

Supporting personalised medicine with real-world data

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Personalised or precision medicine?

(Deisenhower et al Behaviour Research and therapy 2024)

Personalised medicine

- any effort to select, adapt, or adjust treatment **to an individual** with the goal of improving outcomes, including approaches originating from a holistic and person-centered approach (e.g. client preferences)

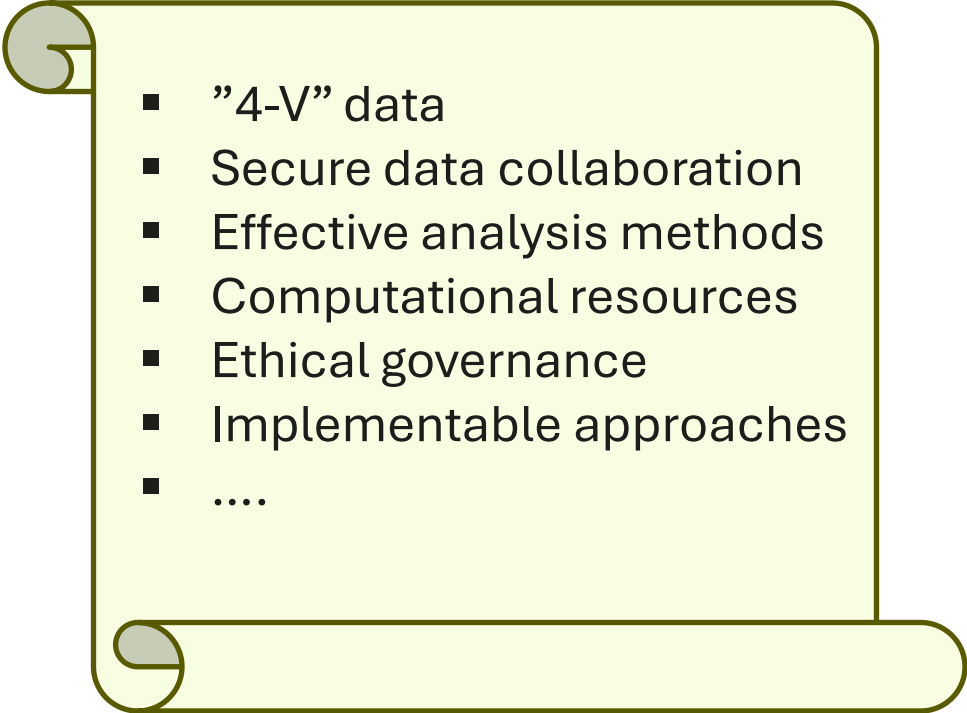
Precision medicine

- data-informed and data-driven treatments
- decision rules for the treatment can be created and implemented AND/OR dynamic prediction systems during the course of treatment

