newsletter

The Newsletter of the Patient Empowerment through Predictive Personalised Decision Support (PEPPER) Project

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Content

Editorial

Dr. Clare Martin

Project Coordinator

Welcome to the last issue of the PEPPER Project newsletter. We have had an exciting few months to reach the end of the project with our goals reached. You will find news about project review. Also, you can also read the recent results achieved by technical work packages, and particularly, some preliminary results achieved in the feasibility study. And finally, the summary of some events we have participated.

If you would like to offer us any feedback please contact contact_pepper@googlegroups.com

I. Project Review

On August 29th the PEPPER project was submitted to a report review on Brussels. On the previous day, the PEPPER team meets for a rehearsal, with happy faces after the summer vacation (see the photo).

The contents of the review includes the work done from the 19th month of the project to the 42 month. In particular, the work carried out during this period includes the completion of the technical work packages, the clinical feasibility study, and the starting of the clinical validation study, which ended on September 2019.

Reviewers of the project were Stefanos Gouvras, the Project Officer, Sara Salevati, from Simon Fraser University (Canada), Asimina MiTrakou from University of Athens Medical School (Greece), and Salvatore Baglio from the University of Catania (Italy).

The scientific results achieved have been highlighted by the reviewers, while some aspects of the exploitation plan required further work, mainly due to Cellnovo, a pillar for the PEPPER system exploitation, going into administration and having to leave the project.

We are currently working on an alternative exploitation plan which will be presented in the next review report at the end of the project.

II. Recent results achieved by technical work packages

PEPPER main research components include the study of human factors on the design loop of medical devices (work package 2), an insulin dosing system (work package 3), the safety system (work package 4). Other technical work packages are related to the platform required to run and synchronize the intelligent and safety components, and they are the client (work package 6) and server (work package 5) ones. All of them (except WP2) are identified in the architecture of the system in figure below.

Here we summarize the recent results achieved in this technical work packages during the second, ending part of the project.

