mhealth platform for Parkinson's disease management

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***Abstract*— Parkinson's is a complicated, chronic disease that most people live with for many years/decades. For this reason, a multidisciplinary disease management, involving several professions working together (neurologists, physiotherapists, speech and language therapists, occupational therapists, dieticians), is important to ensure that the patient retains his/her independence and continues to enjoy the best quality of life possible. To address these needs we describe an mhealth ecosystem for Parkinson's disease (PD) management facilitating the collaboration of experts and empowering the patients to self-manage their condition.**

I. Introduction

PARKINSON'S disease affects people of all races and cultures. The facts are startling. Around 6.3 million people have the condition worldwide – that's less than one percent of the total population [1]. More than one million people live with Parkinson's in Europe today and this number is forecast to double by 2030 [2]. It is the second most common neurodegenerative disease (after Alzheimer's disease) and its prevalence will continue to grow as the population ages. The economic impact of the disease is high and its annual European cost is estimated at €13.9 billion [3].

Even though many different studies can be found in the literature addressing specific aspects of the disease there are only a few research efforts that adopt a holistic approach in order to address the disease management. The PERFORM [4], the REMPARK [5] and the SENSE-PARK [6] systems are intelligent closed-loop systems that seamlessly integrate a range of wearable sensors (mainly accelerometers and gyroscopes) constantly monitoring several motor signals of the patients and enabling the prescribing clinicians remotely assess the status of the patients, adjust medication schedules and personalize treatment. In addition, the REMPARK system includes a belt-worn movement sensor that detects in real time movement alterations that activate an auditory cueing system controlled by a smartphone in order to improve patient's gait. CuPiD [7] is a closed-loop system for personalized and at-home rehabilitation focusing on freezing of gait.

The PD_manager system proposes a holistic mobile approach based on a set of unobtrusive, simple-in-use, off-the-self, co-operative, mobile devices (a smartphone, an insole and a wristband). It covers aspects such as patients' and caregivers training and focuses on adherence to the medical recommendations. Moreover, the open, based on the Internet of Things concept, knowledge management platform that will be developed as well as the studies analysing the clinicians diagnostic and prescribing behaviour and the mobile apps for empowering patients adhere to nutrition and physiotherapy plans are novel and along with the effort to build a Decision Support System (DSS) that suggests modifications in the medication plan take the PD management a step beyond the existing systems.

The approach that is being followed for the development of the PD_manager system is:

Phase 1 - Modelling of the behaviours of intended users of (patients, caregivers, prescribing neurologists and other healthcare providers). User needs analysis will examine current practices around every-day and specialist management of Parkinson's disease, and identify where these practices may be enhanced or complemented by technological and/or process support. Detailed studies of the analytical strategies and knowledge sets used by expert health-care providers (e.g., neurologists undertaking diagnosis activities) will inform the design of a DSS embedded within PD_manager. At the same time, the policy and ethical framework under which Parkinson's disease is managed will be assessed. These outcomes of behavioural modelling will be validated within a computational modelling framework, which will establish the viability of, and constraints on, the PD_manager support environment.

Phase 2 - Assessment of symptoms (initially of motor with data collected prospectively from 20 advanced patients

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with motor complications). Obtaining long-term, objective information on motor status using an unobtrusive approach, that minimizes visits to the clinicians' office, is very important for the assessment of disease progression. Specifically, the patient, with the support of his/ her caregiver, will be able to monitor occurrence of motor symptoms such as tremor, dyskinesia, bradykinesia, gait, posture, balance, with the sensor insole, as well as the accelerometers of the wristband and of the smartphone that will provide the necessary raw data needed for that purpose. Data for non-motor symptoms, including the emotional state, cognitive status, speech disturbances and sleep disorders the patient may be experiencing will provide to clinicians a more complete picture.

