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Functionalities development for IBD Tool, an italian web-app for Inflammatory Bowel Disease monitoring

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To all the people who support me

Abstract

This thesis is based on functionalities development for IBD Tool, a web platform created and developed specifically to manage patient monitoring for IBD (Inflammatory Bowel Disease) tele-care. This project was born in 2020 from the collaboration between *LINKS Foundation* company and the *Gastroenterology department of the Mauriziano Hospital* in Turin. The main goal of the entire project is a study that wants to demonstrate, using this web platform, how a telemedicine service can offer advantages compared to a traditional care service. Additionally, this project wants to make IBD Tool a gold standard in the clinical practice of IBDs. This thesis aims to enrich the platform with new functionalities supporting the physicians' requests, to build a more efficient web platform.

The platform is based on the automatic administration of specific questionnaires, which assess: the state of the disease (remission or relapse), the effectiveness of therapy, the impact of the disease on the quality of life, and psychological aspects. The various types of questionnaires are sent by email and notified directly by the platform. There are also clinical questionnaires which are filled in by the physician and which are compared with the patients' ones. The platform composes of two main parts: the backend and the frontend. The backend encapsulates all the logic of the system, it has been developed using Java, an OOP (Object-Oriented Programming) language, and Spring Boot. The frontend was developed by using Angular, Typescript, HTML (Hypertext Markup Language) and CSS (Cascading Style Sheets) files, which contains all the interfaces that the user sees. The communication between these two parts takes place through the HTTP (Hypertext Transfer Protocol) protocol. All the data are stored in a database based on documents, which is Mongo DB. Two main users are present in IBD Tool: physicians and patients.

Through this thesis it has been possible to enrich and improve the platform. One of the first results has been the revision of questionnaires by updating them and inserting new ones. Some features have been added on the side of medical staff. The most innovative feature has been a dashboard which permits to monitor in real time the total number of global and personal patients divided by pathology, the total number of inactive users, the total number of never logged ones, and the total number of patients with a certain pathology in remission or relapse. All

these data are included in a in a very organized interface, which makes information easily accessible. Then, following the physicians' need to carry out a concordance study, it has been created a special section that allows clinicians to download tables in Excel format. In these tables the scores of the questionnaires compiled both by physicians and patients, within the same time span, are associated. Another important section that has been added during this thesis comprehended the new clinical variables previously not present in the application, which now are easily to insert and re-display from the patient dedicated page.

IBD Tool is an ever-growing application, and in the future, it may be integrated with any other functionality that makes it more and more avant-garde. The platform is constantly evolving following the requests of physicians. IBD Tool has led to many results in patients monitoring and aroused a lot of interest in clinical practice, being a first step towards a more telemedical future.

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List of Acronyms

5-ASA: 5-Aminosalicylic Acid
be: backend
CD: Crohn's Disease
CRP: C-reactive Protein
CRUD: CREATE, READ, UPDATE and DELETE
CSS: Cascading Style Sheets
DI: Dependency Injection
EQ-5D: EuroQol instrument
EQ5D5L: 5-level EQ-5D (European Quality - version 5D - 5 Levels)
fe: frontend
GCS: Glucocorticoids
HADS: Hospital Anxiety and Depression Scale
HBI: Harvey-Bradshaw Index
HTML: HyperText Markup Language
HTTP: HyperText Transfer Protocol
IBD: Inflammatory Bowel Disease
IBD-DI: Inflammation-Bowel-Disease Disability Index
IBDQ: Inflammatory Bowel Disease Questionnaire
ICT: Information and Communication Technologies
IoC: Inversion of Control
IPAQ-SF: International Physical Activity Questionnaire Short Form
JSON: JavaScript Object Notation
MET: Metabolic Equivalent Task
MIAH: Monitor IBD At Home
MMAS-8: 8-item Morisky Medication Adherence Scale
MST: Malnutrition Screening Tool
OOP: Object-Oriented Programming
PC: Personal Computer
PHQ9: Patient Health Questionnaire-9
PRISM: Pictorial Representation of Illness and Self Measure
PSQI: Pittsburg Sleep Quaity Index
SCCAI: Simple Clinical Colitis Activity Index
SF-12: Short Form Health Survey
SFQ: Shortened Fatigue Questionnaire
SIDBQ: Short Inflammatory Bowel Disease Questionnaire
SMTP: Simple Mail Transfer Protocol
SNAQ: Short Nutritional Assessment Questionnaire
SSL: Social Support List
TSQM: Treatment Satisfaction Questionnaire for Medication
UC: Ulcerative Colitis

URI: Uniform Resource Identifier
WHO: World Health Organization
WPAI: Work Productivity and Activity Impairment

Chapter 1

Introduction

1.1 Inflammatory Bowel Diseases in Covid-19 scenario

During the last year, worldwide and especially in Italy, attention has been decentralized on chronic diseases to address the health emergency due to Covid-19. However, these diseases continued to affect people in silence and caused a lot of complications due to the impossibility to offer to patients a proper care. It is possible to attribute the major causes to the healthcare system that was unprepared to deal with a pandemic and it did not have the proper infrastructure to deal with a big emergency. Proper infrastructure is synonymous of an available telemedicine healthcare service which could offer a continuous monitoring of patients. Telemedicine should not be taken into consideration only for patients with early Covid-19 symptoms, but it should be adopted also for patients with chronic diseases, which care should not be neglected or postponed due to pandemic [1]. Telemedicine's use increased a lot during the pandemic, especially in terms of video-based telemedicine. Some data from USA show how in few weeks the number of patients and providers raised 8000 in a single day [2].

Referring to some Italian data related to the 2020, telemedicine's interest usage among general practitioners increases in all its applications [3]:

- Tele-consultation with other general practitioners increased from 17% in Pre-COVID-19 to 59%

- Tele-consultation with specialist physicians increased from 16% in Pre-COVID-19 to 72%

- Tele-assistance increased from 12% in Pre-COVID-19 to 60%

- Tele-examination increased from 11% in Pre-COVID-19 to 54%

- Tele-monitoring increased from 11% in Pre-COVID-19 to 63%

- Tele-rehabilitation increased from 5% in Pre-COVID-19 to 34%

Among chronic diseases, the focus is on IBD (Inflammatory Bowel Disease), as Crohn's disease and ulcerative colitis. In Italy there are 200-250 thousand of people suffering of these diseases, whose peak of onset is between 15 and 30 years, even if one case out of 5 is already recorded in pediatric age [4].

Nowadays, the incidence of these pathologies is around 10-15 new cases per 100 thousand inhabitants per year, with a prevalence of about 302 patients per 100 thousand inhabitants. These pathologies are chronic and accompany patients for the rest of their life, so there is not a definitive cure, even if mortality is low [5]. In the Italian Covid-19 scenario some necessary cures and surgeries related to IBD patients were postponed, augmenting the risk of complications and of emergency services. This confirms that it is difficult to maintain a high standard quality of care with the traditional system of care [6].

In this context, the idea that telemedicine is an essential tool is increasingly gaining ground, the only one which guarantees continuity of care in emergency situations and which, in non-emergency situations, encourages an increase in the level of care itself. To be able to take advantage of a tool like this, a basic preparation is required, which includes the presence of the necessary infrastructures and reliable security systems.

This thesis aims to offer a complete telemedicine web application that can help physicians to attempt at monitoring patients with IBDs, ensuring the quality and the continuity of care. The main target is to provide a service which could be integrated in the traditional care by demonstrating how a telemedicine approach can facilitate the dialogue between patients and clinicians, and offer a continuous overview of how the disease is evolving. Despite its use until now, telemedicine should be considered as a mean through with the entire healthcare system should improve and bring itself up to date and not only a service designed for emergencies [1].

1.2 Telemedicine and IBD

Telemedicine is a term that was first used in the 1970s and its meaning is "healing at a distance". It refers to a new way of conceiving diagnosis, care, and treatment that was not born to replace traditional treatments, but to support and accompany them. Several studies showed that telemedicine does not require very expensive equipment, but it is accessible, and it even manages to reduce costs and improve the quality of care [7].

Telemedicine spread after the evolution of ICTs (Information and Communication Technologies) for healthcare. Talking about telemedicine or "e-health" (which

means electronic-health) is the same thing and it always refers to every medical assistance at a distance, in most of the cases using Internet. The WHO (World Health Organization) in 2010 declared that the Telemedicine is an ever-developing science and embraces a lot of different definitions. However, there are four essential elements that can be attributed to it. They are [8]:

- the intention to provide clinical support

- the intent to go beyond all barriers, especially geographical ones

- the use of ICT

- the intent to improve the health system

Also, the WHO in 2010 dealt with distinguishing telemedicine in various categories. Taking into consideration the type of interaction, telemedicine can be between physician and physician or physician and patient. On the other hand, considering the timing of the interaction, this can be synchronous (real-time) or asynchronous (store and forward). Moreover, the type of exchanged information can be different (e.g. text, audio, video, etc.) [8].

Telemedicine has been used a lot for chronic diseases, demonstrating how it is really a good practise which leads a lot of advantages (e.g. lowering of healthcare costs). Telemedicine in IBD has been applied in terms of:

- telemonitoring

- teleconsulting

- tele-education.