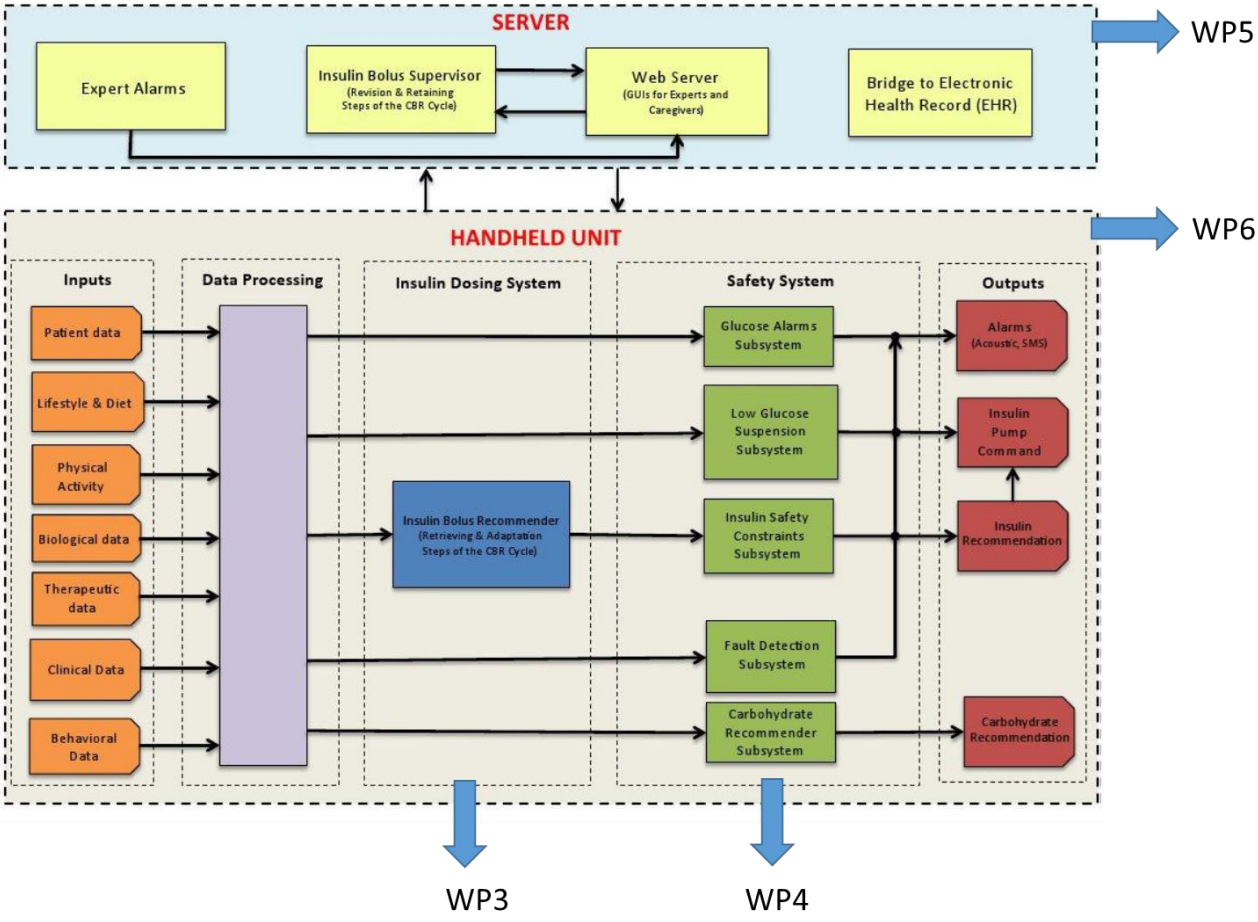


Fig 1. PEPPER architecture and the technical work packages related.

WP2. Customized remote usability analysis

The majority of the work on human factors since the last newsletter has been centred around processing the usability data obtained from the clinical validation study. This has two components: customized remote usability analysis and task-based user evaluation.

The first component uses PEPPER's customized analytics framework to illustrate how remote usability data can expose redundancies in the user interface design and reveal trends in user behaviour. We were able to combine data concerning user interactions with clinical data, including records of blood glucose levels. Preliminary findings showed that users spent significantly longer on the app during periods of hyperglycaemia and hypoglycaemia than at other times. We also found that participants using an insulin pump tended to have a more variable daily schedule of bolus recommendations than participants who used multiple daily injections. We are now in the process of extending the initial analysis to the data obtained over the entire study.

In addition, the results of the task-based user evaluation have been compared to the corresponding results from the first clinical feasibility study. This has shown many improvements in the usability metrics of the final PEPPER prototype in comparison with the original version.

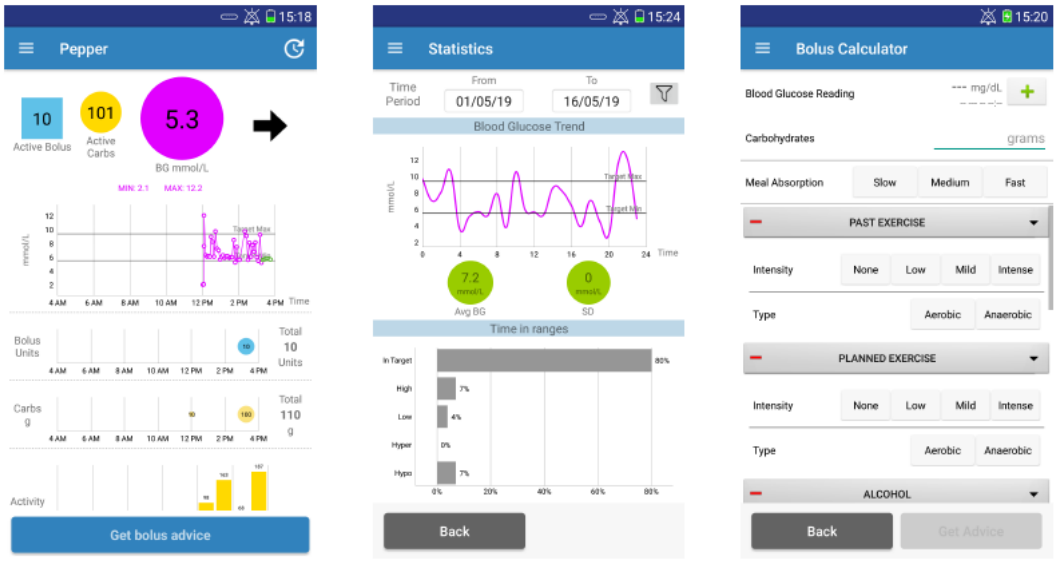


Fig 2. PEPPER app screens. Home Screen (left), Statistics Screen (centre), Bolus Calculator (right).

WP3. Case-base Maintenance of a Personalised and Adaptive CBR Bolus Insulin Recommender System for Type 1 Diabetes.

On 20th of December 2018 the work called "Case-base maintenance of a personalised and adaptive CBR bolus insulin recommender System for type1 diabetes" has been published[1]. The paper, outcome of the work done in WP3, proposed a maintenance system for the CBR (case-based reasoning system), that is the core of the insulin recommender system, in order to keep the system's response efficient and accurate.

The maintenance phase, seen in Figure 3, consists in: (I) decide if new cases will be stored in the case-base, (II) remove the redundant and useless cases and (III) weight the attributes according to its importance.

The proposed approach has been tested using the UVA/PADOVA type 1 diabetes simulator and demonstrated to accomplish with better glycemic control than other insulin recommender systems, when a large number of attributes is take into consideration.

