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PancreApp: An Innovative Approach to Computational Individualization of Nutritional Therapy in Chronic Gastrointestinal Disorders

Konrad Stawiski[a], Alicja Strzałka[a], Anna Puła[a], Krzysztof Bijakowski[b]

[a] *Faculty of Medicine, Medical University of Lodz, Lodz, Poland*
[b] *Faculty of Computer Science, Electronics and Telecommunications, AGH University of Science and Technology, Cracow, Poland*

Abstract

Medical nutrition therapy has a pivotal role in the management of chronic gastrointestinal disorders, like chronic pancreatitis, inflammatory bowel diseases (Leśniowski-Crohn's disease and ulcerative colitis) or irritable bowel syndrome. The aim of this study is to develop, deploy and evaluate an interactive application for Windows and Android operating systems, which could serve as a digital diet diary and as an analysis and a prediction tool both for the patient and the doctor. The software is gathering details about patients' diet and associated fettle in order to estimate fettle change after future meals, specifically for an individual patient. In this paper we have described the process of idea development and application design, feasibility assessment using a phone survey, a preliminary evaluation on 6 healthy individuals and early results of a clinical trial, which is still an ongoing study. Results suggest that applied approximative approach (Shepard's method of 6-dimensional metric interpolation) has a potential to predict the fettle accurately; as shown in leave-one-out cross-validation (LOOCV).

Keywords:

Personalized medicine; nutritional therapy: machine learning; chronic gastrointestinal disorders.

Introduction

The experience of pain and complaints associated with gastrointestinal disorders determines patient's fettle and has an impact on the recovery rate. Nutrition therapy, although complex in nature, has a meaningful role in various gastrointestinal disorders such as chronic pancreatitis [1], inflammatory bowel diseases (Leśniowski-Crohn's disease and ulcerative colitis) or irritable bowel syndrome.

Pancreatitis is commonly defined as a continuous, chronic, inflammatory process of the pancreas, characterized by irreversible morphologic changes. For the majority of patients with chronic pancreatitis, abdominal pain is the most common symptom. This intermittent pain may worsen after eating or drinking. There is a sizeable list of reported etiological factors of pancreatitis which can be categorized into: (1) toxic and metabolic (connected mostly with alcohol intake), (2) genetic, (3) autoimmune, (4) recurrent acute or severe acute pancreatitis, (5) obstructive and, lastly, (6) idiopathic. According to a paper from 2008 by Shallu et al. the main issues in chronic pancreatitis are exocrine insufficiency and pain – which are also the two main reasons of diet regime and malnutrition in pancreatitis patients. Unquestionably, the dietary regime can soothe inconveniences and thus self-control is as crucial as clarity of recommendations [2]. However, guidelines may not be appropriate for every individual, thus personalization is needed. Lack of the individualization can affect directly the compliance, as guidelines are usually complex and can be misinterpreted by patients. Personalized therapy applied in other scenarios, has recently shown positive results [3, 4, 5].

Individualized diet can increase fettle and improve the compliance of patients suffering from chronic gastrointestinal disorders. Diet-related patterns are also being constantly searched for in inflammatory bowel diseases and in the irritable bowel syndrome. This is driven by the fact that etiology of these diseases is still unclear.

The aim of this study is to develop and evaluate a solution with the purpose of supporting patients' self-control and adjust diet to the best possible fettle based on an individualized machine learning model. The proposed solution iscalled – PancreApp (fig. 1).

Figure 1 – Logo of PancreApp project.

Materials and Methods

This paper describes the process of idea development and application design, feasibility assessment using a phone survey, preliminary evaluation on 6 healthy individuals and the earliestresults of the clinical trial, which is still an ongoing study (21 patients involved so far).

