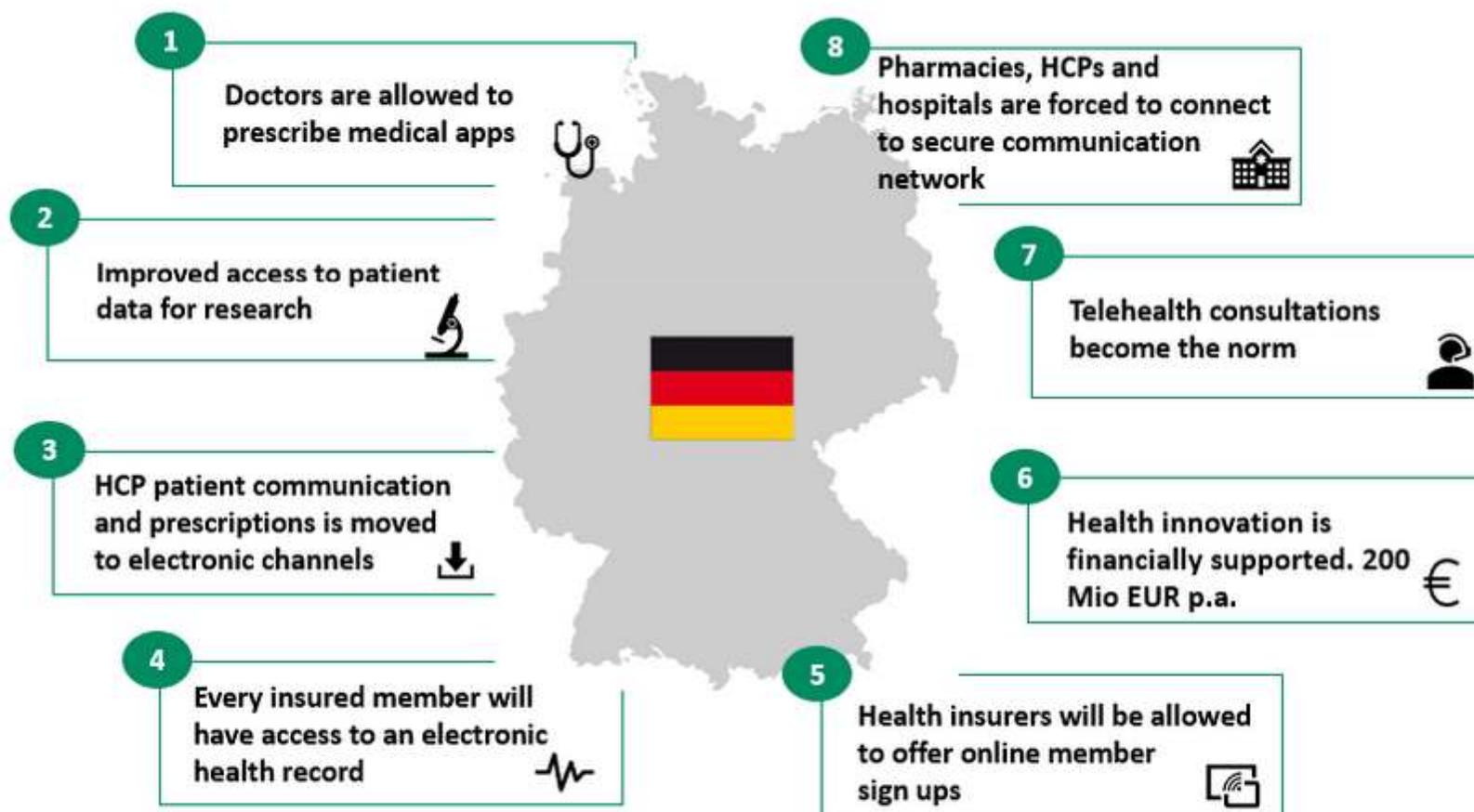## Digital Therapeutics: Emerging New Therapy for Neurologic Deficits after Stroke