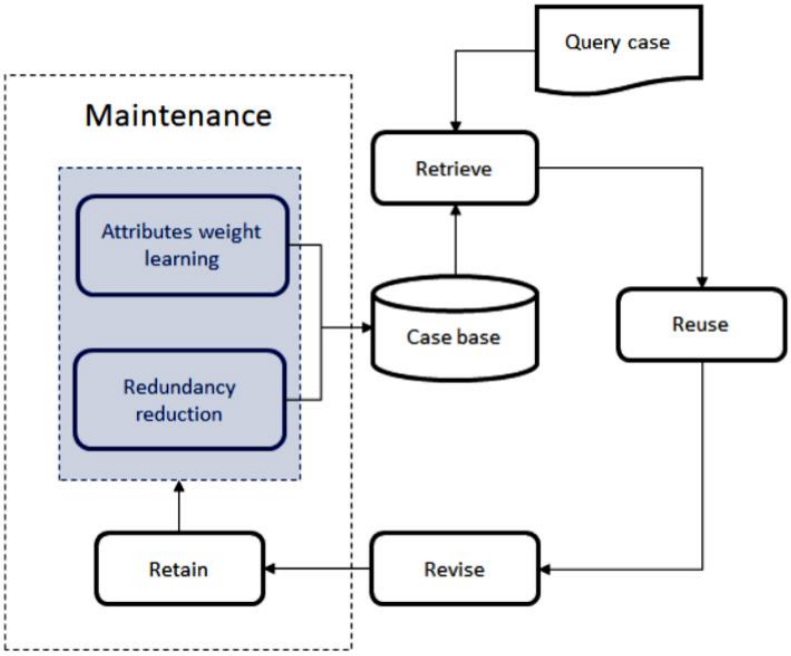


Fig 3. Methodology of the proposed bolus recommender system with new maintenance phase highlighted in a blue square.

[1] Ferran Torrent-Fontbona, Joaquim Massana, Beatriz López. Case-base Maintenance of a Personalised and Adaptive CBR Bolus Insulin Recommender System for Type 1 Diabetes. Expert Systems With Applications, 121, 338-3. http://hdl.handle.net/10256/16214

WP4. A Modular Safety System for an Insulin Dose Recommender: a Feasibility Study

One of the main outcomes of WP4 during the last period of the PEPPER project has been the clinically evaluation of the modular safety system that is the main outcome of WP4 [Liu et al JDST2020[2]].

The proposed safety system is composed of four modules which use a novel glucose forecasting algorithm. These modules are: predictive glucose alerts and alarms; a predictive low-glucose basal insulin suspension module; an advanced rescue carbohydrate recommender for resolving hypoglycaemia; and a personalised safety constraint applied to insulin recommendations. The technical feasibility of the proposed safety system was evaluated in a pilot study including eight adult subjects with type 1 diabetes on multiple daily injections over a duration of six weeks. Glycaemic control and safety system functioning were compared between the two-weeks run-in period and the end-point at eight weeks. The obtained clinical results show that the proposed safety system is viable solution to reduce the number of adverse events associated to glucose control in type 1 diabetes.

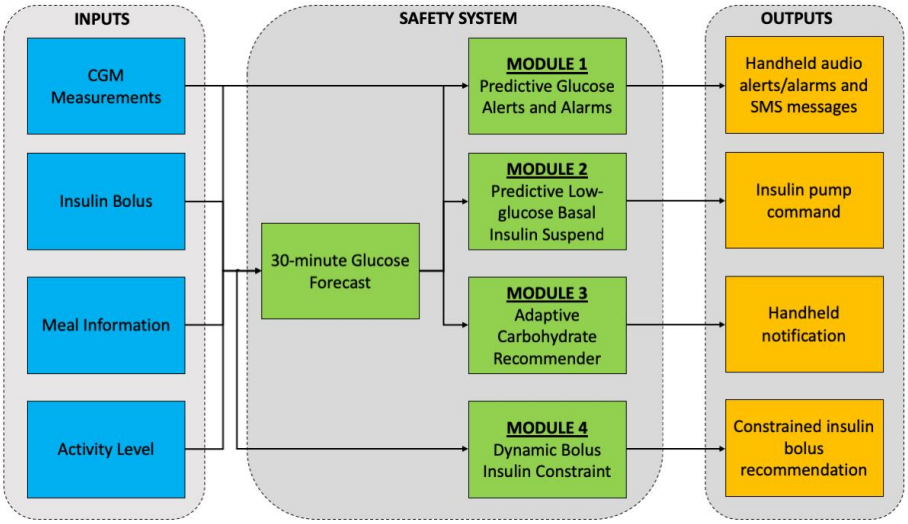


Fig 4. Block diagram of the safety system with the four modules, and corresponding inputs and outputs

[2] Chengyuan Liu, Parizad Avari, Yenny Leal, Marzena Wos, Kumuthine Sivasithamparam, Pantelis Georgiou, Pau Herrero, Nick Oliver. A modular safety system for an insulin dose recommender: a feasibility study. Journal of diabetes science and technology, 14(1), 87-96. 2020

A second main contribution of this WP4 is Long-Term Glucose Forecasting unit.[Liu et al Sensors 2020[3]].

