REAL WORLD EVIDENCE

RWE4Decisions

Public Webinar

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

Co-moderated by **Eric Sutherland (OECD)** and **Alina Pavel (RWE4Decisions Secretariat)**

25 June 2024 | 15:00 - 16:30 CEST

On Zoom

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

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Co-moderator

ERIC SUTHERLAND

Senior Health Economist, OECD

Principles

Payer-Led Multi-Stakeholder Learning Network

Highly innovative technologies often have immature clinical evidence (and high prices)

Could robust real-world evidence (RWE), generated during the life cycle of technology development and use, resolve HTA/Payer uncertainties?

Can requirements be aligned across stakeholders and health jurisdictions/payers?

RWE4Decisions REAL WORLD EVIDENCE 2024 STEERING GROUP

HTA bodies / Payers

Jo De Cock

Senior Adviser, **INAMI-RIZIV**

Diane

President of Comm. of Drug Reimbursement, **INAMI-RIZIV**

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Chief Pharmacist, **TLV**

Piia Rannanheimo

Chief Specialist, **Fimea**

Cláudia Furtado

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Laurie Lambert

Special Projects Adviser, **CADTH**

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Carlos M. Saborido

Adviser, **Spanish Ministry of Health**

International Org.

Eric Sutherland

Senior Health Economist, **OECD**

Industry

EUCOPE

AstraZeneca

Boehringer Ingelheim

GILEAD

NOVARTIS

Pfizer

Roche

Takeda

Patient Representatives

Antonella Cardone

CEO, **Cancer Patients Europe**

Chris Sotirelis

Patient Advocate for **Thalassemia**

EURORDIS RARE DISEASES EUROPE

Insurer

Hans-Georg Eichler

Consulting physician, **Austrian Social Insurance Inst.**

Clinician

Matti Aapro

Director, **Genolier Cancer Centre**

Analytics Expert

Ashley Jaksa

Market Access Scientific Strategy Lead, **Aetion, US**

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Entela Xoxi

Pharmacologist, **Uni. Cattolica Sacro Cuore**

Facilitators

FIPRA International

Karen Facey, Senior Adviser (HTA)

François Meyer, Special Adviser (HTA)

Secretariat provided by FIPRA funded by EUCOPE and member companies

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

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Keynote speaker

ROSSELLA DI BIDINO

Head of the HTA and AI Unit,
ALTEMS Università Cattolica

Strategies for Development, Governance, and Assessment of digital health technologies at hospital level

Dr. Rossella Di Bidino

The Graduate School of Health Economics and Management, Catholic University of the Sacred Heart, Rome - Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

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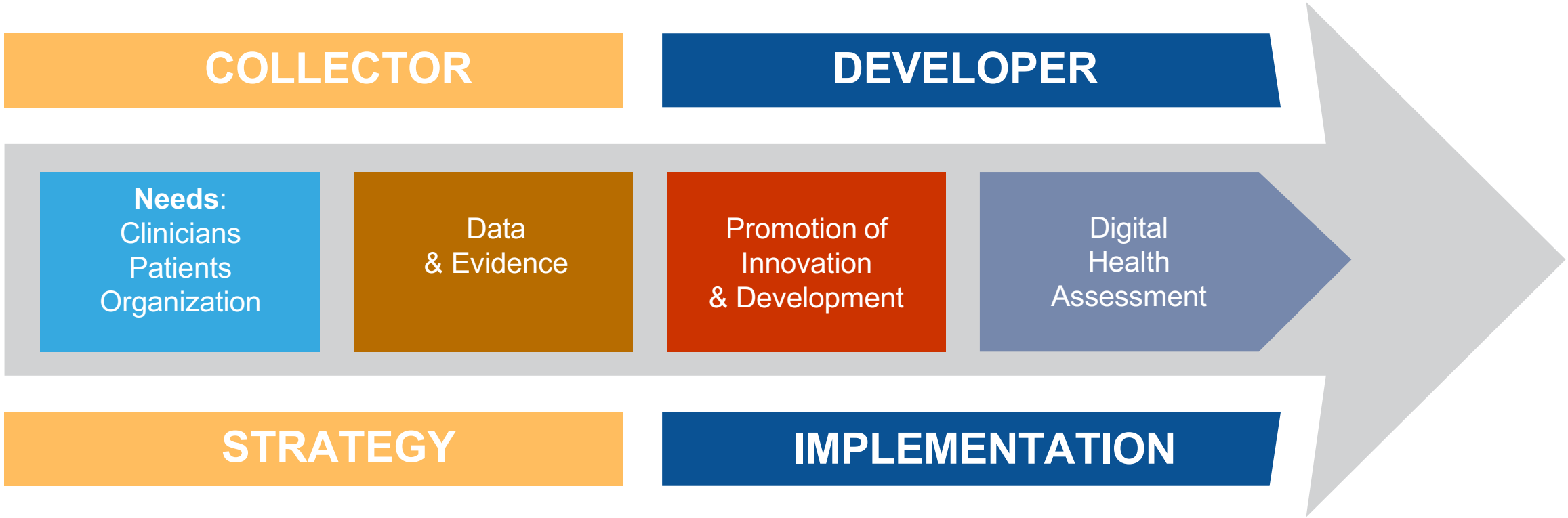
Agenda

- Hospitals not only users of digital health
- Hospitals as assessors
- What about digital endpoints?
- Conclusions

Hospitals not only users of digital health



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Hospitals & needs

COLLECTOR

Needs:
Clinicians
Patients
Organization

STRATEGY

Needs	Digital solutions for:
• Personalise care • Address the needs of chronic patients • Planning of activities • Optimization of resources • Training • Promote wellness • Sports medicine	• Early discharge • Remote monitoring • Virtual ward

Data
& Evidence

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Hospitals as developers

and their contribution in the definition of endpoints

GemelliGenerator
Clinical research beyond tomorrow

Digitally enabled care model

Aims:

- Personalised remote heart failure care.
- Based on good clinical practice standards and guidelines.
- Optimization of in-hospital care delivery models and out-of-hospital and home settings.

Co-development:

- Clinicians: Gemelli
- Technology: Innovation Spirit
- Industry: AstraZeneca

AZIMUTH

DEVELOPER

Promotion of Innovation & Development

IMPLEMENTATION

Gemelli Digital Medicine & Health — GDMH

A large general hospital spin off, fully owned by Policlinico Gemelli. GDMH provides turn-key solutions in Digital Medicine & Health.

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Hospitals as assessors

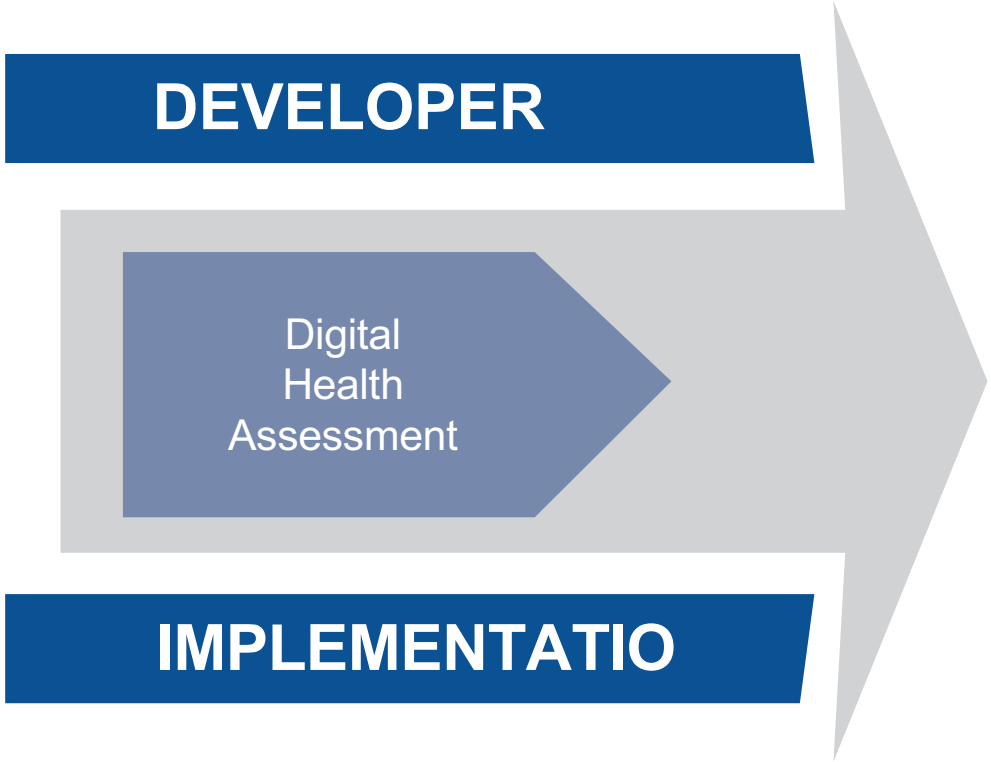
- **When** – Technology Readiness Level & piloting

AI-Mind

- **How** –PICOTS-ComTeC & Framework(s)

EDiHTA

- **Evidence** – Trials, RWD/RWE, quality, and …



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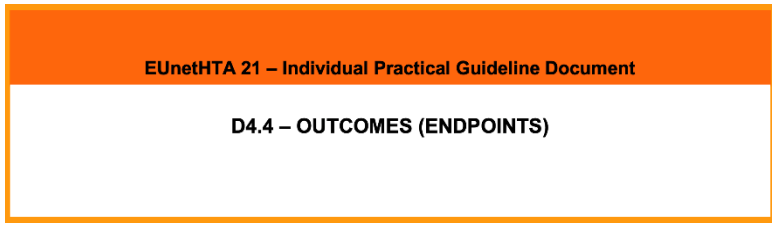
What about digital endpoints in HB-HTA?

