NUOVI APPROCCI DI STUDIO DELLA COMPLESSITÀ IN GERIATRIA: DAI BIG DATA ALLA MEDICINA DI PRECISIONE

R. Liperoti, MD, MPH, PhD
Università Cattolica del Sacro Cuore, Roma
Fondazione Policlinico Universitario A. Gemelli IRCCS

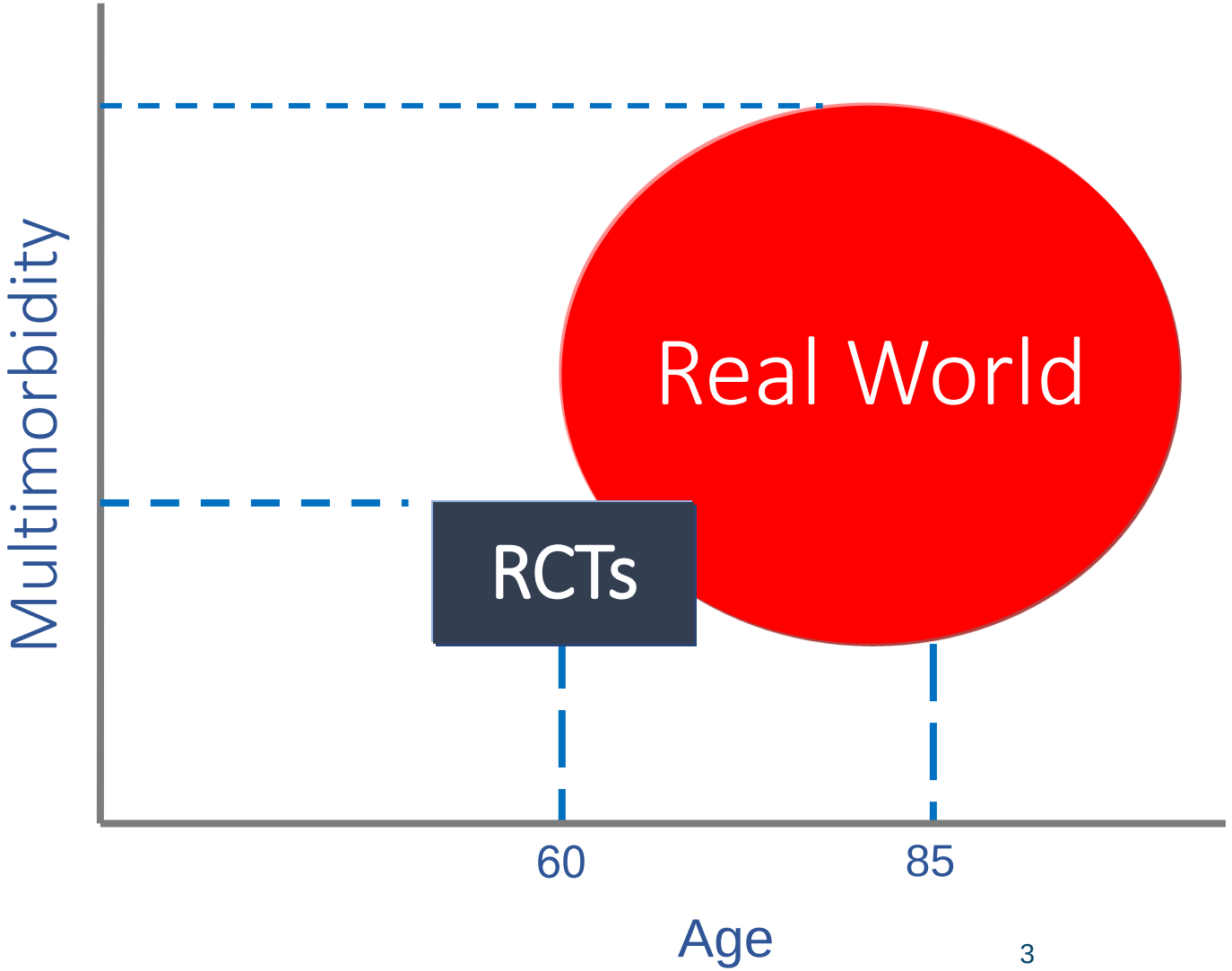
SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022
UNIVERSITÀ CATTOLICA DEL SACRO CUORE

COI disclosure: consulente per MSD, anno 2022;

Grants da EU, Ministero della Salute

RCT e Geriatria: Un Bersaglio Mancato



The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Potential Pitfalls of Disease-Specific Guidelines for Patients with Multiple Conditions

Mary E. Tinetti, M.D., Sidney T. Bogardus, Jr., M.D., and Joseph V. Agostini, M.D.

Comment

www.thelancet.com Vol 367 February 18, 2006

Comorbidity and guidelines: conflicting interests

thebmj

BMJ 2015;350:h1059 doi: 10.1136/bmj.h1059 (Published 11 March 2015) Page 1 of 2

EDITORIALS

Guidelines, polypharmacy, and drug-drug interactions in patients with multimorbidity

A cascade of failure

Alessandra Marengoni *assistant professor*[1 2], Graziano Onder *assistant professor*[2 3]

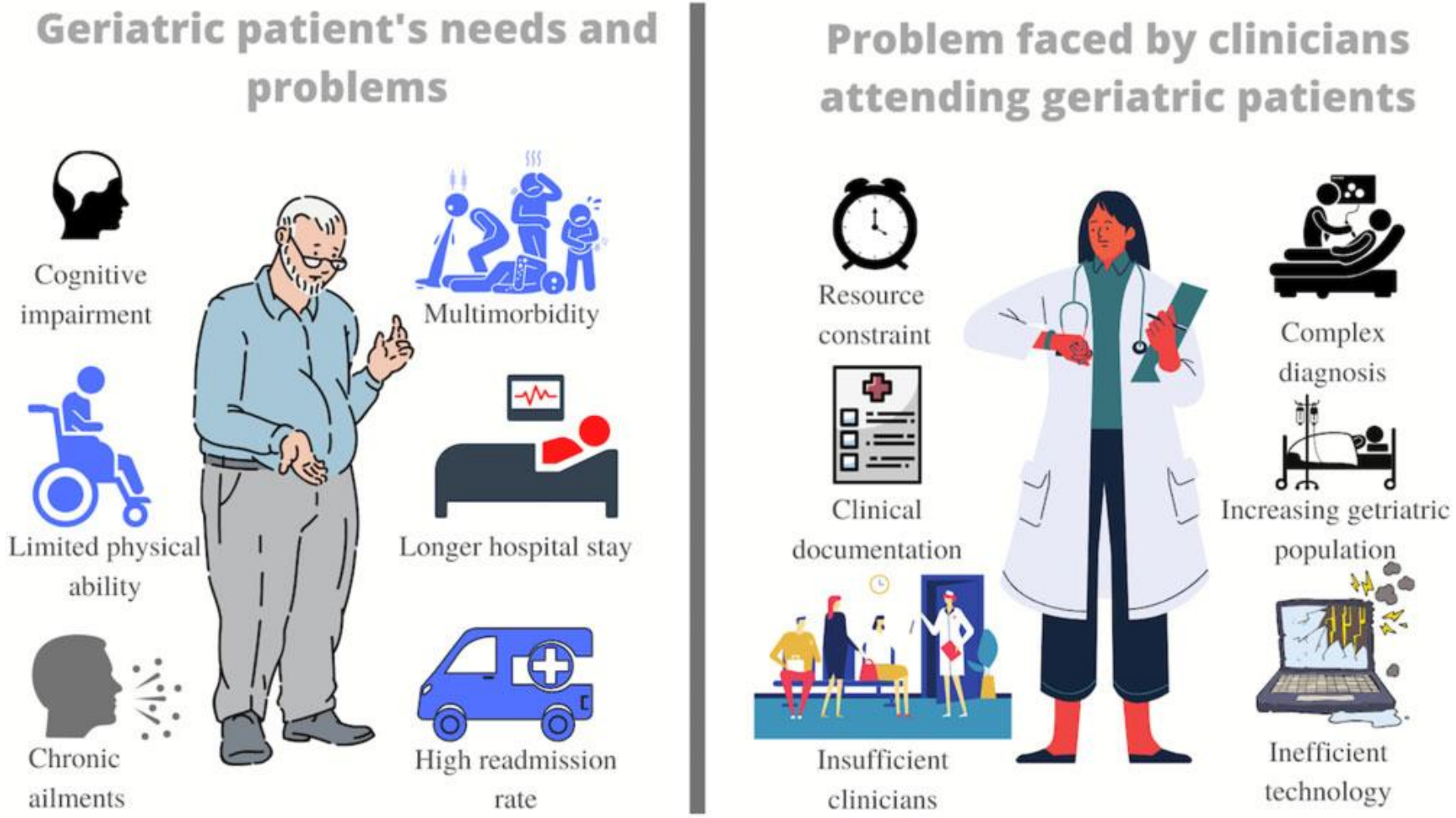
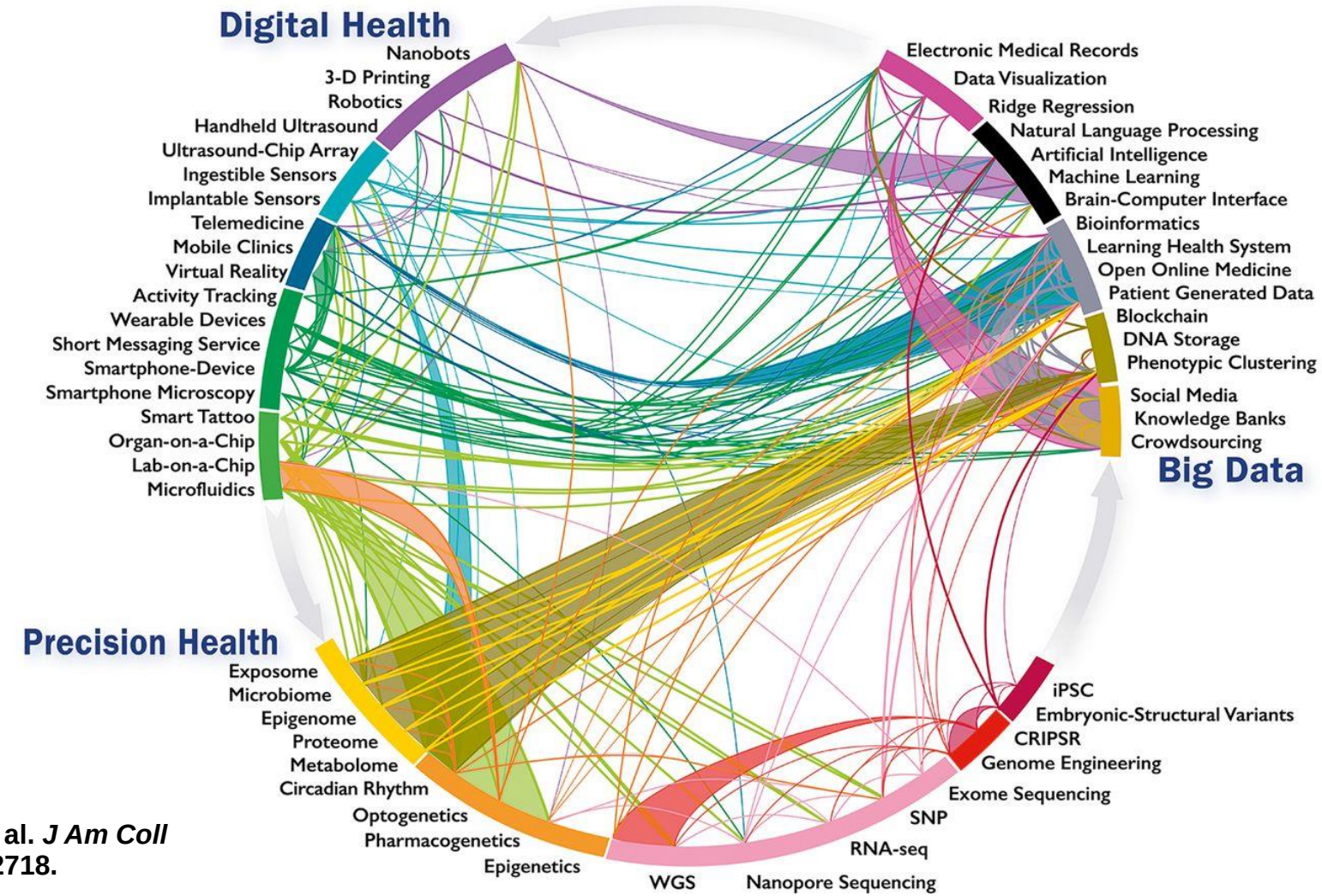


