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CAncer PAtients Better Life Experience

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Final version of refined backend DSS including all components

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

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1. Versions History

Version	Date	Author	Comments
0.1	1/1/2024	David Glasspool Alexandra Kogan Szymon Wilk Roy Leizer	Initial draft
1.0	8/2/2024	David Glasspool Alexandra Kogan Szymon Wilk Roy Leizer	Final draft for review

2. Executive Summary

This deliverable reviews the final version of the CAPABLE backend decision support system. Experience with running the system in production with real clinical users and patients has informed a number of updates to the system, and has provided confirmation that the main features of the system are suitable for live use.

This report gives an overview of the changes made during this period of the project, including their motivation and their effect on the practical running of the system, describes the clinical scenario used to exercise the system, and gives an overview of the demonstration video and a summary of the results.

This report accompanies the demonstration video available here which shows the system in use:

https://capable-project.eu/d5-9_demo/

3. Scope of the Demonstration

This deliverable has two elements. Firstly it describes the changes and refinements that have been made to the backend decision support components since the last report on their status, deliverable D5.6 (Glasspool et al., 2023). These changes have been made in the light of experience operating the CAPABLE system in a production clinical environment and it is useful to summarise the changes themselves, the motivation for the changes, and the degree to which they have been successful in improving the performance of the system. The first part of this document provides this summary.

Secondly, this deliverable demonstrates the operation of the final, clinically deployed backend decision support system (DSS) in the context of a realistic patient scenario. The demonstration is provided in the form of a video, and the last part of this document provides a commentary to go alongside the video itself. Log files from the main components involved in the demo are also available for download.

The components included in the scope of this deliverable are those which have been used to generate live clinical decision support in the clinical pilot studies:

- VC (Virtual Coach)
- PDSS (Physician DSS)
- GoCom (Goal Comorbidities - Multimorbidity Controller)
- KDOM (Knowledge Data Ontology Mapper)

The final state of the VC component has already been reported in detail in deliverable D5.8 (Wilk et al, 2023), and to prevent repetition some material from that deliverable will be briefly summarised and/or referenced in this document.

4. Overview of the backend DSS

The DSS has been already described in detail in previously published deliverables:

- Deliverable D5.3 (Glasspool et al., 2022): Overview of the DSS backend system with details of PDSS and GoCom components and their interaction with the Predictive Model Component (PMC).
- Deliverable D5.4 (Barkan et al., 2022): Details of PMC component.
- Deliverable D5.5 (Wilk et al., 2022): Details of VC component.
- Deliverable D5.6 (Glasspool et al., 2023): Overview of the prototype backend system.

This section provides a brief recap of the main features of each component that are important for the D5.9 summary and demonstration.

Figure 1 shows the main components of the CAPABLE DSS system, with the backend components that have been used in the clinical pilot studies highlighted in orange. The components are not directly connected to each other but interact through message-passing via the Data Platform (DP) as shown by the black arrows in Figure 1. The orange arrows indicate that three components, Physician DSS (PDSS), Virtual Coach (VC) and GoCom, also connect to the Deontics Server which provides an execution engine for clinical guidelines specified in the PROforma language.