While we acknowledge their potential relevance, but:

- Are digital endpoints perceived as a **source of evidence**?
- Are **hospitals** currently incorporating them into their HTAs?
- If not, what are the barriers to **acceptance**?
- If yes, **when** they are used?
- Which criteria should satisfied a digital endpoint to be included in a hospital PICOT (or **PICOTS-ComTec**)?

What about digital endpoints?

Endpoint / Outcome



"Outcome" is any concept that can be used for estimating **treatment effectiveness,** such as mortality, remission, disease control, function, health-related quality of life (HRQoL), symptoms and safety.
Outcomes are distinct from **the way in which they are measured**.

What relevant endpoints/outcome measures are used? E.g. change in mortality, morbidity, side effects, quality of life, cost-effectiveness**, length of stay, number of (re)admissions,** ICER, **budget impact, costs per correct diagnoses** etc.

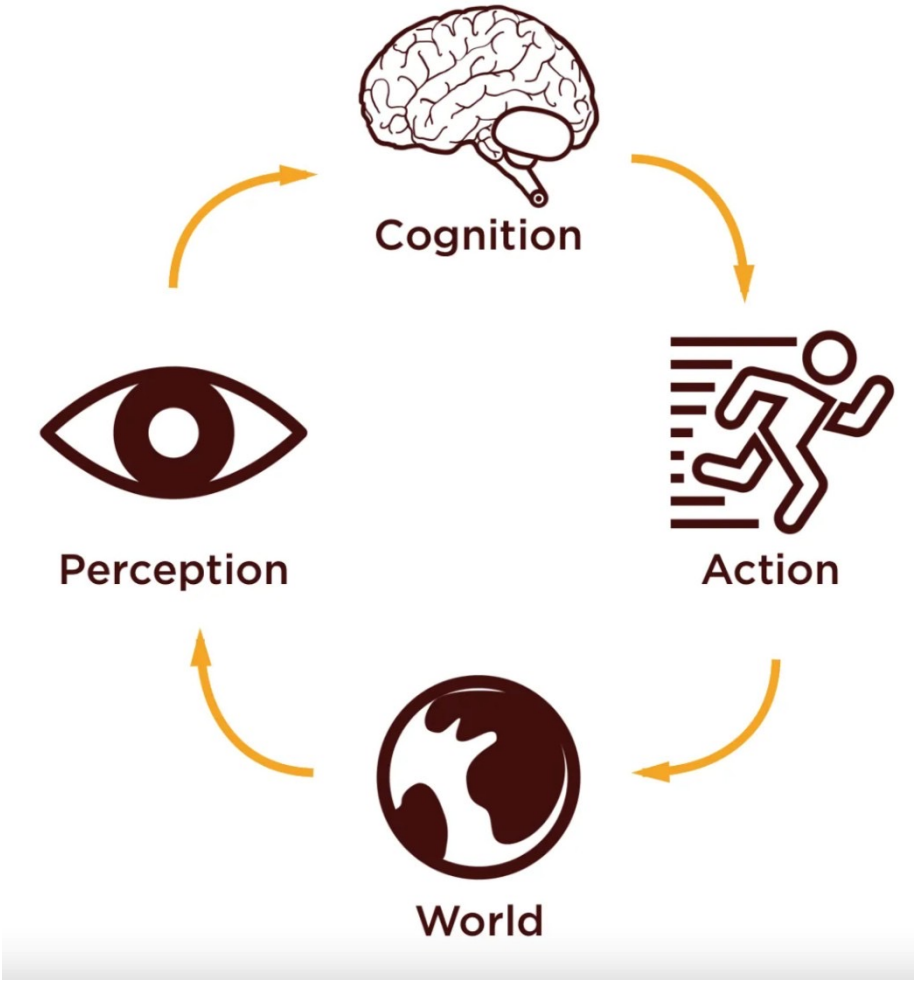
What about digital endpoints?

HTA CG | MEMBER STATE COORDINATION GROUP ON HEALTH TECHNOLOGY ASSESSMENT

Guidance on outcomes for joint clinical assessments

- There is increasing use of **patient-generated health data** provided directly via health technologies (also called digital outcomes). Some medical devices can offer automated measures of outcomes in non-clinical settings, such as the home.
- Digital outcomes might include those used for COAs (an example would be *actigraphy instead of 6-minute walk test*), those that impact the actual use of the product in everyday life (improve adherence) or a combination of both.
- Digital outcomes can be collected at a **high frequency**, even continuously, but **analyses can be challenging** due to data handling in the context of the European general data protection regulation requirements, or because large datasets may be collected that are challenging to analyse. **They do not constitute a particular source of information per se.**
- For example, "**well validated**" in the context of novel medical devices measuring an outcome of interest means that the device has at least undergone testing and validation processes to demonstrate its validity and reliability in measuring the intended outcome. During validation process, studies should compare the performance of the device against established standards or reference methods.

How are perceived the digital endpoints?



Intermediate endpoint

Intermediate endpoints are measures that **may be associated** with disease status or progression toward a primary endpoint (such as mortality or morbidity). It may be a measure of a body function or disease symptoms (e.g. measures of lung function in chronic obstructive pulmonary disease (COPD)) that is expected to correlate with changes observed on primary endpoints.

Surrogate endpoint

Surrogate endpoints are biomarkers or intermediate outcomes that are used as substitutes for clinical outcomes of interest, often to expedite research **or decision-making**.

Hospitals and digital endpoints

FIVE MOST IMPORTANT DOMAINS IN DECISION-MAKING BY TYPE OF MANAGER.

DOMAINS OF THE AdHopHTA SURVEY	CLINICAL MANAGER	HOSPITAL MANAGER
D1: Health problem	**74%**	**51%**
D2: Technology characteristics	16%	19%
D3: Safety	**82%**	**77%**
D4.1: Clinical outcome effect size	**84%**	**74%**
D4.2: Quality of evidence	**74%**	**72%**
D5.1: Economic - societal point of view	24%	23%
D5.2: Economic - hospital point of view	**42%**	**61%**
D6: Ethical	24%	19%
D7: Organisational aspects	11%	30%
D8: Social	11%	5%
D9: Legal	26%	21%
D10.1: Strategic	26%	35%
D10.2: Political	0%	7%

- Digital endpoints
- Research questions
- Quality of data

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Hospitals and digital endpoints

- Hospitals (and HB-HTA doers) know well the deficiencies of traditional endpoints.
- As co-developers, hospitals are aware of the potential value of digital endpoints.
- They (can) contribute to define them.
- **But…**
- To what extent do digital endpoints **influence decision-making**?
- It's a matter of **endpoints or comparators**?

PICOTS-ComTec

Comparator Domain	Non-DHI(s) or alternative DHI(s) with same function
Model of Care	Current model of care and/or clinical pathway, may be redesigned by DHI
Alternative Digital Health Interventions	DHI(s) with the same purpose (e.g., smart phone vs PC retinal screening)
Usual Care Alternatives	Usual treatment or care (e.g., compare with paper-based surveillance)
Outcomes Domain	Outcomes relevant to patients and other stakeholders
Health Benefits	Clinical and patient reported outcomes
Improved Care Structure or Process	Health care system improvements (e.g., access to care, adherence to guidelines, patient health literacy, self-management)
Social/ Societal Benefits	Humanistic, social, or societal effects (e.g., DHI could improve social support, or reduce stigma of a condition)
Safety	May reduce health related risks or improve patient safety
Non-health Related Risks	Non-health related risks including data privacy (e.g., unauthorized access and use of personal data)
Efficiency, Convenience, and Economic Benefits	DHIs could deliver the same outcome with greater efficiency, or less effort

Conclusions

Hospitals know:

- To need Digital Health (DH).
- How to contribute to the development of DH.
- Why they need digital endpoints.

But the relevance of digital endpoints in relation to hospital decision-making needs has still to be fully perceived.

Hospitals still need to know how to fully exploit the digital endpoints they contribute to define.

Thanks for your attention

rossella.dibidino@policlinicogemelli.it

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

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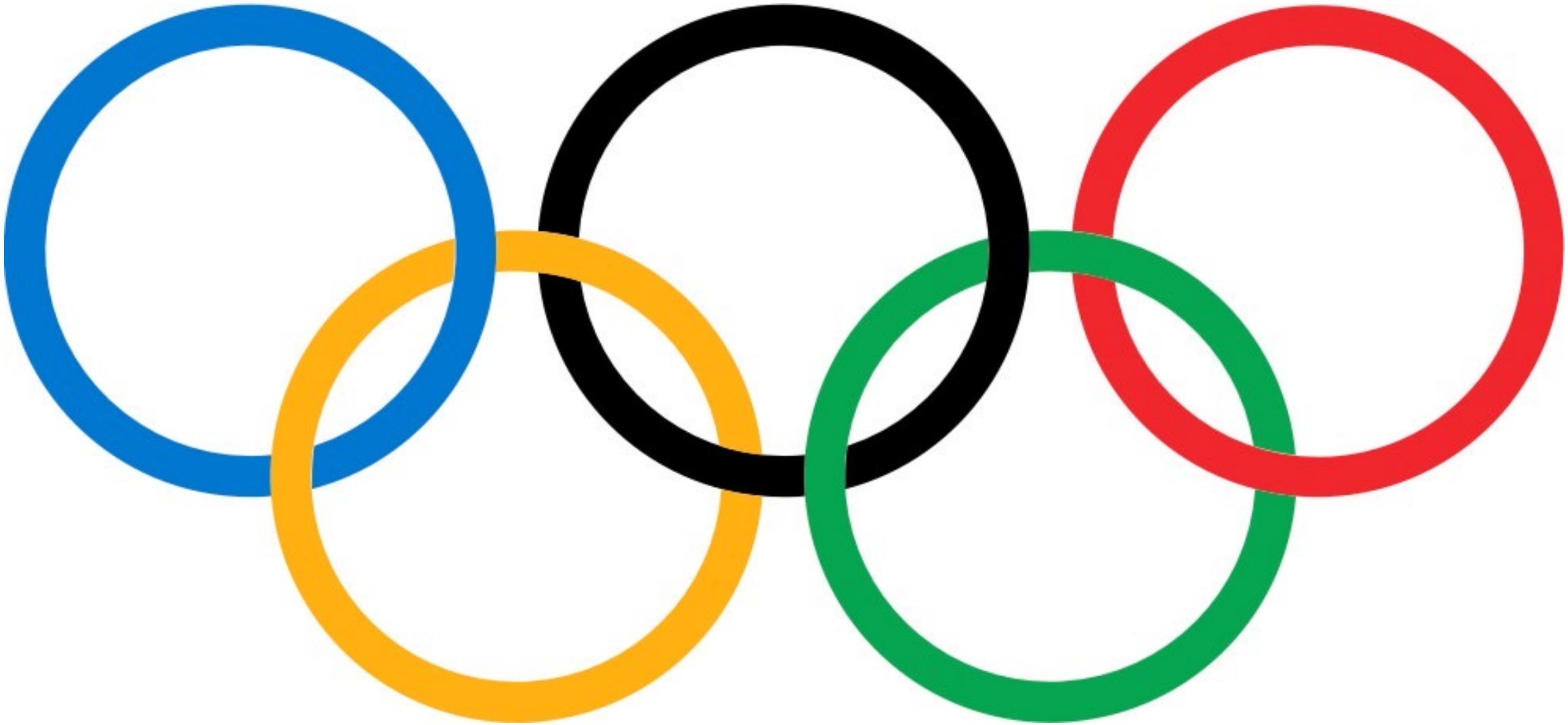
Keynote speaker

