CAPABLE
CAncer PAtients Better Life Experience

CAPABLE: Supporting Cancer Patients and Their Physicians

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The CAPABLE Team

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Consortium

1	**UNIPV**	University of Pavia
2	**UoH**	University of Haifa
3	**BIOM**	BIOMERIS s.r.l.
4	**AMC**	Academic Medical Center
5	**IBM**	IBM Israel – Science and Technology LTD
6	**BIT**	Bitsens, JSC
7	**PUT**	Poznan University of Technology
8	**ICSM**	Istituti Clinici Scientifici Maugeri
9	**NKI**	Netherlands Cancer Institute
10	**DEON**	Deontics Ltd
11	**AIMAC**	Associazione Italiana Malati di Cancro, Parenti e Amici
12	**UPM**	Universidad Politécnica de Madrid

Motivation

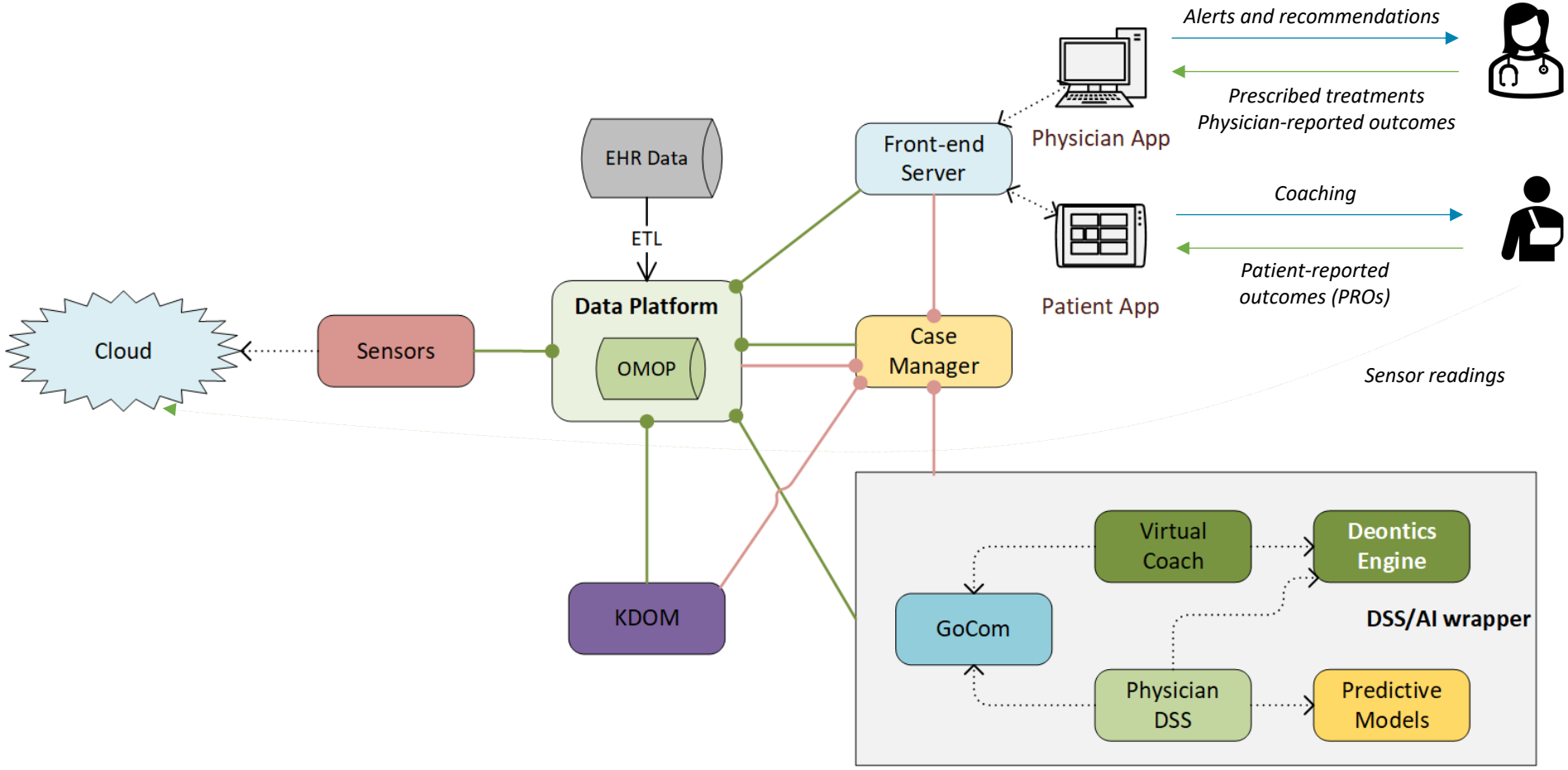
- Cancer becomes chronic disease with most treatments provided at home, follow-up visits and stays are occasional
- Patients between visits should be constantly monitored and provided comprehensive support
- Physicians should be offered support to address challenges associated with treatment planning and management

Objectives

- A system providing decision support, coaching and information for cancer patients and their physicians
  - Mobile and web apps for ubiquitous accessibility
  - Wearable sensors for unobtrusive monitoring

- Combination of domain knowledge (guidelines, behavior models, …) with knowledge discovered from data [not included in clinical studies]
- Improving of the quality of care, patient wellbeing and engagement in interventions that results in better quality of life (QoL)

CAPABLE Architecture

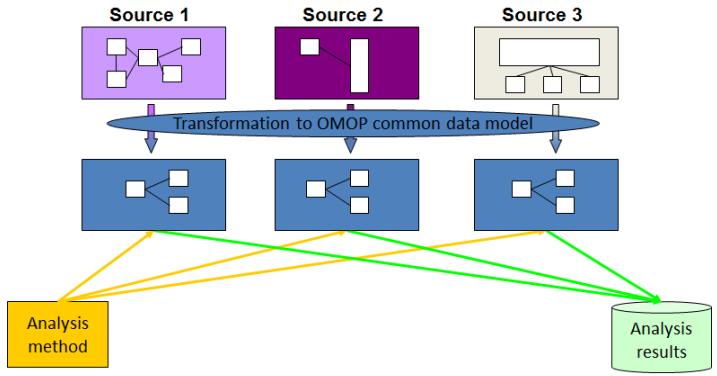


Data Platform (DP)

- Provides a shared data storage for all components
- Supports FHIR and OMOP Common Data Model (CDM) standards
  - FHIR for regular CRUD operations
  - OMOP for subsequent data sharing

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

https://www.ohdsi.org/data-standardization/



- Based on the customized OMOPonFHIR project https://omoponfhir.org/
- Integration with EHRs at specific institutions through ETL

Case Manager (CM)