Idea development and application design

PancreApp is designed as a multiplatform, cloud-based digital diet diary, which not only enables regular control of the disease, but also tries to predict diet-related changes of fettle using computational methods. The application considers the details of diet and associated disease manifestations as input. The aim of the data processing is to provide patients with an individually computed multidimensional profile of their

disease which can be applied in the estimation of fettle for the next meals. In this model continuous acquisition of new data enables constant calibration of prediction; in general a concept of machine learning algorithms. (fig. 2)

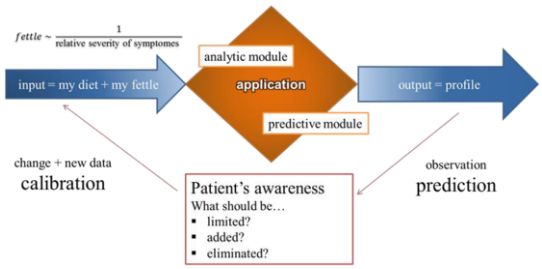

Figure 2 – Graphical representation of PancreApp core concept.

We developed two distributions of the software. The first one, for Microsoft Windows OS (using C# programming language based on .NET Framework CRL, Microsoft Visual Studio 2013 Professional) and the second one - a mobile version for Android OS users (JAVA programing language). Applications, being in bilateral connection with server (python-based, HTTPS protocol, XML format), allow the user to use software in every scenario. The application is harvesting data as the user is determining the diet and fettle after the meal (on a scale).

Entering data is facilitated by the fact that food products available in the market are almost always described quantitatively, based on basic ingredient content. It offers a possibility to count how much of the basic compositions (fat, carbohydrates, fiber, proteins and energy) the users consume during a selected meal and also provides patients with a possibility to archive their diet faster (via simple selection, rather than manual calculation). Our product database contains over 2200 products that are available in the Polish market. When the diet is known, users can define their fettle (associated with a particular meal). The fettle can be determined by the user on a scale from 1 to 10 (where 10 is the best) and should reflect the severity of symptoms. Screenshots of the general user interface are shown in figure 3.

The application, in addition to the prediction model, contains a reach analysis module wherein the patient can find statistics and charts visualizing his diet. The user can ,for example, put together the amount of of consumed fat and the associated fettle. This particular relationship may be clinically relevant in chronic pancreatitis.

The prediction model allows the user to estimate the fettle of future meals based on previous meals and fettle (training set). Its screenshot is presented in figure 4. Among all the methods, we were looking for a simple one that would give users results quickly, even on devices where central processing units have low clock rates. -, PancreApp's prediction model is using Shepard's method of 6-dimensional (multivariate) metric interpolation; as inverse distance weighting is the simplest interpolation method. Specifically, multi-dimensional euclidean distance is calculated and then applied for weighting. Fettle is predicted on the previously described scale and its value is specific for each patient.

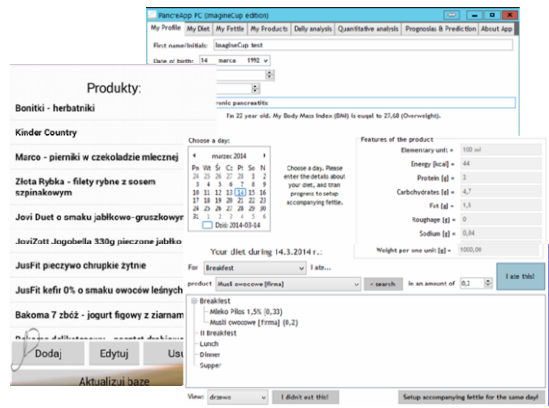

Figure 3 – Screenshots of PancreApp's general user interface. Right-sided pictures present the application for Microsoft Windows OS, left – for Android OS.