ANDREAS HAGER

Board Member, Cystic Fibrosis Europe

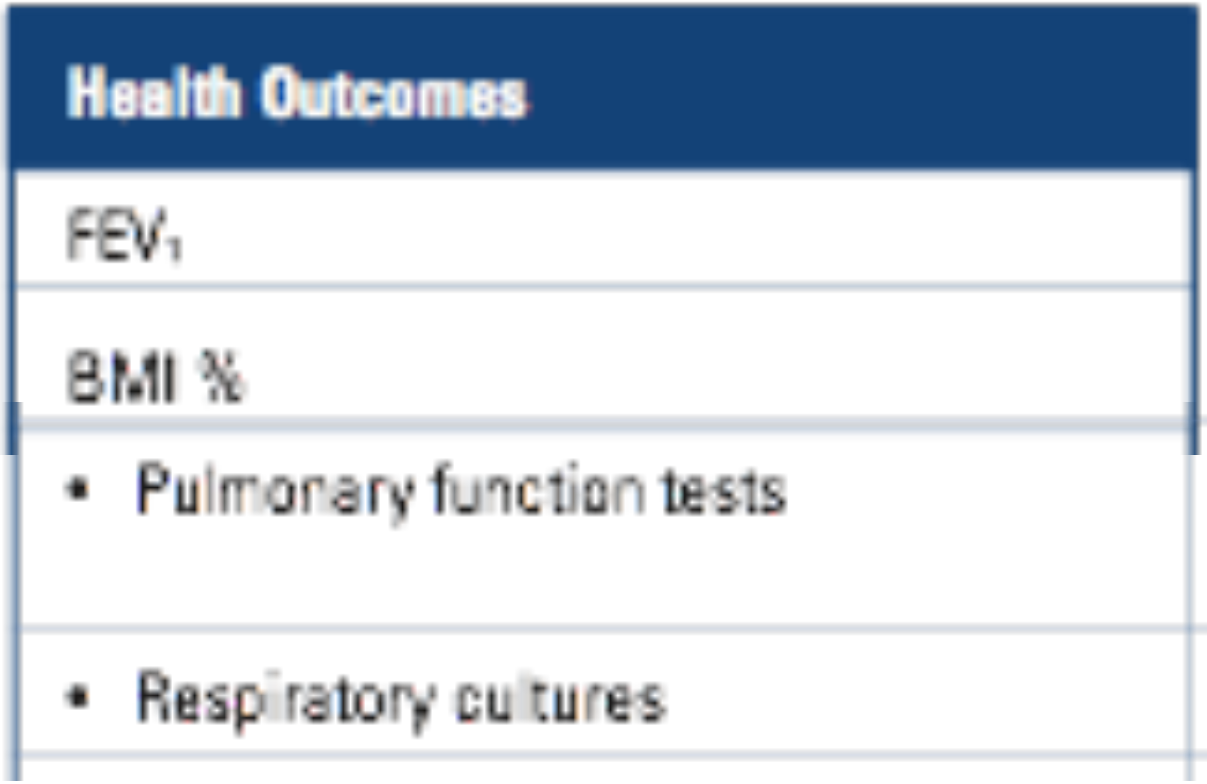


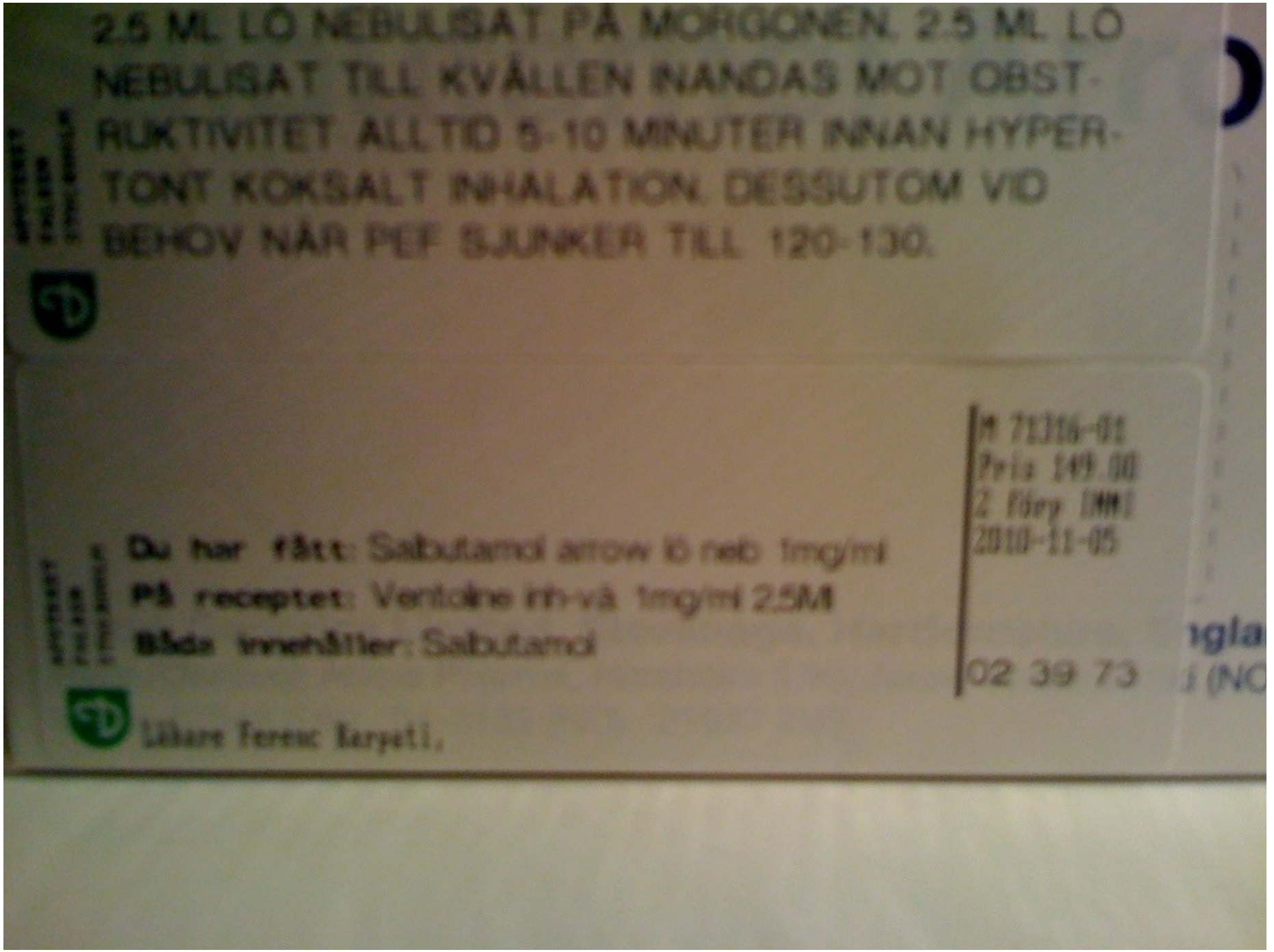

Sonia (2003)


Sam (2016)


Hjärtstopp
Ring 86000

There are measures that mean something for all the stakeholders





Vision statement from Sonia, 9 yrs old:

“I would like to help others understand us better. Sometimes you don’t listen and don’t see what we want to teach you. I want you to go home and know how it is to be a patient. I just want to live my life.”

The Genia Platform

by Upstream Dream

Genia:

Disease agnostic platform created 10 years ago by CF patients, families, and care teams to support this partnership with trustful information-sharing.

Development partners:

Karolinska Institutet (SE), University of Alabama at Birmingham (US), Boston Childrens and Johns Hopkins (US)

Health IT integrations:

Registries, Epic and REDCap

Mission:

Reduce the burden of illness by improving the ability of people with CF, families, and health care professionals to co-produce better clinical practice and care at home.