Mi Joo Choi,[a] Hana Kim,[b] Hyun-Wook Nah,[c] and Dong-Wha Kang[b,c,d]

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ISTITUTO DI RICERCHE
FARMACOLOGICHE
MARIO NEGRI · IRCCS

Legge approvata il 7 nov 2019

RECENT REGULATORY CHANGES THAT MAKE GERMANY A TOP COUNTRY FOR DIGITAL HEALTH SOLUTIONS

NEW GERMAN REGULATION THAT POSITIVELY IMPACT MARKET OPPORTUNITIES FOR DIGITAL HEALTH COMPANIES STARTING FROM 2020/2021

1 Doctors are allowed to prescribe medical apps

2 Improved access to patient data for research

3 HCP patient communication and prescriptions is moved to electronic channels

4 Every insured member will have access to an electronic health record

5 Health insurers will be allowed to offer online member sign ups

6 Health innovation is financially supported. 200 Mio EUR p.a.

7 Telehealth consultations become the norm

8 Pharmacies, HCPs and hospitals are forced to connect to secure communication network

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R²G

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Terapie digitali

- Le terapie digitali sono un **sottoinsieme della digital health** e riguardano quelle opzioni terapeutiche che **utilizzano tecnologie digitali** per **curare** una patologia, una malattia mentale o una condizione psicologica. Il trattamento si basa **su modifiche del comportamento o degli stili di vita** attraverso l'implementazione di linee guida e programmi, e grazie alla raccolta sistematica di dati utili a raggiungere l'obiettivo.

#DTx - Digital Therapy – Digital Therapeutics

- Interventi Terapeutici

- **Software come Principio Attivo**

- Sviluppati attraverso RCTs

- Autorizzati da enti regolatori

- Sottoposti a valutazione HTA

- Rimborsati da SSN / assicurazioni

- Prescritti dal medico

What is digital therapy and why does it matter?

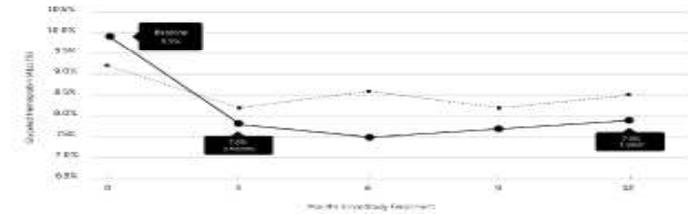Eugenio Santoro, Polihub - Milano 20 febbraio 2020

WellDoc
FDA-cleared in 2013

Target indication:

Type 2 diabetes

WellDoc

1.9% A1C Improvement [1]
WITH BLUESTAR

0.7% A1C Improvement
USUAL CARE

1 Quinn CC, et al. Diabetes Technol Ther. 2008;10(3):160-168. Quinn CC, et al. Diabetes Care. 2011;34(9):1934-1942.. Richard Katz, MD; George Washington University Medical Center; Journal of Health Communication, December 2011. Quinn, CC, et al. Glycemic Control: Impact on Physician Prescribing Behavior, Presentation ADA 72nd Scientific Sessions, 2012. Tang PY, et al. eHealth-Assisted Lay Health Coaching for Diabetes Self-Management Support American Diabetes Association 76th Scientific Sessions Poster Presentation 2016.

Propeller
FDA-cleared in 2012

Target indications:

Asthma and COPD

1 Merchant et al (under review) "Impact of a Digital Health Intervention on Asthma Resource Utilization"
2 Van Sickle D, Humblet O, Barrett M, Henderson K, and Hogg C. 2016. Randomized, controlled study of the impact of a mobile health tool on asthma SABA use, control and adherence. European Respiratory Journal 48: PA1018. http://erj.ersjournals.com/content/48/suppl_60/PA1018

Propeller

Reduced Acute Care Utilization [1]

Improved Adherence [2]

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Akili Interactive
FDA-clearance - submitted

aKILI

Children with Sensory Processing Dysfunction (SPD)

