HORIZON 2020
The EU Framework Programme for Research and Innovation

CAPABLE

Cancer Patients Better Life Experience

Grant Agreement No. 875052
Start Date: 01/01/2020 (48 Months)

Deliverable No. 4.2

2nd iteration of the Platform Proof of Concept

Due Date: 30/6/2021
Submitted On: 13/7/2021

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Deliverable Type		
R	Document, report	
DEM	Demonstrator, pilot, prototype	**X**
DEC	Websites, patent fillings, videos etc.	
OTHER		
Dissemination Level		
PU	Public	**X**
CO	Confidential (Consortium members including the Commission Services)	
CI	Classified Information (Commission Decision 2015/444/EC)	

This deliverable is a part of a project receiving funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 875052.

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1.Version history

Version	Date	Author	Comments
1.0	7/7/2021	Matteo Gabetta (BIOM)	

2. Executive summary

The aim of this deliverable is to support and provide context to the CAPABLE system demonstration video which is available at this link. A brief description about the scope of the demonstration is followed by a detailed description of the scenario that will be managed during the demo.

The demonstration video was recorded in the first half of June 2021 by involved partners and faithfully reflects what was shown during the CAPABLE consortium meeting held on June 22nd and 23rd, 2021.

Given the decoupled nature of the CAPABLE architecture, the efforts that led to the completion of this demo were twofold: on the one hand, each involved partner carried out the development of the component under their own responsibility, on the other hand there was a global effort to make the different components communicate with each other. All these efforts have been coordinated by two Task Forces within the project: Task Force 1 focused on the development of the final CAPABLE architecture and Task Force 2, focused on the delivery of the specific demonstration.

3.Scope of the demo

The demonstration involves most of the components of the CAPABLE architecture given in Figure 1 and covers many interactions between them; in particular, the included components are as follows:

- Data Platform, storing and providing patient-level data,
- Case Manager, managing events related to Data Platform and providing notifications to other components,
- Knowledge-Data Ontology Mapper (KDOM), computing abstractions from data stored in Data Platform,
- Patient App (Patient GUI in the video), providing user interface for patients in form of a mobile app,
- Physician App (Doctor GUI in the video), providing user interface for physicians in form of a web-based app,
- Deontics Engine, executing computer-interpretable clinical practice guidelines (CIGs) defined using the PROforma language,
- GoCom Multimorbidity controller, checking for possible adverse interactions between clinical tasks for multimorbid patients and resolving them. Currently, it focuses on drug-drug interactions, but can be extended for other types of interactions involving non-clinical tasks (e.g., physical exercises).
- Physician DSS, providing guideline-based decision support for clinicians when managing cancer patients.
- Virtual Coach, providing coaching support combining clinical (guideline-based) and non-clinical recommendations to cancer patients staying at home.

The Deontics Engine is used by both Physician DSS and Virtual Coach (more precisely, they use different instances of the Engine). Moreover, GoCom queries the Deontics Engine when checking for possible adverse interactions between tasks to get detailed characteristics of CIG tasks. Interactions between Deontics Engine and other components are handled by a web-based (REST) API. GoCom is invoked by Physician DSS and Virtual Coach -- in such case communication employs Data Platform and Case Manager.

All components, except the two user interfaces, have been effectively deployed in the premises made available by the partners responsible for their development; thus, all the interactions between these components that are shown in the demo are happening live. Of course, the functionalities implemented by each component are partial and comply with the early stage of this demonstration.

The two user interfaces, following the development schedule of the responsible partner (Bitsens), are currently in the form of a mock-up, deployed through *InVision*, a digital product design platform.