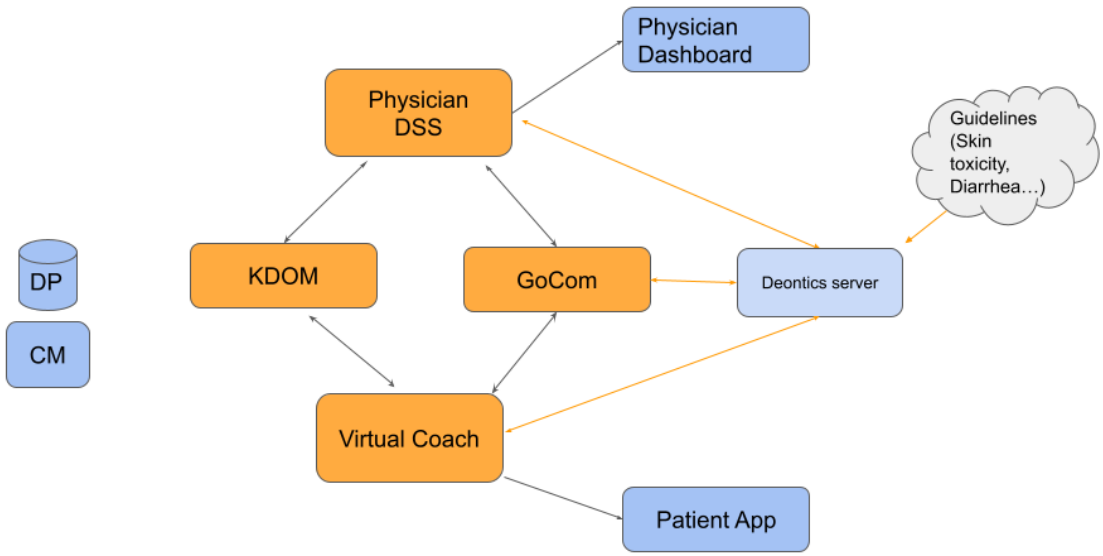


Figure 1: *Conceptual view of the CAPABLE backend DSS with surrounding components. The DSS components (demonstrated in this deliverable) are shown in orange. All connect to DP (Data Platform) and CM (Case Manager), and the black arrows conceptually indicate interactions that take place via DP.*

The DSS components react to patient data captured by FHIR resources, primarily Observations (such as blood pressure readings, symptom reports etc.) and Medication Requests, stored in the DP.

4.1. PDSS

PDSS is responsible for applying computer-interpretable guidelines (CIGs) written in the PROforma CIG language to patient data in the CAPABLE system. It uses the Deontics engine to execute the CIGs. Whenever new clinical data arrives for a patient, a single assessment is carried out on each available CIG using the patient's clinical data.

PDSS interacts with the DP (pulling patient data when it is notified by the CM that a new data item is available), KDOM (requesting updated values for any "abstraction" data items that are required by the currently executed CIGs - these values must be calculated by KDOM dynamically using current patient data values), and GoCom (determining if actions recommended by the PDSS may lead to adverse interactions, and if the clinician should consider alternatives).

4.2. GoCom

GoCom detects interactions among the patient's diseases and treatments and suggests alternative solutions. GoCom is goal-oriented and mitigates interacting treatments while attempting to provide clinically viable solutions for as many of the patient's diseases as possible. PDSS forwards pharmacological treatments recommended by the guidelines to GoCom for interaction checking in order to prevent adverse events. Afterwards, GoCom provides as output the clinical guideline recommendations along with information about all found interactions involving active medications as well as medications recommended by the system for the patient.

4.3. VC

VC is a component of the CAPABLE system that provides active and comprehensive support for patients and their home caregivers. The provided support referred to as *coaching*, involves monitoring reported symptoms and readings obtained from wearable sensors (consumer-grade smartwatches), recommending pharmacological (only if already prescribed by the physicians) and non-pharmacological interventions (so-called well-being capsules), and delivering alerts, reminders and various types of tips (related to prevention, education, and symptom management).

4.4. KDOM

KDOM allows the computing of abstract medical concepts (such as "Patient is on chemotherapy" or "Persistent diarrhoea"), which are useful when defining computer-interpretable guidelines and for communicating with clinicians, to the detailed data (such as lists of individual drugs and patient symptoms) which appear in the patient data record. KDOM provides a service within the CAPABLE system allowing the VC and PDSS components to request specific abstractions which KDOM will then compute from the available patient data.

5. Refinement of the backend DSS during the final year of the project

5.1. PDSS

The following changes have been made to the PDSS component since the last report in Deliverable D5.6. Some of these changes constitute final work involved in putting PDSS into action in the clinical pilot studies, as the final refinements to the set of CIGs were completed after D5.6 and required some software updates which are reported here. Other changes however were made in response to experience gained with running the full decision support backend in a real clinical environment. As anticipated, a number of issues became apparent in real-world use which had not emerged during testing. These were all addressed with updates to the PDSS software which were implemented, tested and deployed quickly thanks to the development and test environment developed earlier in the project - the CAPABLE simulator system along with a set of "test" components running on separate servers unconnected with the pilot systems. This environment allowed software updates to be tested against formal test scenarios to detect any possible regressions.