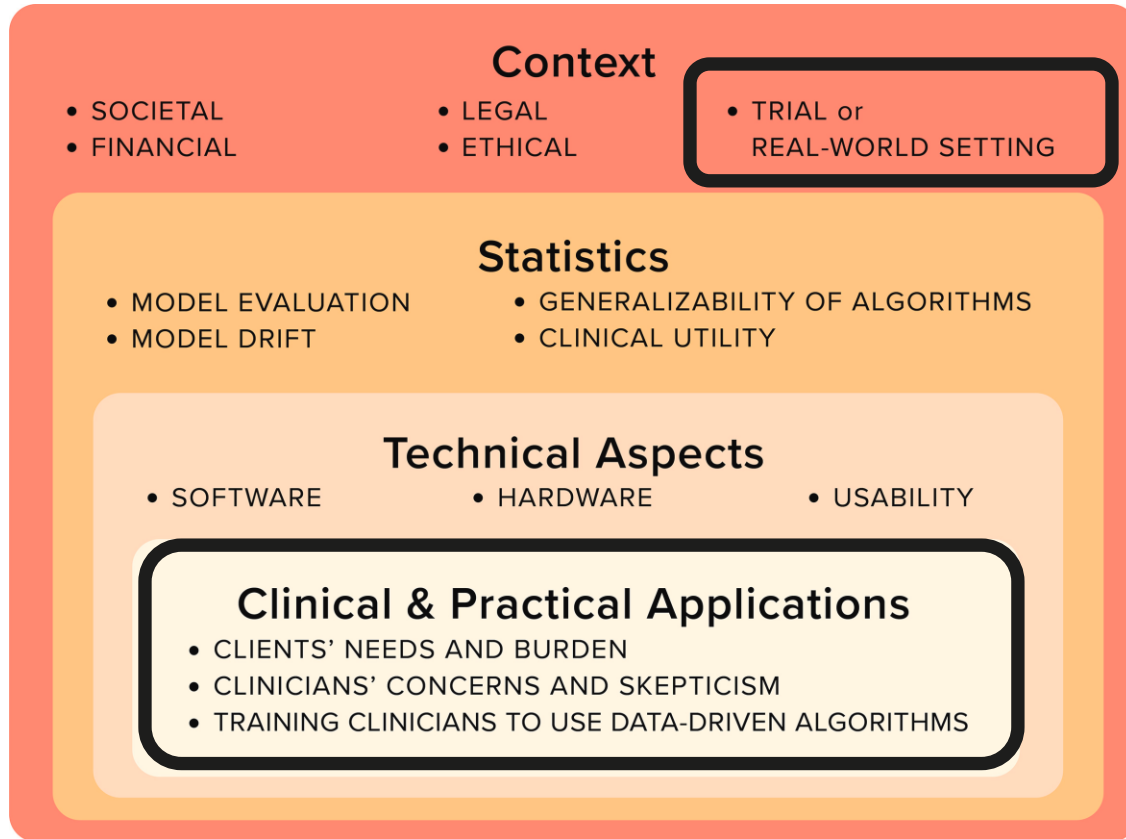
Advances in precision medicine inform treatment personalisation!

Challenges & letter to Santa

- Sufficient sample size
- Availability of relevant data types & measurement frequency
- Appropriate external validation
- Implementation barriers

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- "4-V" data
 - Secure data collaboration
 - Effective analysis methods
 - Computational resources
 - Ethical governance
 - Implementable approaches
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The wishlist in a more academic format



Deisenhower et al Behaviour Research and therapy 2024

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What is real-world data?

“data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources” (U.S. Food and Drug Administration)

These data can be obtained from a number of sources, for example:

- National registers
- Electronic health records (EHRs)
- Claims and billing activities
- Product and disease registries
- **Patient-reported and patient-generated data**
- Data gathered from other sources that can inform on health status, such as mobile devices
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Multiple regulatory frameworks& strategies for integrating evidence from real-world data into personalized medicine exist!

TABLE 1 Global regulatory frameworks and strategies integrating real-world evidence (RWE) into personalized medicine (PM).