When it comes to telemonitoring, everything from diagnosis to patient follow-up is included. To be able to carry out an adequate telemonitoring, there is certainly a need for a specific infrastructure and a good communication system. Telemonitoring can also be carried out with web-based systems which are advantageous because they reduce installation costs. Teleconsulting refers to the search for information and the information exchange that takes place between medical specialists. Therefore, data, approaches and information are often sought not only within one's own medical team, but also outside to form a real multidisciplinary team. Finally, tele-education serves to ensure the dissemination of proper knowledge through the provision, for example, of distance courses [9].

1.3 The role of IBD Tool

Covid-19, beside all its negative aspects, has finally led the telemedicine at the center of interest. Discovering that telemedicine, teleconsulting, and telepresence

are good instruments to manage patients without distinction has been the first important step to a more modern care service. The real telemedicine's advantage is that the care process becomes fast, safe, effective, and less expensive [10].

IBD Tool is an example of how physicians can remotely manage and control the evolution of the disease, contact the patients if something goes wrong through e-mails and chat. Also, the patient feels safe, always monitored, and he can control his conditions through the web platform by consulting his data. An important aspect of this web application is the focus not only on the single patients, but also on the globality because it allows to have an overview on the global impact of the disease. One of the main goals is to prevent sudden visits to the emergency, detecting in advance any patient relapses. Another goal is certainly the patient-empowerment: the patient, thanks to his personal page in the web-app, is able to consult all the completed questionnaires and he can contact the physician at any time through a dedicated chat. In this way, the patient feels much more active in the treatment of his illness and much more aware.

IBD Tool also allows to collect a large amount of data, and this represents a starting point for many studies that can be conducted, some of which has already been started. One is the concordance study between senior-physician and junior-physician and also between a physician and patient, by comparing the scores of the questionnaires. These questionnaires are administered by the web-app and filled in by both the physician and the patient. Another study is the evaluation of the questionnaires scores, trying to find some new patterns amongst the state of the disease and questionnaires.

Despite all the positives, there are still barriers that need to be overcome (Figure 1.1). One of this is the patients' fear that telemedicine will completely replace traditional medicine, losing the physical contact with the clinician. This fear must certainly be eviscerated because "telemedicine" does not mean "replacement", but rather "support" for treatment. The actual use of IBD Tool is as a support instrument to the usual visits that are conducted between clinician and patient. Another important aspect is that there are still some technological barriers which cause the impossibility to use IBD Tool everywhere. Some of them are:

- the difficulty in using devices such as smartphones or PCs (personal computers) for uneducated people

- the difficulty in having a stable internet connection to be able to establish remote communication

- the distrust of users on the effectiveness of telemedicine and new technologies.
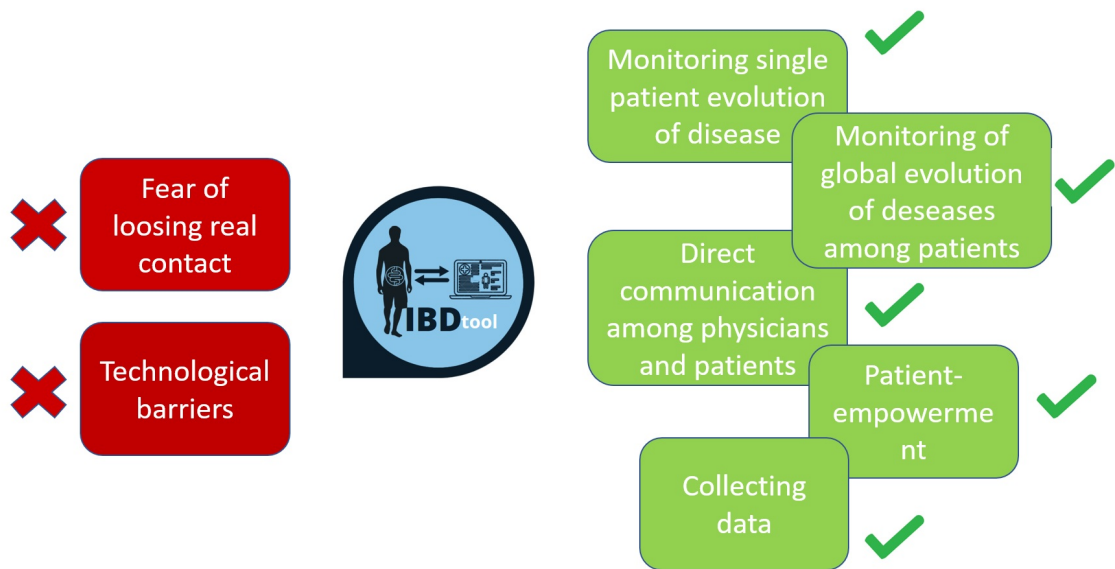
Figure 1.1. Positive and negative aspects related to the usage of IBD Tool.

Chapter 2

IBD: a medical point of view

Crohn's Disease (CD) and Ulcerative Colitis (UC) are the two main autoimmune pathologies which stand down the acronym of IBD. CD can involve any part of the gastrointestinal part (in the 90% of cases ileum is the most affected), while UC mainly focuses on colon tract. IBD is characterized by a chronic intestinal inflammation and its etiology is still unknown. Its pathogenesis involves four main different risk factors: genetic susceptibility, external environment, intestinal microbial flora, and immune response. Among environmental factors one of the most important is smoke, which has a different role in the two diseases: it is an important risk factor in CD, while in UC it seems to have a protective effect. Other risk factors are the presence of Vitamin D, the use of nonsteroidal anti-inflammatory drugs, the use of antibiotics, stress, depression, anxiety, and air pollution [11][12].

2.1 Symptoms and Complications

The real challenge about these diseases is trying to do a diagnosis as soon as possible, because all these symptoms are easy to exchange with other common pathologies. The most frequent symptoms of CD are:

- diarrhea

- abdominal pain

- articular pain

The UC is mostly characterized by:

- abdominal pain

- bloody diarrhea, containing blood and mucus

- tenesmus

- anemia

Both the diseases can be silent in some periods and then reappear flaring-up together with other symptoms like fever, weight loss, profound tiredness, and loss of appetite. Complications related to CD are due to ulcers which can lead to the formation of abscesses, fistulas, and strictures which often require surgery; complications related to UC are toxic megacolon and cancer, especially when disease is not treated [11][12].

2.2 Diagnosis

A series of common tests are conducted to diagnose the two diseases, including colonoscopy with ileum visualization and intestinal biopsy and ultrasound of the intestinal loops. Some specific tests for UC are:

- narrow band imaging

- fecal calprotectin

- abdominal x-ray [12].

Specific tests for CD are:

- abdominal magnetic resonance with contrast agent

- entero-CT with contrast medium

- esophagogastroduodenoscopy

- enteroscopy with videocapsule

- surgical exploration under anesthesia [12].

However, the 10% of people suffering of IBD can not reach easily a diagnosis because there is not a gold standard procedure and the biggest problem is the uncertainty. Furthermore, another big issue is that over time the diagnosis can change and a patient with CD can become a patient with UC. In addition to CD and UC, there are other forms of colitis that are not classifiable and go under the term of "inflammatory bowel disease unclassified". The issue of differential diagnosis is very important for the definition of the correct treatment. In general, to make a diagnosis, a lot of clinical evaluations are carried out based on endoscopies (upper and small-bowel endoscopy), radiological examinations, Ileo-colonoscopy, histological examinations, and biomarkers analysis as the CRP (C-reactive protein), fecal biomarkers and immunologic biomarkers (Figure 2.1) [13].
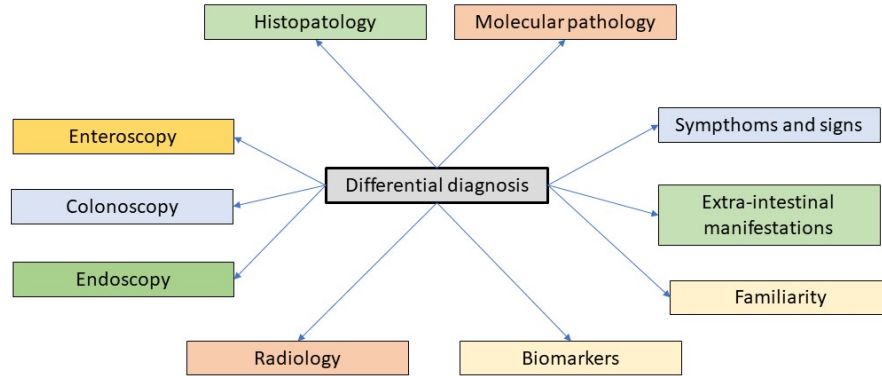
Figure 2.1. Tools for IBD diagnosis. The figure shows which are the various diagnostic paths that can be followed, most often in combination with each other, to make a differential diagnosis of IBD (figure adapted from Tontini, Gian Eugenio et al., Differential diagnosis in inflammatory bowel disease colitis: state of the art and future perspectives, 2015).

2.3   Therapies

Different therapies are proposed to induce remission in patients and avoid as much as possible secondary effects. Corticosteroids, aminosalicylates (as 5-aminosalicylic acid, 5-ASA), immunosuppressive agents, metronidazole and antibiotics are the most used. Then, there are some alternatives therapies conducted by fish oils, methotrexate, arsenical salts, bismuth, colestyramine, and sodium cromoglycate. Finally, there are some new approaches which use monoclonal antibodies (biologicals). The main goal of pharmacotherapy is to maintain the remission, avoid complications and treat acute symptoms [14].

Some drugs have only been approved for UC and others for CD and it has been demonstrated that treating the disease with its specific drug is more effective than treating it with generic drugs. For this reason, it is clearer why it is so important to make a differential diagnosis, especially regarding on future developments in clinical practice about the creation of specific drugs [13].