Phase 3 - Analysis and validation of strategies that help physicians and healthcare professionals to search and evaluate the most diagnostic information (i.e., the information that is most relevant to help PD patients to cope with their symptoms, relief from them and make the best of their resources). Usually consultations are very short so the feedback needs to be short and integrated into the daily working routine of the health professional. Moreover, medical staff and patients usually decide the treatment plan and its modifications together – shared decision making. This decision making is on the basis of subjective experiences by the patient / carer (self-report), and on the basis of objective assessment (available thanks to PD_manager) of motor, cognitive, and non-cognitive symptoms, as well as the level of adherence to the suggested management plan (with information about medication, nutrition, physiotherapy and daily activity). Furthermore, objective data ought to be combined with subjective symptoms (e.g., depression, impulse control disorders, and cognitive dysfunction) referred to by the patients to gain a holistic view on the patient's state. This holds true especially at the stage in which PD patients' response to medications becomes unpredictable and clinicians have to make decisions about whether and what changes in the disease management should be made. Thus personalized suggestions for an optimal PD management plan will be provided by the PD_manager DSS that will be based on expert decision-making strategies and data mining and will be calibrated by the treating neurologist before referring it to the patient.

Phase 4 - System evaluation. 100 patients and 100 controls will be recruited during the pilot activities of the system. In addition to the evaluation of the usability and usefulness of the developed platform and mobile apps a detailed study for the potential of PD_manager as a new care model in terms of health outcomes, quality of life, care efficiency gains and economic benefits will also be conducted.

II. Material and Methods

A. Overall architecture

The PD_manager overall architecture is provided in Fig. 1. The mobile part, i.e. the gathering of data using as hub iOS, Android and Windows Phone devices and data transmission to the PD_manager cloud infrastructure, the implementation of mobile apps and their hosting will be handled by Globo's proprietary platform [8]. The cloud infrastructure (services, data management and storage etc.) will be hosted by Biotronics 3D [9].

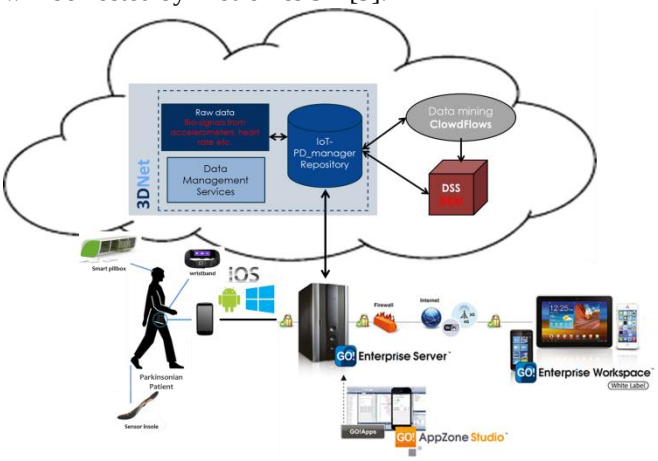

Fig. 1. The overall PD_manager architecture

The sensors, Clowdflows for data mining and analytics and Dexi for building DSS are presented in the next sections.

B. Data Collection

For the initial needs of the research activities, and especially for the monitoring and assessment of motor symptoms, data from 20 patients will be captured prospectively. Each of the Fondazione Ospedale San Camillo (in Venice), Fondazione Santa Lucia (in Rome), University of Ioannina and University of Surrey, will enrol 5 patients. The consenting hospitalised, enrolled patients will be asked to use the wristband and the sensor insole for 30 days at their home environment. The annotated data, which will be captured 24/7, include:

- Measurements for distribution of pressure, acceleration, weight-bearing, balance and motion sequences that will become available from the insole sensor manufactured by Moticon [10].
- Continuous heart rate patterns (with optical blood flow sensor), motion (with 3-axis accelerometer and gyrometer), skin conductivity measurements (with galvanic skin response (GSR) sensors), activity (metrics for steps, calories burned, duration accurately measured thanks to the built in GPS) and periods of restful and light sleep that will be captured with the Microsoft Band [11].

C. Motor Symptoms Evaluation

Tremor, Bradykinesia, Dyskinesia, Gait and Postural Balance will be assessed mainly with the OpenGo system (Moticon). The OpenGo is based on a fully integrated, ultrathin and flexible sensor insole (that can measure frequencies at 5, 10, 25, 50, 100 Hz). With respect to the analysis of motor symptoms, the sensor insole is capable to

continuously measure the centre of foot pressure (COP), the partial weight-bearing as well as the tri-axial acceleration. These parameters can serve for further analysis of staggering, dysbalance, gait variance, foot loading as well as for fall detection or position monitoring. Analysis of the motor symptoms of the upper limbs and body will be based on signals received from the accelerometers and gyroscopes built in smartphones and the wristband.