Anguera JA, et al., (2017) A pilot study to determine the feasibility of enhancing cognitive abilities in children with sensory processing dysfunction. PLoS ONE 12(4): e0172616. https://doi.org/10.1371/journal.pone.0172616

Target indications:

ADHD, Autism Spectrum Disorder, Major Depressive Disorder, Parkinson's

reSET

START YOUR THERAPY

Review your progress

Report your status

p<0.01

% Abstinent in Study Weeks 9-12

Face-to-Face Therapy

reSET®
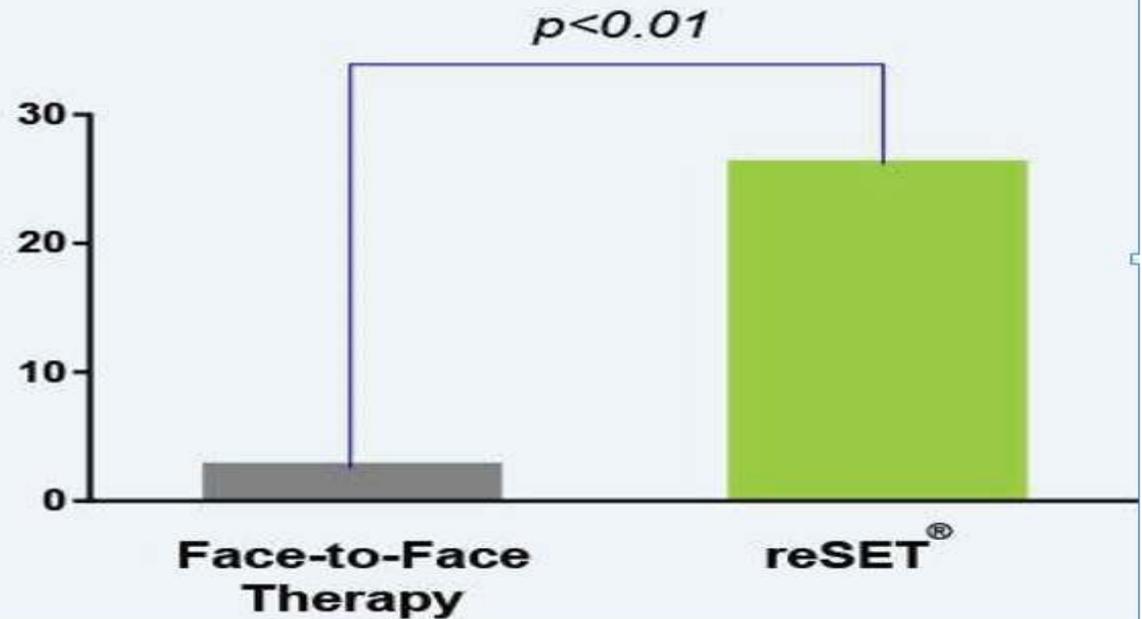
Quali Indicazioni Terapeutiche?

#DTx – Come si Ricercano & Sviluppano?

RCT Fase I

Analisi

RCT Fase II

Disegno

Studio clinico pilota

La sperimentazione clinica nella specifica indicazione e la dimostrazione del beneficio terapeutico qualifica il Digital Therapeutic

Sviluppo
Quale assurance
Interfaccia
Privacy/security
End user testing

RCT Fase III

RCT Fase IV

Affidabilità
Safety

- Convalida SW medicale

Sperimentazione clinica allargata (RCT)

Introduzione nella Pratica Medica

Efficacia vs standard care

Real world data

Adverse Events

- Marcatura CE
- FDA Certification

- Aggiornamento Marcatura
  - Digital Therapeutic

- Sorveglianza post market

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Impact of a Novel Smartphone App (CureApp Smoking Cessation) on Nicotine Dependence: Prospective Single-Arm Interventional Pilot Study

Intervention= CureApp: data collection, personalized counseling advices created by a AI system and based on national guidelines, diary of smoking cessation + messages and education videos + counseling chatbot answering individual's questions and providing encouraging messages. App used daily for 24 weeks. CureApp support s the pharmacological treatment.