Chapter 3

Web-apps and IBD: state of the art

3.1 MyIBDCoach

IBD Tool has been developed following the example of MyIBDCoach, a telemedicine application born in Netherlands to monitor IBD patients at home, reachable through a link to a secure webpage. Main aspects which stand beside the idea of MyIBD-Coach were:

- improving the dialogue among doctors and patients

- improving the self-management care

- improving the patient-empowerment.

The design and the content development of MyIBDCoach evolved in seven different phases: stakeholders' identification, brainstorming, questionnaire selection, development of questionnaires, content optimization and finalization, e-learning modules, and testing (Figure 3.1). The questionnaire selection phase was carefully regarded, trying to select the most effective questionnaires in terms of evaluating the quality and the adherence of medication, quality of life, anxiety and depression, and work. The web-application is based on different functions: monitoring through modules (monitoring modules, intensified monitoring modules and outpatient visit modules), e-learning modules, communication, and personal care plan. Monitoring function is done by the compilation of different questionnaires which are scheduled monthly, once per 3 months or weekly in relation to the status of the disease. Provided questionnaires are:

- MIAH, Monitor IBD At Home.

- MMAS-8, Morisky Medication Adherence Scale.
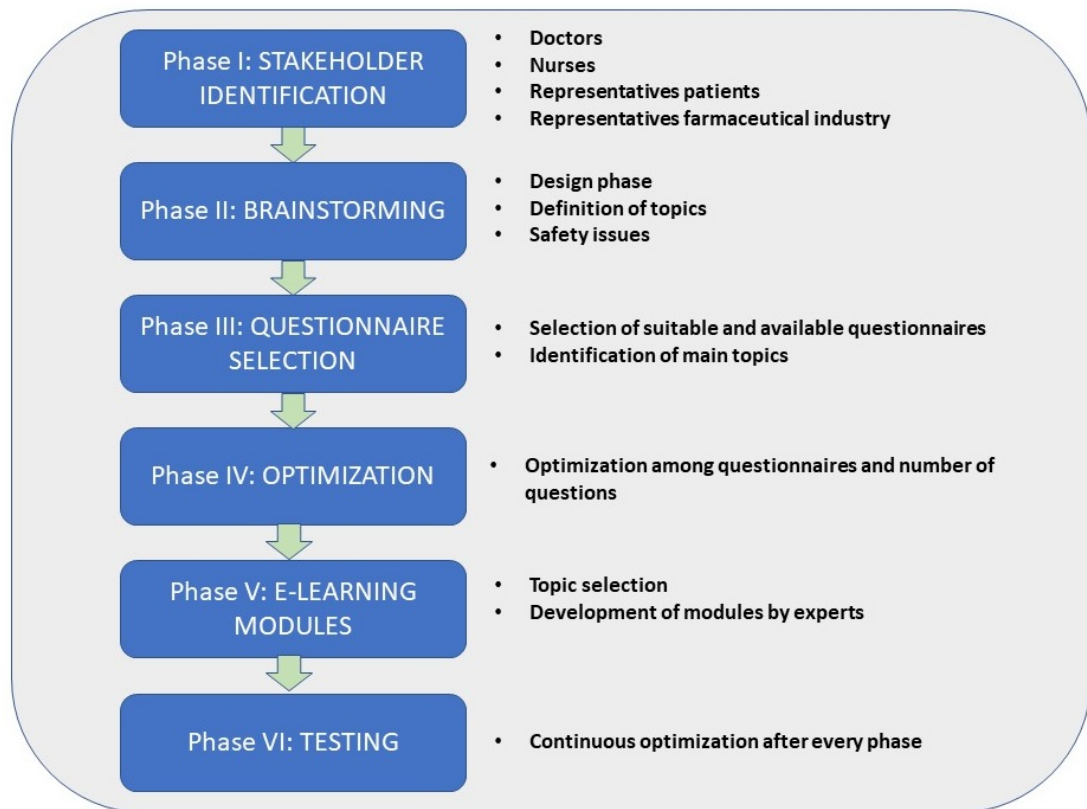
Figure 3.1. Development phases of MyIBDCoach (adapted from de Jong M., Development and Feasibility Study of a Telemedicine Tool for All Patients with IBD: MyIBDcoach, 1 April 2017).

- TSQM, Treatment Satisfaction Questionnaire for Medication.

- MST, Malnutrition Screening Tool.

- SNAQ, Short Nutritional Assessment Questionnaire.

- EQ-5D, EuroQol instrument.

- SF-12, Short Form Health Survey.

- WPAI, Work Productivity and Activity Impairment.

- SIBDQ, Short Inflammatory Bowel Disease Questionnaire.

- HADS, Hospital Anxiety and Depression Scale.

- SSL, Social Support List.

- SFQ, Shortened Fatigue Questionnaire.

E-learning module is thought in a patient-empowerment view, and it is extremely useful to the patient who is interested in a deep knowledge about his pathology, available treatments, risk factors or anything connected to IBD. The learning module can be started both by the care provider or the patient. Communication is extremely easy thank to the presence of a back-office which evaluates all the messages sent by the patient at each time. In case of a critic situation, the health care provider can decide to fixate a face-to-face evaluation. Furthermore, each communication is documented. Personal care plan is synonymous of a dashboard which reassumes all main features trough graphs and tables, and it is available for both doctors and patients improving the self-management care. The study of feasibility of MyIBDCoach was published in 2017, showing very good results in terms of satisfaction: patients gave a mean score of 7.8/10 and health care providers of 8.0/10 judging the accessibility and the design of the entire system. Furthermore, the 93% of patients considered the option to recommend the application to other patients [15].

3.2 IBD Tool

IBD Tool was born from the collaboration between LINKS Foundation company and the Gastroenterology department of the Mauriziano Hospital in Turin, inspired by MyIBDCoach. IBD Tool is currently mainly focused on monitoring and communication trough notifications, e-mails, and telephone, with only some aspects about personal-care-plan and nothing about e-learning. The functionalities of the web-application are:

- if the user-role is "patient" the main functionalities are:

  - access and log-out
  - password reset
  - compiling new scheduled questionnaires
  - signalizing already compiled questionnaires
  - visioning already compiled questionnaires
  - contacting the center by the compilation of new questionnaires or by chat
  - receiving notification when: a new questionnaire must be compiled, the doctor has evaluated or signalized some questionnaires, a new questionnaire has been added, a questionnaire has been removed
  - removing notifications

– receiving e-mails when: the doctor wants to contact the patient, a new questionnaire is sent, main resuming scores of questionnaires are sent, the patient has been registered and the system provides username and password, password is reset.

All the relations among different use-cases are resumed in Figure 3.2.
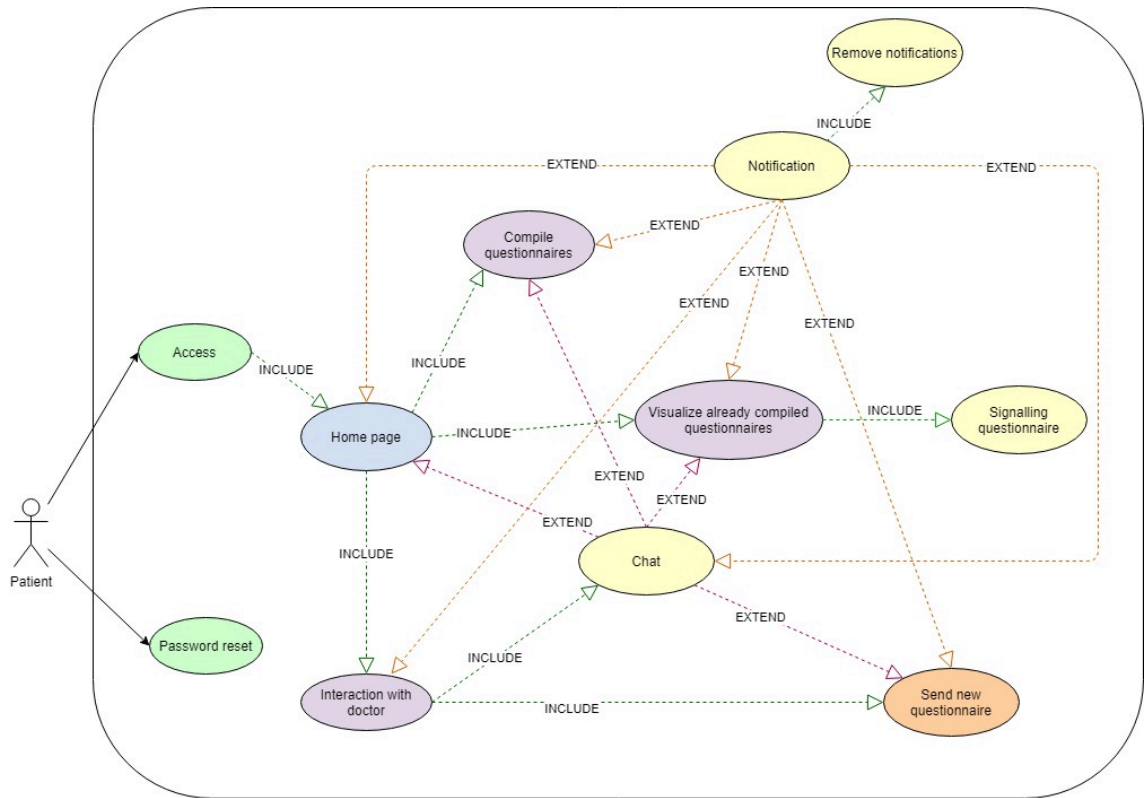
Figure 3.2.   Use case diagram of all the functionalities related to the patient.