Figure 1. Graphical illustration of geriatric needs and clinician's problems.

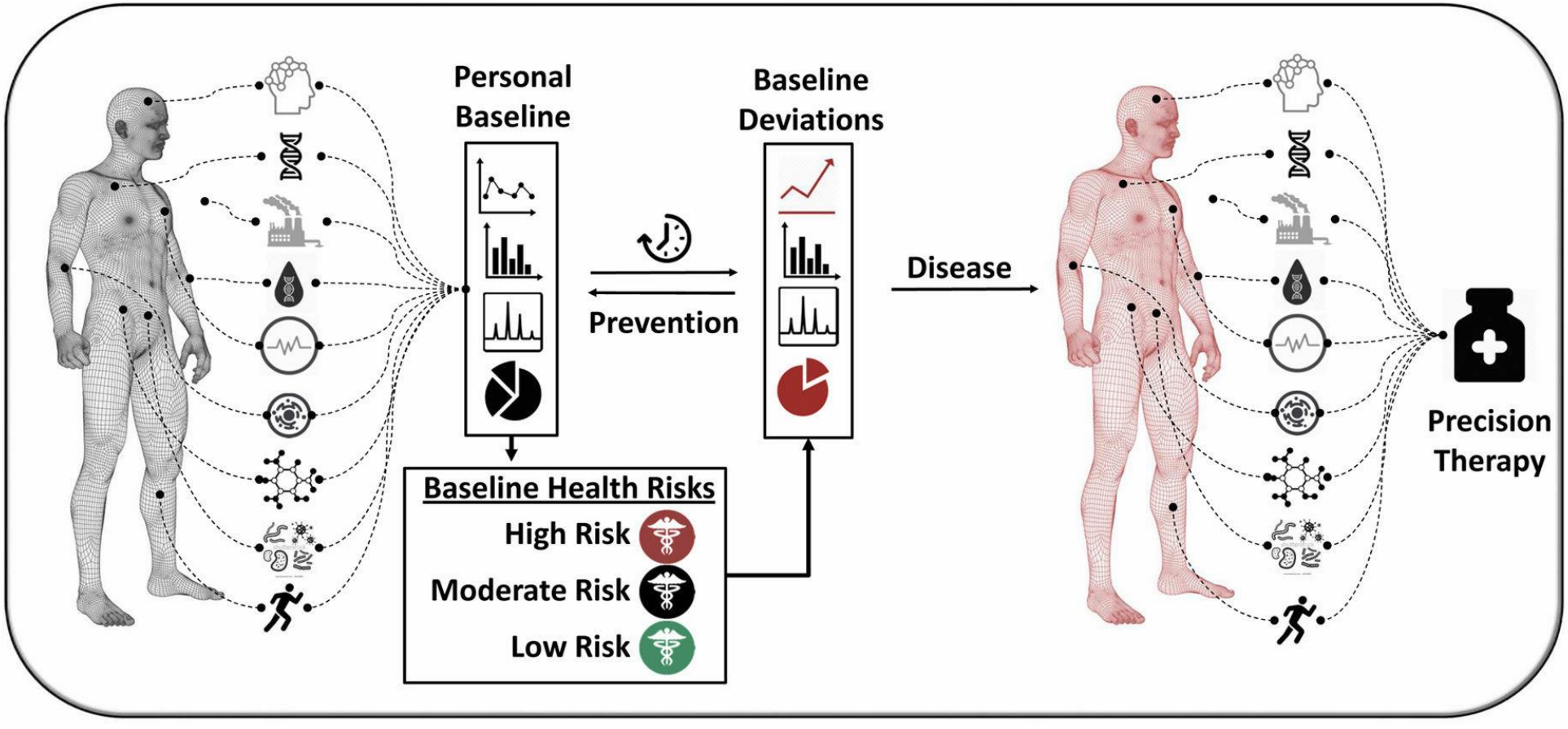
Cohoundhury et al. JAMA open 2020

Interconnessioni tra innovazioni emergenti



Sanjeev P. Bhavnani et al. *J Am Coll Cardiol* 2017; 70:2696-2718.

High Definition Medicine



Cell. 2017 August 24; 170(5): 828–843.

The NEW ENGLAND JOURNAL of MEDICINE

Goal-Oriented Patient Care — An Alternative Health Outcomes Paradigm

David B. Reuben, M.D., and Mary E. Tinetti, M.D.

… focus on a patient's individual health goals within or across a variety of dimensions (e.g., symptoms; physical functional status, including mobility; and social and role functions) and determine how well these goals are being met…

NEJM FREE FULL TEXT

Rubern DB NEJM 2012

EBM

- Trial clnici, metanalisi, rischi relativi
- Rigore sperimentale
- Risultati non generalizzabili ad anziani complessi nel ‘real world’
- Interazioni tra variabili difficili da studiare
- Difficile applicabilità delle linee guida

Nuovo approccio epidemiologico

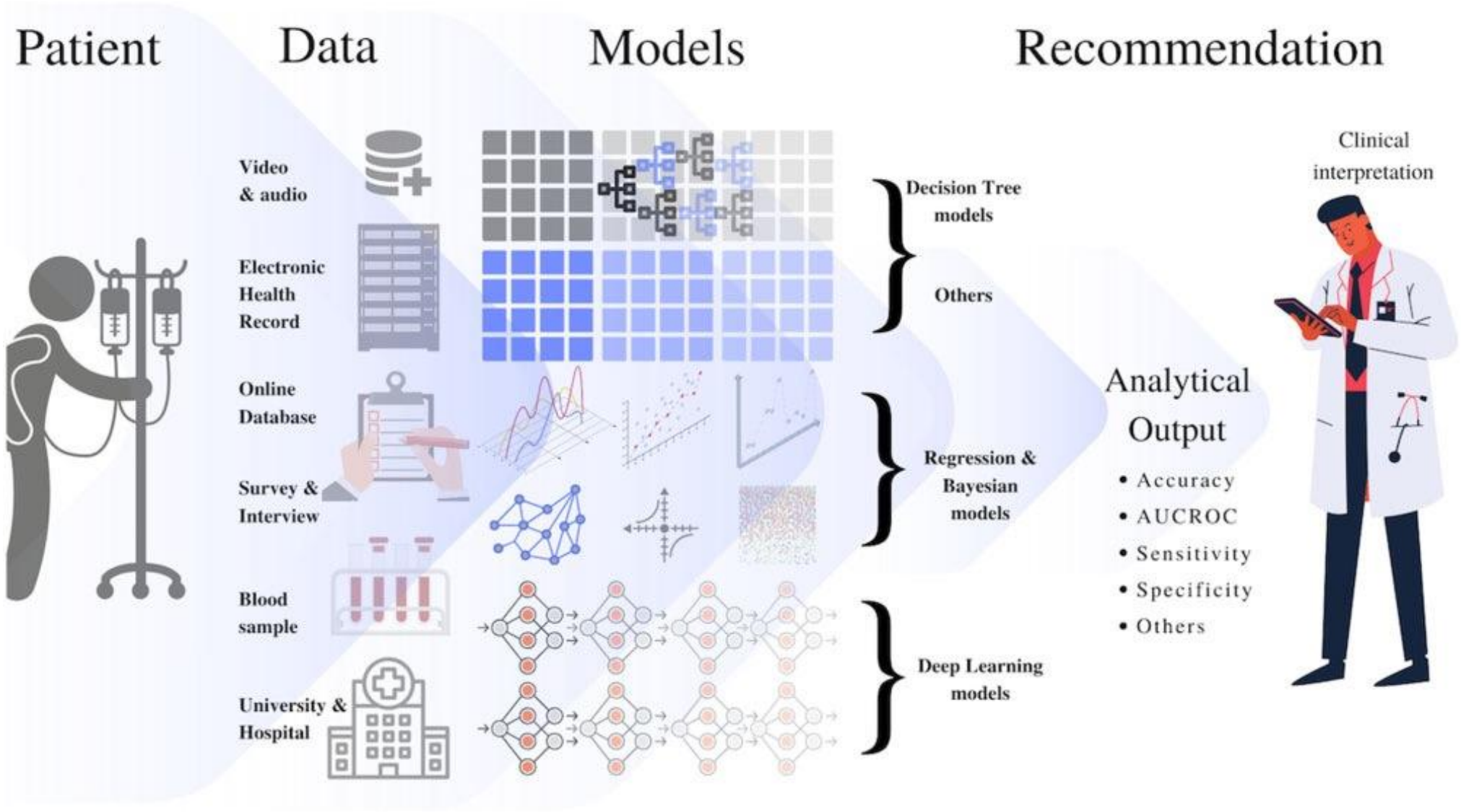
- Osservazioni, rischi assoluti
- Big data
- Informazioni dal ‘real world’
- Intelligenza artificiale
- Fine caratterizzazione dei pazienti e studio della complessità
- Adeguata predizione di outcome di salute, effetto di trattamenti, reazioni avverse etc..
- Necessità di standardizzazione
- Problematiche regolatorie, etiche, di sicurezza