Primary outcome: abstinence rate from 9 to 24 weeks
Secondary outcome: abstinence rate from 9 to 12 and from 9 to 52 weeks
Smokers recruited: 56

Figure 7. Continuous abstinence rates from weeks 9 to 12, 9 to 24, and 9 to 52.

febbraio 2020
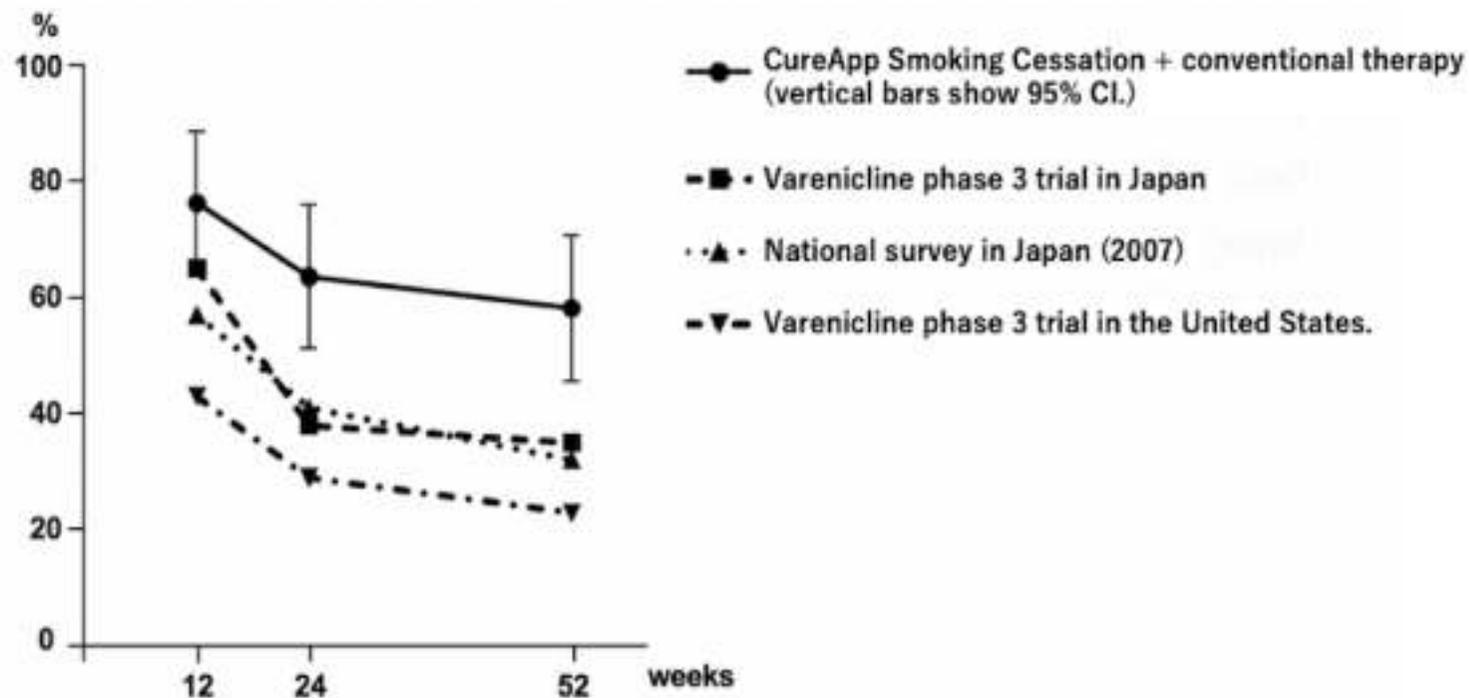
oleena™

A prescription mobile app that provides personalized symptom recommendations.

THE OLEENA JOURNEY
HERE'S HOW OLEENA™ WORKS

Prescribe
The healthcare provider sets up Oleena™ to meet the patient's unique needs. The patient gets access to the Oleena™ app.