SRQ – the Swedish Rheumatology Quality register is a national quality register

- A national database on **individual patients** belonging to the same defined group
- A nationally agreed description of **interventions** applied to the defined patient group
- Nationally agreed **outcome measures** of health and other relevant data e.g. costs

Data is used for individual needs and improvement for groups

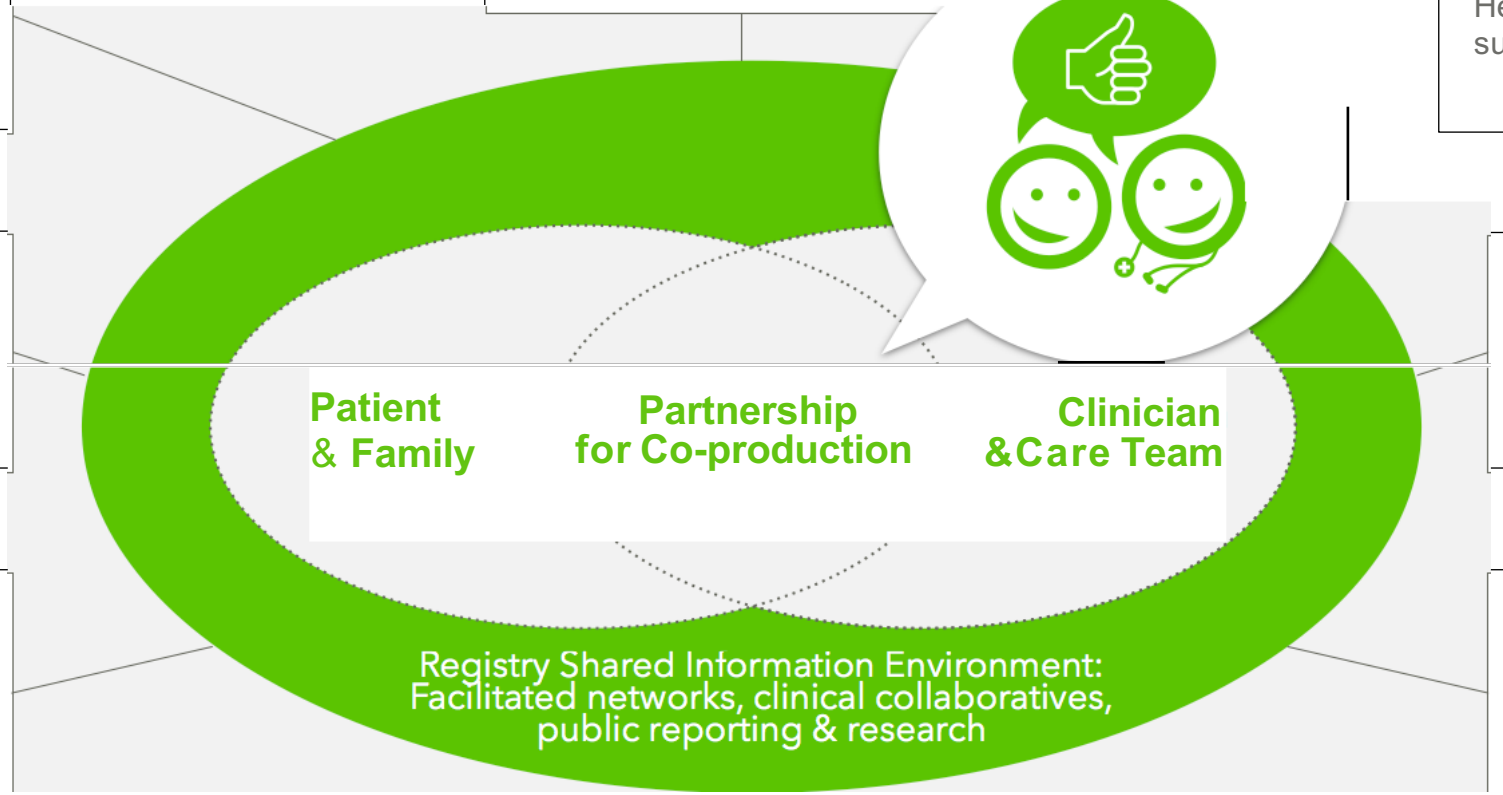
Stakeholder conversations supported by the PHIE

Patient-Clinician Conversation:
Goals, treatment decisions, outcomes tracking

Patients-Family Conversations:
Self-care actions & outcomes tracking

Community of Patients Conversations:
Helpful knowledge, support, resources

Clinical Team Conversation:
Population management, pre-visit planning



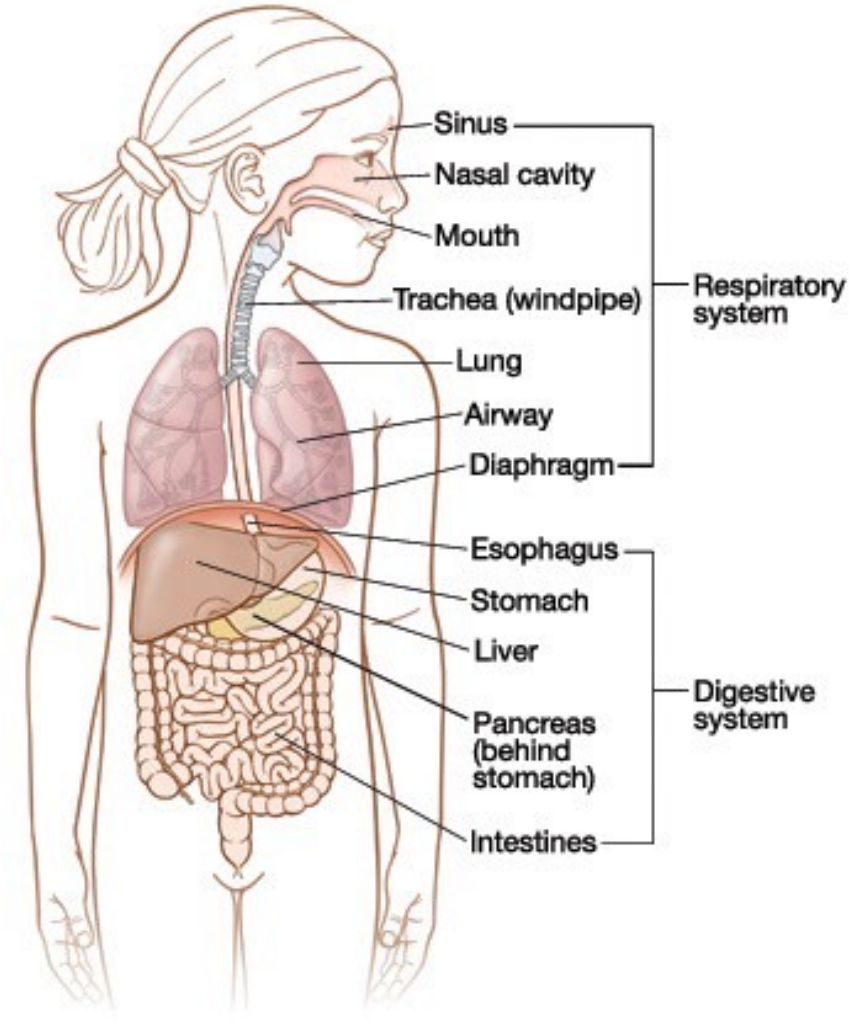
Registry/ Industry Conversations:
Post-approval surveillance; population modeling

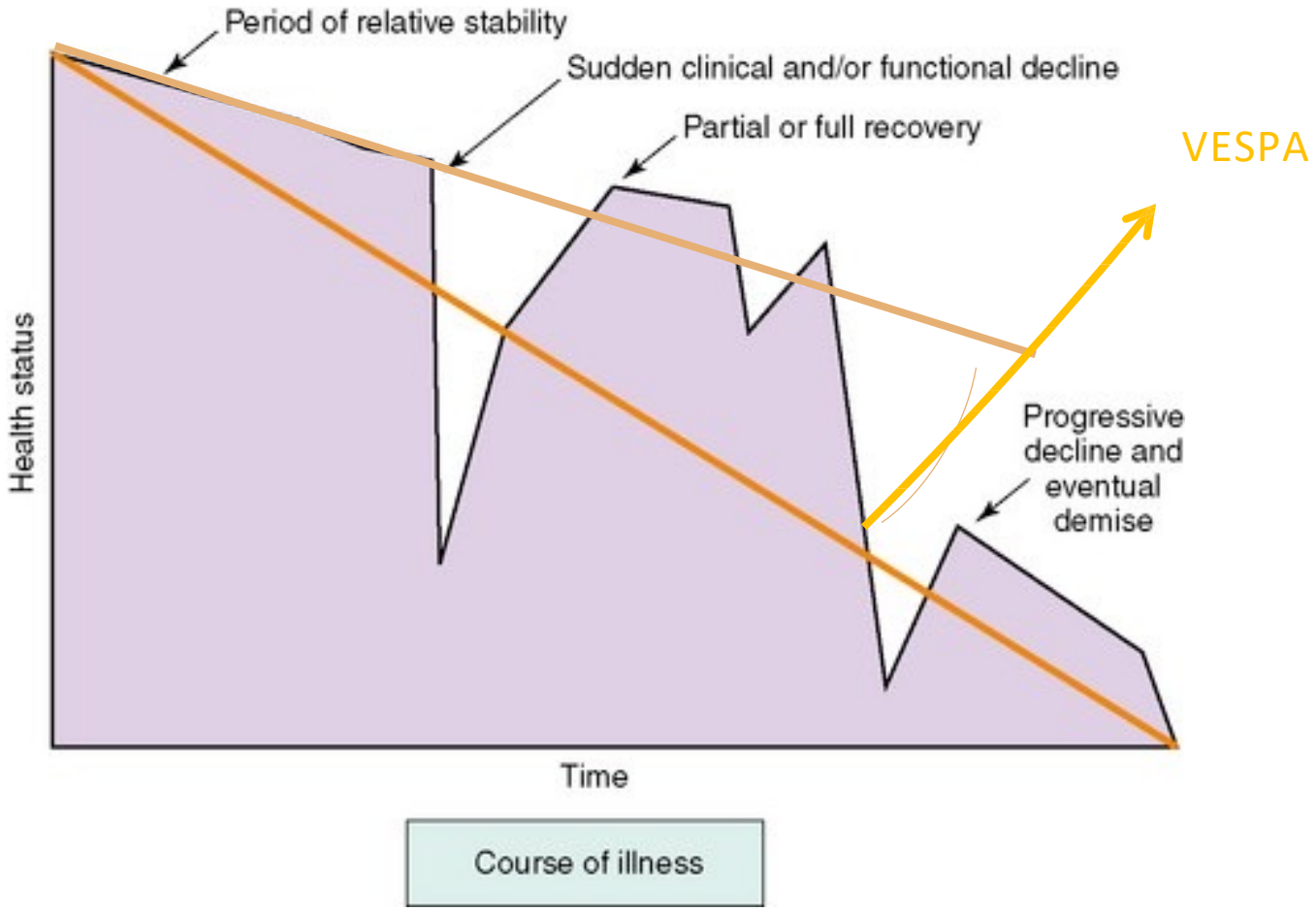
Benchmarking & Transparency Conversations:
Variations in outcomes, good value services