Intelligenza Artificiale in Medicina

- La componente virtuale dell' Intelligenza Arificiale è rappresentata dal Machine Learning
- Si tratta di algoritmi matematici che migliorano l'apprendimento attraverso l'esperienza

Artificial intelligence	The technical replication of human intelligence.
Data-driven	Relying on big amounts of data.
Decision support	The automated suggestion of a beneficial option.
Deep learning	An approach to technically replicate the cognitive abilities of the human brain by consecutively passing information through several layers of an artificial neural network.
Machine learning	The application of algorithms that can learn from data. In supervised machine learning, the algorithms are trying to correctly estimate predefined classes (e.g. naïve Bayes, support vector machine, regression trees). In unsupervised machine learning, the algorithms try to find patterns in the data coming up with classes themselves (e.g. clustering). Deep learning can either be supervised or unsupervised.
Predictive analytics	The prediction of future outcomes by analysing existing data.

Br J Clin Pharmacol. 2020;**86**:2000–2007.



Cohoundhury et al. JAMA open 2020

I CARE 4 OLD

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Individualized CARE for Older Persons with Complex Chronic Conditions at home and in nursing homes

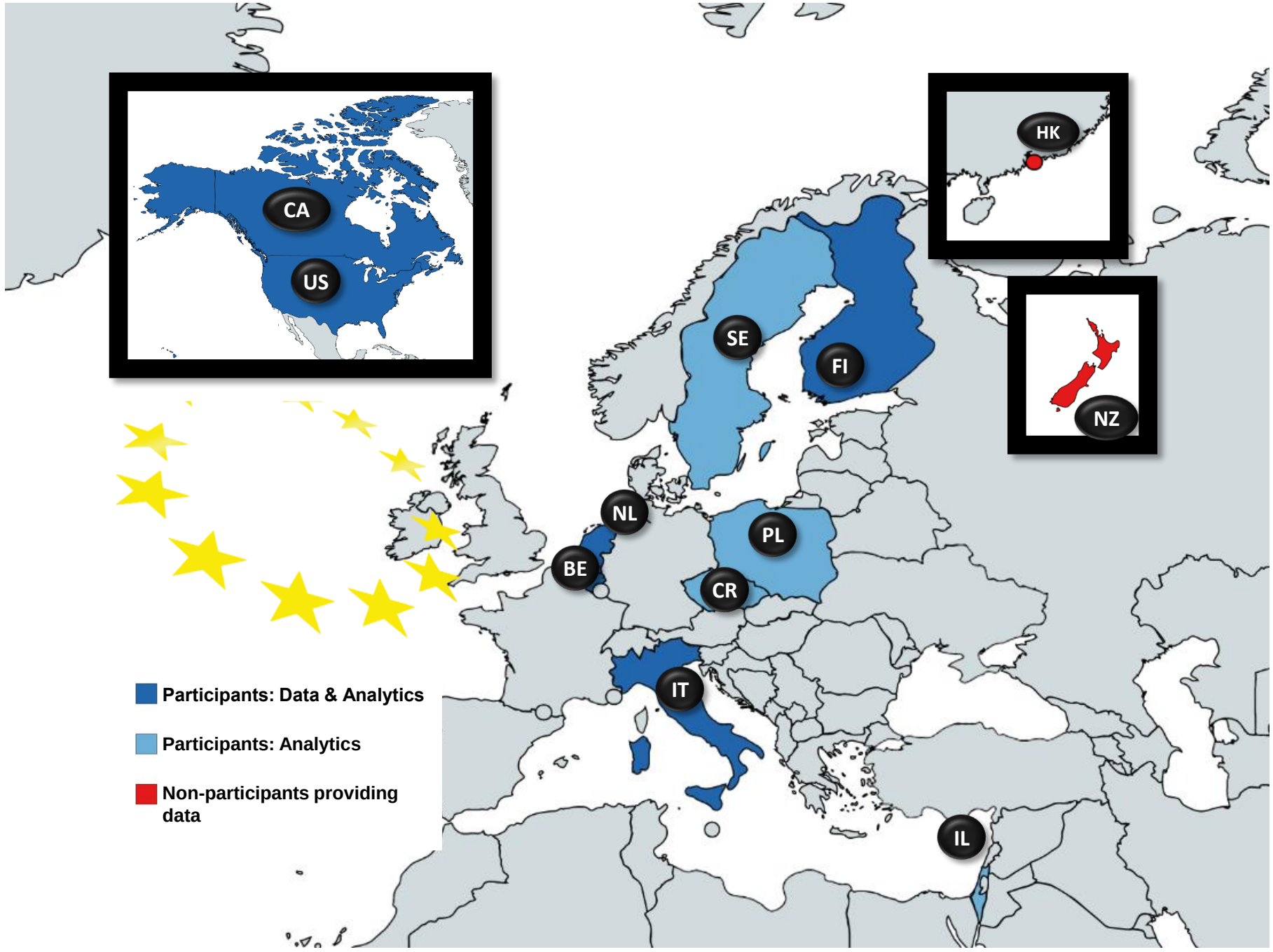
Healthcare professionals taking care of older persons with complex chronic conditions often lack appropriate decision support. In the EU-funded I-CARE4OLD project, a multidisciplinary international team of experts will develop an innovative decision-support tool for healthcare professionals, to enable personalised care.

Learn more about I-Care4Old

www.icare4old.eu

Improve prognostics on 6 outcomes :

	(i) Life expectation
	(ii) Unplanned hospital admission
	(iii) Change in self care functioning- ADL
	(iv) Change in cognitive functioning – CPS
	(v) Health instability – CHESS
	(vi) Change in health related quality of life- HUI-III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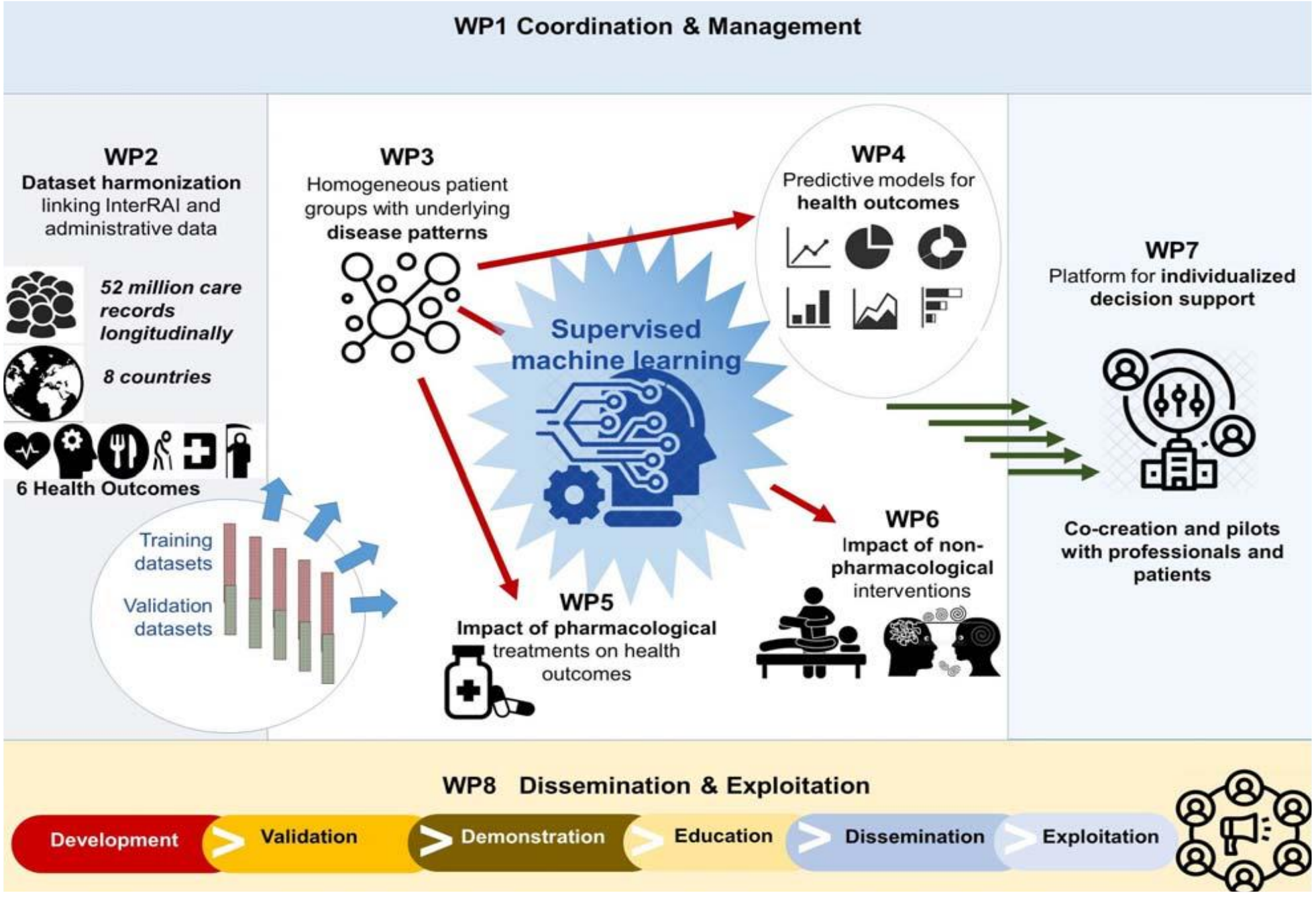
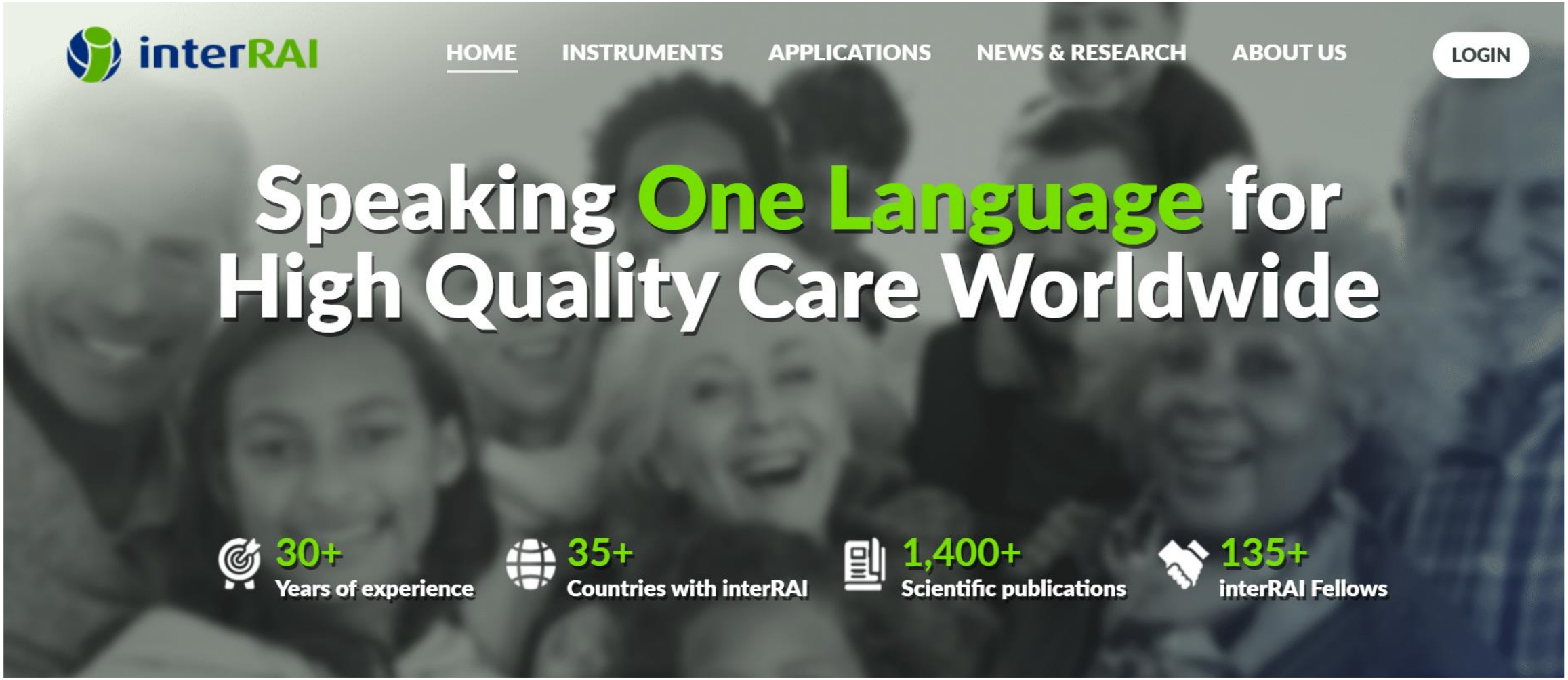
SE
FI
NL
BE
PL
CR
IT
IL
Participants: Data & Analytics
Participants: Analytics
Non-participants providing data