Blood glucose forecasting in type 1 diabetes (T1D) management is a maturing field with numerous algorithms being published and a few of them having reached the commercialisation stage. However, accurate long-term glucose predictions (e.g., >60 min), which are usually needed in applications such as precision insulin dosing (e.g., an artificial pancreas), still remain a challenge. In this work, we present a novel glucose forecasting algorithm that is well-suited for long-term prediction horizons. The proposed algorithm is currently being used as the core component of the PEPPER safety system. In particular, it is being used by the predictive glucose alerts module, the predictive low-glucose basal insulin suspension module, and the carbohydrate recommender module. The obtained clinical results show that the proposed glucose forecasting algorithm is potentially well-suited for T1D management applications which require short and long-term glucose predictions.

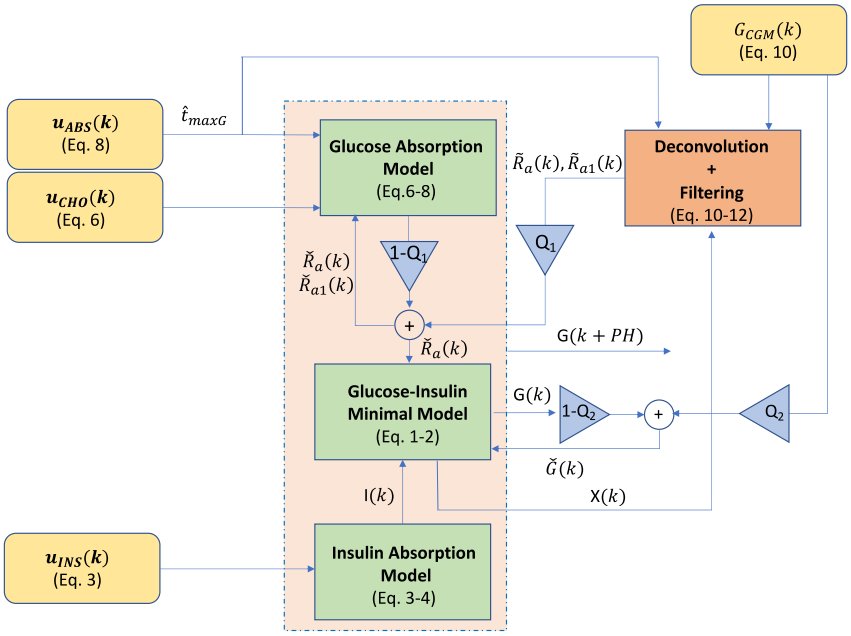


Fig. 5: PEPPER Glucose Forecasting Algorithm

[3] Chengyuan Liu, Josep Vehí, Parizad Avari, Monika Reddy, Nick Oliver, Pantelis Georgiou, Pau Herrero. Long-Term Glucose Forecasting Using a Physiological Model and Deconvolution of the Continuous Glucose Monitoring Signal. Sensors, 19(19), 4338. 2019 http://hdl.handle.net/10256/17048

WP5. New exploitation perspective

Based on the PEPPER project results, the RomSoft partner is building a new web platform (named EMIM) which intends to work as an ecosystem where the three main actors of the health care field patients-clinicians-pharmacists collaborate in order save, transmit and analyse patient data (https://www.emim.ro).

The new application will implement multiple functionalities for the health sector: medical data storage, physician-patient dialogue, online appointments, medical history, self-management disease and other.

