Optimizing IBD care – through digitalization and reinforced patient empowerment

There is currently a need to develop IBD care - partly in respect of increasing accessibility adapted to needs, and partly to offer patients a higher degree of active participation in their current treatment, for a greater freedom and quality of life.

The overall aim of the concept described in this document is - with reference to prediction, a more efficient healthcare chain and active patient involvement - to offer more needs-based and more accurate healthcare than at present.

The introductory work has been conducted as a Proof Of Concept (PoC) and the analysis is based on historical data from Karolinska University Hospital patients.

The PoC has shown a positive result why it is interesting to move forward and test the model in a real world setting and further validate the model and way of working.

Can IBD care be streamlined?

The hypothesis was that routine repeat visits to a centralised specialist clinic can be replaced by needs-based visits initiated by statistical predictions based on regular samples taken at a local healthcare centre or where the patients decide. Patients are divided into four categories:

1a – Active disease, has a current relapse or newly diagnosed.

1b – Active but not acute disease that requires continual contact with the medical team - for example adjustment of treatment or monitoring of immune suppressant drugs or biological treatment.

2a – Inactive disease that requires continual contact with the medical team - for example monitoring of immune suppressant drugs or biological treatment.

2b – Inactive disease in remission with no requirement for direct contact for monitoring of therapy - virtual follow up with yearly blood tests, faecal calprotectin and symptom questionnaire. Patient can contact the clinic between virtual contacts according to their need, (for example new onset relapse or change in circumstances such as pregnancy.

It is our assumption that these categories correspond to prediction periods for the occurrence of relapse at 3, 6 and 9 months respectively. Category 2b is not part of a prediction.

The health-economic evaluation of a new working method for IBD patients, grouped based on needs and status, shows that care becomes streamlined – days in hospital and expenses have dropped as well as patient quality of life has improved.

If a group division can be made based on the risk of relapse, supported by a prediction model/ algorithm, a division can be made continually, and normally without the patient routinely needing to visit their healthcare provider and without healthcare staff unnecessarily being taken away from other patient work.

The recommendation for the next stage is to establish a cloud-based service for use as decision support in the clinical IBD business setting. Based on the value flow and patient groups, and together with the profession, we can quickly and on an ongoing basis implement the adjustment of items such as the design of alarm lists and over-

view reports in line with the users' experiences being built up and an increase in appetite. With access to further patient data we can also fine-tune the created prediction model for use in both UC and Crohn's disease. We make the link to different types of data sources (such as mobile phone for registration of patients' Short Health Scale) in line with suitable apps becoming available on the market.

Background

IBD (Inflammatory Bowel Disease) is a group of inflammatory bowel disorders that cause patients a variety of symptoms, including pain, diarrhoea and anaemia, and is associated with different complications. A key aspect of these illnesses is that patients have very varying healthcare needs during the course of the illness. Patients may feel good for certain periods (which can be anything from a few weeks to years) to then suddenly develop a relapse. During the relapse, the patient needs increased contact with the IBD team and an intensification of treatment, which may include surgery. The aim of treating a relapse is for the patient to return to good health. Occasionally, between relapses, patients receive maintenance treatment with medication in order to prevent further relapse. This treatment is monitored through regular blood and stool samples even when the patient feels well.

Today it is hard to predict relapses and this means that some patients have routine healthcare contact unnecessarily, whilst it can be hard to find emergency ward times for the patients who have entered a new relapse phase.

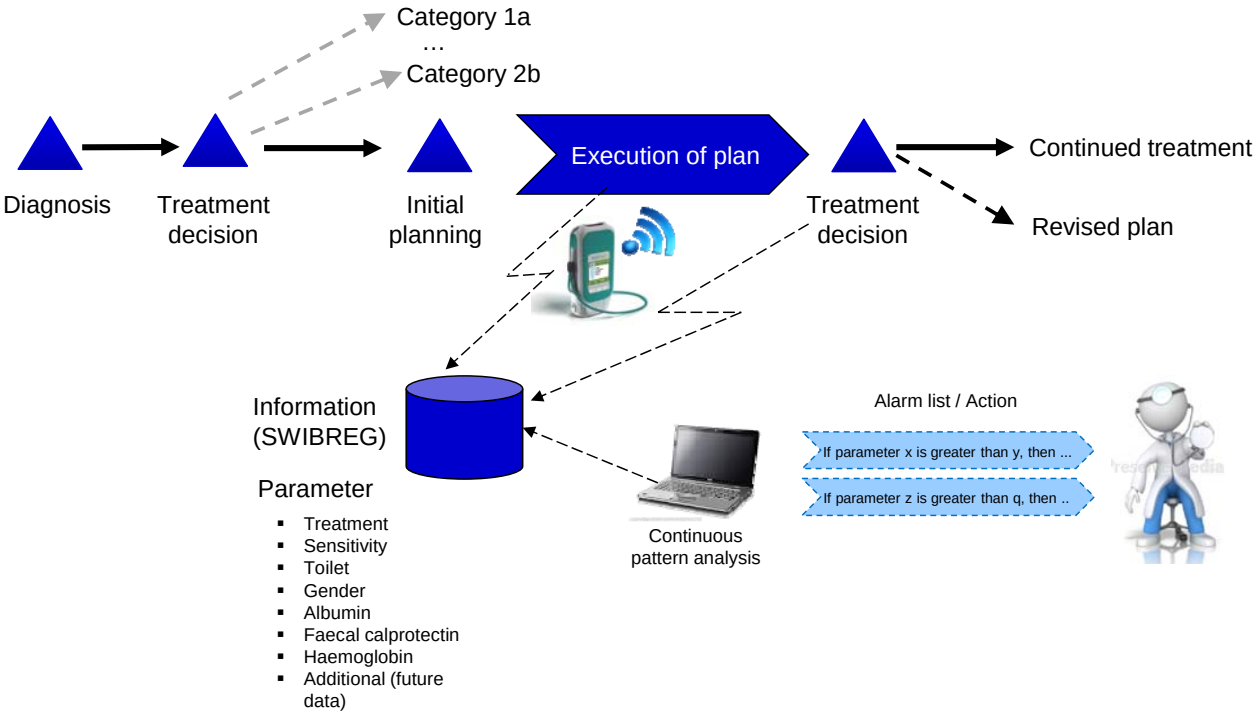
Current IBD care needs to be developed - partly in respect of increasing accessibility adapted to needs, and partly to offer patients a higher degree of active participation in their current treatment.