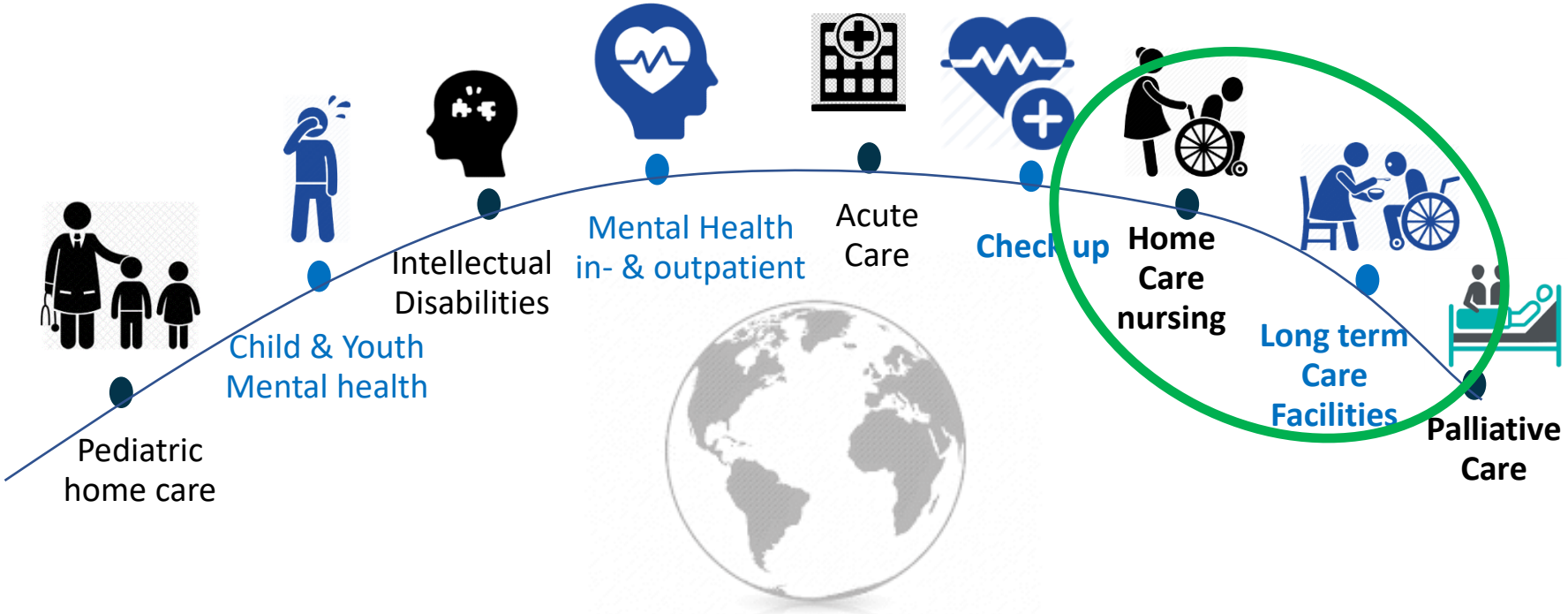
This project has received funding from the European Union's Horizon 2020 Research and Innovation programme, under Grant Agreement number 965341.

Horizon 2020
European Union Funding
for Research & Innovation



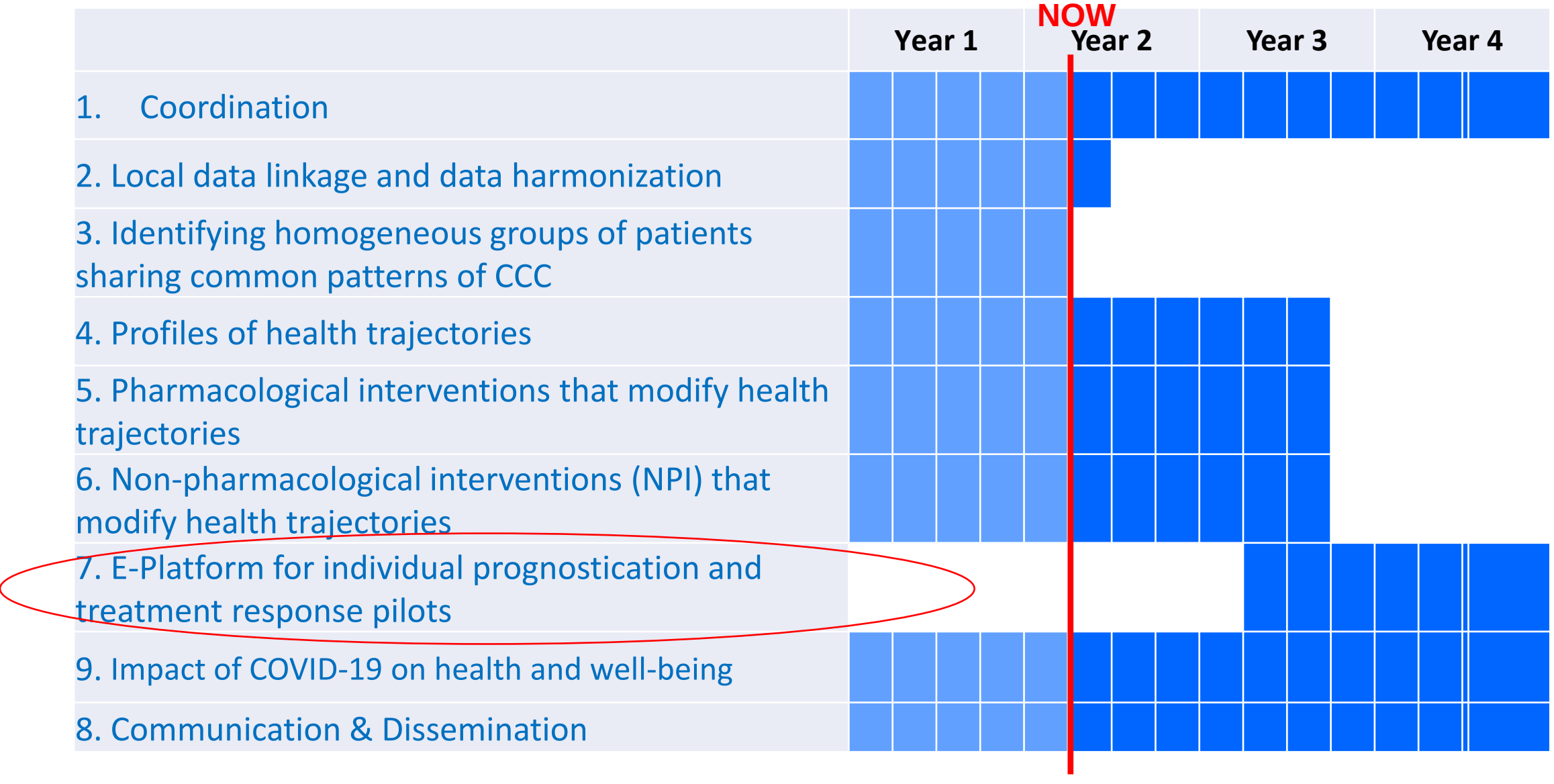

interRAI
HOME
INSTRUMENTS
APPLICATIONS
NEWS & RESEARCH
ABOUT US
LOGIN
Speaking One Language for High Quality Care Worldwide
30+
Years of experience
35+
Countries with interRAI
1,400+
Scientific publications
135+
interRAI Fellows