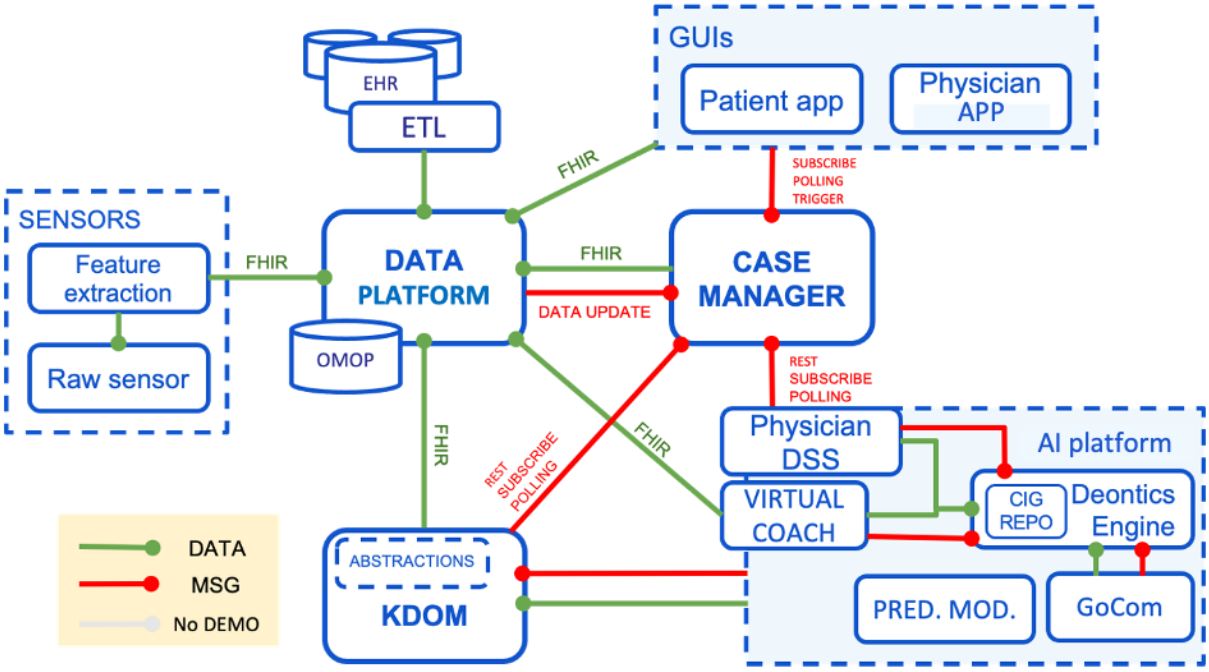

Figure 1. The CAPABLE overall architecture.

4.Scenario

The demo, designed together with clinicians and patients involved in the project, focuses on a single clinical guideline: the "ESMO Management of toxicities from immunotherapy guideline" [1]; and it revolves around a prototypical fictional patient named Maria.

Maria is 66 years old, and she's affected by stage IV melanoma; apart from her main diagnosis, Maria has no significant clinical history. The demo follows Maria during the period spanning from June 1st to July 23rd, 2021, starting from the enrollment visit (day 0) – see Figure 2 for the overview.

In the following sections all the details about what happens in the demo are reported.

Figure 2. Overview of the demo.

4.1. Enrollment - Hospital

During the enrollment the physician, through the Physician App, enrolls new patient Maria Rossi and inserts the following data:

- Name = Maria,
- Surname = Rossi,
- Gender = female,
- Date of birth =11/11/1947,
- Sleep problem (Sleeping section) = no,
- Physical activity and Nutrition sections = same as M12 Demo,
- Clinical history section = no regular physical activity, no particular diet habits,
- Years as a smoker (smoking section) =0,
- Caregiver contacts = same as M12 Demo [2],
- Weight = 62 kg,
- Height= 160 cm,
- BMI = 24.2 Automatically computed from Height and Weight,
- Diagnosis= melanoma stage IV,
- Type of melanoma = superficial spreading
- Location primary tumor = head and neck,
- BRAF mutation = no,
- Breslow thickness in millimeters = 1.02 mm,
- Ulceration = no,
- Dermal mitoses = 1 or more mitotic figure per mm^2,
- Satellites/ in-transits metastases = satellitosis,
- Lymph node metastases (macroscopic) = no,
- Distant metastases = yes,
- WHO score = ECOG grade 0,
- Comorbidity = no,

- Medication use = false,
- Lab determination: s100 = 0.06 μg/L,
- LDH level = 265 U/L,
- Metastasis site = lung,
- Total number of metastases = multiple,
- NRAS mutation = no,
- Sequence (treatment line)= first line treatment,
- Treatment for cancer = none,
- Treatment for comorbidity = none,
- Other treatment = none,
- Goals selection = all goals "up to patient" (default values).

All the information is transferred from the Physician App to the Data Platform.

Case Manager notifies the Physician DSS and the Virtual Coach about the newly enrolled patient. The Virtual Coach starts execution of patient CIGs related to symptom monitoring and management (symptom CIGs in short) on the Deontics Engine.

Physician DSS stores in and sends a request to KDOM (through Data Platform and Case Manager) to compute two abstractions – LDH-elevated and S-100-increased. Once these abstractions are computed, Physician DSS retrieves the data from Data Platform and passes them to the Deontics Engine to run the immunotherapy CIG.