The following are the main changes made to PDSS:

1. The full final set of CIGs defining the decision support that would be available for physicians were completed by January 2023. The final iteration of CIG development identified a lack of sufficient granularity in the way clinical data was extracted from the patient records in DP by the PDSS. In addition to the value property of an Observation resource (for example, the presence of a symptom reported by the patient) the logic in the final versions of some CIGs required access to different features of the resource (such as the date and time that the symptom was reported). This had not been anticipated during requirements definition and was not supported by PDSS. The data mapping subsystem within PDSS was redesigned to provide the required granularity. This change was in place and tested by January 2023, well before initial deployment to the pilot sites.
2. A final refinement was made during January 2023 to support some updated and extended functionality in other components: PDSS now allows multiple terminology codings for a single Medication Request and will correctly process each of them. Additional information about the logical arguments used to recommend a medication is now passed to GoCom to allow more informative messages to be compiled for the physician.
3. Pre-deployment testing of the PDSS in December 2022 with large numbers of FHIR resources in DP revealed significant and increasing slowing of processing. The issue was traced to inefficiencies in requesting FHIR resources from DP. PDSS was making broad requests and then finding the resources it needed among the set of data returned. The set of resources returned became very large as the amount of patient data increased, causing the slowdown. Improvements were made to the specificity of requests in order to reduce the workload on the components and reduce the number of resources being transferred between components. This change was completed and

tested before pilot system deployment, and the system performed with the expected speed when deployed.

4. An issue was observed, during very early clinical use, where some messages to the physician were repeated needlessly. This was found to be due to a data paging issue which had been missed in earlier testing. PDSS asks DP for a list of Communication resources it has previously sent to the physician about a particular patient. Once the number of such resources in DP became large, the result was returned in limited chunks, a page at a time. PDSS was erroneously checking only the first page and missed the fact that some communications had already been sent. A fix was quickly deployed.

5.2. KDOM

The following updates and modifications were made to the KDOM component since the last report in D5.6:

1. Added ability to create abstractions based on an XML format with special tags to allow support for mapping instances of all 4 types (1:1, Logical, Hierarchical and Temporal) including a mechanism that allows loading those abstractions in real-time.
2. Added support for calculating the abstractions in parallel using a multithreading approach to reduce the execution time and return the abstraction calculation results faster.
3. Added support for symptom duration calculation, including automatic detection of when a patient forgot to close the symptom event.
4. Implemented a special tool for simulating abstraction requests using FHIR Communication resources. The tool prepares resources for abstractions, and manages the CM event queue.

5.3. GoCom

The following changes have been implemented in the GoCom component since the last report in D5.6:

1. Simplification of the option-set format has been done for better integration with the Physician Dashboard. GoCom provides recommendations and interaction warnings in one message, with guideline recommendations (if present) ordered by guidelines and interaction warnings afterwards. This single-message format demands less clicks from the physician and aims to reduce alert fatigue.
2. Logging features along with timestamps have been added in order to enable detailed monitoring of GoCom activities.
3. The process for handling medications prescribed by the physician separately from guideline recommendations has been refined to ensure every active or proposed medication is checked for interactions.
4. New features have been implemented to allow GoCom integration with the latest guidelines and the new meta properties that have been added for detailed guideline processing.

5. Bug fixes have been implemented, including those identified within the guidelines, to improve overall functionality and reliability.

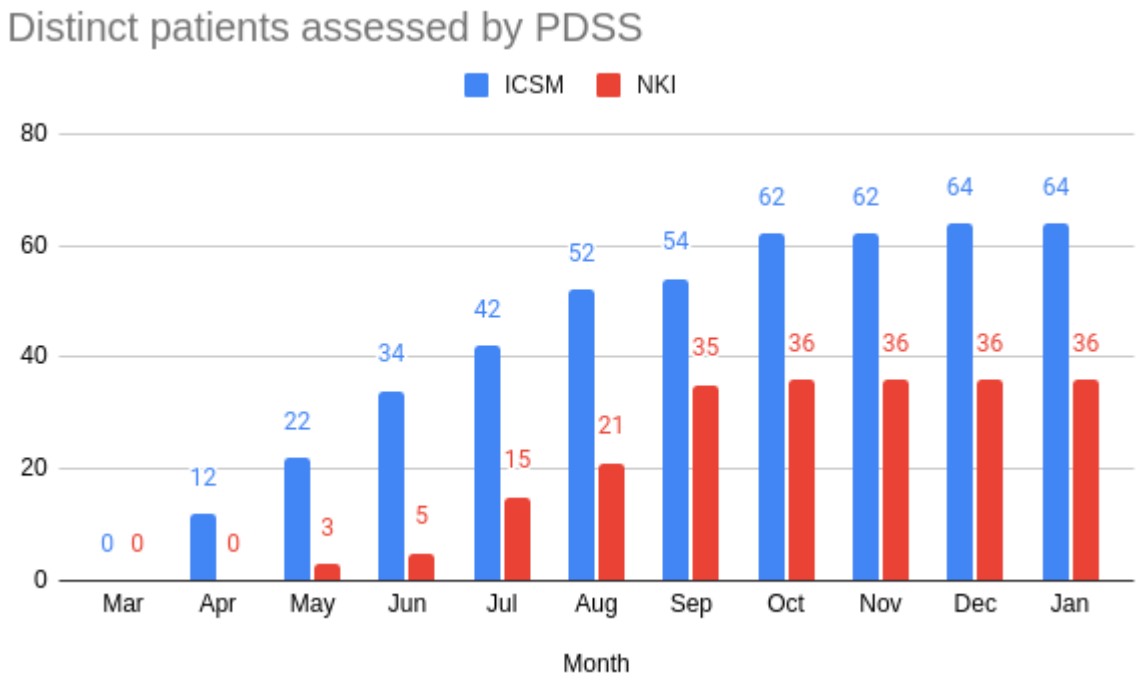
6. Performance of the backend DSS components during the clinical pilot study