Minimal Data Sets
with embedded decision support
an International standard



With **Core items and Core scales** persons can be followed through care settings

Timeline workpackages



EXAMPLE PROGNOSTIC DASHBOARD

Your prognosis		if you start 'Physical therapy'
Life expectancy	24-28 months	**+ 1 month**
Acute hospitalisation in 6 months	Low risk <5%	↔ Unchanged
ADL worsening in 6 months	Medium risk 35%	↔ Unchanged
Cognitive worsening in 6 months	Low risk <5%	↔ Unchanged
Health instability in 6 months	High risk 60%	30% ↓ CHANGED medium risk
HR Quality of Life deterioration	Medium risk 35%	<5% ↓ CHANGED: Low risk

Valutare efficacia e sicurezza di interventi farmacologici medianti metodologia tradizionale e machine learning based

- **Traditional statistical model analyses**

The aim is to model average treatment effect over the clients of different multimorbidity classes: the difference between the outcomes Y(0) without treatment (W = 0) and Y(1) if treatment is administered (W = 1).

- **Machine learning analyses**

The aim is to train models to predict individualized treatment effect: the difference between the outcome Yi(0) if client with the characteristics X does not receive treatment (Wi = 0) and Yi(1) if treatment is administered (Wi = 1).

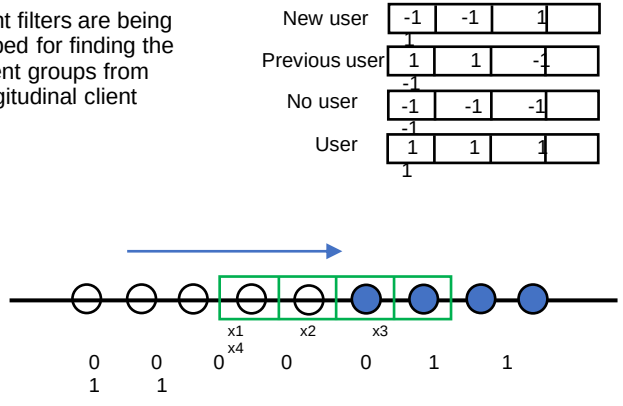
Scopo dello studio:

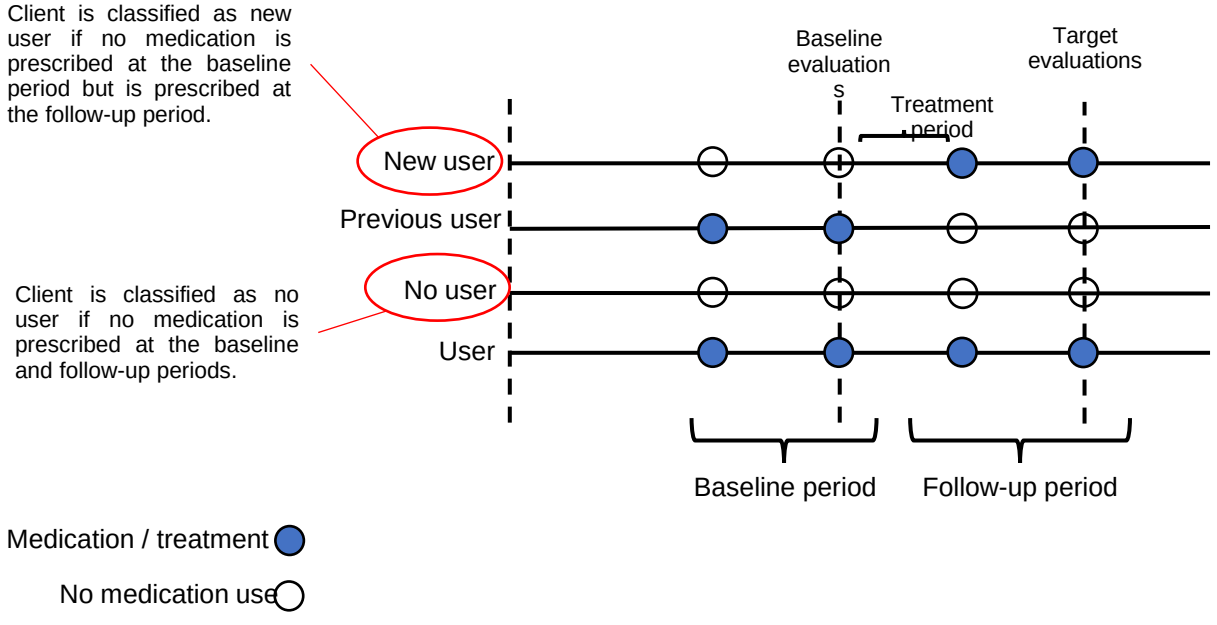
Stimare la risposta a farmaci antidepressivi e il loro effetto su outcome comportamentali e motori in una popolazione di anziani complessi in assistenza domiciliare

Definizione dei gruppi a confronto

- Il primo punto è definire due gruppi, controllo e trattamento, che siano paragonabili.

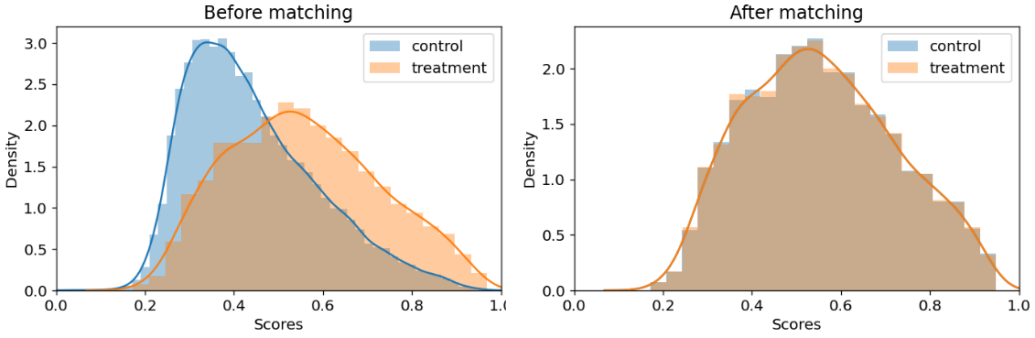
Different filters are being developed for finding the treatment groups from the longitudinal client data





Il problema del ‘confounding by indication’. Propensity score matched groups (HC clients)

Common support is strong assumption for propensity score matching. That is, there must be overlap in the range of propensity scores across treatment and control groups. No inferences about treatment effects can be made for a treated individual for whom there is not a comparison individual with a similar propensity score. Left figure presents propensity score distributions of control and treatment groups before matching. According to the figure, the extent of overlap is good. Right figure presents propensity score distributions of control and treatment groups after matching. According to the figure, the distributions are similar after the matching.



	Before matching			After matching		
	Control	Treatment	SMD	Control match	Treatment match	SMD match
Clients, n	24854	3019		3000	3000	
Age	83.16	82.92	-0.046	82.78	82.95	0.031
Gender, female	68.28%	73.37%	0.158	73.3%	73.23%	-0.002
BMI	26.2	26.4	0,051	26.14	26.38	0.06
Antidepressants	0	0		0	0	
Short term memory problem	50.72%	50.51%	-0.006	50.83%	50.6%	-0.007
Procedural memory problem	40.5%	40.64%	0.004	40.93%	40.5%	-0.012
Decisions about organizing the day	1,1	1,18	0,107	1,18	1,18	-0.003
Worsening of decision making	19.68%	23.98%	0.147	24.1%	23.67%	-0.014
Change in mental function	4.49%	6.72%	0.137	6.33%	6.5%	0.01
Client has become agitated	4.51%	5.76%	0.08	6.03%	5.67%	-0.022
A feeling of sadness or being depressed	8.44%	21.63%	0.531	19.43%	21.17%	0.061
Persistent anger with self or others	10.73%	18.35%	0.308	17.77%	18,00 %	0.009
Expressions of what appear to be unrealistic fears	4.47%	10.24%	0.314	9.27%	9.73%	0.023
Repetitive health complaints	7.08%	17.39%	0.451	16.3%	16.9%	0.023
Repetitive anxious complaints, concerns	7.48%	16.76%	0.406	15.73%	16.33%	0.023
Sad, pained, worried facial expressions	15.25%	31.04%	0.539	29.33%	30.63%	0.04
Recurrent crying, tearfulness	2.76%	7.02%	0.281	6.87%	6.67%	-0.011
Withdrawal from activities of interest	9.04%	15.07%	0.263	14.7%	14.9%	0.008
Reduced social interaction	10.17%	15.63%	0.231	15.2%	15.43%	0.009
Mood indicators have become worse	9.87%	21.2%	0.448	19.87%	20.83%	0.034
Wandering	4.03%	5.03%	0.069	4.9%	5.07%	0.011
Verbally abusive behavioral symptoms	5.02%	7.22%	0.13	7.13%	7,00 %	-0.007
Physically abusive behavioral symptoms	1.42%	1.39%	-0.003	1.6%	1.4%	-0.023
Socially inappropriate_disruptive behavioral symptoms	2.33%	3.08%	0.065	3.7%	3.03%	-0.052
Resists care	9.5%	12.36%	0.13	12.2%	12.27%	0.003
Behavioral symptoms have become worse	4.62%	8.61%	0.228	8.57%	8.33%	-0.012

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Modelli di analisi statistica tradizionali: Antidepressivi: Propensity score matched groups