Research Conversations:
New treatments, comparative effectiveness

Source: Eugene C Nelson et al. BMJ 2016;354:bmJ.13319

Staffan Lindblad (2008): ”Cystic fibrosis can be the leading example of a paradigm shift for children with medical complexity”





VESPA

Gene Nelson (2014): “Bridge the gap between clinical reality and the patient world, triggering learning as well as the right next action”

thebmj

BMJ 2015;350:g7818 doi: 10.1136/bmj.g7818 (Published 10 February 2015)

ANALYSIS

SPOTLIGHT: PATIENT CENTRED CARE

Patient reported outcome measures in practice

Scores of tools to measure outcomes that matter to patients have been developed over the past 30 years but few are used routinely at the point of care. **Nelson and colleagues** describe examples where they are used in primary and secondary care and argue for their wider uptake to improve quality of care

Eugene C Nelson *professor*[1 2], Elena Eftimovska *researcher*[3], Cristin Lind *patient advocate*[4], Andreas Hager *patient advocate*[5 6], John H Wasson *professor*[1], Staffan Lindblad *professor*[3 7]

Box 2: Views of patient advocates

For most patients there is no systematic or effective method for communicating what happens outside the clinical encounter, such as perceived needs, symptoms, response to treatment, undesirable side effects, effect on function, and what matters to patients and their families. Like clinicians, patients want better outcomes for individuals and communities, and better professional development and system performance, although we might not use those same words to describe them.

PROM systems have the potential to enable improvement by providing information that can bridge the gap between the clinical reality and the patient world, triggering learning as well as the right next action.

PROM systems must be codeveloped by patients, the public, and professionals to obtain maximum value. They should be integrated with the rest of the patients’ healthcare information and patients should be able to use the information when and where they choose, including for research to benefit others with their condition.

Swedish HTA evaluation criteria Orkambi 2018

LANDSTINGENS SAMVERKANSMODELL FÖR LÄKEMEDEL

Sveriges Kommuner och Landsting

Treatment goals

1. Stabilization or increase of FEV1 compared to the previous 12-month period
2. Stabilization or reduction of LCI compared to starting treatment
3. Stabilization or increase of Z-score BMI (child), BMI (adult)
4. Fewer exacerbations compared to the year before the start of treatment
5. Fewer antibiotic and / or less intensive courses (eg oral rather than intravenous) compared to the year before the start of treatment
6. Increase in CFQR respiratory domain, reduction of reported symptoms

Additional criteria for when Orkambi treatment should not be offered: patients not considered to follow the treatment or follow-up of treatment

Challenge: How Can More Quality Assured Measures and Observations be Reported by Patients during the first year with new treatment?

Agreed treatment goals for disease modifying treatment (CFTR protein modulator therapy)

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Additional criteria for when Orkambi treatment should not be offered: patients not considered to follow the treatment or follow-up of treatment

"LCI is the only treatment goal that can not be supported by patient reported data"

Information need	Reporting frequency p.a.	Patient reported outcomes	Quality requirements and motivations
FEV1	4-12	Spirometer	?
Weight and length	4-12	Home scale	?
Antibiotic treatments	4-8	Patient reported treatments	?
Exacerbations: • **Infection symtoms** • **Respiratory symptoms** • **Sputum properties** • **Other**	4-8	[eg structured health-check-ins, thermometer, cough tracker]	?
Quality of life assessment	2	CFQ-R, EQ5D	?
Adherence metrics	12-50	[Key performance activity in app]	?

"Reporting frequency ties both to individual health status (eg number of exacerbations) and frequency of clinical workflows where the patient reports data"

Potential Additional RWD-sets

- Patient demographics and care system maps (CF Atlas)
- Deeper patient reported data on exacerbations and remission periods (Expanded Antibiotics RWD)
- Deeper data-sets on patient QoL (school / work attendance etc.)

This is not currently available through the CF registry. Might be necessary to establish a separate channel.

Less is more? Patient-reported antibiotics RWD

Data points in the personal database:

1. Medication details
2. Start and stop dates
3. Perceived health benefits
4. Observations in daily living (e.g. symptoms, weight and spirometry values)

Data points entered in the CF registry:

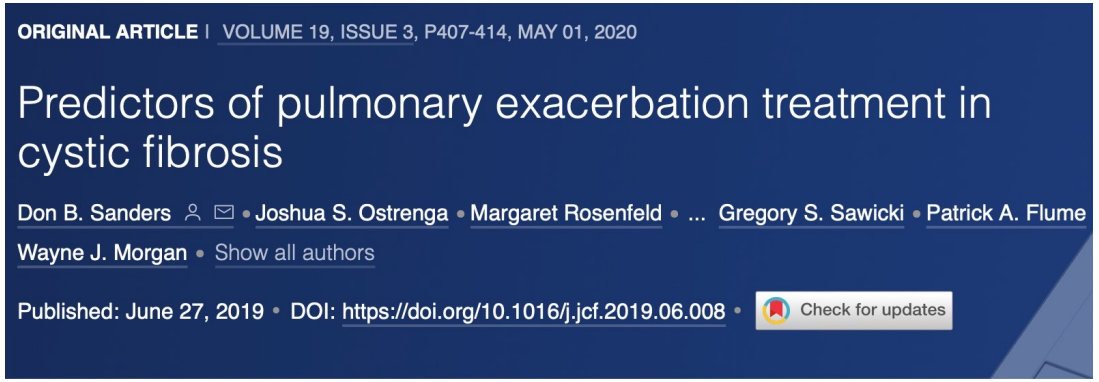
1. Days with antibiotics, IV
2. Days with antibiotics, oral
3. Days with antibiotics, inhalation
4. Total days with antibiotics

Patient-generated data from Genia will be imported into the CF registry, so that the clinic can view and process the data directly in the registry. Clinics export the data to national level for reporting.

The information is around a key topic in the lives of patients and families.

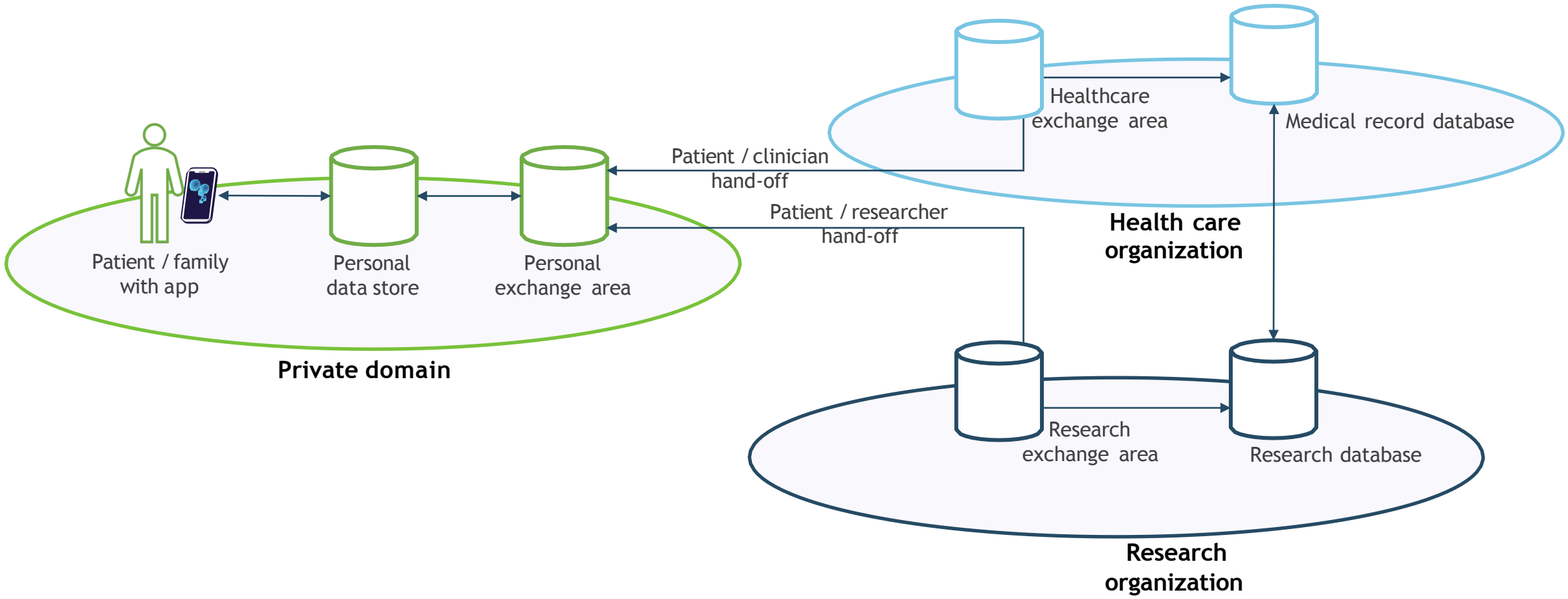
Development of this functionality is ongoing and is planned to be released on May 15. Onboarding has started and the feed-back from patients and providers is strong!