- if the user-role is "physician" the main functionalities are:

    – registration to the web-app

    – access and log-out

    – password reset

    – registering a new patient

    – removing patients from the platform

    – adding questionnaires on patient's account

    – removing questionnaires on patient's account

- management of questionnaires' frequency

- contacting patient trough e-mails

- visualization of patients' data

- visualization of inactive patients

- visualization of not-visualized questionnaires

- visualization of compiled questionnaires

- compiling new clinical questionnaires

- removing notifications

- receiving notifications when: the patient has changed his personal information, the doctor has received the e-mail with summary information about compiled questionnaires of personal patients, the patient has signalized a wrong compiled questionnaire, a new clinical questionnaire is available

- receiving e-mails when the summary information about compiled questionnaires of personal patients is sent once a day.

All the relations among different use-cases are resumed in Figure 3.3.

All the functionalities have been designed and adapted to the needs of the clinicians of the Mauriziano Hospital.
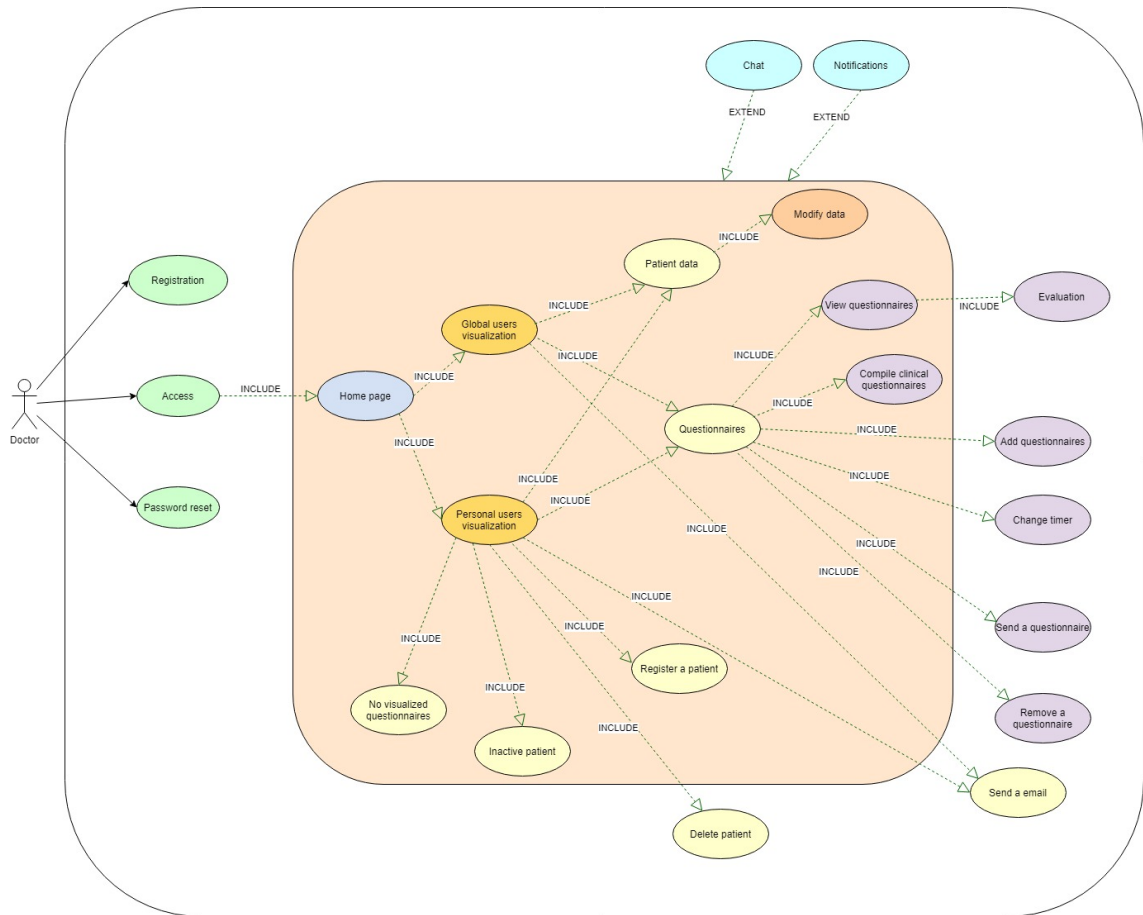
Figure 3.3.   Use case diagram of all the functionalities related to the physician.

Chapter 4

Materials and methods

4.1 Set goals

This thesis aims to expand the IBD Tool platform by adding new functionalities based on the requests and needs of physicians. The work started from a platform already working with the desire to expand it, to make it more and more complete, with optimized functions. The work proceeded in several phases:

- phase 1: study of the platform and of all the present code, familiarizing with the architecture and technologies used.

- phase 2: study of the questionnaires and fulfillment of the first requirement, the insertion of a new questionnaire in the platform.

- phase 3: design, creation, and testing of a personalized dashboard for physicians.

- phase 4: design, creation, and testing of a section from which it is possible to download the entered data.

- phase 5: design, creation, and testing of a section dedicated to clinical data that emulates a real medical record.

It is always important to consider the requests of the final users and try to fit the programming objectives with the users' objectives, especially physicians who always need fast and practical solutions. Because of this, all phases involved continuous interaction with the physicians of the Mauriziano Hospital in Turin, the main recipients of the added functions. The close contact with specialists has allowed us to offer personalized and efficient solutions, aimed at improving diagnosis, treatment, and interaction with the patient in every aspect.

4.2 Questionnaires: the core of the project

The main core of the entire platform is the questionnaires. When a user-doctor registers a new user-patient and defines his pathology, a method automatically starts and takes care of sending questionnaires. In this regard, there are monthly, quarterly, and half-yearly questionnaires. There are multiple questionnaires with different functionalities, moreover, the same questionnaires are not defined for all users and with the same administration frequency. In fact, questionnaires change with respect to the pathology from which the user suffers and respect to the category, "STANDARD" or "TELEMEDICINE". The presence of two categories is necessary as in any clinical study in which there is the need to compare the results with a control group. Right now, the function of randomly dividing the user-patients in the platform by category means that they are monitored by different questionnaires and different frequencies of administration (Figure 4.1).

QUESTIONNAIRES - TELEMEDICINE								
MONTHLY			**THREE-MONTHS**			**SIX-MONTHS**		
CD	**UC**	**OTHER**	**CD**	**UC**	**OTHER**	**CD**	**UC**	**OTHER**
HBI	PATIENT-SCCAI	IBD-DISK	PHQ9	PHQ9	PHQ9	PSQI	PSQI	PSQI
IBD-DISK	IBD-DISK		PRISM	PRISM	PRISM	EQ5D5L	EQ5D5L	EQ5D5L
MIAH-CD	MIAH-UC		IPAQ-SF	IPAQ-SF	IPAQ-SF			
			WPAI	WPAI	WPAI			
			IBDQ	IBDQ	IBDQ			
			MMAS8	MMAS8	MMAS8			
			TSQM	TSQM	TSQM			
QUESTIONNAIRES - STANDARD								
MONTHLY			**THREE-MONTHS**			**SIX-MONTHS**		
CD	**UC**	**OTHER**	**CD**	**UC**	**OTHER**	**CD**	**UC**	**OTHER**
-	-	-	HBI	PATIENT-SCCAI	IBD-DISK	-	-	-
			IBD-DISK	IBD-DISK				
			MIAH-CD	MIAH-UC				

Figure 4.1. Scheduled questionnaires to the two different users' categories, "STANDARD" and "TELEMEDICINE", and respect to the pathology of registered patients in IBD Tool.

Questionnaires are:

- HBI (patient-HBI, clinical-HBI). This questionnaire, also known as the Harvey-Bradshaw index, consists of 5 questions and is used only for Crohn's patients. The questions concern the patient's well-being, abdominal pain, the number of liquid or soft bowel movements, the presence of abdominal mass and the presence of complications. Each answer has a score, and the total score is

calculated by adding all the scores of the questions. A score less than 5 defines remission, between 5 and 7 a mild disease activity, between 8 and 16 a moderate activity and strictly greater than 16 a severe activity [16]. Clinical and patient-HBI are the same questionnaires, but the second one is compiled by physicians and then compared with patient's score. There are two version of this questionnaire in IBD Tool, one for patient and one for clinicians which are always compiled in the same period.

- SCCAI (patient-SCCAI, clinical-SCCAI). This questionnaire, also known as the Simple Clinical Colitis Activity Index, can detect relapse and remission activity for patients suffering from ulcerative colitis. For the patient-SCCAI there are 13 questions that refer to the symptoms of the last week, in particular to bowel movements, episodes of fecal incontinence, blood in the stool, joint pain, erythema and any infections. The final score is calculated based on the combination of all the scores of the various questions. A final score of less than 5 classifies the patient in remission, greater than or equal to 5 in relapse [17]. There are two version of this questionnaire in IBD Tool, one for patients and one for clinicians which are always compiled in the same period.