Report
The patient experiences a symptom and reports it in Oleena™.

Evaluate
Oleena™ evaluates the symptom severity and provides a personalized recommendation.

Act
The patient self-manages their symptom based on the recommendation. When severity is too high for self-management, Oleena™ connects the patient to the care team.

Monitor
Oleena™ continues monitoring the patient until the symptom subsides.

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Two-Year Survival Comparing Web-Based Symptom Monitoring vs Routine Surveillance Following Treatment for Lung Cancer

Figure 2. Kaplan-Meier Curves for the Overall Survival (OS) Analysis

A Intention-to-treat analysis

B Censoring of crossover analysis

A (Intention-to-treat analysis)

Web-based monitoring

Control group

HR, 0.59 (95% CI, 0.37-0.96); P=.03
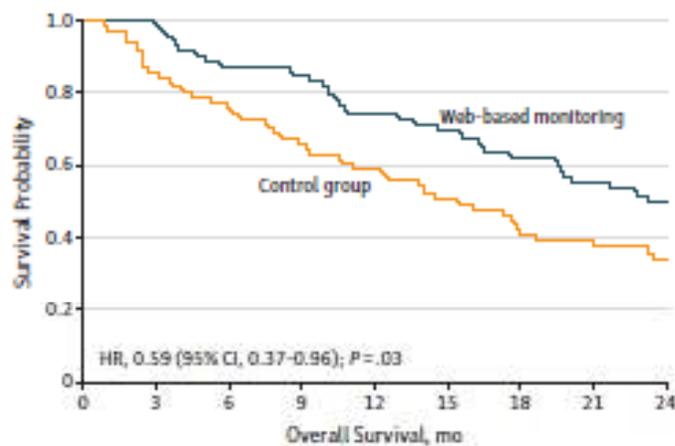
No. at risk

Web-based monitoring	60	60	51	48	43	39	35	31	27
Control	61	52	45	38	34	29	24	22	19

Source	Median OS	12-mo OS, %	24-mo OS, %
Web-based monitoring	22.5 mo	75	50
Control	14.9 mo	56	34

B (Censoring of crossover analysis)

Log-rank P=.004

Web-based monitoring

Control group

HR, 0.50 (95% CI, 0.31-0.81); P=.005
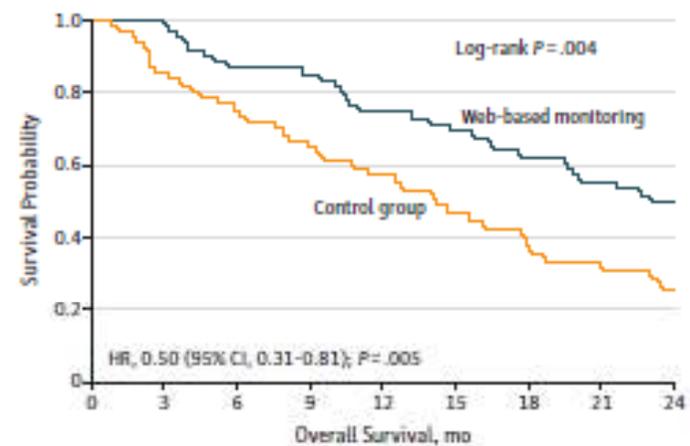
No. at risk

Web-based monitoring	60	60	51	48	43	39	35	31	27
Control	61	52	43	33	26	20	15	13	11

Source	Median OS	12-mo OS, %	24-mo OS, %
Web-based monitoring	22.5 mo	75	50
Control	13.5 mo	53	26

A total of 121 patients were included in the intention-to-treat survival analysis. Ten of 34 living patients in the control group were eligible to cross over following the interim analysis. HR indicates hazard ratio.