The clinical DSS back-end system performed as designed during the clinical pilots. This section reports some measures that indicate the level of demand on the individual components and confirm that the system was operating under load.

5.4. PDSS

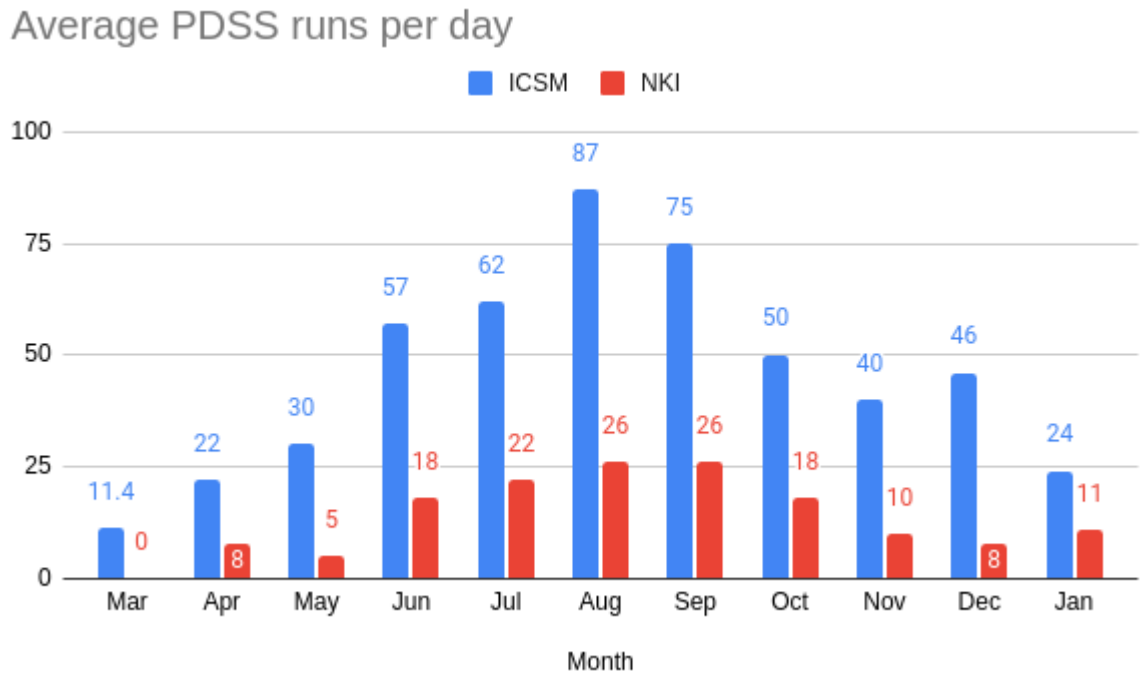
The following charts illustrate the workload for PDSS at each site over the pilot period.

Chart 1 shows the number of distinct patients assessed by PDSS each calendar month. (NB these numbers include both real patients and a small number of test *patients,* i.e., internal volunteers, for the first two months)



■ *Chart 1: Number of distinct patients assessed by PDSS in each calendar month on the two pilot systems.*

Chart 2 shows the number of times PDSS was triggered to carry out an assessment for a patient each day, averaged for each calendar month during the pilot trial. This chart shows only assessments that were triggered by new patient data (so it does not include four assessments per day for each patient that are carried out as mentioned above purely to catch any actions that are triggered by passage of time).