- MIAH: This questionnaire, also known as Monitor IBD At Home questionnaire, was constructed in both a version for patients with Crohn's disease (MIAH-CD) and for patients with ulcerative colitis (MIAH-UC). The first consists of six questions regarding general health, rectal bleeding, mucus loss, number of daily bowel movements, urgent bowel movements and asthenia; the second consists of five questions regarding general health, rectal bleeding, number of daily bowel movements, urgency to bowel and abdominal pain. A score is assigned to each of the answers and a specific algorithm is used to calculate the final score, which associates an appropriate weight factor with each answer. The cut-off for determining the result is set at 3.6. Therefore, scores higher than this cut-off determine a state of relapse, otherwise below it is remission [18].

- PRISM (patient-PRISM, clinical-PRISM). Known as Pictorial Representation of Illness and Self Measure. This questionnaire is not made up of questions, but of a representation that shows two circles: one represents the disease, the other represents the patient. The user must indicate, by moving the circles, how much he suffers due to his illness. The final score is returned in terms of "distance". It has been shown that this questionnaire is very simple, intuitive, effective, and valid in the evaluation because it correlates with other questionnaires' scores [19]. There are two version of this questionnaire in IBD Tool, one for patients and one for clinicians which are always compiled in the same period.

- IBD-DISK: This questionnaire was validated starting from a previous questionnaire (the IBD-DI: Inflammation-Bowel-Disease Disability Index) with some modifications and it is based on 10 items with respect to which the user must express his agreement on a scale from 0 to 10, where 0 stands for "absolute disagreement" and 10 for "absolute agreement". Items are about abdominal pain, regulating defecation, education and work, sleep, energy, emotions, body image, sexual functions, and joint pain [20]. The result is expressed in terms of a score disk, therefore graphically (Figure 4.2). Anyway, there is a final score which is due to the sum of overall answers' scores.
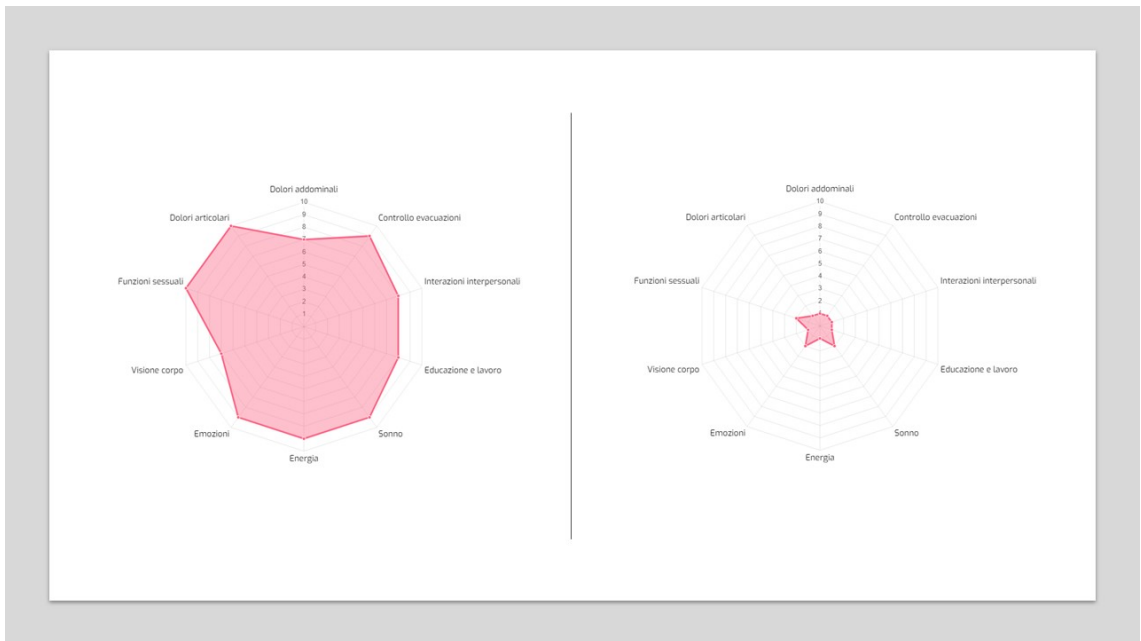
Figure 4.2. Output figure for IBD-DISK assessment. The left figure shows high scores and so high disease burden, the right one shows low scores and so low disease burden.

- PHQ9: This questionnaire, also known as Patient Health Questionnaire-9, is used for the diagnosis of depression, and can be administered by both medical personnel and self-administered. In general, it consists of two questions, the first of which evaluates the symptoms of depression, which are 9; the second question, on the other hand, concerns the effect of depression on the patient's life. The questionnaire score is given by the sum of the scores on the individual questions. For each question the associated choices are 4, from a score of 0 up to a score of 3. So, the final score varies from 0 to 27: scores between 0-4 indicate no depression, between 5 and 9 indicate subthreshold depression, between 10-14 indicate mild major depression, between 15-19 indicate moderate

major depression, greater than or equal to 20 indicate major depression [21].

- IPAQ-SF: This questionnaire, also known as the International Physical Activity Questionnaire Short Form, is aimed at measuring the amount and type of physical activity performed in the last seven days. Intense or moderate physical activity is evaluated, however activities that lasted at least 10 consecutive minutes. The total final score is called MET score (metabolic equivalent task). The result of the questionnaire tells whether the patient is inactive (score less than 700 MET), usually active (score between 700 and 2520 MET), active or very active (score greater than 2520 MET).

- PSQI: This questionnaire, also known as Pittsburg Sleep Quaity Index, is for the evaluation of sleep in the last month, with questions regarding the time a person fell asleep, the time taken to fall asleep, the wake-up time in the morning, the total hours of sleep, the general sleep quality, how many times a person wakes up during sleep, whether a person has been taking sleep medications, etc. This questionnaire also returns a final score, which has a cut-off value of 5 which represents the boundary between good quality sleep and poor quality [22]. Anyway, this score is not used in the IBD Tool platform.

- WPAI: This questionnaire, also known as Work Productivity and Activity Impairment Questionnaire, is used to assess the impact of the disease, both Crohn's disease and ulcerative colitis, on work and daily activities. This questionnaire does not currently provide any score; therefore, the results are evaluated based on the consultation of the questionnaire itself.

- EQ5D5L: This questionnaire, also known as 5-level EQ-5D (European Quality - version 5D - 5 Levels), is about the measurement of the quality of life, work, personal care, physical and psychological health, usual activities, pain and discomfort. Each answer is divided into five levels. This questionnaire does not currently provide any score; therefore, the results are evaluated based on the consultation of the questionnaire itself.

- IBDQ: This questionnaire, known as Inflammatory Bowel Disease Questionnaire, is for quality of life assessment. Its composition consists of 32 questions, whose answers are distributed on 7 different levels, where 7 is a good score and 1 the worst. This questionnaire takes into consideration different fields about social life, emotional health, and symptoms [23]. The final score goes from 32 to 224 and the cut-off is 170: higher values indicate remission [24].

- MMAS8: This questionnaire, also known as the 8-item Morisky Medication Adherence Scale, is based on 8 questions that assess adherence to therapy. The questions relate to times when a person forgets to take the tablet or stops taking it because it is believed to be ineffective or causes discomfort. This

questionnaire returns a final score: if the score is less than 6 it means that the therapy is not adherent, if it is between 6 and 8 it is on average adherent, if it is greater than 8 it is very adherent.

- TSQM: This questionnaire, also known as the Treatment Satisfaction Questionnaire for Medication, is used to assess the level of satisfaction or dissatisfaction with the drug that the patient is taking. In particular, the effectiveness, the side effects, the use of the drug, its planning and the convenience or inconvenience of taking it are evaluated. This questionnaire does not return any final score.

4.2.1 Questionnaire association algorithm

The purpose

One of the aims of IBD Tool is to be able to collect data that can be used to carry out some scientific studies on IBDs. The platform collects a large amount of data monthly, especially relating to the completed questionnaires. Clinical questionnaires are generally filled in at the same time as the patient questionnaires, this happens during the traditional visit that the specialist makes to the patient. During this visit the physician has the possibility, through IBD Tool, to send to both himself and the patient the proper questionnaire. During this first year of use of the application, evaluations were carried out by different physicians even on the same patient. To be able to re-associate the evaluations carried out in the same period by several doctor-users regarding the same patient with the patient's self-evaluations, it has been necessary to create a special algorithm that proceeded with these associations. The main purpose of this association was to conduct a concordance study in parallel:

- between senior physician and junior physician, if more medical evaluations were present for the same patient

- between any physician (senior or junior) and the patient.

Materials

As already discussed, there are questionnaires that are administered for both physicians and patients, they are:

- PATIENT-SCCAI and CLINICAL-SCCAI for ulcerative colitis patients

- PATIENT-HBI and CLINICAL-HBI for Crohn's patients

- PATIENT-PRISM and CLINICAL-PRISM for both.

Data collection includes:

- the use of the following questionnaires for ulcerative colitis patients:

  - PATIENT-SCCAI
  - CLINICAL-SCCAI
  - PRISM
  - CLINICAL-PRISM

- the use of the following questionnaires for Crohn's disease patients:

  - PATIENT-HBI
  - CLINICAL-HBI
  - PRISM
  - CLINICAL-PRISM.

Presentation of the algorithm

The method is implemented trying to consider also possible future developments, such as the presence of several senior physicians who evaluate the same patient and one or more junior physicians who evaluate the same patient. All the results of association are resumed in a table: each row represents a patient. All the physicians are automatically recognized, and each questionnaire's evaluation is associated with the correct column of the table dedicated to the right physician (recognized by a doctor ID). In the columns there is always a reference to the ID of the physician who carried out the evaluation. For the patient there are also some identifiers (name, surname, date of birth).