Region/Country	Authority/Body	Definition or Focus of Personalized Medicine	Use of RWE in Personalized Medicine	Key Initiatives/References	Maturity Level
United States	FDA	Tailoring medical treatment to genetic, biomarker, phenotypic, and lifestyle data	Regulatory decision-making (e.g., label expansions, post-marketing surveillance)	21st Century Cures Act, FDA RWE Framework, Oncology Center of Excellence (1, 2)	High
Canada	CADTH	Typology-based: Molecular, digital, and clinical personalization	HTA in rare diseases, biomarker-driven care, co-dependent technologies	CADTH HTA guidelines, PM Typology Briefing (3)	Moderate
European Union	EMA/EC	Designing right therapy based on genotypic/phenotypic profiles, lifestyle, environment	Adaptive pathways, pharmacovigilance, benefit-risk assessment	ICPerMed, Regions4PerMed, EMA guidance on RWE (4–7)	High
United Kingdom	NHS/NICE	Right care for the right person at the right time; person-centered and genomics-informed	Medicines optimisation, service design, shared decision-making	NHS Genomics Strategy, NICE NG5 (8, 9)	High
Australia	MSAC	HTA of co-dependent technologies and diagnostics	Early economic modeling with RWE	MSAC evaluation reports (10)	Moderate
China	NMPA/NHC	National PM strategies linked to AI and digital health	Pilot real-world data zones, oncology-focused registries	Healthy China 2030, Hainan RWD pilots (11)	Emerging
Japan	PMDA	Precision-focused early access using biomarkers	RWE in rare disease approvals, Sakigake and Conditional Approvals	Sakigake designation, PMDA real-world datasets (12)	Moderate
South Korea	MFDS	Bioethics-compliant genetic data use in oncology and rare diseases	Draft RWE guidance, genomic screening initiatives	Korean Genome & Epidemiology Study, MFDS draft guidelines (13)	Emerging

(1) In this manuscript, we use **personalized medicine (PM)** as the umbrella term, which encompasses approaches also referred to as “precision medicine”, “stratified medicine”, or “the right care at the right time”. Precision medicine is treated as a subset of PM with a narrower focus on biomarker- or genomics-driven stratification. Regional differences in terminology are preserved in the table to reflect regulator and HTA agency usage (e.g., PMDA Japan emphasizes “precision medicine,” whereas the UK NHS and NICE emphasize “right care, right time”).

Why we need real-world data

- Challenges in generalising the results of randomised controlled trials
 - Population
 - Settings
 - Duration
 - Outcomes
 - Timeframe
 - Power to detect adverse events
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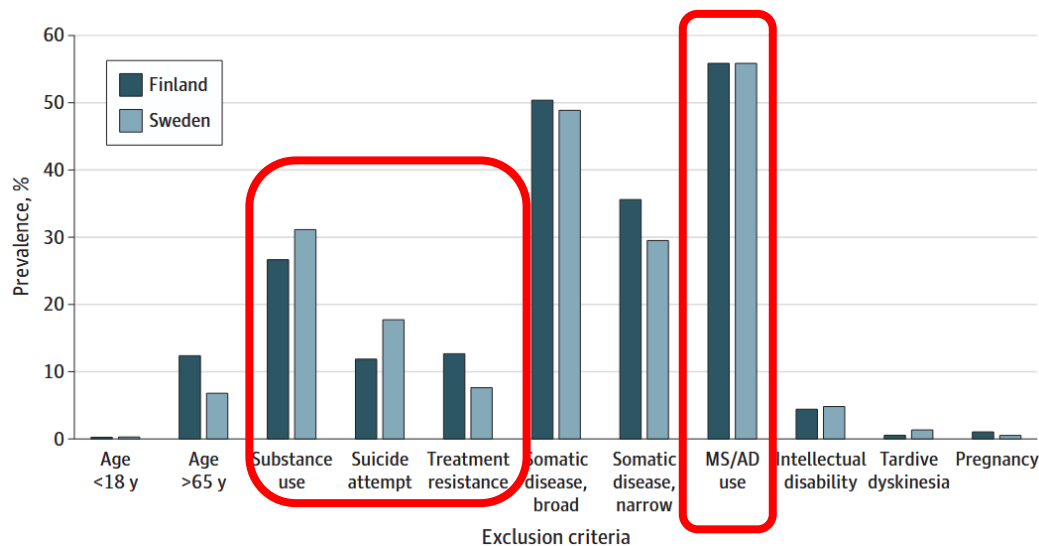
Population selection (external validity) illustrated

JAMA Psychiatry | Original Investigation

Representation and Outcomes of Individuals With Schizophrenia Seen in Everyday Practice Who Are Ineligible for Randomized Clinical Trials