Physician DSS obtains the first task from the CIG (drug prescription of Nivolumab and Ipilimumab) and executes them by creating draft medication requests and requesting GoCom to check for possible interactions.

To this aim, Case Manager notifies GoCom which retrieves tasks in progress from the Deontics Engine, patient data from the Data Platform and checks for possible interactions. The result of this check (no interaction found) is sent, together with the *option-sets* (i.e., sets of drugs that should be prescribed together), to the Data Platform to be stored. Considering Maria's clinical conditions (no BRAF mutation, lung metastases, elevated LDH level and S-100 increased) two possible option-sets: nivolumab monotherapy and nivolumab-ipilimumab combination therapy.

Case Manager notifies the Physician DSS and the Predictive Models about the option-sets.

The Predictive Models component retrieves necessary data from the Data Platform and stores prediction results in the Data Platform.

Case Manager sends a notification to the Physician DSS that prediction results are available. Physician DSS, after retrieving predictions from the Data Platform, combines predictions with option-sets, as they could assist the physician in treatment selection, and stores them in the Data Platform.

Case Manager notifies the Physician App about option-sets and prediction results, and they are presented in the Physician App. Physician opens the Treatment tab and selects cancer treatment with nivolumab, which is stored in the Data Platform by the Physician App in form of an active medication request.

When Maria is at home (after ~6 hours since her enrollment at the hospital during the visit) she uses the Patient App to indicate her hobbies from a shortlist: gardening, listening to music, photography, Tai Chi, walking, and writing. Maria chooses walking and her preference is saved in the Data Platform.

4.2. Visit (1 month later) - Hospital

The Physician App retrieves sensor data from the Data Platform and visualizes them. The page with all the data presents a summary of steps and sleep duration. Looking at the data the physician realizes that in the past month Maria did not perform regular activity and had problems with her sleep.

Physician decides to prescribe (activate) two goals for Maria: improve sleep quality and increase physical wellbeing. These goals are marked as prescribed, and the Physician App stores them in the Data Platform.

Case Manager notifies the Virtual Coach about the new active goals. In response, the Virtual Coach identifies capsules that address these goals and are preferably consistent with the hobbies indicated by Maria. Specifically, there is one such capsule – "30x30 Nature Challenge", consisting in walking in the nature 30 min per day for 30 days (later in the text for brevity we refer to it as to 30x30 capsule). The capsule is stored as draft medication request in the Data Platform together with a request for GoCom to check for possible interactions.

GoCom, after receiving a notification of a request from the Case Manager checks for possible interactions and stores results (no interactions found) in the Data Platform. Case Manager notifies the Virtual Coach about it.

Virtual Coach stores a communication with a 30x30 capsule recommendation in the Data Platform and Case Manager alerts the Patient App about the availability of a new recommendation. The Patient App shows this recommendation to the Patient: "*Consistent with the goals you have decided with your doctor, improve sleep quality and increase physical well-being, and consistent with your preferred activity «walking», we propose you start a journey with the 30x30 Nature Challenge capsule. Are you there?*"

Maria decides to start the 30x30 capsule and her decision is stored in the Data Platform. Case Manager notifies the Virtual Coach about the capsule approval, and the Virtual Coach stores the capsule as *active* medication request in the Data Platform.

4.3. Visit + 1 day (1 day later) - Home

Maria reports in the Patient App her first day with the 30x30 capsule. Through a calendar she selects the day, duration of physical activity and a rating ranging from 1 (worst) to 5 (best) to indicate how much the capsule pleases her.

Maria inserts the following data:

- Date = 2/07/2021,
- Duration = 30 min,
- Rating ("*Do you find that the 30x0 Nature Challenge is working for you?*") = 2.

These data are stored in the Data Platform by the Patient App. Case Manager notifies the Virtual Coach about the capsule execution report.

Since the rating is low, an immediate feedback is shown by the Patient App: "*We are sorry that you didn't appreciate this activity, remember that it has been shown to have many benefits such as improving your stress level*."

Immediate feedback is managed by the Patient App, and it is based on the provided capsule rating, thus no interaction with other components in necessary at this point.

4.4. Day 1 (15 days later) - Home

Maria reports pruritus symptom (grade 1) in the Patient App, and this information is stored in the Data Platform. Case Manager notifies the Virtual Coach about new symptom, and the Virtual Coach passes the data to the symptom CIG executed by the Deontics Engine.