The questionnaires are associated based on their evaluation date. During the patient visit, all types of questionnaires of interest are administered by physician simultaneously and it is interesting to evaluate questionnaires that are filled in very close to each other. Therefore, the algorithm works by associating the questionnaires that are around 2 weeks before and 2 weeks after the date of completion of the reference questionnaire (generally the reference is always a specific physician's questionnaire). If more questionnaires are filled in by the same senior, or junior doctor, or patient and fall within this margin, it is always considered the questionnaire with the compilation date closest to the reference one (in this regard a special algorithm exists (Figure 4.3)).
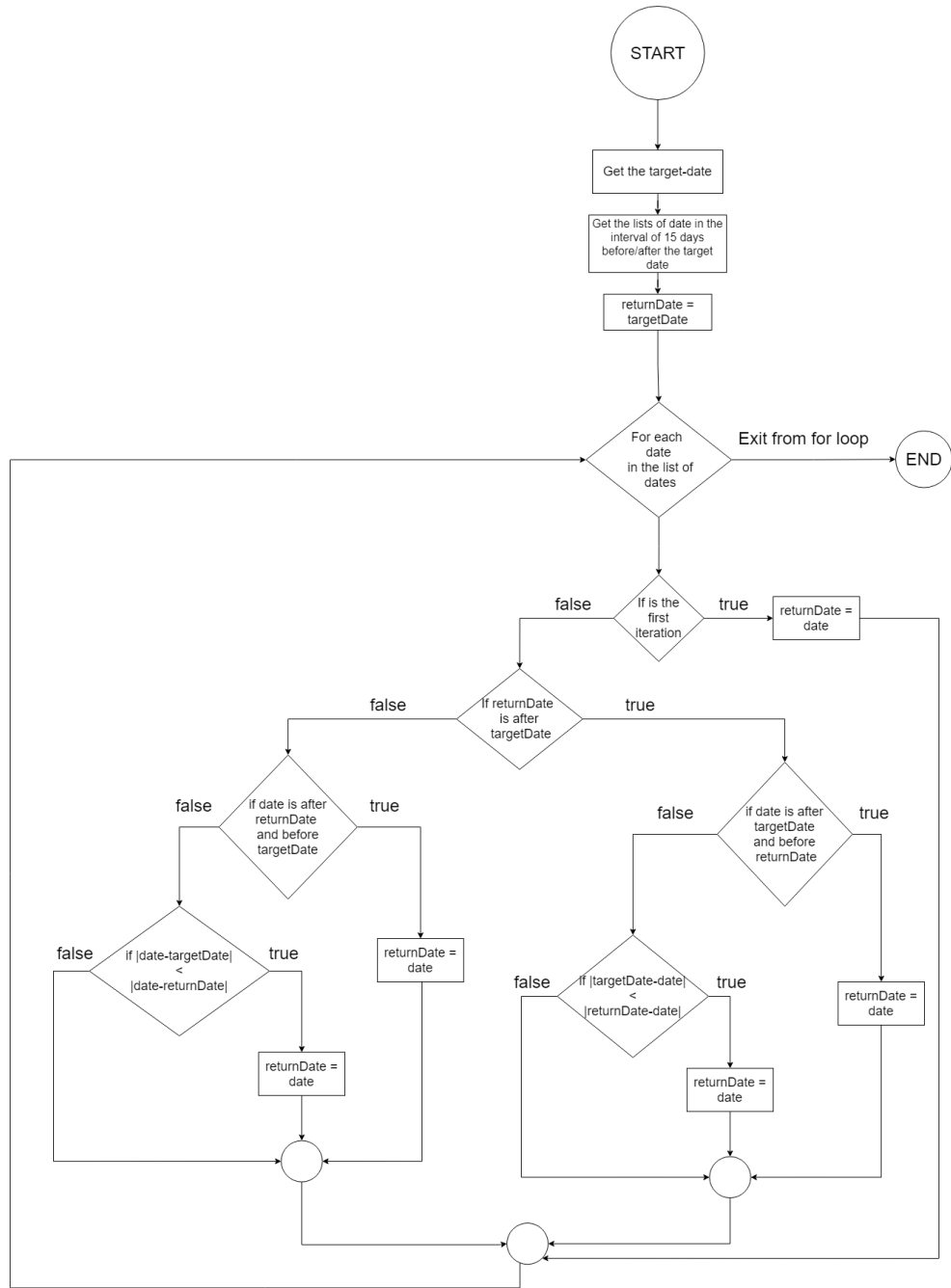
Figure 4.3.   Algorithm scheme. Method which explains how questionnaires' dates are associated. In this scheme, "targetDate" is the reference date of the physician's questionnaire, "date" is the testing date of each iteration, and "returnDate" is the returned date of each iteration. If date is between the previous returnDate and the targetDate, date becomes the new returnDate; otherwise, the distance between the date and the targetDate has to be lower than the distance between the date and the previous returnDate to let date becoming the new returnDate.
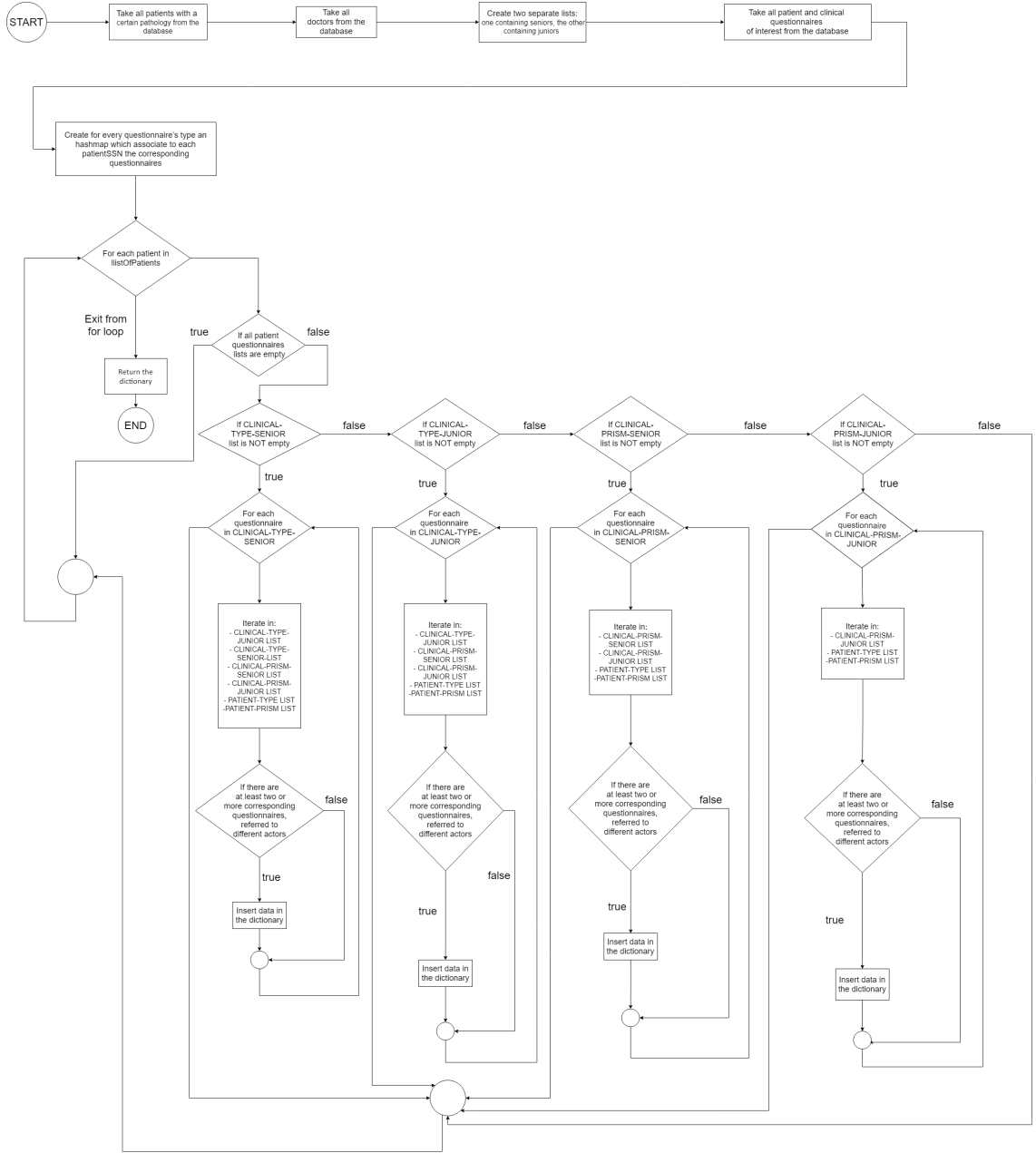
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Figure 4.4. Algorithm scheme. Scheme which explains the method by which questionnaires have been associated.

The reference date used by the algorithm is always a date associated with a physician's questionnaire, in order of preference the CLINICAL-HBI senior is searched first; if there are no CLINICAL-HBI senior evaluations, the method iterates through the CLINICAL-HBI junior; if there are no evaluations of these, then it iterates through the CLINICAL-PRISM senior; if there are neither of these evaluations, it

iterates amongst CLINICAL-PRISM junior questionnaires. It works the same for ulcerative colitis questionnaires (CLINICAL-SCCAI, PATIENT-SCCAI, PRISM, and CLINICAL-PRISM).