■ *Chart 2: Average number of times PDSS assessed patients each day in response to incoming clinical data.*

5.5. GoCom

Chart 3 illustrates the quantity of medication requests submitted to GoCom for interaction checking. Due to the NKI physician team not reporting medications in the Physician Dashboard, the number of medication requests processed in NKI is notably lower. There were 100 distinct medications identified, with Loperamide emerging as the most frequently recommended, representing over 40% of the medication interaction checking. Other medications such as Levothyroxine, Prednisolone, and Dexamethasone followed, albeit with significantly lower percentages, accounting for 2% of the interaction checking collectively. Throughout the pilot phase, GoCom handled more than 460 medication requests and guideline recommendations for interaction checking, with 803 pairs of medication requests (where there was more than one active or proposed medication for the patient), detecting 328 interactions in total.

The spike in medication request numbers for ICSM in December is interesting. This indicates a larger number of medication requests processed by GoCom in this month. However the impact of larger numbers of medications is non-linear and relates also to the number of possible interactions with existing medications. Processing occurs with each communication from the PDSS or each new medication prescription. Therefore, if a patient is prescribed multiple medications sequentially, GoCom processes interaction checks cumulatively, leading to a high processing count, which does not necessarily correlate to the number of medications prescribed to the patient. A relatively modest increase in medication requests may thus cause a much larger increase in GoCom processing as seen in December.

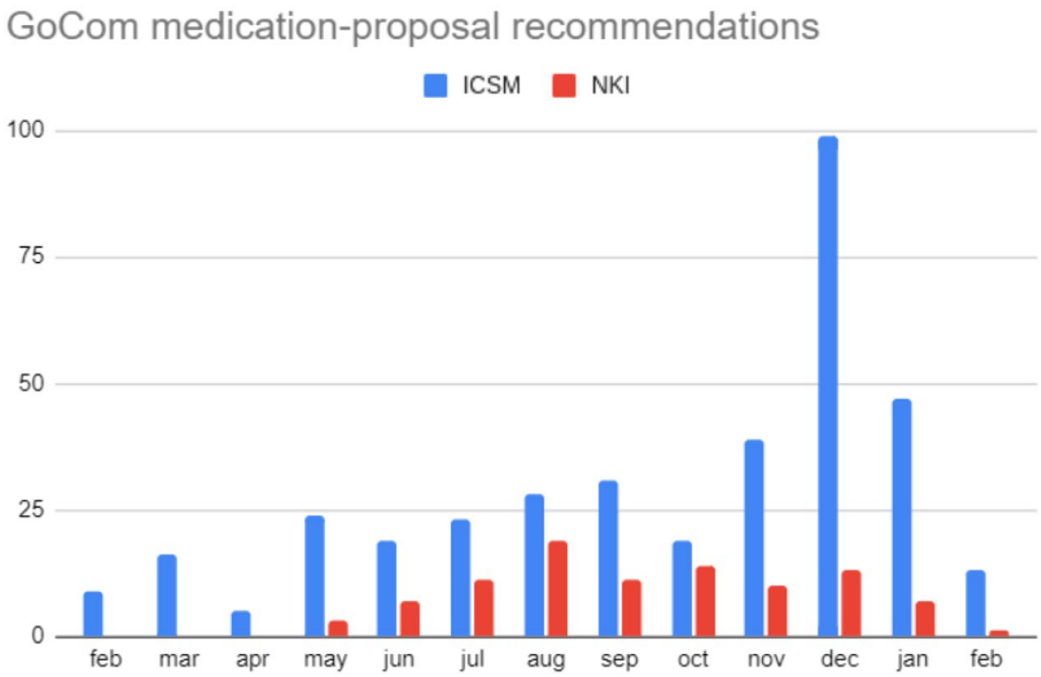
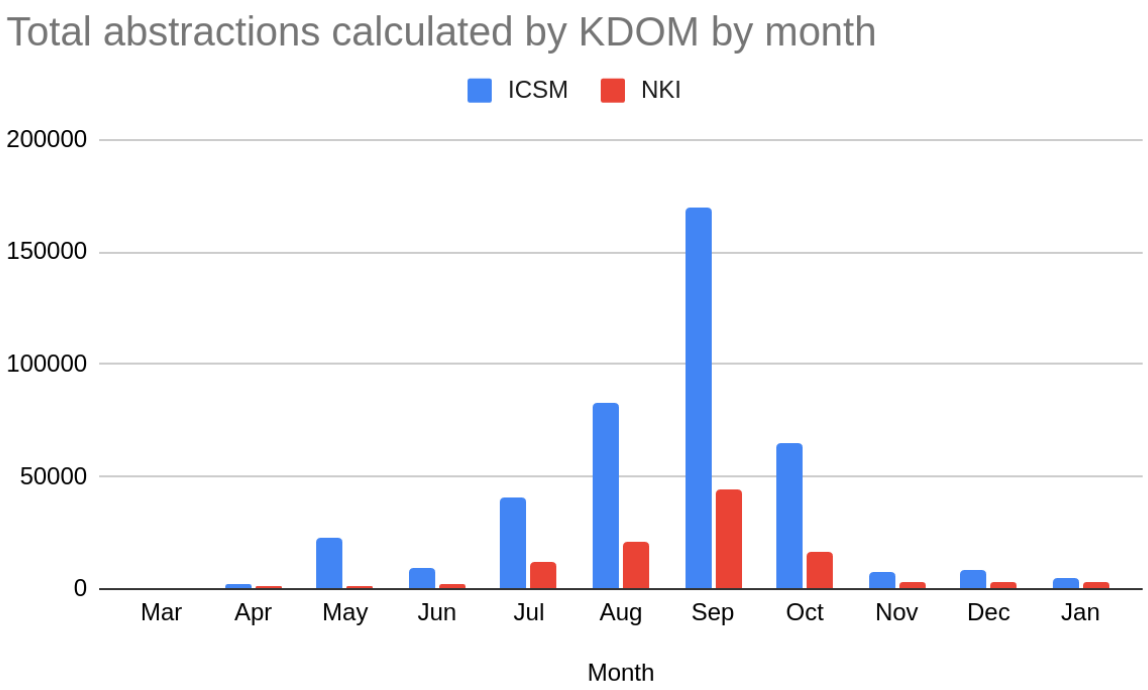