Patient App checks for symptoms related to pruritus and shows to Maria a new reporting request ("*If you have any rash and you have not already reported it, please report it*"). Maria does not report any rash (rash = absent), and her answer is stored in the Data Platform.

Case Manager notifies the Virtual Coach about the new reported symptoms (rash = absent). Virtual Coach passes the symptom-to-symptom CIG. The Deontics Engine responds with a CIG task that recommends the "*OTC topical emollient (moisturizer) without perfume*". Virtual Coach saves in the Data Platform a draft medication request for emollient together with an interaction check request. Case Manager notifies GoCom about

this request – GoCom checks for possible interactions and stores the result (no interaction found) in the Data Platform.

Case Manager notifies the Virtual Coach about the GoCom's result. Then, Virtual Coach stores a communication with a new treatment recommendation in the Data Platform. The Case Manager notifies the Patient App about the new treatment recommendation, so it shows the following recommendation to Maria: "*You reported pruritus. If you haven't since the symptom started, you can use OTC topical emollient (moisturizer) without perfume. Did you use it or are you going to use it?*". Maria approves the treatment, and it is stored in the Data Platform. Case Manager notifies the Virtual Coach about the treatment approval, and Virtual Coach saves the treatment as an *active* medication request in the Data Platform.

4.5. Day 2 (2 days later) - Home

Case Manager notifies Virtual Coach about the periodicity (2 days) asking the patient about pruritus persistence. In response, Virtual Coach stores a communication with a reporting request for pruritus in the Data Platform. Case Manager notifies the Patient App about a new request, so it asks Maria if she still has pruritus: "*You reported mild or localized symptom pruritus. Do you still have the symptom today? If yes you will be prompted with possible change of the severity*". Because the answer is affirmative, the Patient App shows the symptom reporting page. Information entered by Maria (pruritus = grade 1) is stored in the Data Platform.

The Patient App checks for symptoms related to pruritus and then asks Maria about rash ("*Do you have any rash?*"). As the answer to the question is positive, the Patient App offers Maria the possibility to better characterize the symptom by choosing one of its levels:

- No symptoms (pruritus, tightness or burning skin), no limitation of instrumental activities of daily living,
- No symptoms (pruritus, tightness or burning skin), limitation of instrumental activities of daily living,
- Presence of symptoms (pruritus, tightness or burning skin), no limitation of instrumental activities of daily living,
- Presence of symptoms (pruritus, tightness or burning skin), limitation of instrumental activities of daily living,
- Limitation of self-care activities of daily living (this means also having symptoms).

Maria also has a notes field available where she may explain where her symptom is located and its size.

Maria chooses level 4 ("*Presence of symptoms (…), limitation of instrumental activities of daily living*") and all information (rash = yes, level = 4) are saved in the Data Platform by the Patient App.

Case Manager notifies the Virtual Coach about reported symptoms (pruritus and rash). Virtual Coach retrieved this information from the Data Platform and passes it to the symptom CIG executed by the Deontics Engine. In response, the Deontics Engine responds with CIG tasks that recommend contacting the physician, using topical emollient and avoiding sun exposure. Virtual Coach stores in the Data Platform a request to check for interactions for these recommendations. Case Manager notifies GoCom about a new request. GoCom identifies an interaction between the 30x30 capsule and avoiding sun exposure, and it generates another recommendation to suspend a walk on a sunny day.

The results are stored in Data Platform and Case Manager notifies Virtual Coach accordingly. Virtual Coach stores a communication with a set of new recommendations in the Data Platform ("*Use OTC topical emollient (moisturizer)*", "*Suspend 30x30 nature walk if it is a sunny day*", "*Avoid sun exposure*" and "*Contact the clinician*", "). Case Manager notifies the Patient App about these recommendations, and they are presented to Maria.

4.6. Day 2 (2h later on the same day) - Hospital

Case Manager notifies the Physician DSS about Maria's rash. The Physician DSS retrieves all patient information from the Data Platform and passes it to the immunotherapy CIG ran by the Deontics Engine. Deontics Engine responds with a recommendation to contact a patient and to schedule a visit. Physician DSS stores a communication with this recommendation in the Data Platform, and Case Manager notifies the Physician App. Finally, the Patient App presents the recommendation to the clinician who accepts it and decides to schedule a visit for Maria in two days (on July 21st).

4.7. Day 3 (1 day later) - Home

Case Manager notifies the Virtual Coach about an upcoming visit (scheduled for July 21st). Virtual Coach stores a reminder in the Data Platform, and Case Manager notifies the Patient App about it. Then, the Physician App displays the visit reminder to Maria.