- Monitors DP and notifies other components about data- and time-driven events
- Relies on rules provided at runtime by specific components that define relevant events
- Inspired by the concept of a blackboard system (DP = blackboard, CM = controller, other components = knowledge sources)
- Similarity to Arden Syntax Rules, but focus on modern standards (FHIR)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Knowledge-Data Ontology Mapper (KDOM)

- Transforms data and provides data abstractions (logical, temporal, …) to other components
  - Administration of a class of drugs (e.g., targeted therapy)
  - Duration of a symptom episode given a specific reference point
- Abstractions allow for simplification of domain knowledge (guidelines, workflows) by capturing low-level details

13	Warning signs	derivation ::if(Massive_dehydration = "true" or Peritonitis = "true" or patient_symptoms_list includesAny ["Febrile neutropaenia", "Delirium"] or Renal_impairment = "true" or Sepsis = "true" or Electrolyte_disturbances = "true" or (Nausea = "true" and Vomiting = "true" and Dehydration = "true" and Reduced_urine_output = "true") or previous_admission_for_diarrhoea = "yes","true","false");	Massive_dehydration Peritonitis Febrile neutropaenia Delirium Renal_impairment Sepsis Electrolyte_disturbances Dehydration Reduced_urine_output previous_admission_for_diarrhoea

Sensors

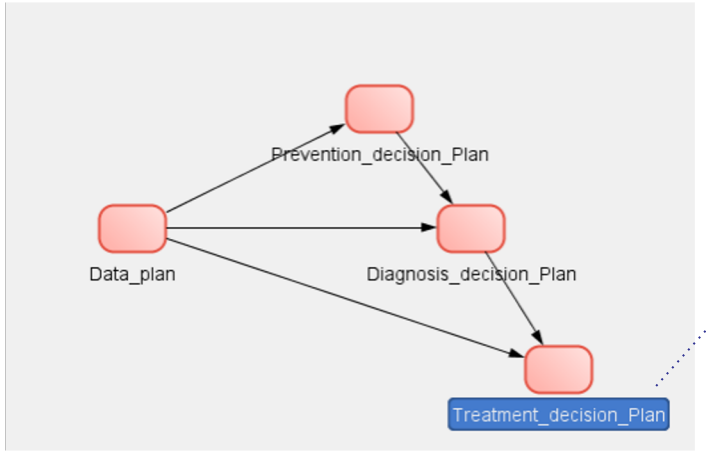
- Retrieves and preprocesses smartwatch data from the cloud-based repository (OmniCare provided by ASUS Life)

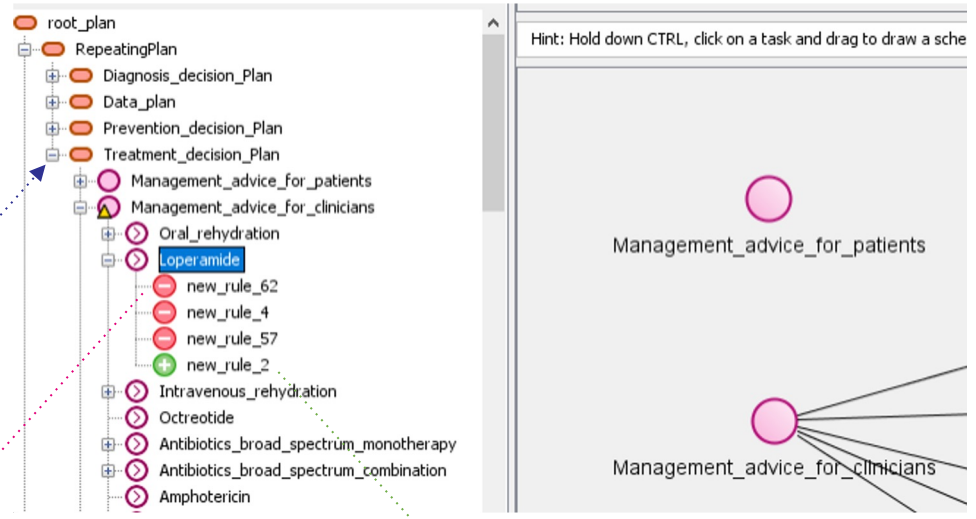
- ASUS VivoWatch 5 used in the study
  - Available sensors: PPG, ECG, GPS, altimeter, skin temperature
  - Measurement of pulse transition time (PTT) as a proxy for blood pressure
- Data from other sensors (air quality) handled by an additional app

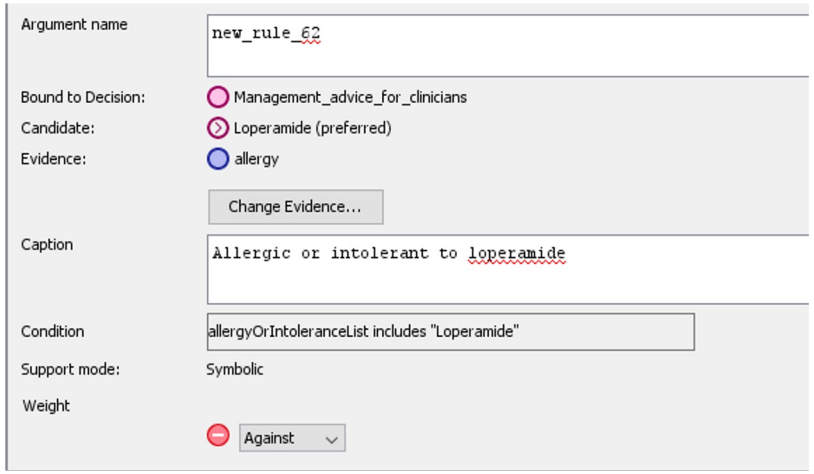
PROforma Formalism

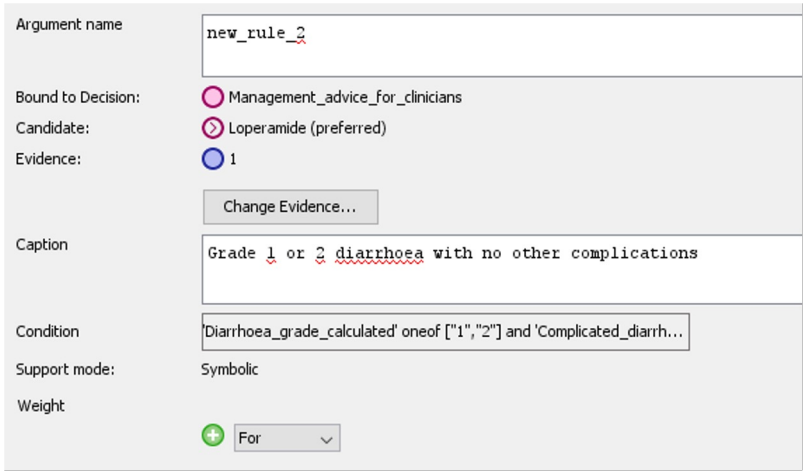
- Representation language for clinical guidelines and workflows (computer-interpretable guidelines, CIGs)
  - Based on a task-network model with more flexible scheduling
  - Argument-based logic with weighted rules (arguments) for and against specific decision candidates
- Authoring and execution environment
  - CIG editor (Composer) with the ability of tagging text-based guidelines
  - Execution engine (Deontics Engine, DE) for running CIGs in interactive and non-interactive modes (simple UI, web-based API)
  - Support for selected standard terminologies (SNOMED CT, LOINC, ICD)