Chart 3: Medication requests sent to GoCom for interaction checking

5.6. KDOM

Chart 4 shows the number of abstractions calculated by KDOM each month at each clinical pilot site. The large spike in abstractions calculated across August and September 2023 is due to an issue which was diagnosed and fixed in early October 2023. A change was made to the VC component in July 2023 which included saving some auxiliary data (resource check-offs used for flagging handled events) as an Observation data resource in the DP. PDSS responded to these internal VC Observation resources as though they were updated patient data, and spurious PDSS runs were triggered. Since no actual changes had happened to any patient data these extra runs did not have any effect on the DSS system other than an increase in internal activity, including an increase in the number of requests from PDSS to KDOM for updated abstractions. Once the issue was fixed in October 2023 the number of KDOM runs returned to the expected level.



■ *Chart 4: Total abstractions calculated by KDOM during each month of the clinical pilot.*

7. Demonstration Scenario

The demonstration uses a clinical scenario which is described in this section.

Patient Maria Rossi is diagnosed with melanoma and the physician prescribes immunotherapy medication (Nivolumab). After Nivolumab is prescribed, PDSS identifies two actions recommended by the guidelines: a medication proposal from the Diarrhea guideline for Loperamide to be prescribed as needed in case the patient experiences diarrhea and a recommendation from the Skin-toxicity prevention guideline for preventing skin dryness. Both recommendations are accepted by the physician and implemented.

The patient reports a skin rash as a side effect of Nivolumab. PDSS registers the new observation, and after re-assessing the patient data with updated abstractions, sends a recommendation from the Rash guideline to contact the patient to determine the type of rash. The physician follows the recommendation and reports the rash to be grade 2 acneiform rash. Two recommendations are proposed by the Rash guideline, the physician decides to decline a recommendation for anti-epileptic agents (that can be prescribed for patients that do not respond to antihistamines) and accept the recommendation to prescribe antihistamines.

Another side effect, diarrhea, is reported by the patient. An action is recommended for diarrhea management, which is communicated as general management advice to the physician for implementation. Moreover, the patient is advised by VC to take Loperamide as needed for diarrhea and accepts the recommendation in the app, which is recorded in the system.

The physician then prescribes Diphenhydramine for the rash symptom. GoCom identifies potential interactions with the existing medications Nivolumab and Loperamide but, after discussion with the patient, the physician decides to proceed with the current regimen.