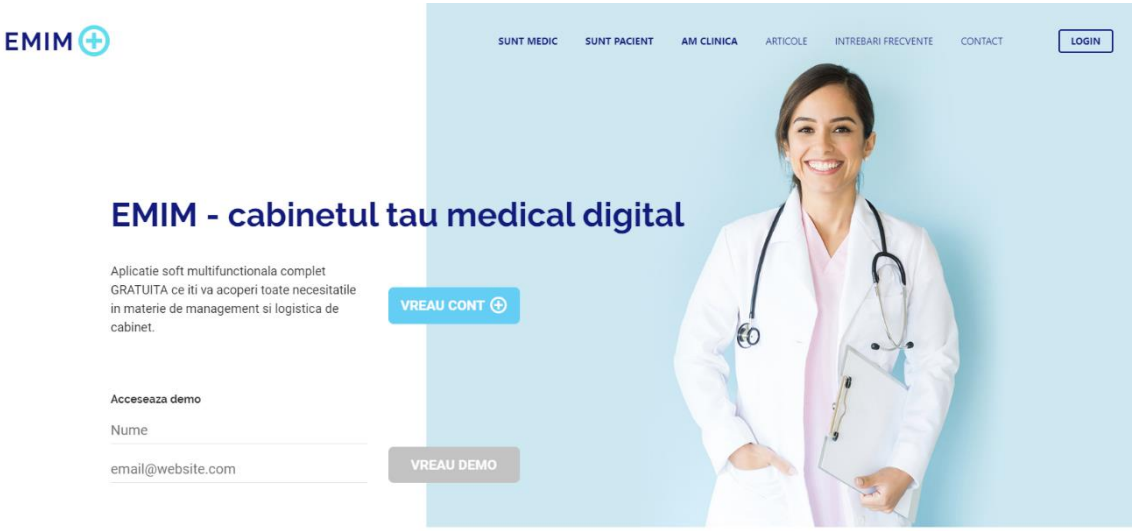


Fig. 6: EMIM landing page

The EMIM platform works as a data acquisition system where all users can upload documents, images, texts, animations, etc. and share these files with other users. Physicians can consult each other on the findings of laboratory results and save their comments on the document history.

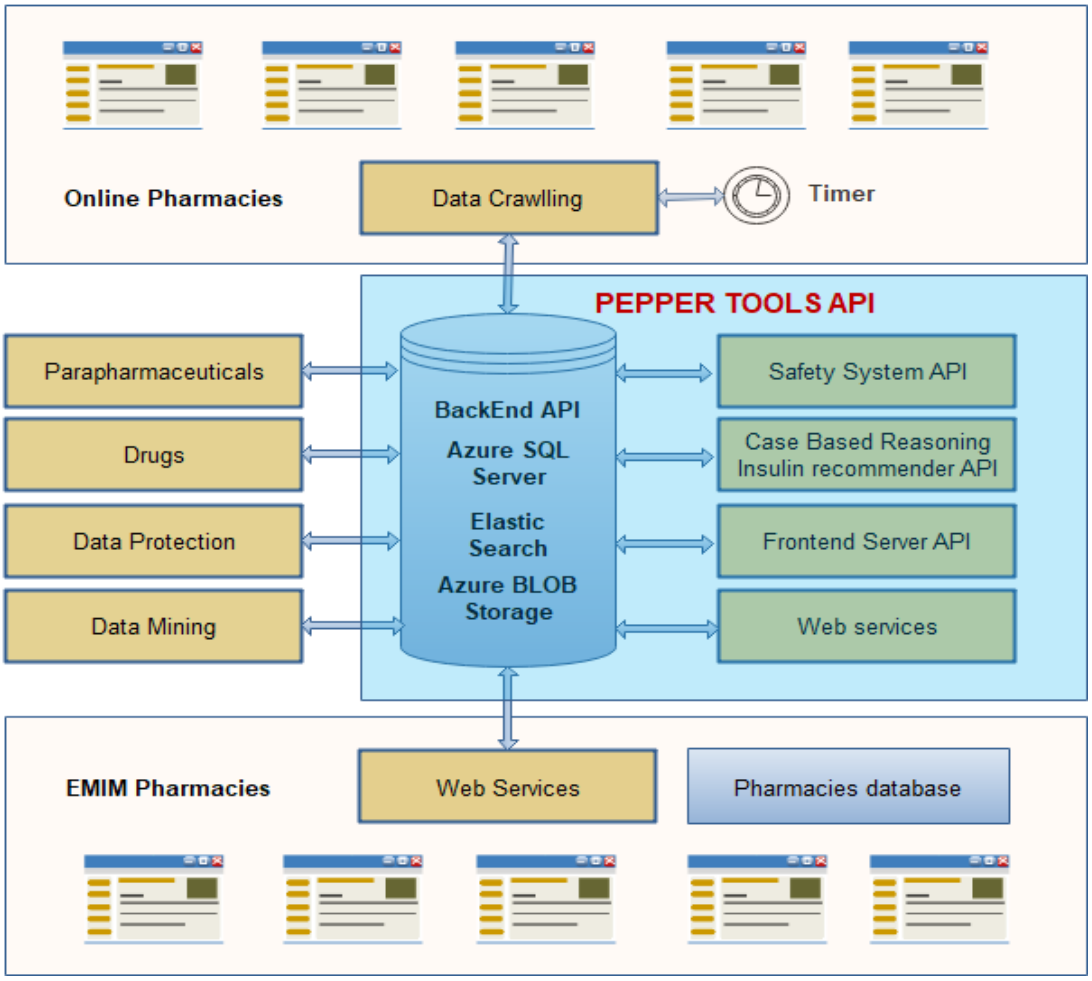


Fig. 7: EMIM Architecture

Also, the platform implements services which help the patients to manage the treatment for their chronic diseases (Self-Management Disease Services). For the beginning, the system implements such services for diabetic patients by assisting in the calculation of injected insulin doses, but in the future, more and more other services will be added. EMIM is an open platform, many other actors could contribute to expand the services area.