Most studies of pulmonary exacerbations (PEx) in cystic fibrosis (CF) focus on intravenous (IV)-treated PEx, though most PEx are treated with oral antibiotics.

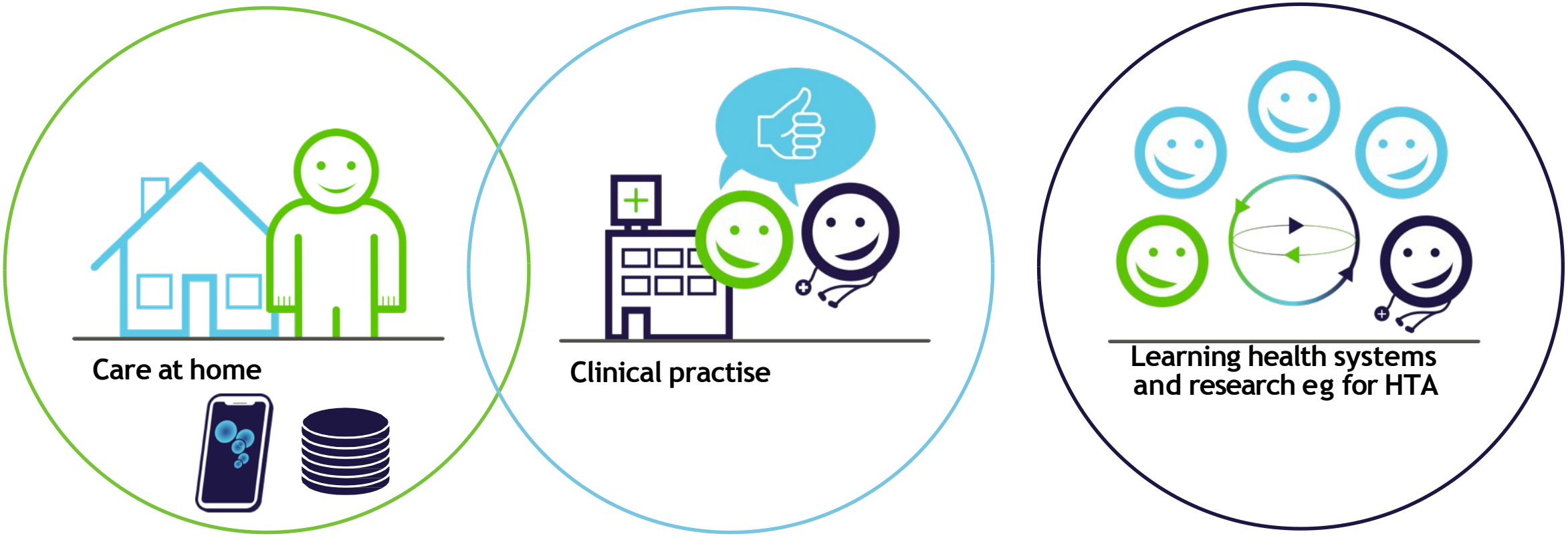


- Over half of pulmonary exacerbations identified in clinic are treated initially with oral antibiotics
- Compared to treatment with IV antibiotics, patients treated with oral antibiotics tended to be healthier
- Nearly one-third had no clinical encounters within 90 days of exacerbation treatment
- Among 14,265 patients with a PEx initially identified in clinic, 21.4% received no antibiotics, 61.5% received new oral and/or inhaled antibiotics, and 17.0% had IV antibiotics within 14 days.

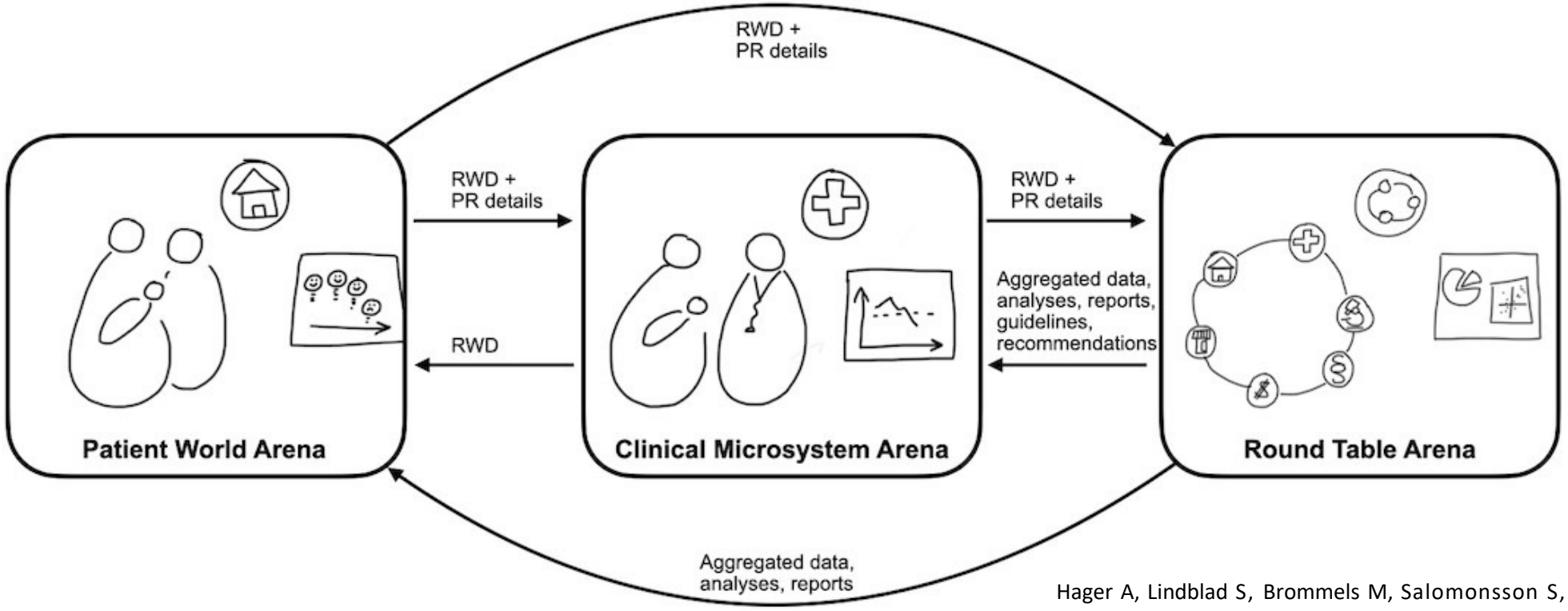
The patient-controlled information flow



Three key action arenas



Patient-controlled information flows building on 20+ years of successful development in rheumatology and neurology – and Sonia's vision



Karolinska Institutet

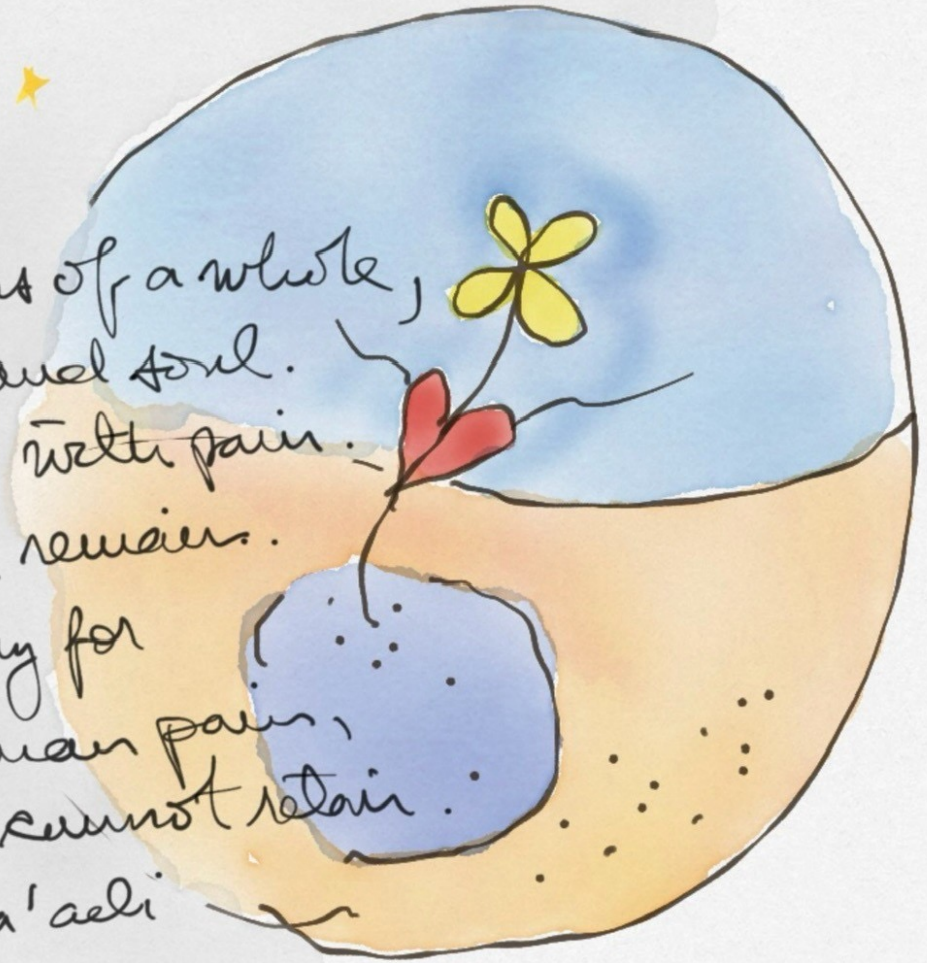
NEXT GENERATION INTERNET
INTERNET OF HUMANS

Hager A, Lindblad S, Brommels M, Salomonsson S, Wannheden C
Sharing Patient-Controlled Real-World Data Through the Application of the Theory of Commons: Action Research Case Study
J Med Internet Res 2021;23(1):e16842
URL: https://www.jmir.org/2021/1/e16842
DOI: 10.2196/16842

A personal information exchange that **empowers people** living with long-term illness, **supports co-production** of care, and **generates valuable health data** in patient-controlled information flows.