PROforma CIG – Example

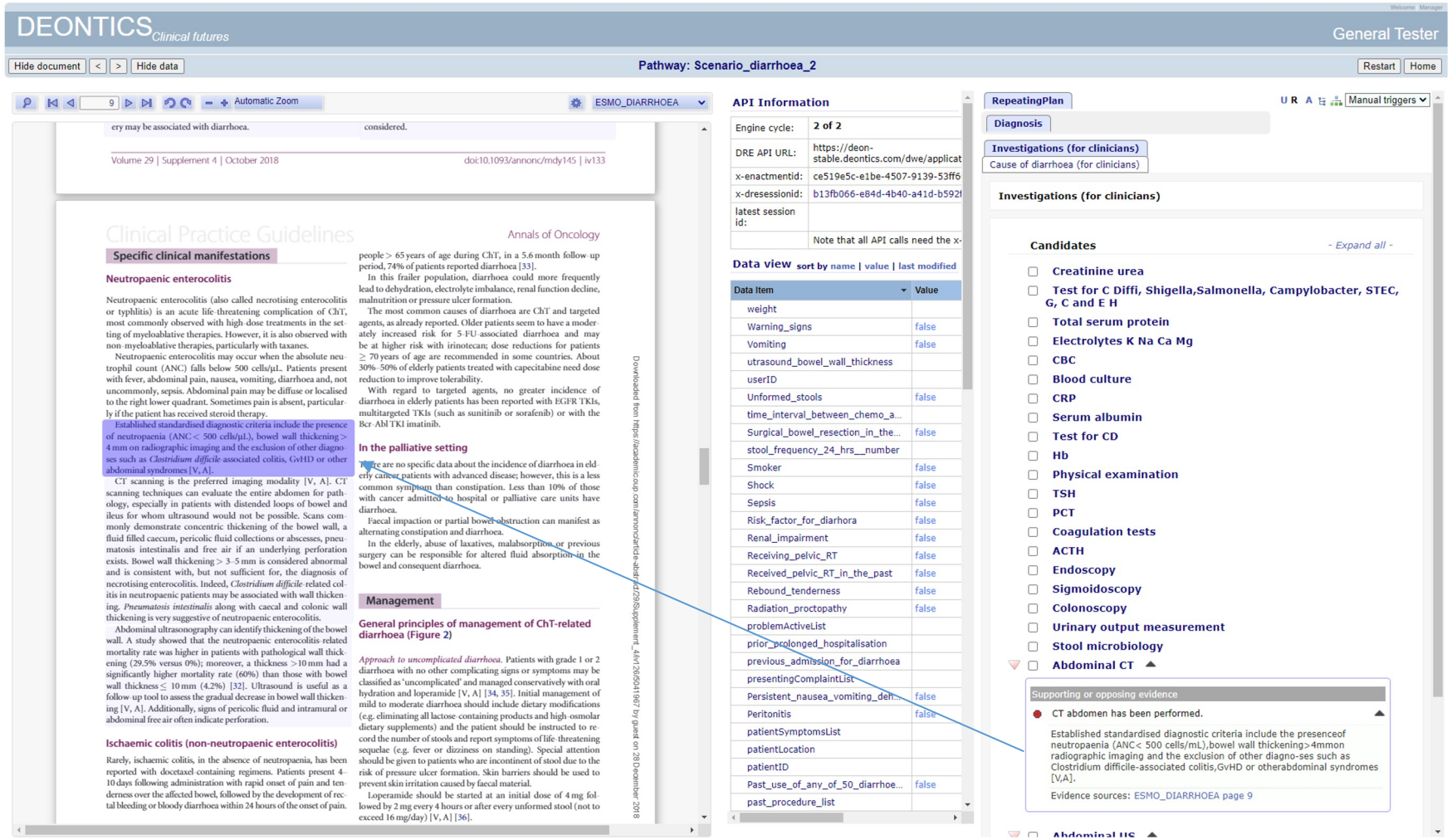






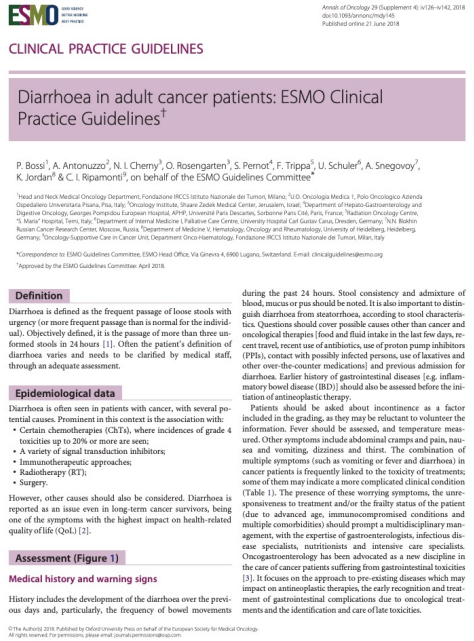


PROforma CIG – Example



CIGs in CAPABLE

- Based on text CPGs published by the European Society for Medical Oncology (ESMO)
- Management of prevalent toxicities related to cancer treatment (diarrhea, fatigue, …)
- Physician- and patient-oriented CIGs
  - Physicians prescribe drugs or services
  - Patients activate pre-authorized (as needed) prescriptions
- Challenge associated with translating CPGs into CIGs → the SMART guideline initiative by WHO



ESMO

CLINICAL PRACTICE GUIDELINES

Diarrhoea in adult cancer patients: ESMO Clinical Practice Guidelines†

Definition

Epidemiological data

Assessment (Figure 1)

Medical history and warning signs

https://www.who.int/teams/digital-health-and-innovation/smart-guidelines

S = Standards-based (FHIR), M = Machine-readable, A = Adaptive, R = Requirements-based, T = Testable