Upon receiving blood test results indicating hypothyroidism, the physician reports the new symptom in the system and PDSS recommends Levothyroxine and further testing. GoCom identifies interactions between the proposed Levothyroxine and the active medication Loperamide and communicates them to the Physician Dashboard (it also finds two other - previously reported - interactions). After reviewing all recommendations and interactions, the physician decides to continue with the current treatment regimen, including the prescription of Levothyroxine.

8. The Demonstration

The demonstration is presented as a video recording, available here: https://capable-project.eu/d5-9_demo/

The full demonstration was carried out on Jan 26, 2024 and ran for approximately 20 minutes. Logs were kept for two components, GoCom and PDSS, which between them capture all events occurring in the backend decision support system.

The video switches between a view of the Physician Dashboard and views of the PDSS and GoCom logs, to show how actions taken in the Dashboard trigger activity in the components, and how actions taken by the components are then reflected back in the GUI. For clarity the video has been edited to remove long pauses (caused primarily by the human operators coordinating the various actions, rather than by the technology, as the logs show). The video runs for 12 minutes.

The full PDSS and GoCom logs from the demonstration are available for reference at https://capable-project.eu/d5-9_log_pdss/ and https://capable-project.eu/d5-9_log_gocom/ respectively. The next section provides a detailed walkthrough to accompany the video.

5.7. Demonstration video walkthrough

Table 1 provides a walkthrough of the demo video (and Annex 1 and 2 logs) showing what exactly is happening at each step.

A note about timestamps

Please note that the video has been edited to remove several sections with long pauses, in order to make it shorter and easier to follow without losing any content. The logs for GoCom and PDSS in Annexes 1 and 2 are unedited and have been directly copied from the original component output. The timings in the video are therefore not synchronised with the log timestamps. However, the log timestamps give the true timings and are of course synchronised with each other.

For this reason, the table gives timestamps for both log files as well as the time each event occurs in the video, for easy reference.

Video timestamp	PDSS Log timestamp (Annex 1)	GoCom log timestamp (Annex 2)	Notes
0:00			Introduction to the demonstration.
0:35			The physician prescribes immunotherapy (Nivolumab) for patient Maria Rossi.
1:14	13:33:20		PDSS responds to the new medication (Nivolumab) by requesting updated abstractions from KDOM.

			PDSS logs the new abstraction values arriving in DP from KDOM.
1:32	13:34:02		PDSS registers that all the requested abstractions have been refreshed and commences a run of each of the CIGs in its knowledge base against the current clinical data and abstractions for this patient.
1:45	13:34:13		PDSS finds two actions have been recommended by the CIGs. It responds by creating a Medication Request proposal for the drug Loperamide and sending a communication to the Physician Dashboard to have it display a recommendation about prevention of skin dryness.
2:04			The medication proposal for Loperamide is sent to GoCom for interaction checking. No interactions are found, the recommended medication and the skin dryness message appear in the Physician Dashboard. The physician accepts the recommendations in the Dashboard.
2:38			The physician prescribes the drug that was recommended by the PDSS, Loperamide, to be taken as needed.
3:19	13:38:16		The patient reports a side-effect of the treatment with Nivolumab - a skin rash. PDSS registers this new side-effect as an Observation appearing in DP, and responds by requesting updated abstractions from KDOM and then running an assessment for the patient on each of the CIGs.
3:55	13:39:09		One of the CIGs (the Rash guideline) generates a recommendation to contact the patient and check the type of rash. The recommendation is sent to the Physician Dashboard and shown to the physician.
4:16			The physician assesses that the rash is grade 2 acneiform, and enters this as a symptom in the Dashboard.
4:46	13:40:01		PDSS registers this new information which has appeared as an Observation in DP, requests updated abstractions and then runs each of the CIGs for the patient.
5:30	13:40:53		PDSS finds two actions are recommended, and sends messages to the Physician Dashboard which are displayed as recommendations to the physician.