Social functioning	OR (95% CI)	p-value
At ease interacting with others		
-- New users	0.93 (0.88-0.98)	0.009*
-- Non-users	Reference	
Openly expresses conflict or anger with family/friends		
-- New users	0.91 (0.86-0.96)	0.001*
-- Non-users	Reference	
Change in social activities		
-- New users	1.05 (0.99-1.11)	0.104
-- Non-users	Reference	
Isolation		
-- New users	0.95 (0.9-1.01)	0.111
-- Non-users	Reference	
Client says or indicates that he/she feels lonely		
-- New users	1.1 (1.04-1.17)	<.001**
-- Non-users	Reference	

Mood and behaviour	OR (95% CI)	p-value
A feeling of sadness or being depressed		
-- New users	1.03 (0.97-1.08)	0.363
-- Non-users	Reference	
Persistent anger with self or others		
-- New users	0.94 (0.89-0.99)	0.027*
-- Non-users	Reference	
Expressions of what appear to be unrealistic fears		
-- New users	1.04 (0.99-1.1)	0.135
-- Non-users	Reference	
Repetitive health complaints		
-- New users	0.97 (0.92-1.02)	0.26
-- Non-users	Reference	
Repetitive anxious complaints, concerns		
-- New users	0.99 (0.94-1.05)	0.759
-- Non-users	Reference	
Sad, pained, worried facial expressions		
-- New users	0.99 (0.94-1.05)	0.76
-- Non-users	Reference	
Recurrent crying, tearfulness		
-- New users	1.02 (0.96-1.08)	0.499
-- Non-users	Reference	
Withdrawal from activities of interest		
-- New users	0.93 (0.88-0.98)	0.009*
-- Non-users	Reference	
Reduced social interaction		
-- New users	0.98 (0.93-1.04)	0.471
-- Non-users	Reference	
Mood indicators have become worse		
-- New users	1.02 (0.96-1.08)	0.492
-- Non-users	Reference	
Wandering		
-- New users	1.02 (0.97-1.08)	0.47
-- Non-users	Reference	
Verbally abusive behavioral symptoms		
-- New users	0.94 (0.89-1.0)	0.037*
-- Non-users	Reference	
Physically abusive behavioral symptoms		
-- New users	1.01 (0.96-1.07)	0.656
-- Non-users	Reference	
Socially inappropriate/disruptive behavioral symptoms		
-- New users	1.02 (0.96-1.07)	0.545
-- Non-users	Reference	
Resists care		
-- New users	0.94 (0.89-1.0)	0.034*
-- Non-users	Reference	
Behavioral symptoms have become worse		
-- New users	0.98 (0.93-1.03)	0.461
-- Non-users	Reference	

Modelli di analisi statistica tradizionali: Antidepressivi: Propensity score matched groups

	HR (95% CI)	P-values
Days to death		
-- New users	0.97 (0.92-1.02)	0.26
-- Non-users	Reference	
Next hospital visit (HILMO)		
-- New users	1.04 (1.0-1.07)	0.03
-- Non-users	Reference	
Next hospital visit (unplanned) (HILMO)		
-- New users	1.03 (0.99-1.07)	0.12
-- Non-users	Reference	
Next ER visits (HILMO)		
-- New users	1.05 (1.02-1.09)	<0.001**
-- Non-users	Reference	
Next hip fracture (HILMO)		
-- New users	0.99 (0.86-1.14)	0.91
-- Non-users	Reference	
Next fall-related injury (HILMO)		
-- New users	1.08 (1.0-1.16)	0.04
-- Non-users	Reference	

Physical functioning		OR (95% CI)	p-value
	Mobility in bed		
	-- New users	0.99 (0.93-1.05)	0.771
	-- Non-users	Reference	
	Transfer		
	-- New users	1.0 (0.94-1.06)	0.879
	-- Non-users	Reference	
	Locomotion in home		
	-- New users	1.04 (0.98-1.1)	0.247
	-- Non-users	Reference	
	Locomotion outside of home		
	-- New users	1.25 (1.18-1.33)	<.001**
	-- Non-users	Reference	
	Dressing upper body		
	-- New users	1.06 (0.99-1.13)	0.077
	-- Non-users	Reference	
	Dressing lower body		
	-- New users	1.07 (0.99-1.15)	0.075
	-- Non-users	Reference	
	Toilet use		
	-- New users	1.05 (0.98-1.12)	0.21
	-- Non-users	Reference	
	Personal hygiene		
	-- New users	1.04 (0.97-1.1)	0.27
	-- Non-users	Reference	
	Bathing		
	-- New users	1.14 (1.06-1.22)	<.001**
	-- Non-users	Reference	
	Falls in last 90 days		
	-- New users	1.08 (1.02-1.14)	0.011*
	-- Non-users	Reference	
	Unsteady gait		
	-- New users	1.24 (1.17-1.31)	<.001**
	-- Non-users	Reference	
	Limits going outdoors due to fear of falling		
	-- New users	1.23 (1.16-1.3)	<.001**
	-- Non-users	Reference	

Sommario

nuovi utilizzatori di antidepressivi sono stati confrontati con i non utilizzatori a 6 mesi dall'inizio del trattamento

Migliorati

- Rabbia verso sè o altri
- Perdita di attività e interessi
- Atteggiamenti conflittuali con familiari o amici
- Aggressività verbale
- Resistenza alle cure

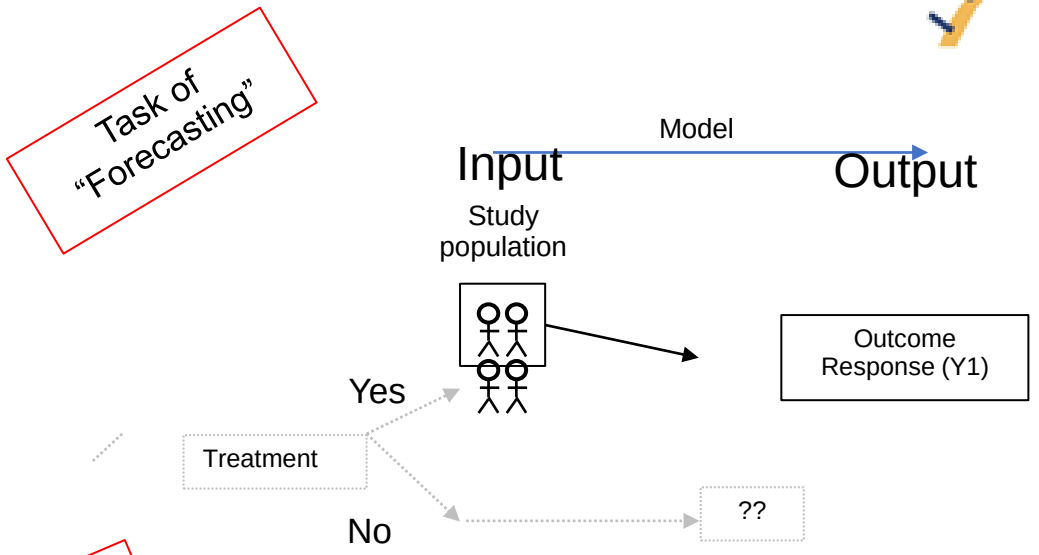
Peggiorati

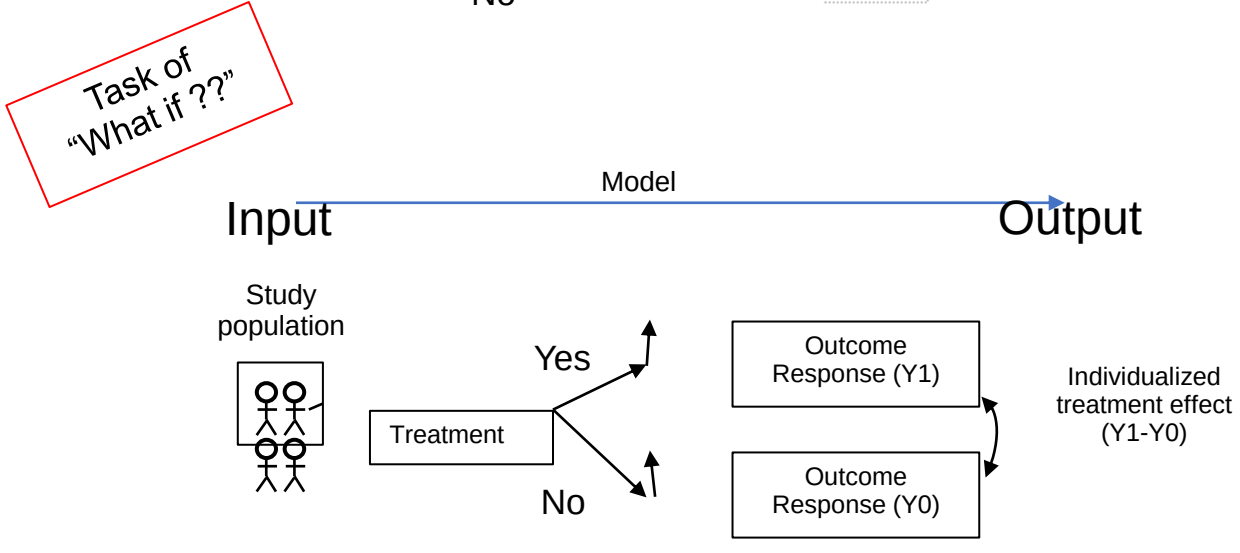
- Ospedalizzazioni e ricorso a PS
- Cadute
- Locomozione
- Abilità nell'igiene personale
- Disturbo di equilibrio
- Limitazione ad uscire per paura di cadere
- Isolamento