CIGs Execution

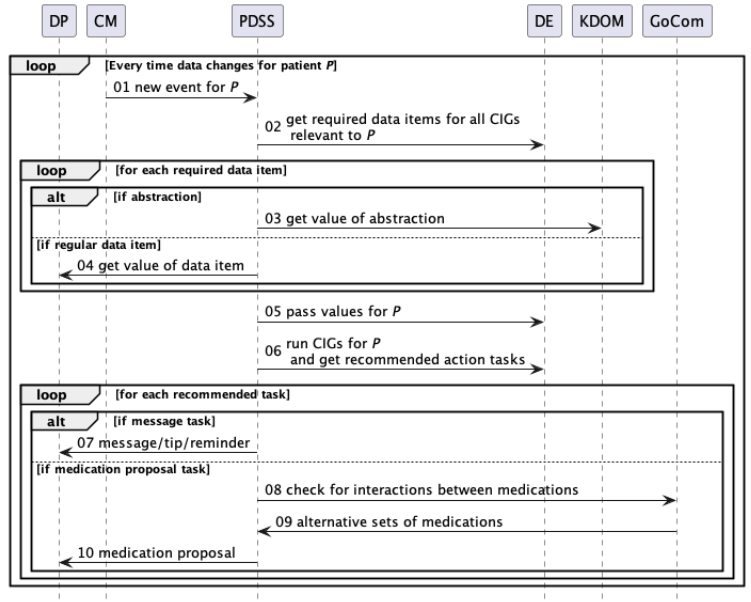
- A hybrid execution environment for CIGs
  - DE providing the core capabilities (CIG traversal, handling of decision tasks)
  - Dedicated “wrapper” components handling non-standard tasks, data (DP) access and events reported by CM
- Custom meta-properties associated with CIG tasks and data items

`interventionType`
- *Description*: indicates intervention represented by a given task
- *Example*: `medication-proposal` (a pharmacological treatment recommendation proposed by the system

`valueExpression`
- *Description*: offers a bridge between FHIR and PROforma by specifying what property of a data item should be reported to DE
- *Example*: `cancer-treatment-related` (a flag in an Observation resource where the physician indicates if the symptom is related to the cancer treatment)

Physician DSS (PDSS)

- Provides active clinical decision support – responds to data-related events and runs physician-oriented CIGs
- Interacts with GoCom to check for interactions between ongoing and proposed treatments
- May invoke prediction models to obtain weights for specific arguments (survival time for a given treatment)

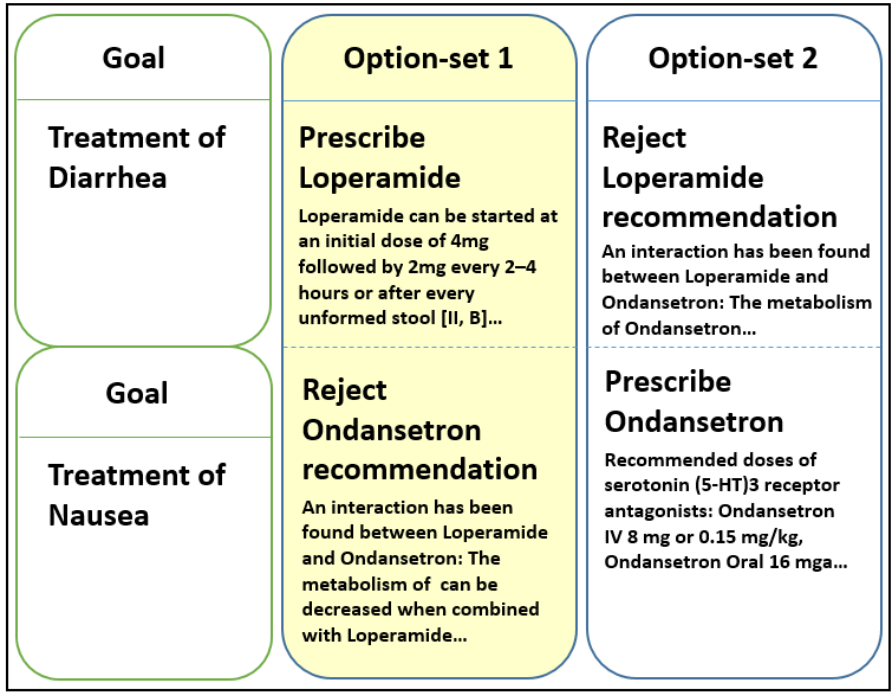


GoCom

- Mitigates (identifies and solves) conflicts between ongoing and proposed (pharmacological) treatments
- Employs goal-oriented planning with action or physiological state goals (meta-properties in PROforma CIGs)
- Identifies contradicting physiological effects and actions using external ontologies (e.g., ND-RFT) and custom rules
- Generates *option sets* with possible treatments for consideration by physician (assistant/critic support mode)

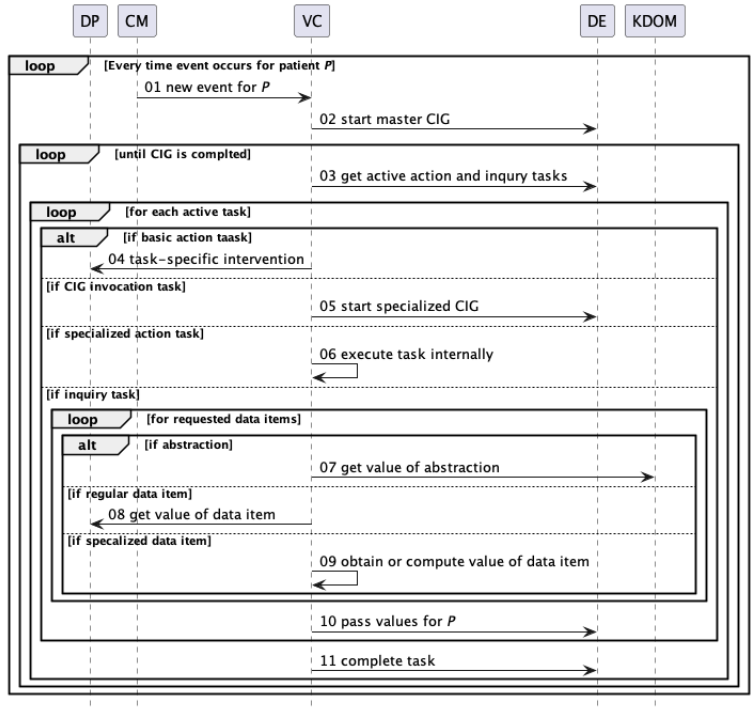
GoCom Mitigation

1. Patient on targeted therapy with loperamide prescribed as needed
2. Patient reports nausea and ondansetron is recommended
3. Recommendation is checked for conflicts and viable option sets are reported to physician