The most interesting results of the relevant, on-going research by the involved groups include:

- a methodology for the automated levodopa-induced dyskinesia (LID) assessment [12], [13]
- a method detecting freezing of gait (FoG) events [14]
- an automated method for analysis and detection of gait parameters, i.e. gait modelling in PD [15]
- a smart algorithm for the bradykinesia detection [16]

D. Data Mining

The PD_manager data mining module will address the problem of prediction of PD symptoms and their severity. The goal is to monitor patient's status, evaluate existing therapy and, when necessary, suggest the new therapy plan.

The study will consist of two phases. In the first phase the work will be done with raw data for patients' symptoms, therapy, adherence to disease management plans and any other available data to analyse the patients' status. The analysis will be done throughout the rule discovery process mainly with association rule mining algorithms. In the second phase methods for the automatic recognition of symptoms based on time series data will be developed. This prediction will be performed mainly by using decision trees. To improve the predicting accuracy, the possibility of using some ensemble methods, like bagging and boosting, will be explored.

The PD_manager data mining module will be implemented as workflows of data processing and data mining algorithms and will be included into the novel web-based data mining platform ClowdFlows [17]. The implementation of this module in the form of workflows provides the benefits of repeatability of such workflows and potential sharing results between different users. The platform has user-friendly graphical user interface which facilitates efficient feature selection, and wider selection of applicable data mining and machine learning algorithms even from non-experts such as the intended end users, i.e. the clinicians.

E. Decision Support System

The PD_manager's DSS supports the physician their monitoring of patients and deciding about their therapies. The DSS will employ mechanisms (models) that transform the stream of measured patient's data into suggested therapy plans. This is a complex and typically a multi-stage process. In the context of PD_manager, the two most important stages are: (a) from patient data to recognise symptoms (to identify patient's status), and (b) from symptoms to proposed decisions (to formulate necessary actions, treatment plans, prescriptions). For both stages, corresponding models will have to be developed and implemented in the DSS. However, it is unlikely that all the needed information could be extracted from data, which could also suffer from other possible imperfections (incompleteness, insufficient quantity, various errors and noise). For this reason, we will supplement the data mining models with expert-developed models. There are several possible ways to combine the two, for instance by model revision [18], where an initial model is developed by an expert and then algorithmically modified to better correspond to some given data stream. A similar approach can be used to address another difficult challenge in PD_manager, the need to personalize the DSS models to features of individual patients.

In PD_manager, the primary method for the development of expert-developed models will be DEX [19]. DEX is a qualitative multi-criteria modelling approach, aimed at the assessment and analysis of decision alternatives. DEX models have a hierarchical structure, which represents a decomposition of some decision problem into smaller, less complex sub-problems. The hierarchy is formulated in terms of qualitative (symbolic) attributes and decision rules. DEX has already been successfully used in healthcare [20, 21].

F. Mobile Apps for Patients, Caregivers and Clinicians

The mobile apps that will expose the decision support functionalities are:

- The clinicians' app through which periodic reports with major events for the patients will be available and suggestions for modifications will be made, mainly, for the medication plan based on the holistic picture of the patient. Moreover, clinicians will be able to collaborate with the other healthcare providers (neurologists, physiotherapists, speech and language therapists, occupational therapists, dieticians) involved in the management of PD patients.
- The patients' app through which recommendations for modifications in medication, diet, physiotherapy and activity will be sent to the patient.
- The caregiver app will have alerts when the patient is in danger, e.g. in case of falls. The app will also provide feedback about symptoms as well as the patient's adherence to the management plan in order to motivate him comply with it and improve his condition. Recommendations for plan modifications will also be sent to the caregiver in order to ensure that the patient will adopt them.

G. Evaluation – Pilot activities

The PD_manager system with the DSS in its core will be evaluated with the following approach:

Evaluation: outline of the stages of the clinical trial

- Ethical approvals and research governance will be completed in each site.
- Recruitment: 200 consenting patients with Parkinson's will be enrolled to the study through clinical centres in

Ioannina, Surrey, Venice and Rome. Patients with motor fluctuations and significant disability (Hoehn and Yahr stage 3 or greater) and with at least 2 hours off time during the day (based on MDS-UPDRS) will be eligible for the trial.