Description of the algorithm

Main steps are:

- The list of patients suffering from a given pathology (e.g. Crohn's disease) is obtained from the database.

- All the questionnaires of interest, previously discussed, are obtained from the database and some maps are created that associate the lists of questionnaires with the different patients (the unique key for patient identification is the patientSSN).

- The algorithm starts to iterate to each patient.

- Starting from a medical evaluation of a given type of questionnaire (e.g. clinical-HBI senior) belonging to a specific list of questionnaires associated with the patient:

  - It takes the date of completion of the current questionnaire and is used as a reference date.

  - It searches in the various lists of questionnaires (clinical-HBI junior, HBI patient, PRISM patient, PRISM senior, PRISM junior, and in the same list from which the search started, to look for questionnaires filled in by a different physician in respect to the reference one).

  - Then all those questionnaires that fall within the chosen time range are associated.

  Multiple lines can be generated for the same patient if there are several different evaluations that can be associated over time (Figure 4.4).

  Covered cases in a single row are:

- Patient assessments - senior doctor/s - junior doctor/s

- Patient assessments - senior doctor/s

- Patient evaluations - junior doctor/s

- Evaluations of senior doctor/s - junior doctor/s

- Evaluations of multiple senior doctors

- Evaluations of several junior doctors.

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Not covered cases in a single row are:

- Only patient assessments

- Only one senior physician assessment

- Only one junior physician assessment.

These cases prevent a priori from being able to make comparisons for concordance studies.

These assessments may concern the completion by the subject of both questionnaires (PRISM and PATIENT-SCCAI or PRISM and PATIENT-HBI), or even just one of the two; to immediately understand if a subject has completed both questionnaires, or only one, or none, it is sufficient to refer to the columns defined with "LOGICAL" (Figure 4.5). In order to enter any medical evaluation in the

Name	Surname	Birthdate	SCORE SCCAI PATIENT	Compilation date	SCORE PRISM PATIENT	Compilation date
Mario	Rossi	yyyy/mm/dd	0	yyyy/mm/dd	2.5	yyyy/mm/dd

SENIOR ID		SCORE CLINICAL SCCAI		Compilation date	SCORE CLINICAL PRISM		Compilation date ***
56hhg		1		yyyy/mm/dd	3		yyyy/mm/dd

JUNIOR ID		SCORE CLINICAL SCCAI		Compilation date	SCORE CLINICAL PRISM		Compilation date	***
45hhb5		1.5		yyyy/mm/dd	3.5		yyyy/mm/dd	

N° of CLINICAL SCCAI assessments	N° of CLINICAL PRISM assessments	Logical control patient	Logical control senior ***	Logical control junior ***
3 (e.g. if there are 1 senior and 2 juniors)	2 (e.g. If there are 1 senior and 1 junior)	1 -> patient correctly compiled both PRISM and PATIENT-SCCAI 0 -> only one of the 2 assessments "-" -> no assessment	1 -> physician correctly compiled both PRISM and CLINICAL-SCCAI 0 -> only one of the 2 assessments "-" -> no assessment	1 -> physician correctly compiled both PRISM and CLINICAL-SCCAI 0 -> only one of the 2 assessments "-" -> no assessment

*** other columns are added automatically if there are other physicians who have made evaluations.

Figure 4.5. Organization of a single row in the concordance table and explanation of each field.

table, it is always checked that there is at least one junior evaluation and/or an evaluation of a senior doctor and/or at least one patient evaluation of any of the questionnaires of interest.

4.3   Platform structure

IBD Tool consists of a client-server architecture, which has been developed using technologies that are very popular among developers. This architecture consists of two fundamental parts:

- the frontend (fe) which represents the graphical interface of the program

- the backend (be) which contains all the logic.

The interaction between the user interface and the backend logic is done by HTTP (Hypertext Transfer Protocol) requests.

Certainly modularity, extensibility, flexibility, and evolution over time are properties that belong to IBD Tool. The first because each feature is generally independent from the others and is characterized by a separate code function. The second because the platform is easily extendable, and it is easy and intuitive to add new features. The third because it offers heterogeneous services and functionalities. The fourth because it adapts very easily to updates and to stay in step with technologies.

4.3.1   Frontend

Angular

The front-end was developed using Angular, which is a modern development platform that relies on the presence of components to create scalable platforms. Angular also allows to use a whole series of libraries and development tools that help developers in their work.

Angular is based on Typescript, which is an object-oriented programming language and on HTML (Hypertext Markup Language), which is a markup language that allows, through specific tags, to define the elements of a web page. These elements render on the screen and their appearance is declared in the style files, which are the CSS (Cascading Style Sheet) files. Angular is based on a root module (generally named AppModule and contained in the file app.module.ts), on components and services.

Each component, indicated with the **@Component** decorator, consists of:

- a Typescript file (.ts)

- an HTML file (.html)

- a CSS file (.css)

When a component is created through the command **ng generate component component-name**, these files are automatically generated with the name of the component and the specific extension [25]. The .ts file shows:

- the **selector** that allows to call this component in any other .html file of any other component of the application

- the **templateURL** which indicates which HTML template is referenced

- the **styleURLs** which indicates which is the reference style sheet.

```
@Component({
  selector: 'app-bar-chart-inactive-patients',
  templateUrl: './bar-chart-inactive-patients.component.html',
  styleUrls: ['./bar-chart-inactive-patients.component.css']
})
```

Each component has a lifecycle, so in the .ts file, after the @Component declaration, there is the declaration of the class and the component's lifecycle. The two main implemented functions are **ngOnInit()** and **ngOnDestroy()**. The first one consists in the initialization of the component, the second one consists in clearing everything before the disposal of the components.

```
export class BarChartInactivePatientsComponent implements OnInit, OnDestroy {
  constructor(private service: someService) { }
  ngOnInit() {
        // code section}
  ngOnDestroy() {}
  // other functions
}
```

Other important Angular elements are the services which work side by side with the components to increase modularity; generally, services are defined as a class with a specific and defined function. The function of services is often to obtain data from the backend (the server). Services are often accompanied by the **@Injectable** decorator, which means that services can be injected into a component, usually in the constructor() function, so that the component can consume the offered service. The service, as the component, can be created through the command **ng generate service service-name** and it includes by default the @Injectable decorator [25].

```
@Injectable
export class SomeService {
  constructor() { }
  someFunction() {
  // code section}
}
```

4.3.2 Backend

The backend is built using in combination Java, a famous object oriented programming language, and a very popular framework called Spring Boot. Thanks to the

use of Spring Boot, the programmer's work is facilitated because he only has to worry about the logic, the creation of classes and their configuration, while Spring deals with managing the life cycle of the components and allows the whole system to function by the use of some abstractions. Spring guarantees inversion of Control (IoC) through Dependency Injection (DI), it allows to build an application based on the concept of microservices and it guarantees efficiency through the development of reactive and secure applications [26].

The multitier architecture and Spring

IBD Tool is organized according to a multitier architecture, composed of four levels:

- A presentation layer; this layer is the outermost one that receives data from the frontend and passes it to the service layer. Once all operations are completed, it sends a response to the frontend. To create a class that does this job, Spring uses the **@Controller** annotation. Since IBD Tool uses a Representational State Transfer (REST) architecture, the **@RestController** annotation is invoked.

```
@RestController
public class DoctorController {
// some methods
}
```

- A service layer; this layer represents the application logic and is recalled by the previously presented layer. Spring uses the **@Service** annotation to instantiate it. It is at this level that the integrity of data is checked. At this level it is very important to import other classes with the annotation **@Autowired**, which is generally used to resolve dependencies (DI property).

```
@Service
public class QuestionnaireService{
        @Autowired
        private MailService mailService;
        @Autowired
        private UserService userService;
        // some methods
}
```

- A Data Domain Layer; it is the layer that deals with the abstraction of data through classes that are a model of the data present in the database. Spring uses the **@Document** annotation to declare what follows, that is an abstraction of a database's data. Additionally, an attribute must be labelled with the **@Id** annotation so that its uniqueness within the collection is signalled.

```
@Document(collection = "users")
public class UserEntity implements Serializable {
    @Id
    private String email;
    private String name;
    private String surname;
    private String SSN;
    private String phoneNumber;
    private String password;
    [...]
}
}
```

- A Data Access Layer; this is the layer that allows the actual acceptance to the database and then passes data to the Data Domain Layer. To access a MongoDB database, an interface is created that extends the **MongoRepository** and contains all the methods that allow to obtain data from the database. Database specific queries can be made using the **@Query** annotation.

```
public interface UserRepository extends MongoRepository<UserEntity, String> {
    Optional<UserEntity> findByEmail(String email);
    Optional<UserEntity> findByEmailAndPassword(String email, String password);
    Optional<UserEntity> findByEnabledAndUuidAndRegistrationTimeGreaterThan
                (boolean enabled, String uuid, long registrationTime);
    @Query("{$and:[{email:?0},{SSN:{$regex:?1,$options:'i'}}]}")
    Optional<UserEntity> findByEmailAndSSNCaseInsensitive(String email,
                                        String SSN);
}
```

A Spring Boot Application has a single entry point which, when invoked, allows all layers of the system to be activated by the use of a run method:

```
@SpringBootApplication
public class IbdtoolApplication {
        public static void main(String[] args) {
                SpringApplication.run(IbdtoolApplication.class, args);
    }
}
```

The HTTP protocol

The HTTP (Hypertext Transfer Protocol) protocol is widely used for communications between a web client and a web server. Among the data formats, the Json (JavaScript Object Notation) format is one of the most widely exchanged. The HTTP protocol is a request-response type protocol that implies the presence of a client that submits requests to the server, which can provide resources or perform functions. A web resource refers to any information that is represented by a unique URI (Uniform Resource Identifier). A URI therefore defines and uniquely identifies a resource, so if any information does not have a URI it cannot be defined as a resource. "Uniform" refers to a lot of benefits: it guarantees to use different identifiers in the same application context, it allows to create new identifiers without compromising existing ones and the applicability of the same URI in different contexts is great. "Resource" refers to everything that is represented by an identifier and it is important to mark that a resource can have a content which can be modified during the time but its own URI is always the same. "Identifier" refers to the URI itself, which it is represented by a set of characters [27].