Virtual Coach

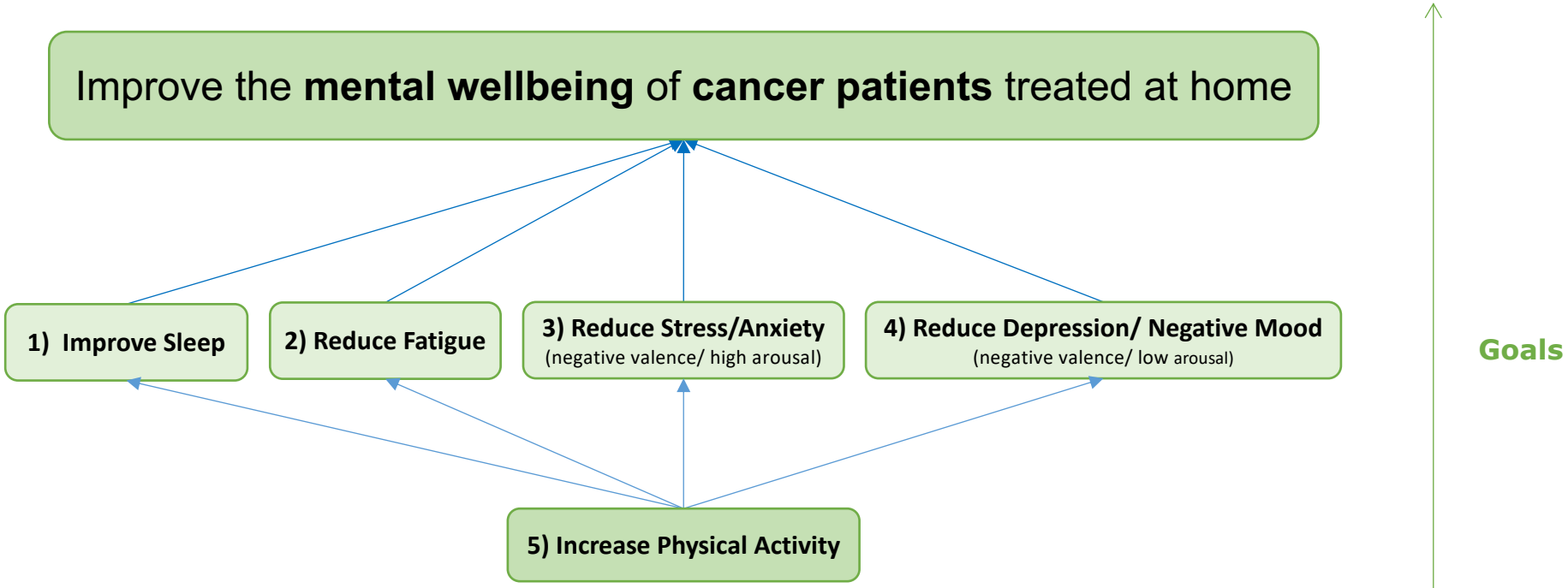
- Provides active coaching – responds to data- and time-related events and runs patient-oriented CIGs
- Diversified coaching interventions – recommendations, reminders, tips, alerts and rewards
- Differences between administrative workflows across institutions – runtime customization of specific CIGs

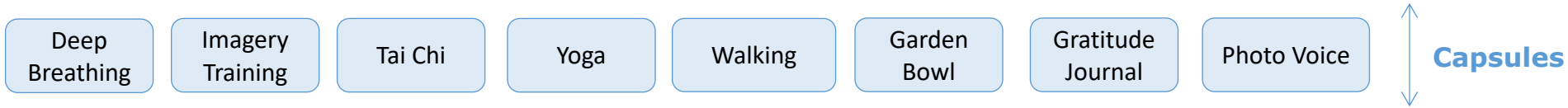


Virtual Capsules

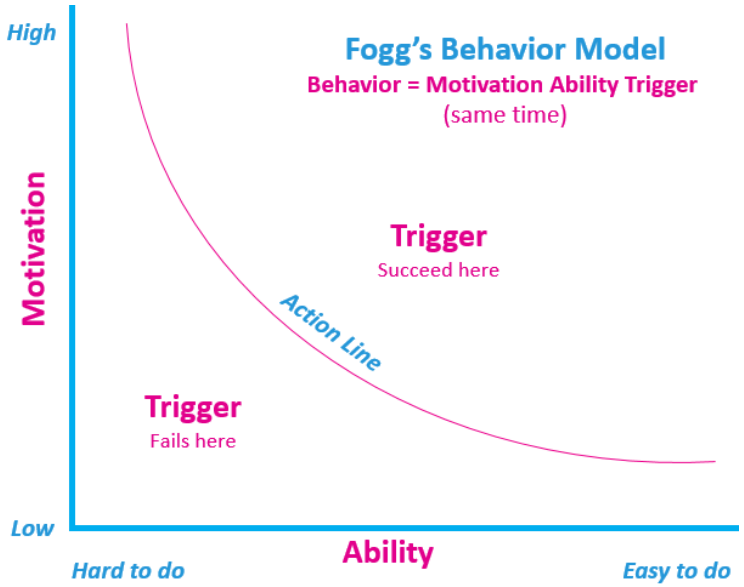
- Interventions aimed at improving mental and physical wellbeing
- Based on evidence and vetted by clinical psychologists
- Need to be approved during enrollment through shared decision-making (→ prescribed, contraindicated, up to patient)
- Direct (deep breathing) and indirect (walking) support in the system

Virtual Capsules





Fogg's Behavior Model



Fogg, B.J., Tiny Habits: The Small Changes That Change Everything, 2019.

- Used to model patient's behavior and to drive personalization of digital behavior change interventions (DBCIs) related to capsules
- Personalization limited to content and time of DBCIs

Simulating Patient Behavior

- No retrospective real-life data for health-related DBCIs
- Simulated data capturing the characteristics of patients – potential users of the CAPABLE system
- An environment (OpenAI Gym) simulating changes of patient behavior in response to triggers based on the Fogg's model

Virtual Coach Simulated patient

$$Behavior = \begin{cases} 1 & if\ (Motivation \times Ability \times Trigger) > action\ threshold \\ 0 & otherwise \end{cases}$$

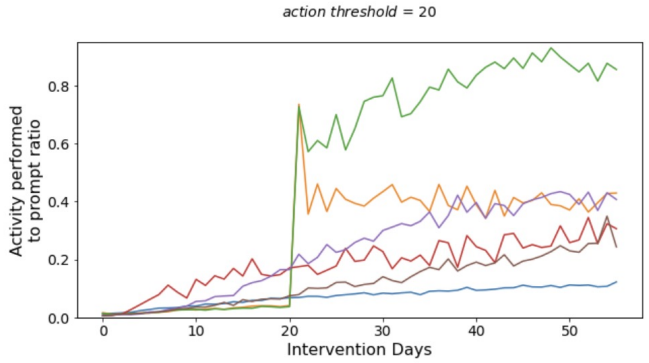
Simulation Experiment

- Patient demonstates a sedentary behavior
- Patient is willing to accept 3 notifications a day
- Patient is most likely to respond to a trigger (DBCI) around noon