The quality of healthcare offered to IBD patients is impacted by the under/overuse and incorrect usage of existing resources. Underuse means that the resources do not reach the intended target groups. Overuse implies a waste of resources and that budgets are not adhered to. Incorrect usage has both financial and medical implications. These details, amongst others, are highlighted in a report from Institute of Medicine (IoM), Committee on Quality of Health Care in America, 2001 (Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC, USA: National Academies Press, 2001.). According to this report, healthcare operations should be based on 6 pillars in order to optimise the usage of existing resources: Safe, timely, effective, efficient, equitable and patient-centred care (STEEEP).

This means focusing on safety, to carry out medical interventions at the right time and for the right patient, to deal with resource usage/ economy (efficiency), to ensure a reasonable distribution between various patients and to have focus on the patient at all stages. If the healthcare meets these criteria, then our IBD patients will achieve a reduction in symptoms and a better quality of life, by us providing the best possible care under the circumstances within the organisation.

Aim & objective

The aim of the initiative is to describe, develop



and evaluate a proactive decision support concept for IBD remote care based on a new technology platform. The technology combines data capture and wireless transfer of patient data with pattern analysis and prediction of changes in patients' state of health. Depending on the predicted likelihood of a relapse over time, the patients are divided into different treatment groups.

The overall aim of the concept is - with reference to prediction, a more efficient healthcare chain and active patient involvement - to offer more needs-based and more accurate healthcare than at present, primarily from four perspectives:

- Patient – Increased accessibility, experienced patient satisfaction/increased quality of life for the patient and receiving healthcare with less travelling (SEK per hr for patient and healthcare)
- Doctors and nurses – Experienced work satisfaction, improved productivity (patients/mth and yr) including through increased resource efficiency (the right patient is given the right time and care resource based on clinical need) plus a positive waiting time effect in respect of fewer repeat clinic visits
- Healthcare system/Clinic – Quality/ effectiveness of treatment
- Society – Total resource usage within IBD care as a whole (SEK/yr).

Method and basis

Patient data was collected from SWIBREG (Swedish Inflammatory Bowel Disease Registry) and KUL (Karolinska University Laboratory). The selection of data is only taken from Karolinska University Hospital's IBD patients.

A study of the data quality was initially done to ensure that the information could be used in the analysis. Relatively few faulty values (such as date errors or unrealistic values) could be identified. SWIBREG lacks some data in respect of lab information prior to 2014, which is why supplementary lab information from KUL has been used. We assessed the quality of the lab data to be acceptable, and have therefore created the basis for analysis.

During the project, the definition of 'relapse' has been developed and established as follows:

- 1st definition element: Patients who are prescribed cortisone medication
- 2nd definition element: Supplemented with - if a prescription is written <90 days from the last prescription, then it is treated as the same relapse
- 3rd definition element: The strength of the medication as per the dosing in the table below
- 4th definition element: Establishing a diagnosis classed as a 1st relapse. Means that we are looking for subsequent relapses as goal variables for the analysis.

Patient data selection and cleansing

The prediction model is based upon clinical data for patients with Crohn´s decease, initially a data set with 1043 patients. A total of 74 000 lab data records for these patients were registered between 2006-02-03-> 2016-04-04. This data have been used as base for the model development.

Data cleansing have thereafter been performed:

- patient records has been removed if time between date of flare and lab date is <2 months or >12 months
- lab data has been grouped together if lab data samples have been registered within a 30-day interval.

As a result of the data cleansing a total of 837 unique patients remained.