The latest version of the application is available for MEDINFO participants to download and test. Links are attached in the references. [6]

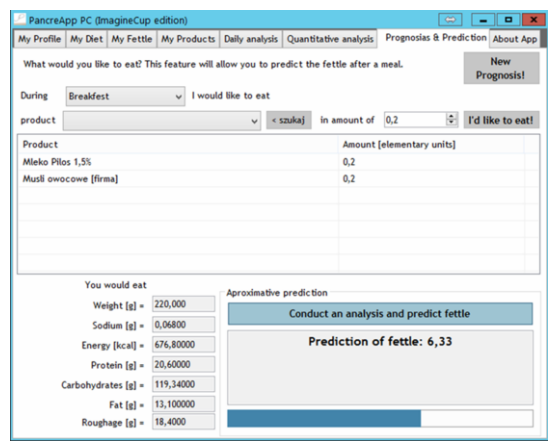

Figure 4 – Example of prediction.

Preliminary evaluation

Preliminary evaluation has been conducted on 6 healthy individuals that were using the software on a daily basis for 2 weeks. We focused on a comparison of relative difference between a real fettle set by the user and a potential prediction that could be calculated using the rest of the training set. This applied technique is henceforth referred to as the leave-one-out cross-validation (LOOCV). STATISTICA (StatSoft Inc.) and our proprietary software were used for data analysis.

We have also conducted a phone survey on 9 patients with chronic pancreatitis after pancreatic drainage/resection during the last 3 years to assess if the proposed idea reflects the needs of the target group. We asked about pain, depression (PHQ-9), food intolerance and access to a personal computer or to a mobile phone with Android.

Clinical trial

Since October 2014 this project has been financed by the Polish Ministry of Science and Education as a grant for student researchers. We enrolled adult patient-volunteers with chronic pancreatitis, inflammatory bowel diseases

(Leśniowski-Crohn's disease and ulcerative colitis) or irritable bowel syndrome. The only requirement was possessing a device with continuous access to the internet and the completion of the application tutorial. Enrolled patients were randomly divided into the control and experimental group and were then using the application for the 3 following weeks. The experimental group was able to use the prediction model, while the control group could use PancreApp only as a simple diet diary. At the beginning and at the end of the trial we measured patients' basic physical parameters and PHQ-9 score (assessment of depression that may affect compliance). To this day, 21 out of 100 patients (planned) have been enrolled into the trial, while 10 of them have finished it. In the analysis we want to assess how well this algorithm can predict fettle (by correlation coefficient and root mean squared error as well as LOOCV), how often the prediction model is used (frequency) and if patients experience time-related changes in fettle. We also want to analyze z-scores of fettle, compared to the amount of consumed basic compositions.

Results

During preliminary evaluation, the study group consisted mainly of young people with normal BMI (mean: 20.06; mean age; 24.3; mean energy consumed: 1408.4 kcal). Related-Samples Wilcoxon Signed Rank test showed that median difference between the well-being (fettle) value described by the tester and the well-being value predicted using Shepard's algorithm (based on all data except for tested; LOOCV) was not statistically significant (p=1.00). The absolute error of prediction was equal to 0.6454, while the relative error of prediction equaled 7.59% of fettle value.

The survey showed that studied patients with pancreatitis (mean age: 52.4) have a depression according to PHQ-9 score (fractions: minimal 0.11 vs. mild 0.55 vs. moderate 0.33). Food-specific intolerance was noted by 8 out of 9 surveyed patients. All surveyees were interested in participation. Only one of surveyed patients had a phone with Android OS. The rest of the patients would prefer using PC with Windows OS.

In this paper we would also like to describe the early results of the clinical trial that will end in May 2015. As described above, 10 patients finished the trial so far, however only 4 of them completed it successfully (used the application over the full testing period). The analysis of patients who dropped out has shown that 2 out of 6 patients were using the application irregularly (despite of reminders), 3 out of 6 never used the application after training meetings and were unreachable for further contact, while one patient was affected by a compatibility issue between .NET Framework 4.5, ClickOnce installer and Windows XP. None of the enrolled patients have , so far, decided, to use the Android version of the application. There was no significant difference between patients who completed the study and patients who dropped out, also in the PHQ-9 score. Patients presented a mean age of 29.8, weight of 68.6 kg, height of 176.2 cm and PHQ-9 score of 8.