4.8. Day 4 (1 day later) - Hospital

Through the Physician App the oncologist obtains all the information about Maria available in the Data Platform. The physician inserts the correct grade of the rash (grade 2) according to CTCAE, which is stored by the Physician App in the Data Platform.

Case Manager notifies Physician DSS about a new symptom (rash) – Physician DSS retrieves patient information from the Data Platform and passes it to the immunotherapy CIG ran by the Deontics Engine. In response, Deontics Engine provides a treatment recommendation ("*Treatment includes topical emollients, oral antihistamines and high strength topical steroids [II, B]. Systemic corticosteroids 0.5–1 mg/kg can be considered, depending on the severity of the symptoms*"). Physician DSS stores this recommendation as *draft* medication requests together with a request to check for interactions. Case Manager notifies GoCom about new request. GoCom finds no interactions and stores the result in the Data Platform.

After being notified by Case Manager about completed interaction check, the Physician DSS stores a communication with treatment recommendation and the Physician App is notified by Case Manager. Physician App presents the recommendation to the physician who decides to prescribe oral antihistamines and topical corticosteroid cream to Maria. Finally, Physician App saves in the Data Platform *active* medication requests for these two drugs.

4.9. Day 5 (1 day later) - Home

Case Manager notifies the Patient App about the new treatments available in the Data Platform: oral antihistamines and topical corticosteroid cream. Patient App presents these treatments to Maria.

4.10. Day 6 (1 day later) - Home

Case Manager notifies the Virtual Coach about the periodicity for reporting pruritus and rash (2 days for both symptoms). Virtual Coach checks the symptom CIGs ran by the Deontics Engine and stores communications with reporting requests for these symptoms.

Case Manager notifies the Patient App about these new requests. Patient App processes the request for pruritus first and displays the following notification to Maria: "*You reported a mild or localized symptom pruritus. Do you still have the symptom today? If yes you will be prompted with possible change of the severity*". Maria answers "*no*" and information about absent pruritus is stored in the Data Platform. Then, Patient App handles the request for rash and displays the following question to Maria: "*You reported symptom rash. Do you still have the symptom today? If yes you will be prompted with possible change of the severity*". Maria answers "*no*" as well, and information about absent rash is saved in the Data Platform.

Virtual Coach is notified by Case Manager about new symptom reports. Since Maria's symptoms are solved, Virtual Coach stores in the Data Platform a communication with recommendation to share her experience with other patients: *"It's good that your symptom is solved. If you have any suggestion for other patients to solve the symptom, write it on the AIMAC forum (https://forumtumore.aimac.it)"*). Case Manager notifies the Patient App about the new recommendation which is presented to Maria.

5.Summary

This document describes CAPABLE Platform 2nd Iteration demonstration (M18). Since the 1st iteration, the platform has undergone several major upgrades:

- predictive models have been included in the workflow
- sensor-generated data are now part of the patient's data model
- new FHIR resources are now supported (e.g., List and Goal)
- simulation of time, a feature that, by its nature, is not evident by looking at the demo, has been re-designed to be more effective
- GUIs, despite shown as a mock-up in this demonstration, will be integrated , starting from the symptom entering functionality, by September 2021, for the project's review by the EU commission

Furthermore, the overall demonstrated scenario has been re-designed from scratch, and not as an extension of M12, to include the whole spectrum of functionalities made available by CAPABLE components.

M12 demonstration has been revised according to these new features and is now compliant with the current version of the Platform.

From this moment on, new features will be integrated into the Platform by means of the new CAPABLE deployment strategy: two environments, each one holding all the CAPABLE components interacting with each other, will be maintained by the consortium: "Integration Test Platform", a stable environment for integration testing and demos, and "Component Development Platform", an unstable environment for continuous integration.

Since, in both environments, CAPABLE components will be available to be asked, by testers/developers, to operate autonomously (exactly as expected to happen during the CAPABLE studies) on non-predefined use cases, another important aspect covered by the new CAPABLE deployment strategy is a shared, concise way of documenting component functionalities by means of documentation cards, whose actual format is under definition by Task Force 1.

6.References

[1] HAANEN, J. B. A. G., et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*, 2017, 28: iv119-iv142.
[2] CAPABLE D4.1: 1st Iteration of the Platform Proof Of Concept - https://zenodo.org/record/4540457#.YOx_BhOA6MI