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ClinicalTrials.gov

413 Studies found for: digital therapeutics | digital therapeutics

Also searched for **Treatment**, **Therapy**, **Therapeutic** and more. See Search Details

106 Studies found for: digital therapeutics | Recruiting Studies | digital therapeutics

Also searched for **Treatment**, **Therapy**, **Therapeutic** and more. See Search Details

Applied Filters: ☑ **Recruiting**

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DTX Diabete – Meta-analisi

Figure 5. Effects of app-based mobile health interventions on hemoglobin A_{1c} (HbA$_{1c}$) for patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM). MD: mean difference.

Trial or subgroup	Weight (%)	MD (95% CI), %
Drion 2015	8.8	0.10 (-0.57 to 0.77)
Kirwan 2013	9.8	-1.39 (-1.96 to -0.82)
Rossi 2013	13.7	-0.01 (-0.05 to 0.03)
Charpentier 2011	11.2	-0.75 (-1.18 to -0.32)
Rossi 2010	12.0	0.10 (-0.24 to 0.44)
Subgroup of T1DM: pooled MD (heterogeneity I^2=88%, P<.001)		-0.36 (-0.81 to 0.08)
Hsu 2016	4.7	-1.20 (-2.44 to 0.04)
Holmen 2014	10.6	-0.20 (-0.69 to 0.29)
Waki 2014	9.7	-0.50 (-1.08 to 0.08)
Yoo 2009	11.7	-0.70 (-1.07 to -0.33)
Quinn 2008	7.9	-1.35 (-2.12 to -0.58)
Subgroup of T2DM: pooled MD (heterogeneity I^2=47%, P=.11)		-0.67 (-1.03 to -0.30)
All trials: pooled MD (intersubgroup P=.30)		-0.52 (-0.85 to -0.18)

Favors intervention — Favors control
MD in HbA$_{1c}$ changes (%)

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DTX Weight Loss – Meta-analisi

Mobile Phone Apps to Promote Weight Loss and Increase Physical Activity: A Systematic Review and Meta-Analysis

(J Med Internet Res 2015;17(11):e253)

Figure 2. Meta-analysis of the net change in body weight (kg) associated with mobile phone app intervention, expressed as the change during the mobile phone app intervention minus the change during the control diet. The area of each square is proportional to the inverse of the variance of the weighted mean difference. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from inverse variance (IV) weighted random-effects models.

Author year	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Allen 2013	-5.4	4	16	-2.5	4.1	18	5.5%	-2.90 [-5.63, -0.17]
Brindal 2013	-2.9	6.4	28	-2.1	1	30	6.7%	-0.80 [-3.20, 1.60]
Carter 2013	-4.6	5.2	43	-2.9	5.85	43	7.0%	-1.70 [-4.04, 0.64]
Glynn 2014	-2.2	3.4	45	-1.5	4.3	45	11.8%	-0.70 [-2.30, 0.90]
Hebden 2014	-1.6	3	26	-1.4	3.18	25	10.9%	-0.20 [-1.90, 1.50]
Laing 2014	-0.03	4.64	105	0.27	4.64	107	15.5%	-0.30 [-1.55, 0.95]
Lee 2010	-1.9	2.3	19	-0.9	4.64	17	6.5%	-1.00 [-3.44, 1.44]
Partridge 2015	-1.9	2.84	125	0.2	2.99	125	22.9%	-2.10 [-2.82, -1.38]
Turner-McGrievy 2011	-2.57	2.6	47	-2.45	4.39	49	13.4%	-0.12 [-1.56, 1.32]
Total (95% CI)			**454**			**459**	**100.0%**	**-1.04 [-1.75, -0.34]**

Heterogeneity: Tau² = 0.43; Chi² = 13.55, df = 8 (P = 0.09); I² = 41%
Test for overall effect: Z = 2.90 (P = 0.004)

Mean Difference IV, Random, 95% CI
-10 -5 0 5 10
Favours [Mobile apps]   Favours [control]

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Digital and mobile interventions could support regular health services in helping people stop smoking and reduce their risk of obesity, says NICE

Health professionals can consider digital and mobile interventions as a supplement to regular services to support behaviour change in people at risk of developing chronic conditions.