Human beings are members of a whole,
In creation of one essence and soul.
If one member is afflicted with pain,
Other members uneasy will remain.
If you have no sympathy for
human pain,
The name of human you cannot retain.

Sa'adi



Tack!

Reach out:

andreas.hager@me.com

Spreading the Conceptual Model: Moving from Chronic Disease to Beyond…

Cancer — Dartmouth-Hitchcock Norris Cotton Cancer Center

Advanced cancer & kidney disease — Northwestern Medicine

Palliative Care & Serious Illness — Gordon and Betty Moore Foundation

Blood & Bone Marrow Transplant — Dartmouth-Hitchcock Norris Cotton Cancer Center

Multiple Sclerosis — MS-CQI Collaborative: Improving MS Care Together

Rheumatology: Pediatric & Adult — Arthritis Foundation

Inflammatory Bowel Disease: Adult — Crohn's & Colitis Foundation

Cystic Fibrosis: Pediatric & Adult — Robert Wood Johnson Foundation; Cystic Fibrosis Foundation

Planning Grant — Robert Wood Johnson Foundation

2013	2014	2015	2016	2017	2018	2019	2020	2021

RxReports are modular

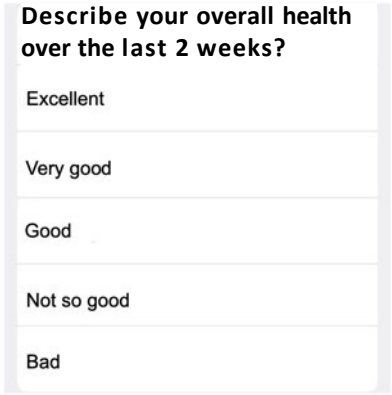
Example: Structure of a bi-weekly Self check-in

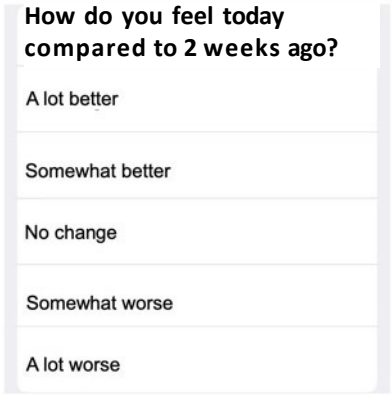
Bi-weekly check-in	Purpose	Number of questions	Source
Global well being +	Standardized evaluation of functional health status	2	Dartmouth COOP
Symptom tracking +	Disease-specific questions to track disease activity	4-6	Agreement in CF coordination group
Modulator kit +	Adherence questions for those who have Modulator kit	2-3	Quittner
Additional kits +	Various purposes specific to clinic or patient	Max 4	
Comment	The user can always add a comment to the report	1	

RxReports are modular

Example: Swedish Basic Self Check-in (bi-weekly)

General Well-being





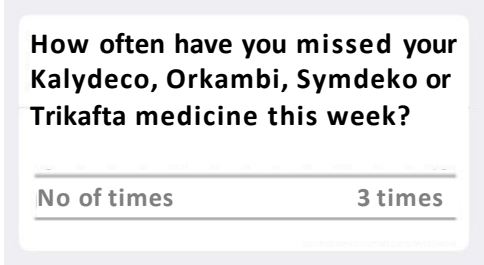
Source: Dartmouth COOP Functional Health Assesment Charts/WONCA. World Organization of Family Doctors (WONCA) and the European Working Group on Health Outcome Measurement (ERGHO)

CF Symptom tracking

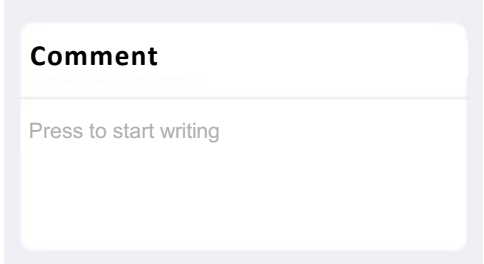
Sick factors

Well factors

CFTR Modulators



Comment

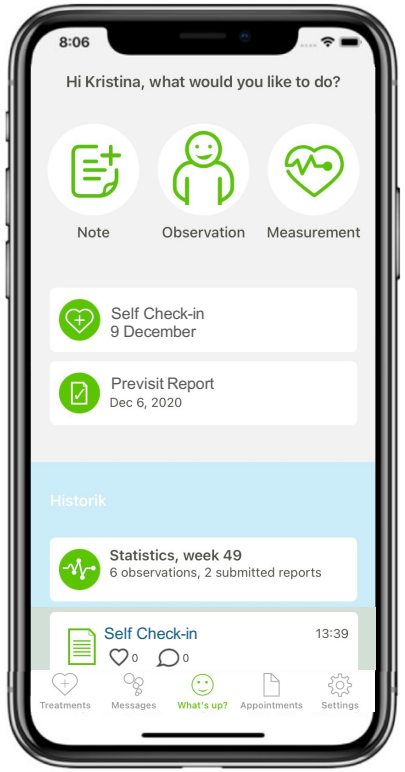


Customer Journey

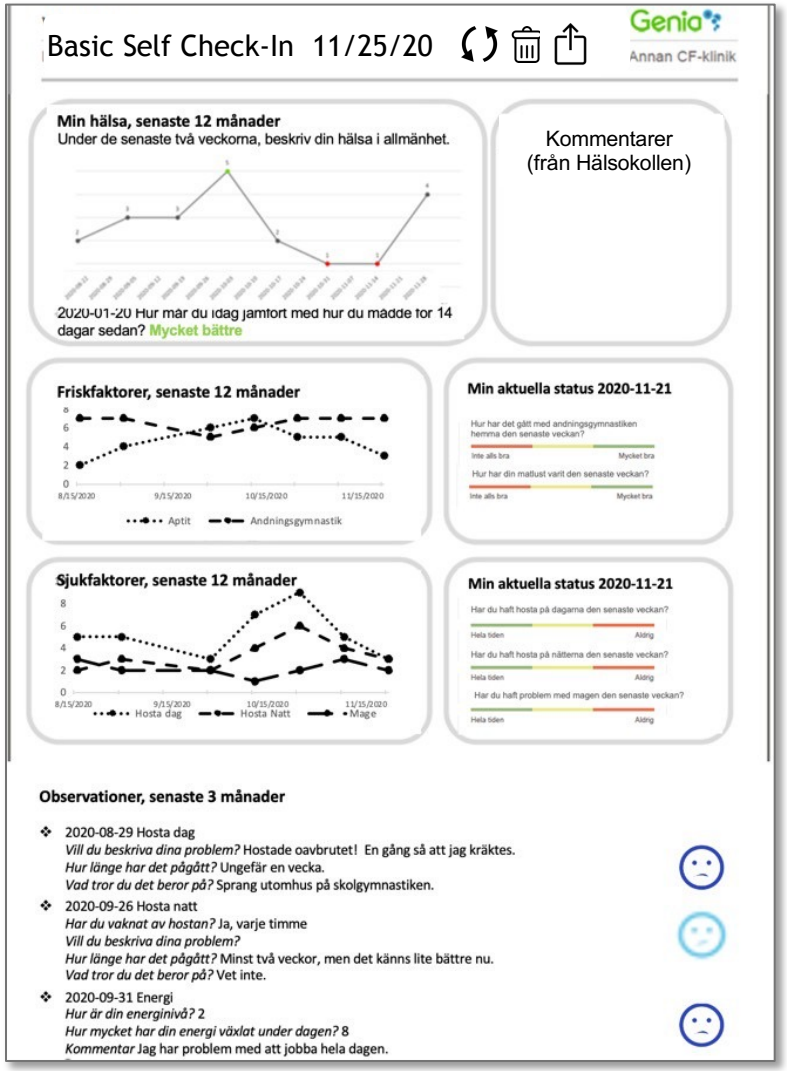
Example: Swedish Basic Self Check-in (bi-weekly)