Modelli di ML per predire l'impatto di trattamenti farmacologici

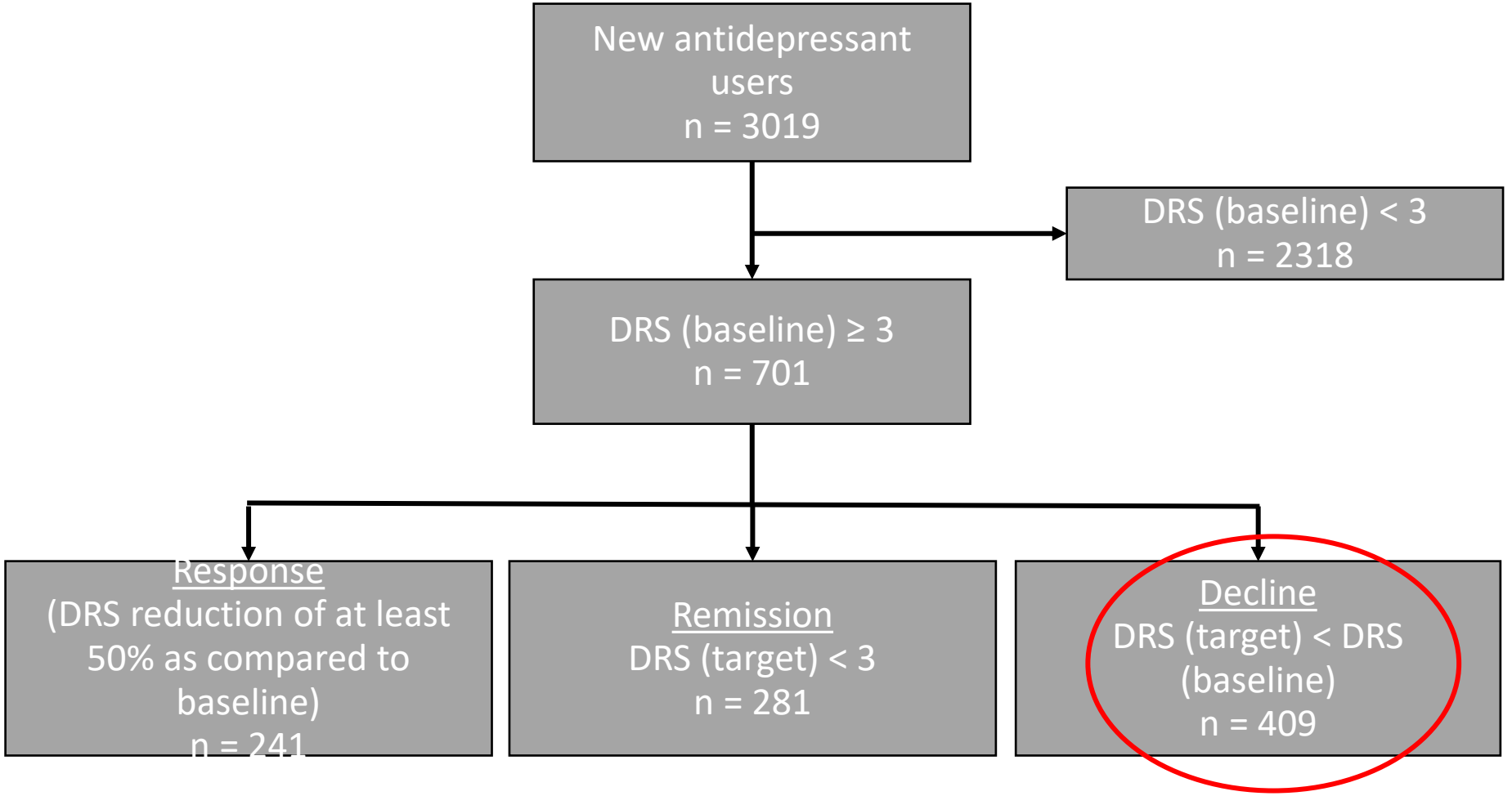
Due diversi approcci

- **(1) Modelli di ML per predire la risposta individualizzata al trattamento**; I dataset di training includono solo pazienti trattati; evidenzia pattern di correlazione.
- **(2) Modelli di ML per stimare l'effetto del trattamento farmacologico negli utilizzatori del farmaco rispetto ai non utilizzatori**; cioè, se iniziare o interrompere il farmaco ha effetto positivo o negativo su un determinato outcome; tutti i pazienti nel dataset sono utilizzati per il training; **"What if scenario".**

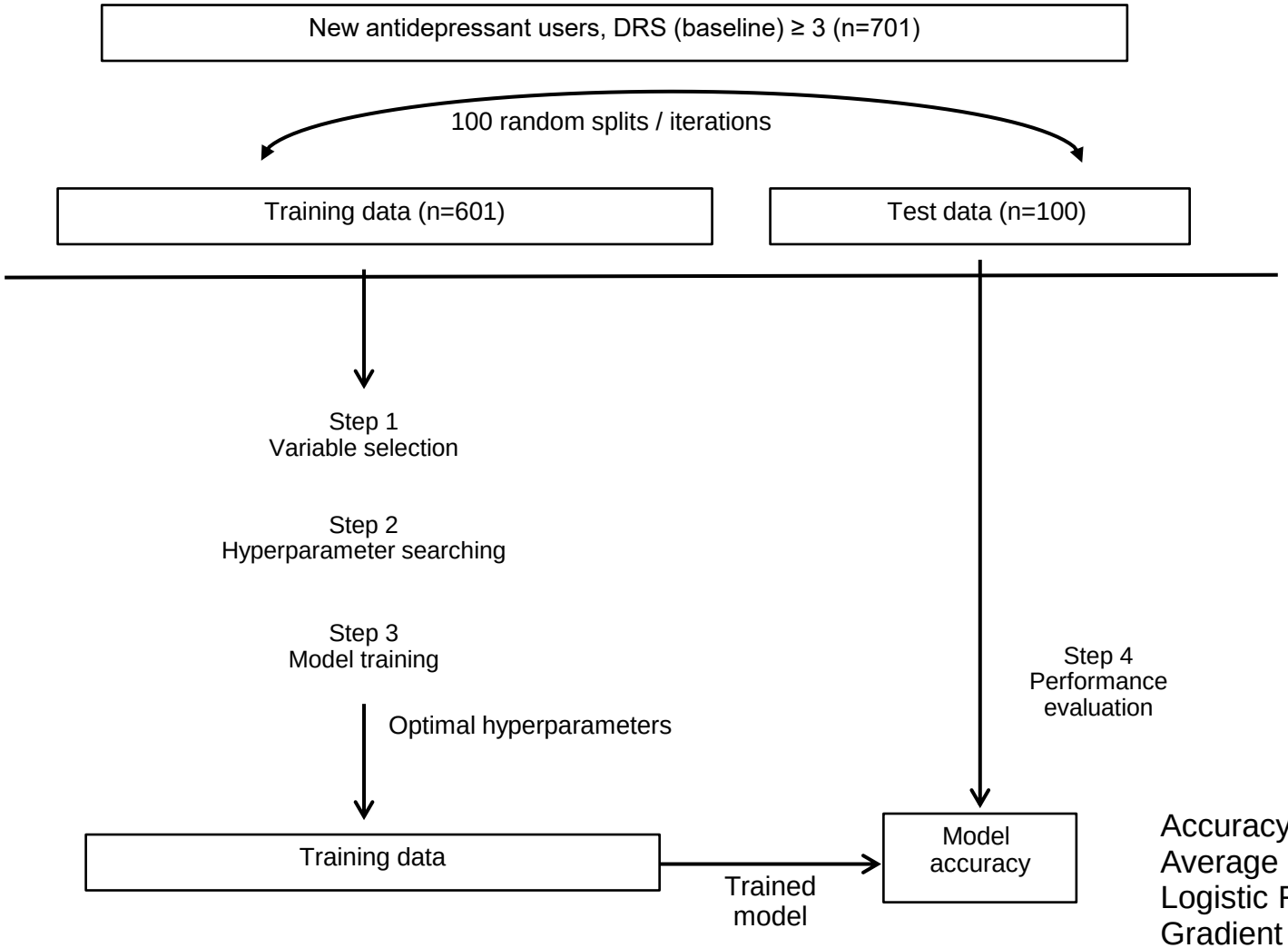




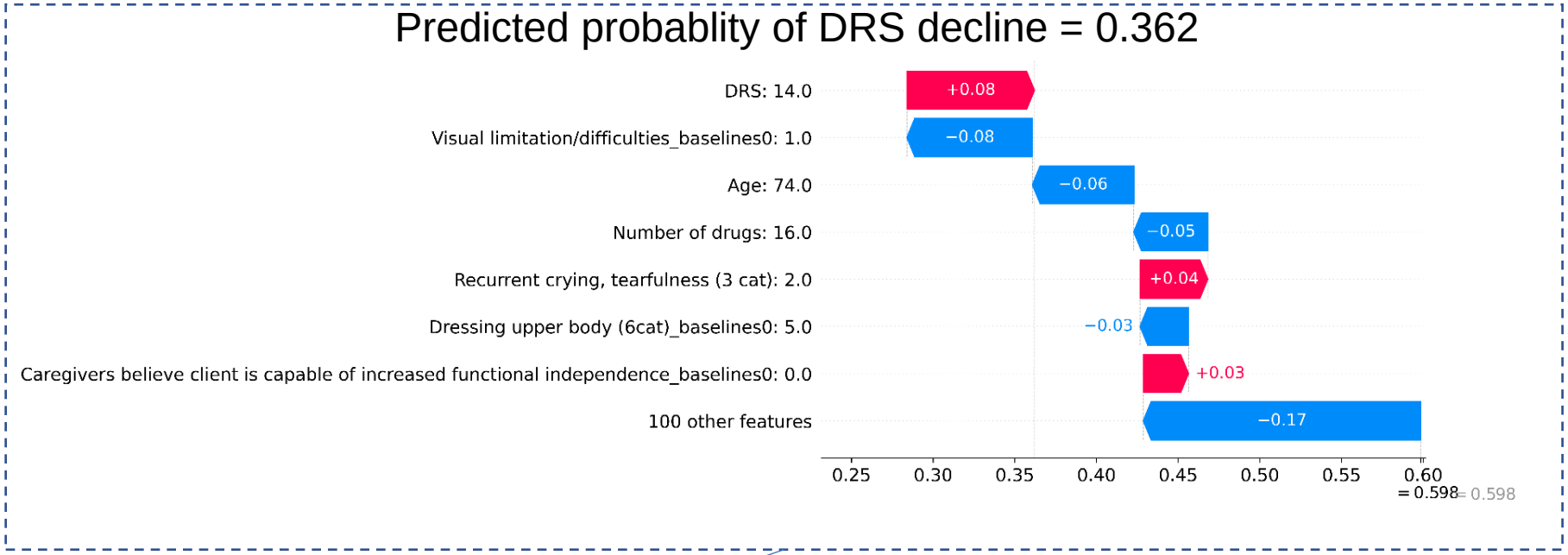
Predire la risposta a farmaci antidepressivi