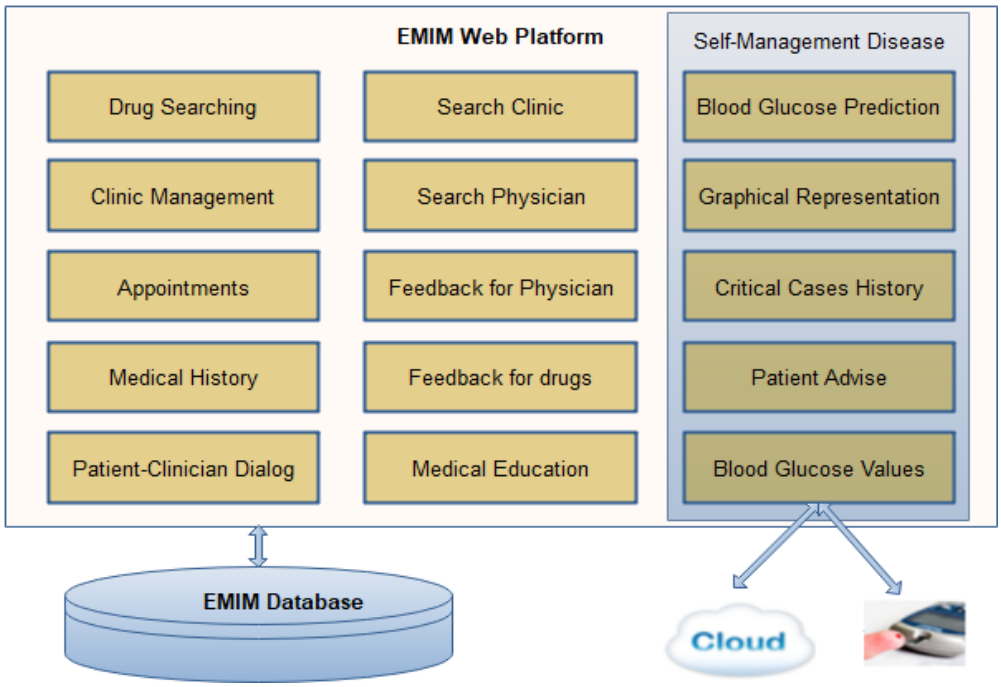


Fig.8: EMIM functionalities

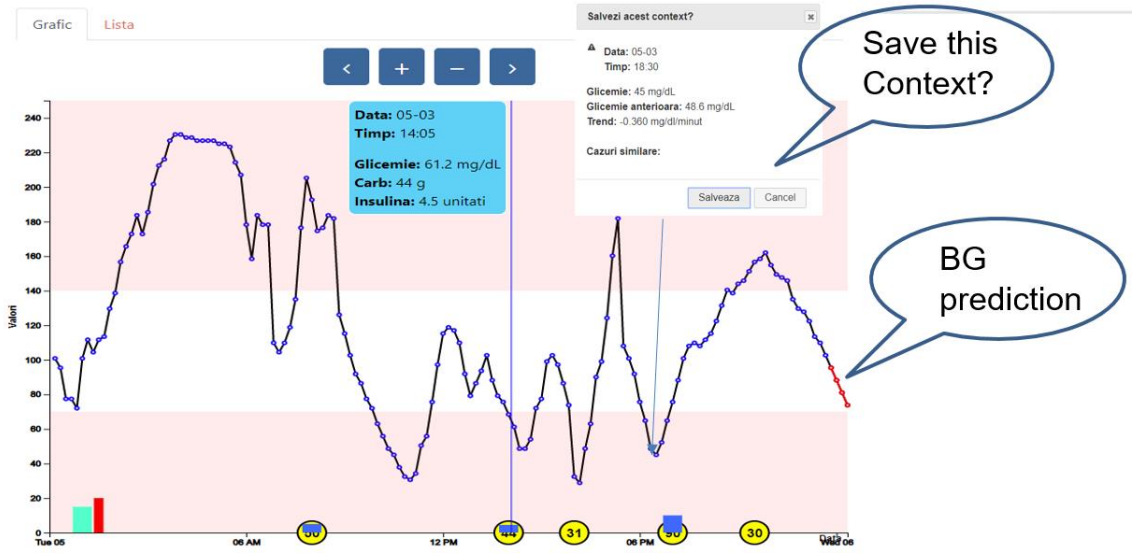


Fig. 9: Self management disease functionalities for diabetics

WP6. The PEPPER System Application Program Interface[4]

The PEPPER system, although initially designed to be used as a whole, is also possible to use its individual components independently. For this purpose, individual application program interfaces (APIs) for the different system components have been developed. In particular, these PEPPER API comprises: the insulin recommender; the safety system; the handset graphical user interface; the web interface (backend and frontend); and a high-level system architecture which allows interoperability between APIs. All APIs are developed in JAVA and use a JSON messaging system for communication between handset and server.

The PEPPER API provides a convenient way to integrate a variety of clinically evaluated software modules into an insulin decision support system or artificial pancreas.