Medication	Dose	Unit	Type	Comments
Budenofalk	9	mg	Capsule	9mg per day or more
Colifoam			Rectal foam	Regardless of dose
Cortiment	9	mg	Capsule	9mg per day or more
Entocort	9	mg	Capsule	9mg per day or more
Pred-Clysma	31.25	mg	Rectal suspension	Regardless of dose
Prednisolone	30	mg	Tablet or chewable tablet	30mg per day or more
Prednisolone	20	mg	Suppository	Regardless of dose
Other cortisone (rectal susp.)				Regardless of dose

The remaining data were then split in two groups where 70% were used for training the model and 30% for testing the model.

Finally an extended validation of the prediction model was performed for both Crohn´s (51 patients) and UC (26 patients) patients with new live data registered between 2016-04-07 – 2016-05-31. Only patients with complete lab data parameters (Albumin, F-Calprotectin and Haemoglobin) were included in the test.

Statistical analysis

The analysis was performed using the tool Statistica Enterprise and its in-built functions for statistics and predictions. Several models were built and tested with the aim of creating a model with strong predictive abilities and statistical significance. The final model chosen was Cox Survival method and has been designed for patients with Crohn's disease.

The final model contains the following variables:

- Gender
- Albumin
- F-Calprotectin
- Haemoglobin.

The model has been tested with these variables, plus time to relapse in number of months. The selected time periods were 3, 6 and 9 months respectively.

The result of the model is a likelihood score for 'survival' (not relapse) between 0-1 where 1 is high likelihood of survival, while 0 is low likelihood of survival (=relapse).

We have made a cut-off value, identified as 0.7. This means that values over 0.7 are predicted as non relapse, and values under 0.7 are predicted as relapse.

As shown in the table below, we obtained the following prediction outcome for the diagnosis of Crohn's disease (CD) and Ulcerative Colitis (UC).

	9 months	6 months	3 months
CD — Proportion of correct predictions	41%	55%	84%
CD — Proportion of missed relapses	12%	12%	8%
UC — Proportion of correct predictions	64%	80%	92%
UC — Proportion of missed relapses	4%	16%	8%

Health Economic evaluation

In order to conduct the health-economic evaluation, two cost-effective models for a flow change within, Stockholm County Council (SCC) were created. One simplified model (Model 0) not fully comprehensive.

In the more advanced model (Model 1), the conditions are split up further in the clinics relevant to the patient group being studied. Model 1 therefore has higher resolution, is more precise and is therefore used for analysis. For IBD patients, model 1 has 700 conditions, plus mortality.

When a patient visits a hospital within SCC, Karolinska Solna, Karolinska Huddinge or other, there are four possibilities:

- the patient comes as an emergency and is admitted as an inpatient
- the patient comes as an emergency visit as an outpatient
- the patient comes as a planned visit and is admitted as an inpatient
- the patient comes as a planned visit as an outpatient.

Each condition in the model is associated with a cost distribution and quality of life distribution specific to the illness studied - here, IBD patients. These are determined by analysing large quantities of patient data from hospitals and healthcare centres within Stockholm County Council (SCC).

IBD care within adult healthcare at Karolinska University Hospital currently has around 4,000 patients and 7,500 annual visits.

By focusing on the conditions associated with Karolinska in model 1, we obtained results from a Karolinska perspective.

As admission days are selected as endpoint, the cost-efficiency model (model 1) gives the following result.

For 2,790 patients, the cost savings would be SEK 76 million and 5,238 reduced admission days at Karolinska in a year, an average of SEK 27,104 and 1.88 care days per patient.

If QALY (Quality-adjusted Life Years) is selected as endpoint, the following result is obtained: For 2,709 patients, the QALY increase is 2 at Karolinska in a year, and on average the increase in QALY is 0.0007 per patient.

At Karolinska, the likelihood of reduced care days and costs for a patient is 99%, whilst the likelihood of an increase in QALY as per model 1 is 100%.

The health-economic evaluation of the new working method for IBD patients, where we group patients based on needs and status, shows that care becomes streamlined – days in hospital and

expenses have dropped as well as patient quality of life has improved.

If the group division is based on risk of relapse with support from a prediction model/algorithm, the division can also be made on an ongoing basis without patients visiting hospital and without healthcare staff needing to take time away from patient work.

Editorial information

This whitepaper is a compilation based upon the Proof of Concept Pilot study report **IBD pattern analysis and prediction** jointly performed by Karolinska University Hospital, Takeda Pharma AB and Bestor AB.

Edited by Fredrik Öhrn, Karolinska University Hospital and Bengt Olwig, Bestor AB.

Project team:

Anna Nauwelaerts de Agé	Consultant, Bestor AB
Bengt Olwig	Consultant, Bestor AB
Carolina Malmgren	Medical Advisor, Takeda Pharma AB
Fredrik Öhrn	Business Developer, Karolinska University Hospital, Center for Innovation
Johanna Brinne Roos	PhD, Karolinska University Hospital, Center for Innovation
Marjo Kapraali	MD PhD Senior Consultant Medical Department, Gastro Section at Danderyd Hospital Former Head of Gastro Section at Karolinska University Hospital
Per Rydingsvärd	Business Unit Director, Takeda Pharma AB
Örjan Andersson	Consultant, Bestor AB