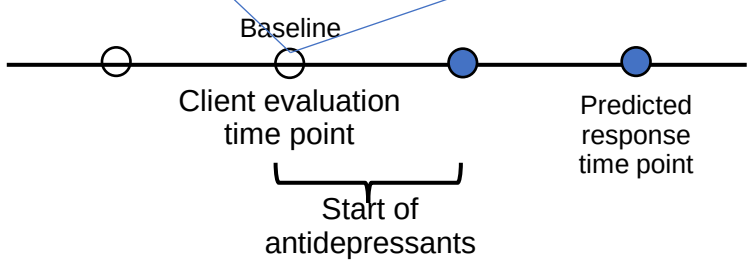
Data flow of machine learning model training pipeline



Accuracy
Average performance (AUC, Area Under Curve) of Logistic Regression (LR), Random Forest (RF) and Gradient Boosting (GB)



Mean value over all clients = 0.598



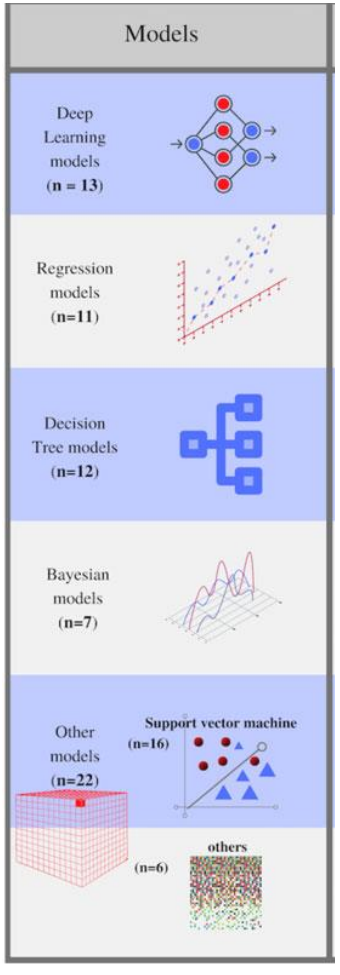
Review

Use of machine learning in geriatric clinical care for chronic diseases: a systematic literature review

Avishek Choudhury, Emily Renjilian, and Onur Asan*

Table 1. Disease classification

Disease name	Disease type	Number of publications
Mild cognitive impairment	Psychological disorder	22
Alzheimer's disease		
Creutzfeldt Jacob disease		
Autism spectrum disorder		
Depression		
Schizophrenia		
Parkinson's disease		
Age-related macular degeneration	Eye diseases	6
Diabetic retinopathy		
Glaucoma		
Geographic atrophy		
Angina pectoris	Other ailments	7
Asthma		
Chronic obstructive pulmonary disease		
Cirrhosis		
Hearing loss		
Osteoarthritis		
Rheumatoid arthritis		
Inflammatory bowel disease		
Hepatitis C virus infection		
Coronary artery disease		



JAMIA Open, 3(3), 2020, 459–471
doi: 10.1093/jamiaopen/ooaa034
Review

LUPINE PUBLISHERS
ISSN: 2641-1725
Lupine Online Journal of Medical Sciences
DOI: 10.32474/LOJMS.2021.05.000225
Research Article

A Perspective: Use of Machine Learning Models to Predict the Risk of Multimorbidity

Journal of Clinical Medicine
MDPI

Review

AI and Big Data in Healthcare: Towards a More Comprehensive Research Framework for Multimorbidity

Wilfling *et al. BMC Family Practice* (2020) 21:180
https://doi.org/10.1186/s12875-020-01247-1
BMC Family Practice

RESEARCH ARTICLE Open Access

Big data analysis techniques to address polypharmacy in patients – a scoping review

D. Wilfling*, A. Hinz and J. Steinhäuser

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Exploring polypharmacy with artificial intelligence: data analysis protocol

Key use cases for artificial intelligence to reduce the frequency of adverse drug events: a scoping review

Ania Syrowatka, Wenyu Song, Mary G Amato, Dinah Foer, Heba Edrees, Zoe Co, Masha Kuznetsova, Sevan Dulgarian, Diane L Seger, Aurélien Simona, Paul A Bain, Gretchen Purcell Jackson, Kyu Rhee, David W Bates

Accuracy of machine learning-based prediction of medication adherence in clinical research

Vidya Koesmahargyo[a,*], Anzar Abbas[a], Li Zhang[a], Lei Guan[a], Shaolei Feng[a], Vijay Yadav[a], Isaac R. Galatzer-Levy[a,b]

[a] *AiCure, LLC, 19 W 24th Street, New York, NY, United States*
[b] *Psychiatry, New York University School of Medicine, 1 Park Ave, New York, NY, United States*

World Health Organization

- Artificial Intelligence (AI) refers to the ability of algorithms to learn from data so that they can perform automated tasks without every step in the process having to be programmed explicitly by a human
- AI can augment the ability of health-care providers to improve patient care, provide accurate diagnoses, optimize treatment plans, support pandemic preparedness and response, inform the decisions of health policy-makers or allocate resources within health systems.
- Use of AI can lead to situations in which decision- making power could be transferred to machines. The principle of autonomy requires that the use of AI or other computational systems does not undermine human autonomy.
- Humans should remain in control of health-care systems and medical decisions.
- It also requires protection of privacy and confidentiality and obtaining valid informed consent through appropriate legal frameworks for data protection.

Ethics and governance of artificial intelligence for health: WHO guidance
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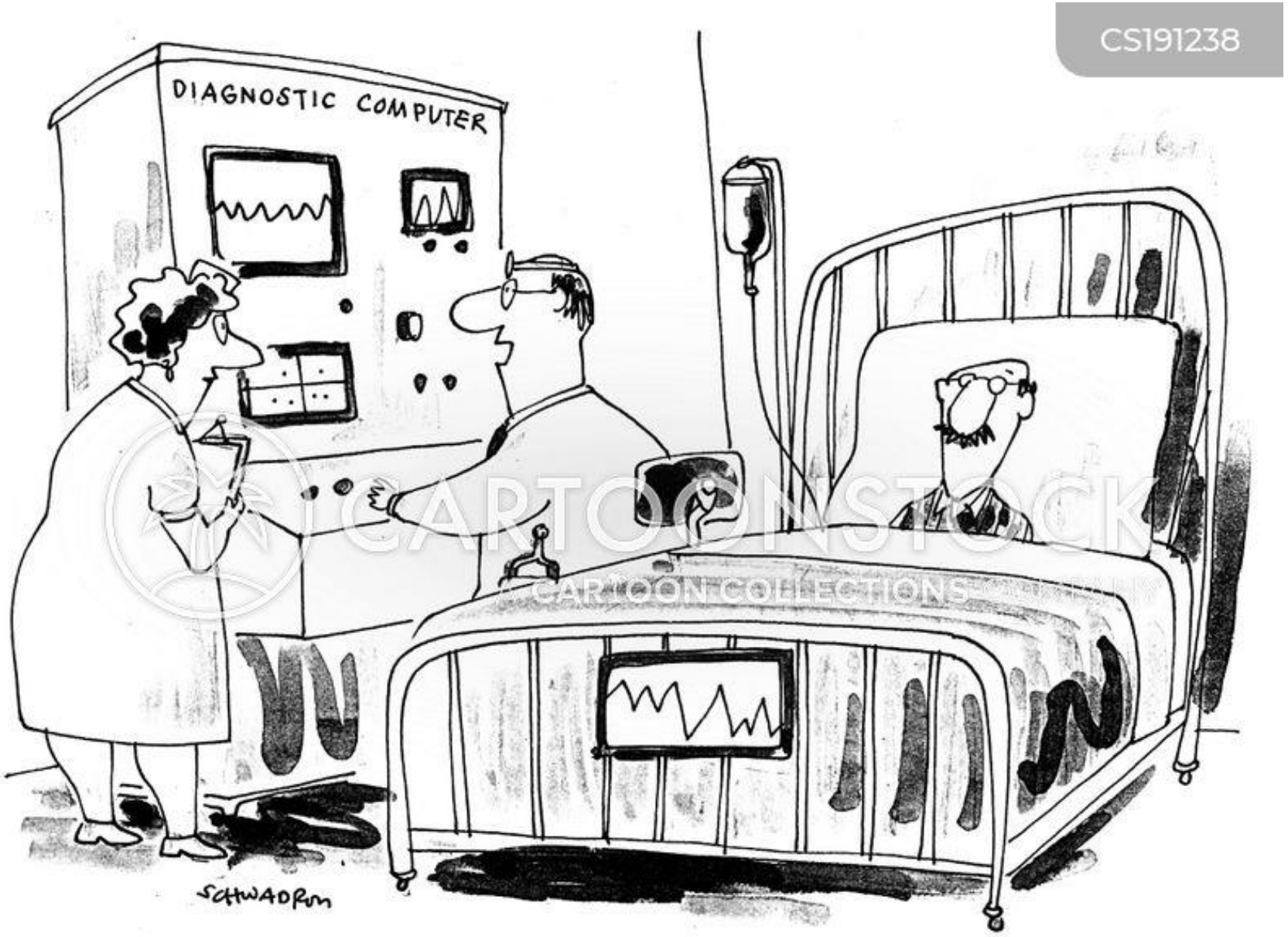

"NURSE, RUSH THIS PATIENT TO THE MATERNITY WARD! SHE'S ABOUT TO DELIVER A BABY!"

frontiers in Medicine

From Big Data to Precision Medicine

Tim Hulsen[1], Saumya S. Jamuar[2], Alan R. Moody[3], Jason H. Karnes[4], Orsolya Varga[5], Stine Hedensted[6], Roberto Spreafico[7], David A. Hafler[8] and Eoin F. McKinney[9]**

- …in order to fully realize the potential inherent in the Big data we can now generate, we must alter the way we work. Forming collaborative networks—sharing samples, data, and methods—is now more important than ever and increasingly requires building bridges to less traditional collaborating specialities such as engineering, computer science and to industry.

- Such increased interaction is unavoidable if we are to ensure that mechanistic inferences drawn from Big data are robust and reproducible. Infrastructure capacity will require constant updating, while regulation and stewardship must reassure the patients from whom it is sourced that their information is handled responsibly. Importantly, this must be achieved without introducing stringency measures that threaten the access that is necessary for progress to flourish.

REVIEW
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