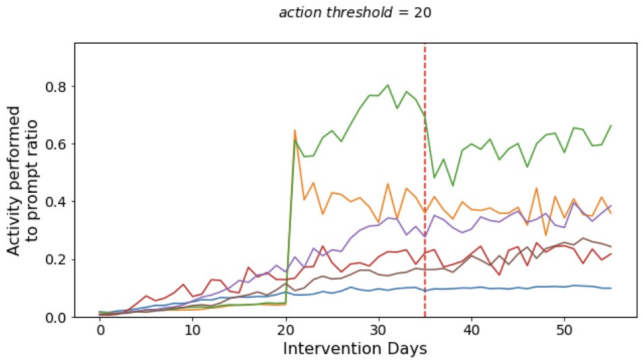
Goal: Learn a notification strategy to instill a walking habbit within 60 simulated days

Compare efficacy and viability of supervised (SL) and reinforcement learning (RL) techniques

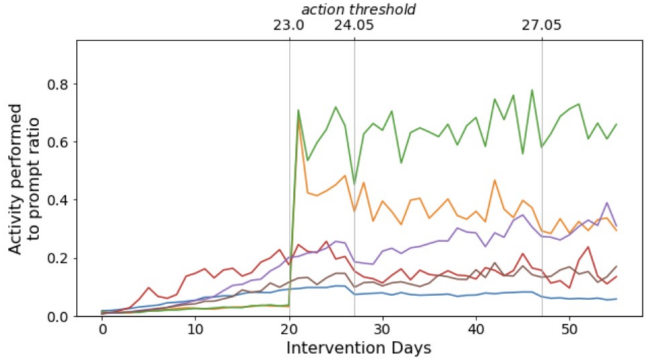
Simulation Results



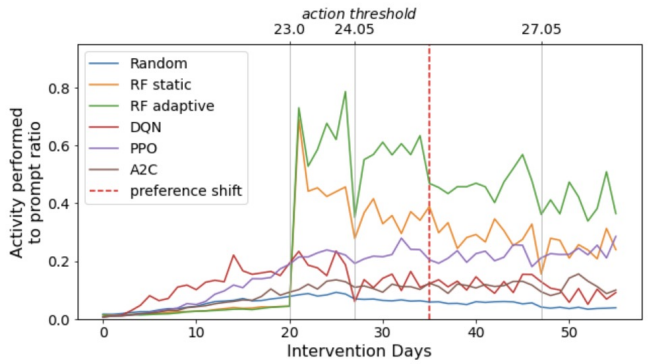
(a) Stable response pattern



(b) Preference shift



(c) Habituation



(d) Habituation + Preference shift

- SL most efficient, but not realistic in practice
- RL can be seen as alternative to static SL
- Warm start with patient preferences (?) and cross-patient transfer learning

A. Lisowska, Sz. Wilk, M. Peleg, From Personalized Timely Notification to Healthy Habit Formation: A Feasibility Study of Reinforcement Learning Approaches on Synthetic Data, in: SMARTERCARE 2021. Workshop Proceedings, CEUR-WS, vol. 360, CEUR, 2021, pp. 7-18.

Motivational Tips for Walking

- Addressing attitude, capability and social support factors and choosing the most appropriate delivery time (→ Fogg's model)
- A pool of predefined tips (6 per factor) based on literature and verified by a clinical psychologist

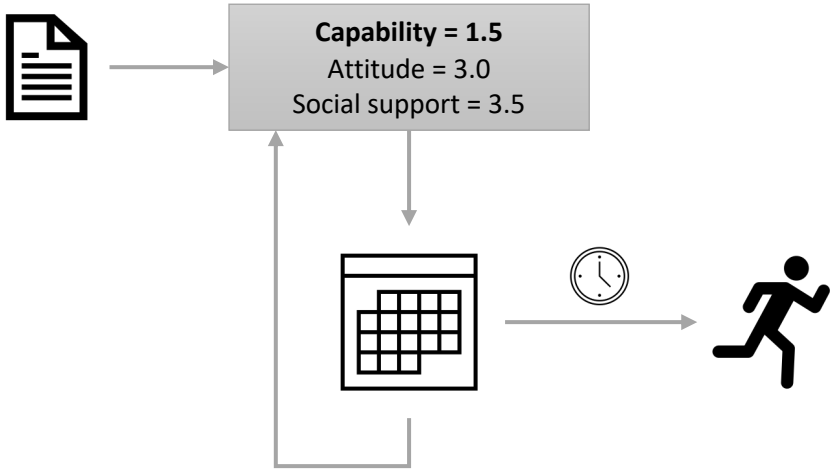
Decision Factor	ID	Message (original from Mor/Aneta)	Message with the changes done by our psychologist (Paola Gabanelli)	Motivation for the change (NB:
Attitude	1	Living through cancer can be stressful, but you can manage the stress. Short nature walks can help you unwind and relax.	Living with cancer can be very difficult, but some activities can help. Short walks in nature or even around your home can help you uwind and relax. Are you feeling up to it at this time? Do you think it could help you?	1. In the psychologist's opinion, talking about "difficulty" or "dolour" is better than "stress" 2. "you can manage the stress" is too direct and it's not appropriate for patients that feel
	2	Feeling fatigued? It is normal when	Feeling fatigued? It is normal when going through the	The last sentence
	3	Walking improves cancer survivor	Walking improves cancer survivor wellbeing. If the	1. the app does
	4	Improve your sleep quality by taking	If you don't sleep well, know that discharging tension and	1. Put in this way,
	5	The weather looks good today. Take	If you feel like it, take 30 minutes to walk from time to	see line 4
	6	Going on a regular 30 minute walk is	This sentence in C7 has been accepted	This sentence has

Motivational Tips for Walking

1. At enrollment, the patient fills in the BREQ2 questionnaire
2. Factors are scored and ordered (weakest to strongest)
3. Tips for a given factor are presented in a 2-week cycle
   - 3 messages per week, presented at fixed days
   - Presentation time based on the maximum activeness in the preceding period