The PEPPER API is currently available under different licensing agreements and its documentation can be freely accessed online at www.pepper.eu.com/API

[4] Pau Herrero, Joaquim Massana, Yenny Leal, Lucian Nita, Parizad Avari, David Duce6, Arantza Aldea, Pantelis Georgiou, José Manuel Fernández-Real, Mercedes Fernández-Balsells, Nick Oliver, Beatriz López, Clare Martin. The PEPPER System Application Program Interface. The 13th International Conference on Advanced Technologies & Treatments for Diabetes, Madrid (Spain) 2020.

III. Clinical preliminary results

The clinical partners, IDIBGI and ICL, have presented the preliminary results for phase 1 non-randomised open-labelled 8-week study to assess the safety system outcomes (without CBR-based insulin dosing decision support). Eight adults with T1DM on multiple daily injection of insulin (MDI) participated. Following two weeks of unblinded continuous glucose monitoring (CGM, Dexcom G5), participants completed six further weeks using CGM with the PEPPER safety system active. Baseline outcomes derived from the run-in period were compared with end-point. Participants were (median (interquartile range)) aged 38(31.8-53.5) years, with a diabetes duration of 22.5(18.0-26.5) years and HbA1c 63(57-66) mmol/mol. Percentage time in hypoglycaemia (<3.0mmol/l) significantly decreased from 0.82% at run-in to 0.33% at endpoint (p=0.02), with a significant increase in percentage time in target (3.9-10.0mmol/l; p=0.027). The total number of alarms to carers significantly decreased (p=0.005). There was also a reduction in number of carbohydrate recommendations. The PEPPER safety system is safe and feasible to use as a component of the overall system and to integrate with the PEPPER adaptive bolus calculator. The data suggest that the PEPPER safety system has the potential to enable improvements in hypoglycaemia and percentage time in range.

The results have been disseminated via two oral presentations at the International Conference on Advanced Technologies & Treatments for Diabetes (ATTD) 2019 and the XXX Congreso Nacional de la Sociedad Española de Diabetes (SED). The preliminary results for phase 1 of the feasibility study have also been published[5].

[5] Chengyuan Liu, Parizad Avari, Yenny Leal, Marzena Wos, Kumuthine Sivasithamparam, Pantelis Georgiou, Monika Reddy, José Manuel Fernández-Real, Clare Martin, Mercedes Fernández-Balsells, Nick Oliver, and Pau Herrero. A modular safety system for insulin doses recommender: a feasibility study. Journal of diabetes, science and technology. May 2019. http://hdl.handle.net/10044/1/71349

IV. Event participation

Members of the Pepper consortium have participated in the Barcelona HealthHub Summit at Barcelona, and the Engineering in Medicine and Biology Conference (EMBC) at Berlin, distributing information about the last project results.

Through the insights, it is important to highlight the diversity of new sensors that augure new opportunities to improve future versions of the Pepper system. On the other hand, Pepper has been built on the basis on explainable AI, conversely to other black boxes approaches. Finally, PEPPER team is sensible to the gender issues in engineering, and has participated in the special events organitzed in the conferences related to Women in Engineering, as the one held at EMB as illustrated in the Figure Below.