24 January 2020   Share

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Limiti metodologici

- Limitato engagement dei pazienti → problemi di compliance e drop out

- Periodo di follow-up in genere troppo brevi

  - con: non si sa se ipotetico vantaggio rimane

  - pro: obsolescenza strumenti/ritardi approvazione

- Reclutamento limitato di pazienti

- Pazienti troppo specifici che impediscono generalizzazione risultati

#DTx – Come si Ricercano & Sviluppano?

PERSPECTIVE **OPEN**

Agile research to complement agile development: a proposal for an mHealth research lifecycle

Kumanan Wilson[1,2], Cameron Bell[2], Lindsay Wilson[2] and Holly Witteman[3]

Mobile health (mHealth) technology is increasingly being used, but academic evaluations supporting its use are not keeping pace. This is partly due to the disconnect between the traditional pharmaceutical approach to product evaluation, with its incremental approach, and the flexible way in which mHealth products are developed. An important step to addressing these problems lies in establishing agile research methods that complement the agile development methodologies used to create modern digital health applications. We describe an mHealth research model that mirrors traditional clinical research methods in its attention to safety and efficacy, while also accommodating the rapid and iterative development and evaluation required to produce effective, evidence-based, and sustainable digital products. This approach consists of a project identification stage followed by four phases of clinical evaluation: Phase 1: User Experience Design, Development, & Alpha Testing; Phase 2: Beta testing; Phase 3: Clinical Trial Evaluation; and Phase 4: Post-Market Surveillance. These phases include sample gating questions and are adapted to accommodate the unique nature of digital product development.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

NHS England   **NICE**   Public Health England   **MEDCITY**   DigitalHealth. London

EVIDENCE STANDARDS FRAMEWORK FOR DIGITAL HEALTH TECHNOLOGIES

March 2019

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Una corsia preferenziale per le terapie digitali – *Eugenio Santoro*
Terapie digitali: il panorama regolatorio europeo e nazionale – *Intervista a Eleonora Agricola e Maria Di Marzo*

Una corsia preferenziale **per le terapie digitali**

Interventi terapeutici digitali per migliorare gli esiti clinici, dallo sviluppo alla rimborsabilità

Pinned Tweet

Eugenio Santoro @eugeniosantoro · Jan 23

Cosa sono le terapie digitali? come si sviluppano? come si studiano? E' necessaria una corsia preferenziale per le #dtx #digitaltherapeutics ? Ne scrive @eugeniosantoro di @MarioNegriIRCCS sull'ultimo numero di @forwardRPM forward.recentiprogressi.it/numero-16/le-t...

Grazie per l'attenzione

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Rappiungimento della soglia di evidenza clinica

Misurazione

Diagnosi

Assistenza sanitaria personalizzata
Patient reported outcomes, analisi predittiva, supporti alla decisione clinica.

Wearable e dispositivi wireless
Sensori diagnostici e prodotti per la diagnosi.

Mobile health
Fitness tracker, app per la nutrizione o per l'aderenza alle terapie.

Health information technology
Cartelle cliniche informatizzate, sistemi informatici per la prescrizione, app per la consumer health.

Telemedicina
Visite virtuali, monitoraggio remoto del paziente, programmi di assistenza da remoto.

Terapie digitali

Terapia
- farmacoterapia
- riabilitazione
- terapia nutrizionale

Definizione	DIGITAL HEALTH	DIGITAL MEDICINE	DIGITAL THERAPEUTICS
	La salute digitale comprende tecnologie, piattaforme e sistemi che coinvolgono i consumatori per stili di vita, benessere e scopi legati alla salute, che servono per	La medicina digitale comprende software e/o hardware basati su prove di efficacia intesi a realizzare misurazioni e interventi per la salute umana.	Le terapie digitali offrono interventi terapeutici basati sulle prove di efficacia per prevenire, gestire o trattare

FNOMCeO and 9 others

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