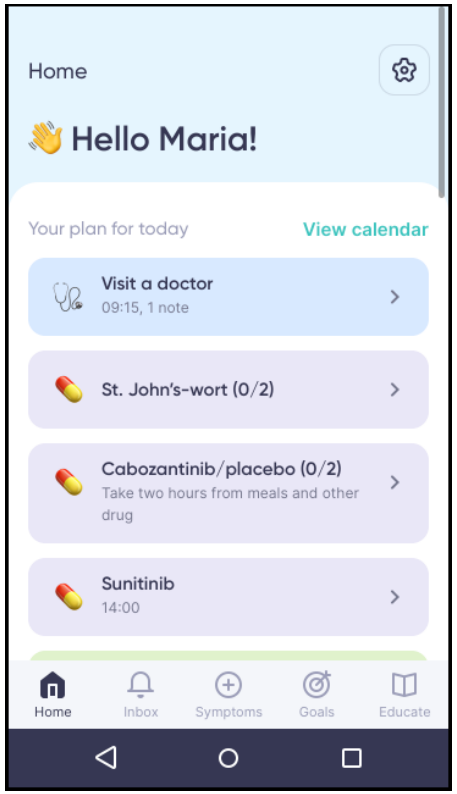
…

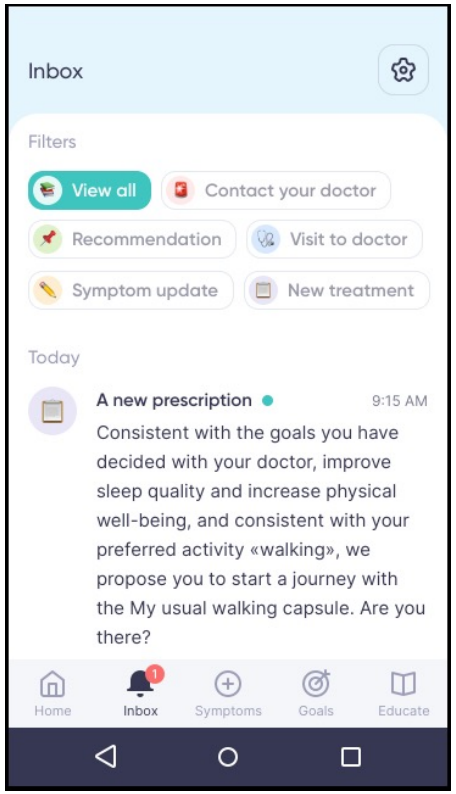
4. At completion, the patient fills in the BREQ2 questionnaire again (to monitor the change of the factors)

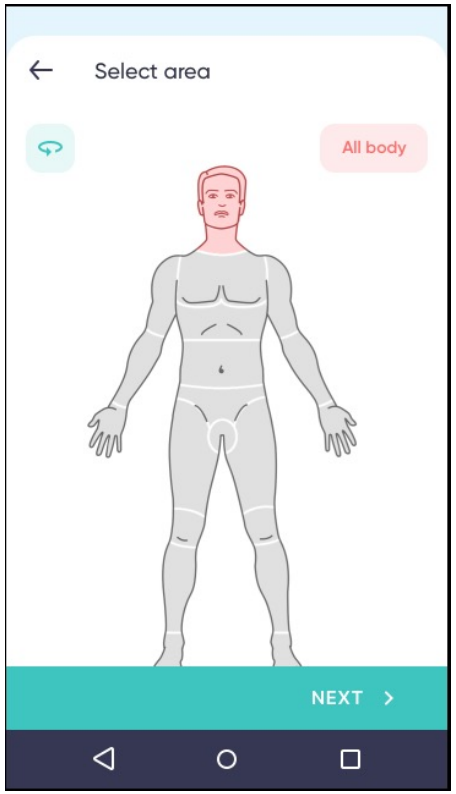


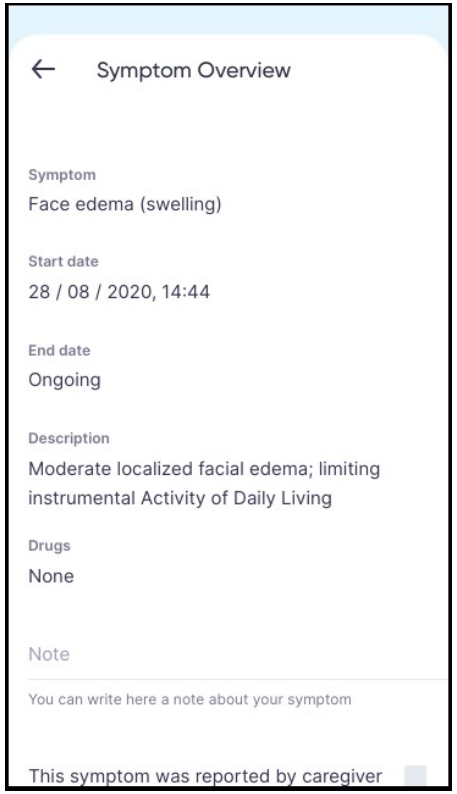
- Tips may be evaluated as helpful or not helpful
- Factors with the majority of not helpful tips are dropped

Patient Application







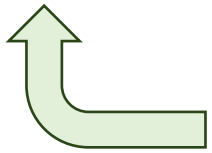


Patient Application

- Proper formulation of symptom descriptions – PRO-CTCAE translated to desctiption levels

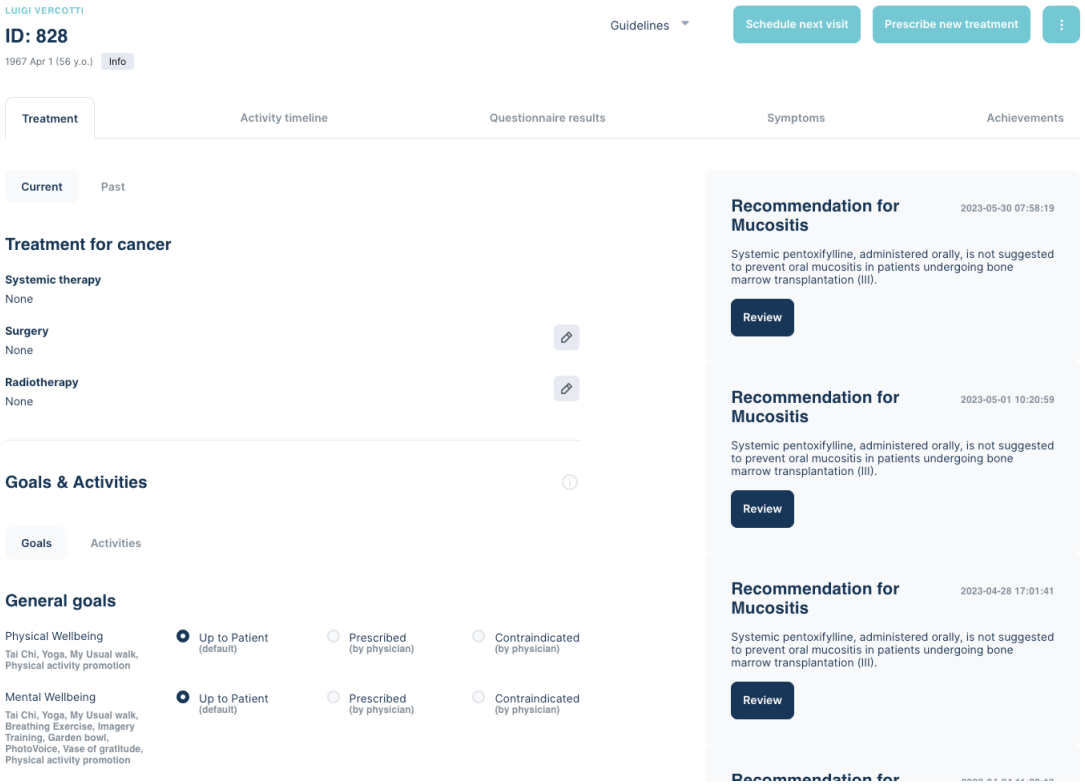
CTCAE = Common Terminology Criteria for Adverse Events