The analysis of the 4 patients who have completed the trial so far, has shown good properties of Shepard's method. Two of those patients have Crohn's disease, one has ulcerative colitis and one irritable bowel syndrome. The chart in figure 5 presents the comparison between the predicted value of fettle and the real one, set by the user. Please note the distance between native data and ideal prediction showed by the red line. It is visible that a 95% confidence interval of regression almost contains the line of ideal prediction. The root mean squared error is equal to 0.80, while Spearman's correlation coefficient between predicted and real values is equal to 0.87 (p=0.000). Time-related changes and the usage of the prediction model will be assessed when the trial is completed. The performed analysis considered only whole days, without division into separate mealtimes.

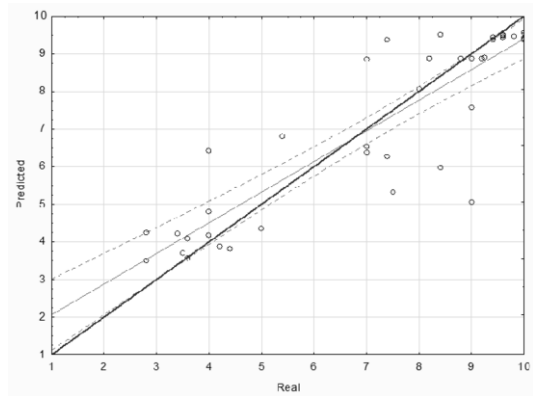

Figure 5 - Comparison between the predicted value of fettle and the real one. The solid thick line presents ideal prediction (f(x) = x), while the thin one (with concomitant dashed lines) shows the linear regression (and 95% confidence intervals). Analyses were performed for whole days. Please note that days without determined fettle change were excluded.

Discussion

Doctors of medicine frequently complain about therapeutic compliance. Lack of faith in treatment is one of the factors predisposing reduced compliance [7], while the therapeutic effect may be strictly dependent on feedback from a patient. PancreApp targets both problems. Machine learning and data-mining techniques are very promising and widely used in various aspects of science. The algorithm applied here is one of the simplest. It can, however, be quickly deployed in an everyday scenario (on low-end devices). It is also necessary to notice the need to test and compare different regression methods on data harvested from this study (retrospectively).

So far, the idea of PancreApp is appreciated by patients and doctors. Despite the fact that we have analyzed early results, from a clinical point of view the prediction accuracy of PancreApp is good. However, several limitations should be noted. Firstly, usage of fettle as a self-assessment of clinical state is disputable, and modern medicine is going to be focused on the quality of life rather than on simple survival. Also, the Hawthorne effect, or selection and technology bias cannot be excluded as a convenient sample is being enrolled. Patients without basic computer skills cannot either benefit from this study. However, based on the results, PancreApp seems to be intuitive enough for usage. Current compliance is in the expected range, as all patients (qualified so far) are in a remission state.

It is also notable that not one patient has chosen an Android device so far (even if they have such an opportunity), suggesting that personal computers are more approachable when it comes to complex data entry.

Conclusion

In this paper we present an innovative approach to computational individualization of nutritional guidelines. Early results from evaluation have shown that the applied approach has a potential to predict the fettle accurately and with low error. A possible broad spectrum of application (pancreatitis, obesity, kidney and liver disorders) encourages us not only to finish the current trail, but also to check whether PancreApp could be applied in different scenarios (diseases). Furthermore, PancreApp can be used in evidence based medicine as an easy available data-gathering service. The main advantage is the flexibility achieved by individualized models. Data collected by this tool could also be used in retrospective analysis of studied disorders, and as a source of valuable inferences. The software has been approved by the local ethical committee. More details about the project can be found at www.pancreapp.pl

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Address for correspondence

Konrad Stawiski, konrad@konsta.com.pl

Alicja Strzałka, alicja.strzalka@stud.umed.lodz.pl

General contact with authors: autorzy@pancreapp.pl