5:46			Physician reviews both recommendations and decides to decline the first but accept the second, which is to prescribe an antihistamine.
6:26	13:41:59		The patient reports a second side-effect, diarrhea. PDSS sees this new Observation and requests updated abstractions, then runs all CIGs.
6:32	13:42:59		An action is recommended by one of the CIGs (the Diarrhea guideline) and PDSS executes this action, sending a message to be displayed to the physician. The message appears as a recommendation for diarrhea management in the Physician Dashboard.
7:01			The patient is now able to take up the earlier prescription of Loperamide as needed in case of diarrhea, and indicates this in the Patient App. Loperamide appears as an active medication in the Physician Dashboard.
7:21			The physician carries out the action recommended earlier for the rash symptom, and prescribes an antihistamine, Diphenhydramine.
7:58		13:45:20	GoCom responds to the new medication event for Diphenhydramine and looks for potential interactions.
8:05		13:45:34	GoCom finds interactions with both Nivolumab and Loperamide for the new medication Diphenhydramine. GoCom sends a communication to the Physician Dashboard.
8:27			The physician reviews the message and after considering the interaction warnings, discusses the risk with the patient and due to the patient's low risk and lack of relevant history the physician decides to proceed with the current medication regimen.
8:37			After receiving blood test results for the patient, the physician reports hypothyroidism.
9:16	13:47:10		PDSS responds to the observation of hypothyroidism by requesting updated abstractions from KDOM and then running all CIGs.
10:04	13:48:02		PDSS recommends Levothyroxine, a test to check the patient's cortisol, and also suggests re-testing before the next treatment cycle.
10:11		13:48:04	GoCom responds to the new medication

			recommendation Levothyroxine. It checks for interactions and finds three interactions. One between Loperamide and Levothyroxine and two between the previously prescribed Diphenhydramine and Loperamide and Nivolumab. It sends a communication to the Physician Dashboard detailing these interactions.
10:23			The interactions and the PDSS recommendations are all displayed in the Physician Dashboard. The physician reviews each of them and decides to continue with the current treatment regimen.
11:34			After reviewing all the recommendations and interactions, the physician decides to prescribe Levothyroxine.

■ ***Table 1:*** *Main points of interest in the demonstration video, cross-referenced to the PDSS and GoCom logs.*

9. Summary

The demonstration we have presented in the video and log files was carried out on the final versions of all decision support backend components and the final set of clinical guidelines, exactly as deployed at the clinical pilot sites. It is based on a scenario that is intended to give a realistic idea of the way the components have been operating in concert during the pilot, and to exercise some features of the system that have been seen in isolation in previous deliverables - simultaneous operation on multiple guidelines, detection of potentially concerning treatment interactions and their mitigations - while adding the interaction with the Physician Dashboard which has not been previously shown.

This report has also presented statistics showing how the system has operated during the pilots, and has detailed the changes that have been made to the system components in response to the challenges of full clinical deployment.

10. Glossary

CIG	Computer-interpretable Guideline
CM	Case Manager
CPG	Clinical Practice Guideline
DE	Deontics Engine
DP	Data Platform
GoCom	Goal Comorbidities - Multimorbidity Controller
KDOM	Knowledge Data Ontology Mapper
PDSS	Physician Decision Support System
PMC	Predictive Model Component
PtApp	Patient App
VC	Virtual Coach

11. References

Barkan, Ella, Quaglini, Silvana, Cornet, Ronald, Glaser, Savannah, & Rabinovici-Cohen, Simona. (2022). CAPABLE D5.4: Prototype of Statistical-based Decision Component. Zenodo. https://doi.org/10.5281/zenodo.7096155

Glasspool, David, Quaglini, Silvana, Kogan, Alexandra, & Wilk, Szymon. (2022). CAPABLE D5.3: Prototype of Guideline-based Decision Component. Zenodo. https://doi.org/10.5281/zenodo.7096129

Glasspool, David, Quaglini, Silvana, Kogan, Alexandra, & Wilk, Szymon. (2022). CAPABLE D5.3: Prototype of Guideline-based Decision Component. Zenodo. https://doi.org/10.5281/zenodo.7096129

Glasspool, David, Parimbelli, Enea, Quaglini, Silvana, Kogan, Alexandra, Leizer, Roy, Barkan, Ella, Rabinovici-Cohen, Simona & Wilk, Szymon (2022). CAPABLE D5.6: Prototype of Backend DSS, Ready for Integration with the Pilot System. https://zenodo.org/doi/10.5281/zenodo.7603469

Wilk, Szymon, Quaglini, Silvana, Veggiotti, Nicole, Peleg, Mor, Glaser, Savannah, Lisowska, Aneta, Śniatała, Konrad, & Glasspool, David. (2022). CAPABLE D5.5: Prototype of the Coaching System with Selected Representative Interventions. Zenodo. https://doi.org/10.5281/zenodo.7096208

Wilk, Szymon, Silvana Quaglini, Mor Peleg, and Aneta Lisowska. (2023). CAPABLE D5.8: Refined Version of the Coaching System with All Interventions Required for the Two Considered Clinical Use Cases". Zenodo, https://doi.org/10.5281/zenodo.10245286