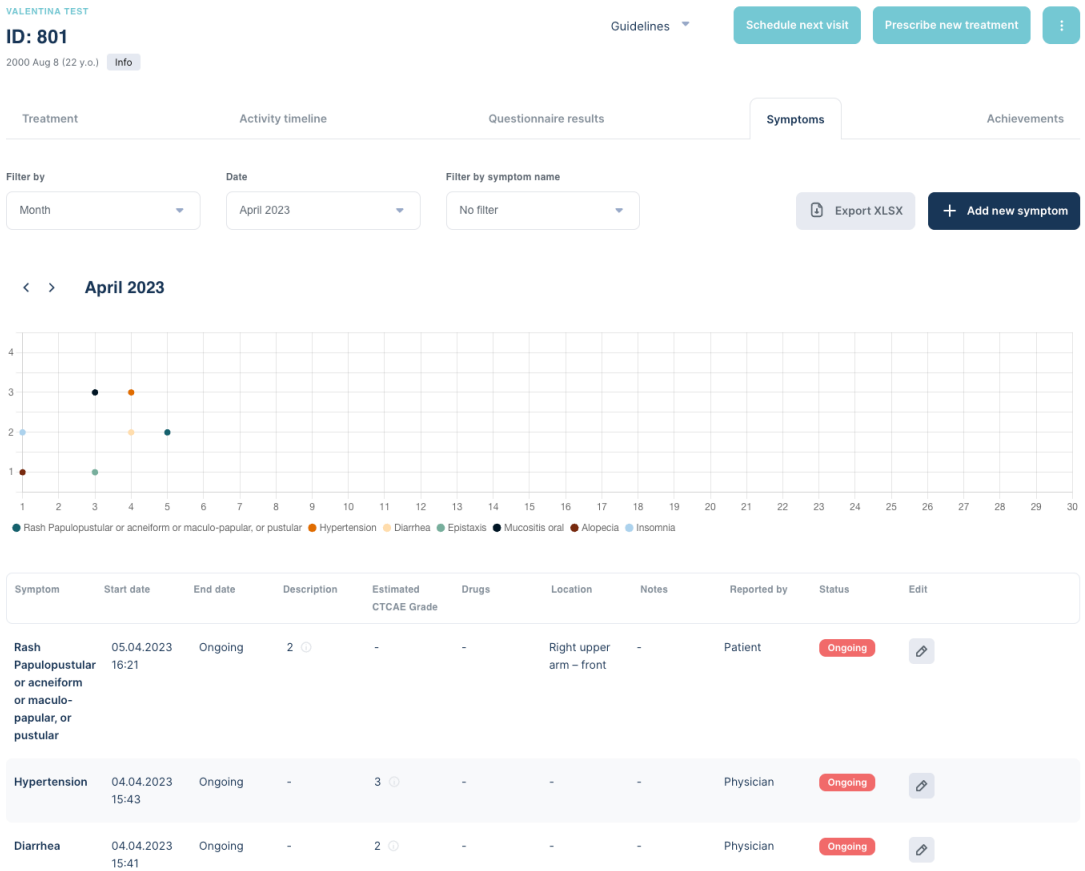
Patient symptom term	PRO-CTCAE match	Codes MedDRA / SNOMED CT	Description 1 EN	Description 2 EN	Description 3 EN	Description 4 EN
Decreased appetite	Yes	10002646	Mild decrease of appetite; I eat and/or drink as usual	Moderate decrease in appetite: I cannot eat and/or drink as usual, but I have not lost weight	Severe decrease in appetite; I cannot eat and/or drink as usual, and I have lost weight	-
Constipation	Yes	10010774	Mild constipation (stools that are hard too pass) that does not interfere or that interferes a little bit	Moderate constipation (stools that are hard too pass) that interferes somewhat with my usual or daily	Severe constipation (stools that are hard too pass) that interferes quite a bit with my usual or daily	Very severe constipation (stools that are hard too pass) that interferes with my usual self-care
Cough	Yes	10011224	Mild cough that does not interfere or that interferes a little bit with my usual or daily activities	Moderate cough that interferes somewhat with my usual or daily activities	Severe cough that interferes quite a bit with my usual or daily activities	Very severe cough that interferes with my daily self-care activities
Diarrhea (loose or watery stools)	Yes	10012727	Increase of <4 stools per day compared to usual amount of stools per day	Increase of 4 - 6 stools per day compared to usual amount of stools per day	Increase of >=7 stools per day compared to usual amount of stools per day	



CTCAE grade 1	CTCAE grade 2	CTCAE grade 3	CTCAE grade 4
Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid	Life-threatening consequences; urgent intervention indicated
Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary	Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL	Obstipation with manual evacuation indicated; limiting self care ADL	Life-threatening consequences; urgent intervention indicated
Mild symptoms; not limiting ADL; nonprescription intervention indicated	Moderate symptoms, medical intervention indicated; limiting instrumental ADL	Severe symptoms; limiting self care ADL	-
Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline; not	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to	Increase of >=7 stools per day over baseline; incontinence; hospitalization indicated; severe	Life-threatening consequences; urgent intervention indicated

Physician Application





Clinical Tests

- Started in March and April 2023 at ICSM and NKI
- Patients with different types of cancer (melanoma, renal carcinoma, breast…) – 30 participants per site in the intervention group
- 6 month follow up to observe a meaningful QoL change (multiple instruments, i.e., QLQ-C30, EQ-5D-5L, …)
- Control group (baseline for comparison) already analyzed

Conclusions

- CAPABLE as response to a new model of care, benefitting patients and physicians — unofficial responses from patients are encouraging
- Methodological and ethical challenges associated with developing and deploying executable decision models
- Organizational challenges associated with clinical studies (not precise formal requirements), need for certified wearable devices
- Practical challenges for the system to be widely accepted by patients (BYOD) and clinicians (fitting the workflow and infrastructure)

Thank you

https://www.capable-project.eu