V. Meet us at ATTD

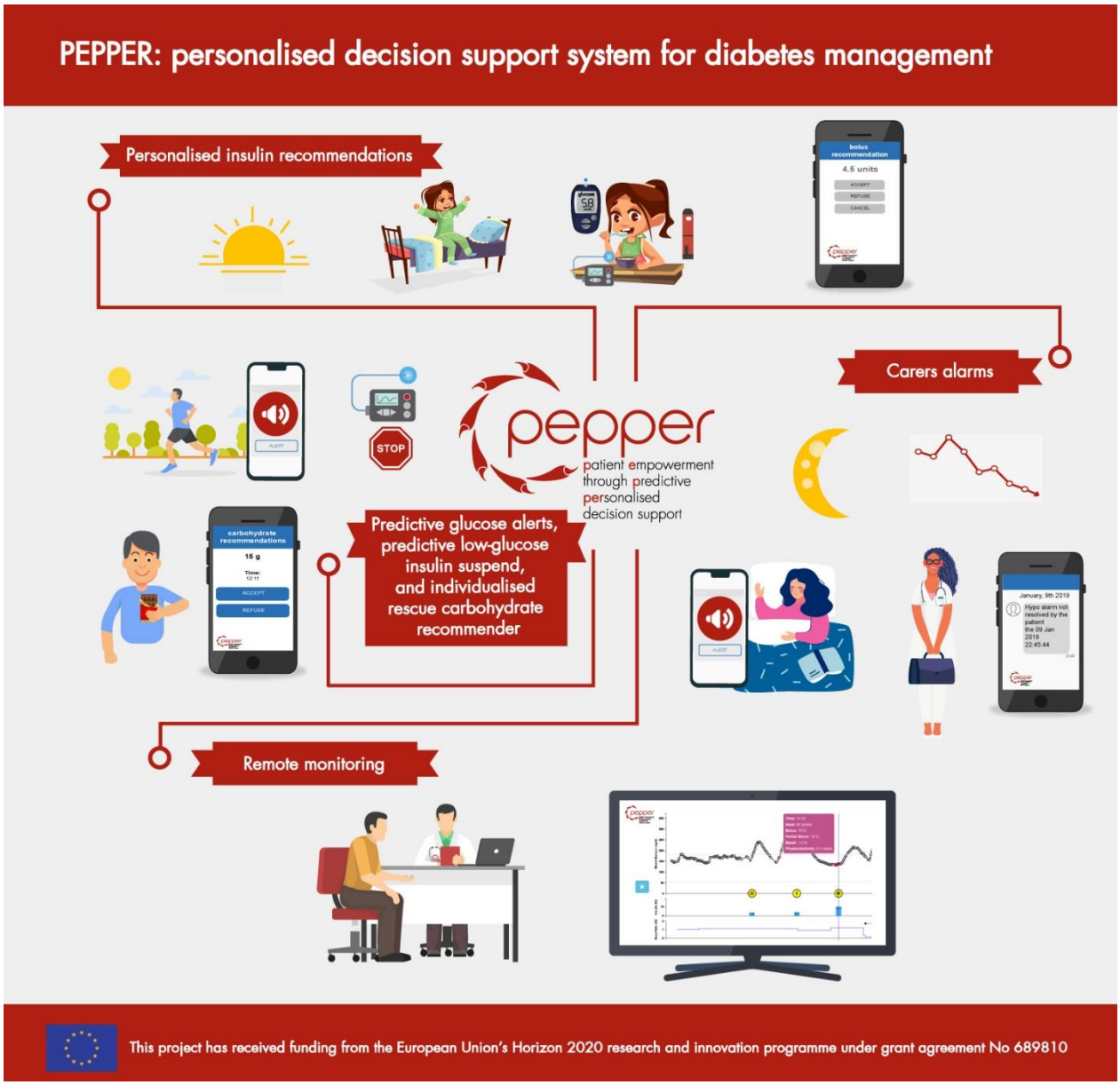
The PEPPER team will be at the 13th International Conference on Advanced Technologies and Treatments of Diabetes (ATTD) in Madrid, Spain on 19-22 February 2020. This year we will be presenting the preliminary results of the Phase 3 clinical trial, as well as qualitative findings from the contextual diary study in Phase 2 and the PEPPER system application program interface (API).

Please do come meet us! Details for presentations include:

1) Oral presentation by Arantza Aldea. Trust and contextual engagement with the PEPPER system: The qualitative findings of a clinical feasibility study. Thursday 20/02/2020 at 13:00hrs in Room Berlin.
2) Poster presentation by Herrero et al. The PEPPER System Application Program Interface. Posterboard Number: 65. Abstract ID: 949.
3) Poster presentation: Avari et al. Efficacy and safety of the Patient Empowerment through Personalised Decision Support (PEPPER) system: An open-label randomised controlled trial. Posterboard Number: 55. Abstract ID: 680.

Look forward to seeing you there!

VI. Infographic



VII. Profile: Clare

Clare Martin is a Principal Lecturer at Oxford Brookes University. She holds a BA in Mathematics (1985), and an MSc (1988) and D.Phil (1991) in Computation, all from the University of Oxford. Her D. Phil supervisor was Sir Tony Hoare FRS FREng.

Clare originally worked as a computer consultant before becoming an academic. Her research interests now include theoretical computer science and healthcare technology. Most of her early work involved using formal methods to reason about programs and specifications. In recent years she has also been conducting research into the usability of mobile applications in general, with particular interest in those designed for health, particularly diabetes management. Clare regularly serves on international programme committees in computer science.

Clare is currently working on a number of externally funded projects in diabetes technology and is the Project Coordinator for the PEPPER project. She is also leading on the user-centred design and evaluation components of the project.

VIII. Other related news

Diabetes: "How my new insulin pump lets me play football!"
https://www.bbc.com/news/av/uk-england-norfolk-49940291/diabetes-how-my-new-insulin-pump-lets-me-play-football

AI and ECG could provide an alternative to finger prick tests

https://www.diabetes.co.uk/news/2020/jan/ai-and-ecg-could-provide-an-alternative-to-finger-prick-tests.html

Sleep: why it's Crucial for Teens with Diabetes

http://www.diabetesincontrol.com/sleep-why-its-crucial-for-teens-with-diabetes/

IX. Future events

19th-22th February 2020 <> Madrid
13th International Conference on Advanced Technologies & Treatments for Diabetes
https://attd.kenes.com/

24th-26th June 2020 <> Oxford, UK
International Health Conference Oxford

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