Heidi Taipale, PhD; Johannes Schneider-Thoma, MD; Justo Pinzón-Espinosa, MD, MSc; Joaquim Radua, MD, PhD; Orestis Efthimiou, PhD; Christiaan H. Vinkers, MD, PhD; Ellenor Mittendorfer-Rutz, PhD; Narcís Cardoner, MD, PhD; Luis Pintor, MD, PhD; Antti Tanskanen, PhD; Anneli Tomlinson, MD, PhD; Paolo Fusar-Poli, MD, PhD; Andrea Cipriani, MD, PhD; Eduard Vieta, MD, PhD; Stefan Leucht, MD; Jari Tiihonen, MD, PhD; Jurjen J. Luykx, MD, PhD

B Prevalence of conditions among excluded individuals by cohort



Key Points

Question What percentage of patients with schizophrenia in the real world are represented in randomized clinical trials (RCTs) and do their outcomes differ from those not represented in RCTs?

Findings In this study of 25 259 real-world individuals with diagnoses of schizophrenia spectrum disorders recorded in national patient registries in Finland and Sweden, about a fifth were represented in RCTs and their outcomes were better than of those individuals with schizophrenia not meeting RCT inclusion criteria.

Meaning Future research should consider the heterogeneity of individuals with schizophrenia and the patient groups typically ineligible for participation; RCTs may become more inclusive by representing a broader spectrum of individuals with schizophrenia and by targeting specific currently underrepresented groups.

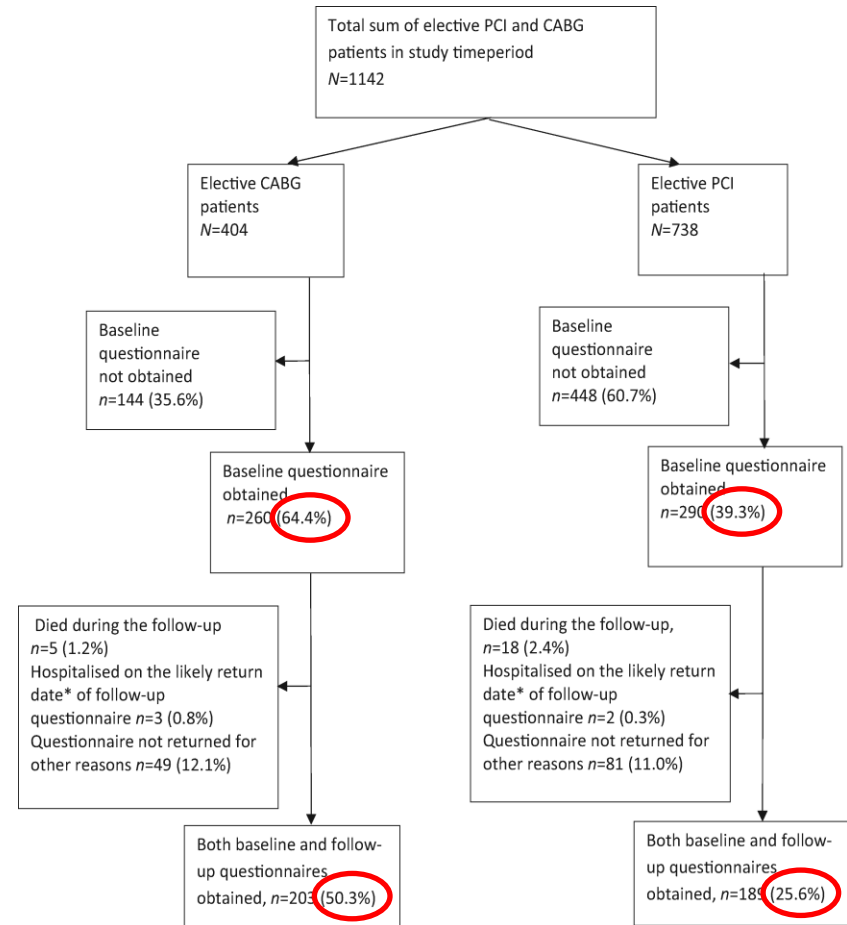
Population selection also occurs in real-world

Kuopio University Hospital Heart Center 6/2012-8/2014:

“All patients undergoing elective coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) were asked, as part of routine clinical practice, to fill in the 15D questionnaire at baseline and 12 months after the revascularization procedure.”