- Baseline data collection will be conducted in each site by a local researcher covering age, gender, indicator of social status, time since Parkinson's diagnosis, disease stage, medications, and comorbidities. Baseline recording of outcome measures will also be undertaken.
- Group assignment: Participants will be randomly assigned to receive either the PD_manager or to be in the control group (i.e. 100 patients in each group). Separate randomisation will be conducted for men and women to ensure an even gender distribution between the groups.
- Intervention: Participants and their caregivers will be trained in how to use the devices and the PD_manager apps. The devices will be unobtrusive. The insole and the wristband do not need to be initiated and they record 24/7. The responsible clinicians in each country will receive a monthly report with the most important information extracted for each patient and with the suggestions of the PD_manager DSS. On the basis of this information, the neurologist will be able to modify the management plan accordingly, and send these modifications to the patients and their caregivers through the mobile apps. The data captured by PD_manager for the 100 patients in the intervention group include: features from motor symptoms; emotional status data (stress, anxiety); sleep quality data; speech abnormalities; data for compulsive behaviours; cognitive status data; data for compliance with the suggested nutrition; adherence to medication data; activity data; physiotherapy data.
- Assessment of outcomes will be undertaken by researchers in each site at the end of the 60 day intervention period. Outcome measures are chosen to show effect of PD_manager:
  a) Clinical effectiveness (both groups) –a range of outcomes will be collected including PD disability, non-motor symptom scale, generic health related quality of life such as SF12, PD specific quality of life e.g. PDQ-8, psychological status, self-efficacy. For carers, the important measurement is the carer strain. Wherever possible, validated scales will be used.
  b) Views about the PD_manager will be collected from patients and carers by telephone interview (in intervention group only). Usefulness, usability and interaction with their neurologist will be explored. PD_manager will generate compliance data and this will be used to assess the extent to which the patients / carers valued using the devices.
  c) All health professionals involved in use of PD_manager will also be invited to take part in a telephone interview to gain feedback on their view of its usefulness, adaptability, interpretation of available data and interaction with the patients.
- An economic evaluation embedded in the clinical trial will assess the resource implications and costs of using PD_manager from the perspective of the health service provider. All health professionals will be asked to keep a log over the 60 day trial period of all activity and tasks they have completed related to the delivery of PD_manager. Using national pay scales, inclusive of on costs and overheads, the cost of the time spent for each professional will be calculated. The health professionals will be asked to keep a similar log for the patients in the control group so that an assessment of the cost difference in the delivery of care to the two groups over the trial period can be estimated. Patients and carers in both groups will also be asked to keep a diary of their use of health and social services during the study period (including that associated with PD_manager). Costs of this service use will be calculated and will be used to explore if PD_manager results in more or less overall service use.
- Data will also be collected from the PD_manager technical team about the costs of running the service (equipment and staff time).

III. Conclusions

The validated PD_manager system will be the first of its kind mhealth solution for the monitoring and management of patients suffering from Parkinson's. The system is applied and engages the whole healthcare ecosystem as it is shown in Fig. 2. The holistic approach described in this paper will combine traditional machine learning and decision support

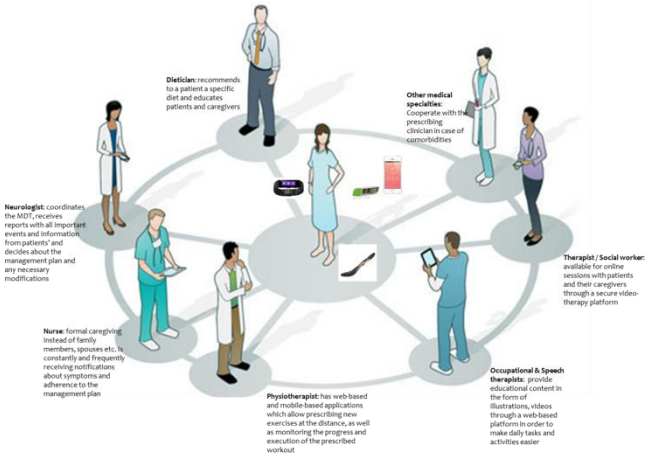

Fig. 2. The patient-centric, holistic approach provided by the PD_manager ecosystem

methods with modern mobile first and cloud based approaches in order to deliver an ecosystem for the management of Parkinsonian patients. Data on the clinical outcomes and from the qualitative feedback and economic evaluation will be brought together in a cost-consequences

framework that will show the benefits and costs of the system to different groups (patients, carers, neurologists, other HCP). The implications of findings for practice and future research needs will be consolidated.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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