5 Feedback

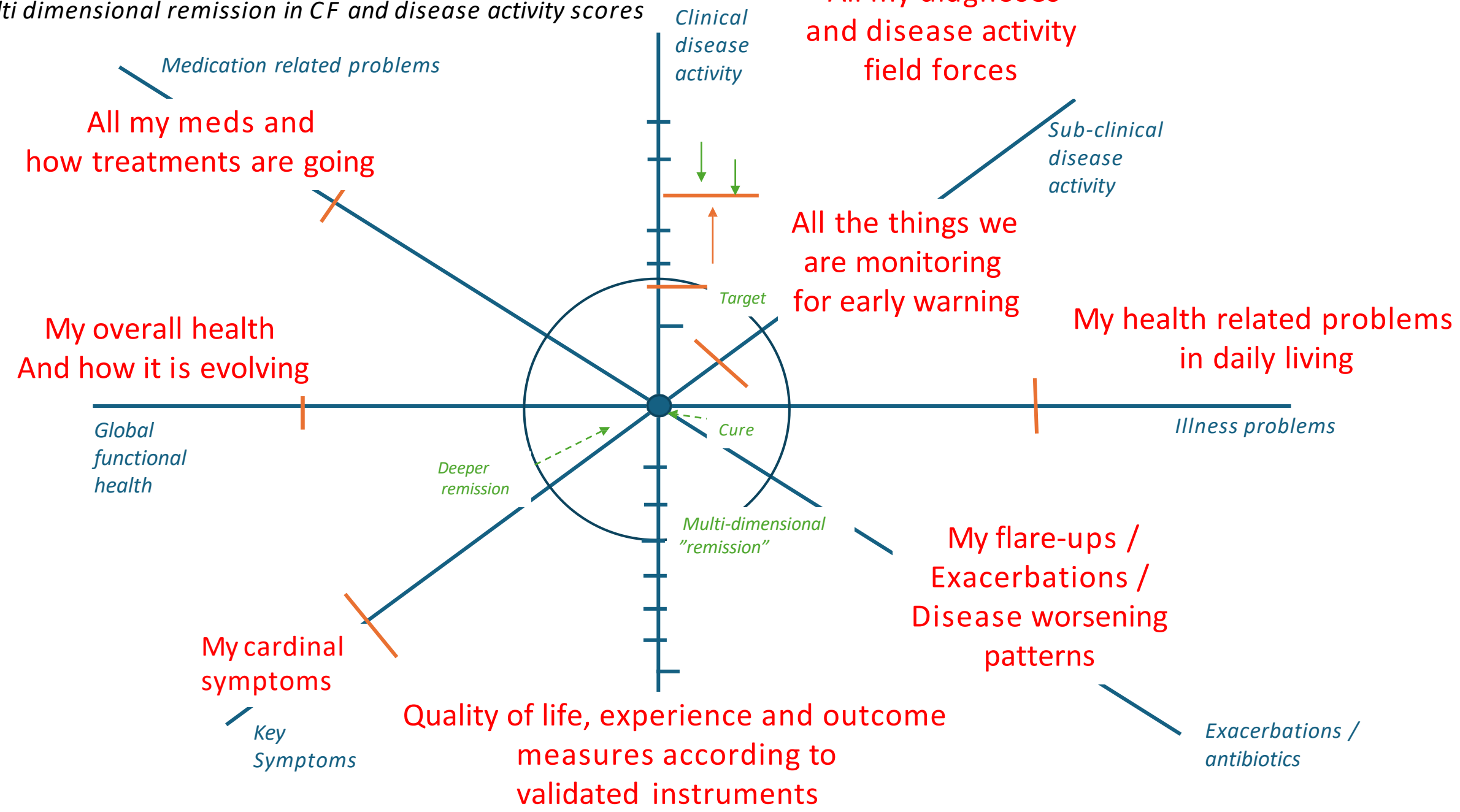
Aggregated check-ins are collected in a shareable pdf



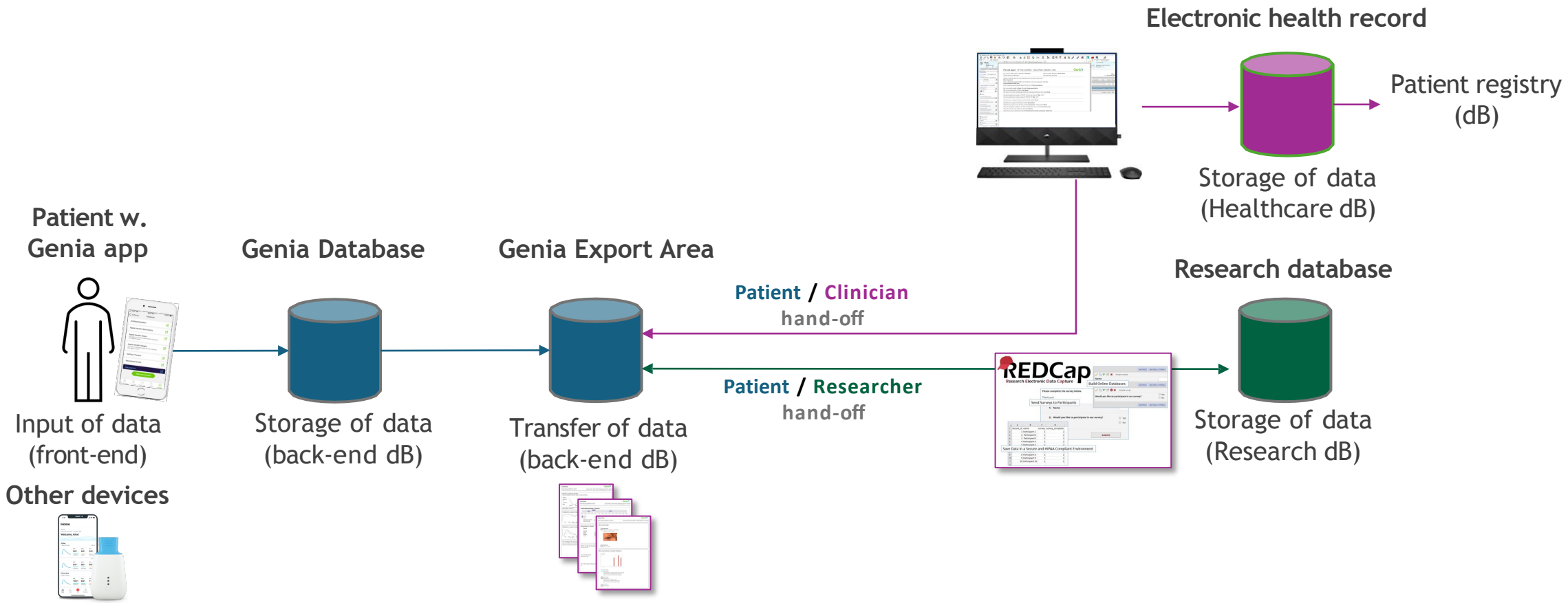
Click on the card



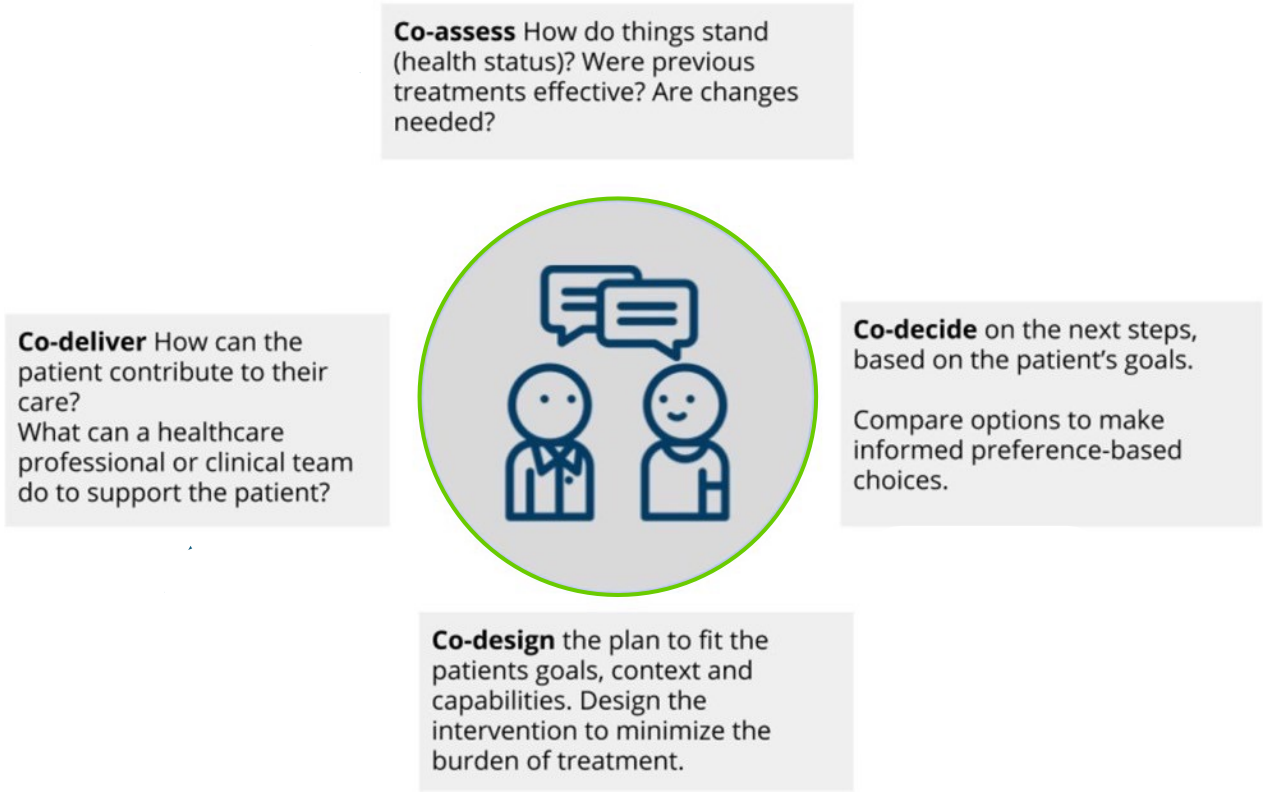
Patient pathways to remission and cure
Multi dimensional remission in CF and disease activity scores



We integrate with existing devices, electronic health records and research databases using self-sovereign identity technology -- building on existing legacy systems



Genia supports coproduction for optimal care



- Better relationships and increased patient satisfaction
- Better communication and quality decision making
- More effective treatments (efficacy, safety and adherence)
- Greater treatment engagement and better adherence to treatment plans

BMJ Quality & Safety

Elwyn, Hager, Nelson and Price. BMJ Qual Saf 2020;29:711-716

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

RWE4Decisions REAL WORLD EVIDENCE

Panelist

ANJA SCHIEL

Senior Advisor, Methodologist in Regulatory and Pharmacoeconomic Statistics, Norwegian Medicinal Products Agency (NOMA)

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

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Panelist

LARA WOLFSON

Co-Chair, PSI/EFPSI HTA Special Interest Group

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Thank you for your contributions!

For any enquires, get in touch at **secretariat@rwe4decisions.com**

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