Oinasmaa et al

Eur Heart J Quality of Care & Clinical outcomes 2018



Population selection also occurs in real-world

- Selection is typically non-random
 - difficult to correct with multiple imputation
- Decision to collect data is not enough, resources are also needed!
- Plan the collection carefully:
 - When, how, what, who?

Context

- SOCIETAL
- FINANCIAL
- LEGAL
- ETHICAL
- TRIAL or
REAL-WORLD SETTING

Statistics

- MODEL EVALUATION
- MODEL DRIFT
- GENERALIZABILITY OF ALGORITHMS
- CLINICAL UTILITY

Technical Aspects

- SOFTWARE
- HARDWARE
- USABILITY

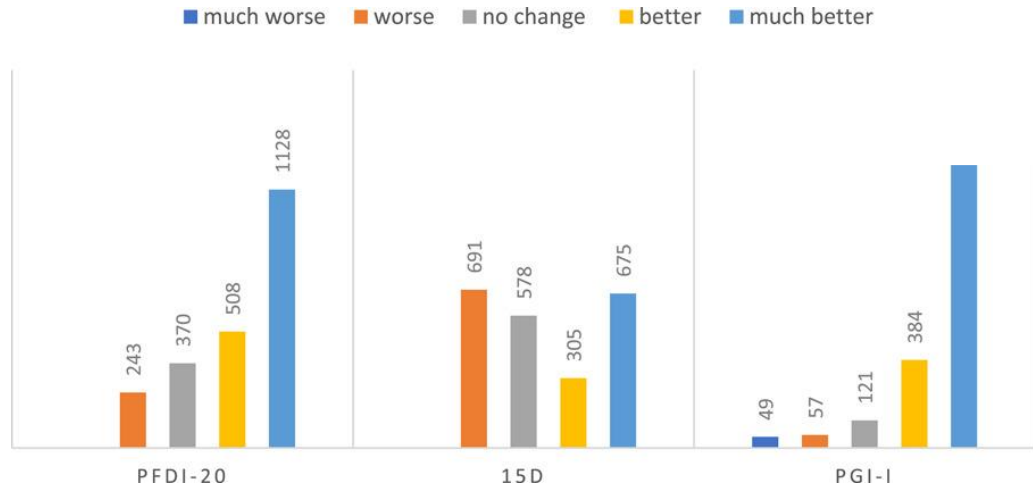
Clinical & Practical Applications

- CLIENTS' NEEDS AND BURDEN
- CLINICIANS' CONCERNS AND SKEPTICISM
- TRAINING CLINICIANS TO USE DATA-DRIVEN ALGORITHMS

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You get what you measure

- Patient-reported outcomes essential for value-based healthcare & personalised medicine
- Plethora of validated instruments exist (disease-specific & generic)
- How many out of the 2249 patients undergoing pelvic organ prolapse surgery considered their condition to be much better after the procedure?



Mattsson et al Neurourol Urodyn 2020

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Summary

- Routinely collected health data increasingly important for personalised (and precision) medicine, but patient-reported data needed in addition to "hard" clinical data
- Successful adoption of data-informed treatment recommendations often depends on whether a client is willing and able to provide necessary data – a challenge that should be solved early in the PM development path
- Need to evidence the gains (for patients & healthcare providers)
 - co-design supports the defining and development of clinically applicable approaches



TAKE-HOME MESSAGE: Using RWD is like building with Legos – although the sets were originally intended for a different purpose, we can combine the blocks to create something new & fantastic.

However, we need to know how to use the blocks optimally to achieve our aims, in collaboration with other builders.