An example of URI is:
https://[hostname]:[port]/[path]/[?query][#fragment]
In this example of URI the hostname can be replaced by the IP address; the port identifies where the service stands on a server and if it not specified it indicates the default port which is the port 80 for HTTP. The path and the query are optional: the first indicates the resource path that is hierarchical "/uri[0]/uri[1]/uri[3]/...", the second refers to some parameters that can be added as "?nameFirstParameter=value&nameSecondParamenter=value...". The fragment is optional and it refers to a specific section of the html page.

In response to the client, the server always sends a response which contains the status information together with the requested information. The request is always made by [28]:

- a request line:
  GET /software/htp/cics/index.html HTTP/1.1
  which contains the method, the path and the version of HTTP protocol;

- header:
  Accept-Language: fr, de
  If-Modified-Since: Fri, 10 Dec 2004 11:22:13 GMT
  which gives some information about how the server responds to the client

- body, if needed which represents the real content of the message.

The response is always made by [28]:

- a status line:
  HTTP/1.1 200 OK

which contains the version of HTTP protocol, the status code and a phrase which represents the meaning of the status code

- header:
  Date: Thu, 09 Dec 2004 12:07:48 GMT
  Server: IBM_CICS_Transaction_Server/3.1.0(zOS)
  Content-type: image/jpg
  which gives some information about the server and the response

- body, used most of the time.

In the request line there is an example of a method, the GET method, which is one of the available methods of the protocol. These methods are [29]:

- GET: this method is used to retrieve some resources which are uniquely identified by a request-URI

- POST: this method is used to create new resources identified by a request-URI

- PUT: this method is used to modify an already existing resource at a given request-URI, but if the resource does not exist, it permits to create a new one

- DELETE: this method is used to delete a resource at a given request-URI.

The status codes can be [29]:

- **1xx**: Informational, it gives some information during the request is taking place

- **2xx**: Success, it means that the request was successful

- **3xx**: Redirection, it means that other actions are necessary to fullfill the request

- **4xx**: Client Error, it means that the client sends a bad request, or it is not authorized

- **5xx**: Server Error, it means that server failed to perform the request.

The REST architecture

IBD Tool was developed using a representational state transfer (REST) architecture (Figure 4.6). This type of architecture ensures interoperability, using the Internet, and using a client and a server. This type of architecture is perfectly compatible with the HTTP protocol used for communications between the frontend and the backend (Figure 4.7). The operations that are carried out to manage resources, in particular web resources, are called *stateless* operations, which means that the server does not store any status information about the client, so any interaction between client and server lasts nothing more than a single request. Each time, the client sends any necessary information to fullfill the request to the server. All formats, including HTML and JSON are perfectly compatible with a REST architecture [30].
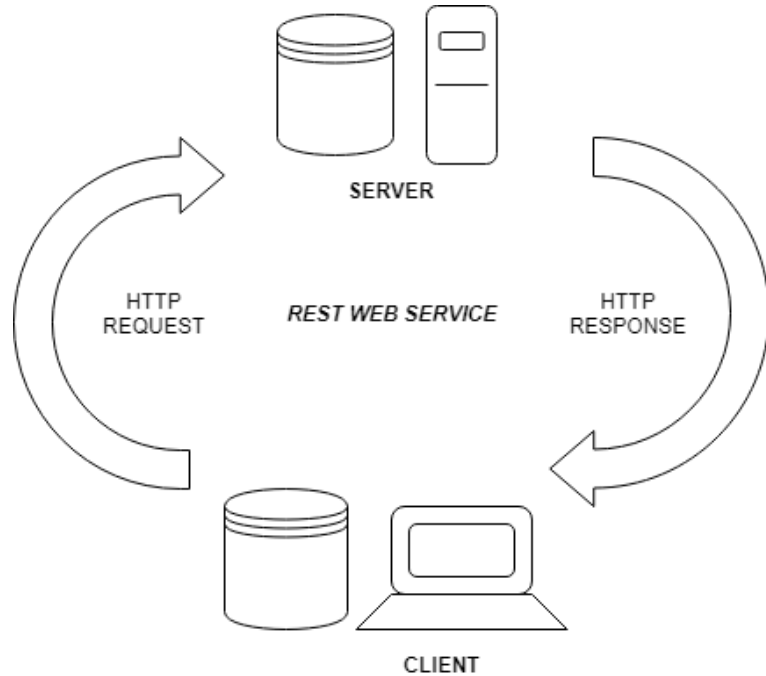
Figure 4.6. Restful web service. The interaction between client and server.

The main REST properties are [30]:

- *scalability*: a REST system can easily be extended to any number of components

- *simplicity*: exchanging data through interfaces makes everything simpler

- *modifiability*: everything can be easily modified, even while the application is running

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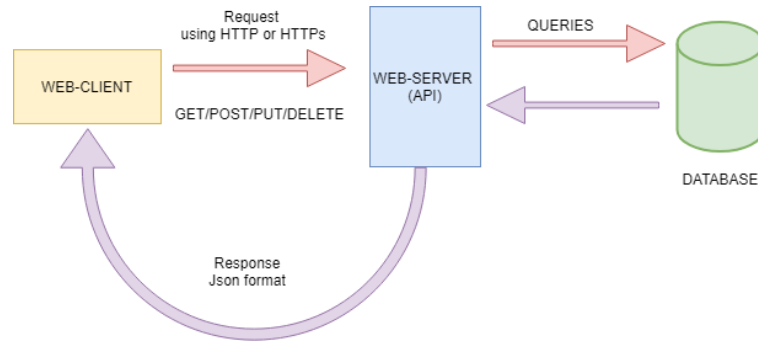
Figure 4.7. Restful web service. The synergy amongst web-client, web-server, and the database.

- *visibility*

- *portability*

- *statelessness*, directly inherited from the HTTP properties

- *chacheability*, also inherited from the properties of HTTP; it makes the client-server interaction faster because some frequently requested resources are saved in the local cache and it is not necessary to query the server every time; obviously, it must first be defined whether a resource is cacheable or not

- *layered system*, used to improve scalability and it is obtained by using of a proxy or a load balancer

- *uniform interface*, generally interfaces are defined, remain constant, and guarantee the simplification of the whole architecture.

In the REST architecture the operations which permit to manipulate resources are called "*CRUD*" (CREATE, READ, UPDATE and DELETE). CRUD methods correspond to HTTP GET, POST, PUT and DELETE in this way [31]:

- if the action is to create a resource, POST must be used

- if the action is to to read a resource, GET must be used

- if the action is to update or modify or replace, PUT must be used

- if the action is to delete, DELETE must be used

Security

All security aspects cannot be neglected, also because it involves managing sensitive data. The main security features of the application are:

- an *authentication system*; a special class has been created for each user in which username and password are saved, together with other necessary data. In particular, the password is concatenated with a string, called *"sale"*, and then a hashing function is performed. So, the password is not visible to those who open the database and work on the data. During the authentication, if successful, the back-end releases a token called JWT (Json-Web-Token) which consists of a string composed of three parts:

  - a header that defines the type of token and the encryption algorithm

  - a payload that contains information either pre-defined or customizable by the developers

  - a signature, which is a BASE64 encoding of the concatenation between header and payload and a secret key.

  This token has been programmed to have a duration of 15 minutes, but thanks to some specific requests done by the front-end every ten minutes it can be renewed.

- The application has been constructed in such a way that the various requests are made by those who really have the right; thus, for each request addressed to the controller, a check is made on the user's role so that some methods can only be called up by patients and others only by doctors. To do this, Spring comes in handy with the annotation *@PreAuthorize ("hasAnyAuthority ("ROLE "))"* , indicating the specific authorization in the ROLE field.

- There is a further control based on URLs, which allows to define which pages can be reached by anyone and which are the pages for which authentication is required.

4.3.3 Database

The database is mongoDB, a database that relies on saving data as JSON-style documents. This makes the database itself both scalable and flexible (as fields can change over time); the documents are objects which can be implemented in a lot of programming languages. Data are stored in a structure field-value and values can be single data, data arrays or embedded documents. A single database can be organized in different collections, which remember the tables of MySQL database [32]. Within the application there are templates (entities) that map the various objects that are stored in the collections of the database. Nowadays, the database is composed by five collections:

- users collection, where all users are store, both patients and doctors

```
{
    "_id":"user@gmail.com",
    "name":"*****",
    "surname":"*****",
    "SSN":"****************",
    "phoneNumber":"********",
    "password":"*********",
    "role":{"userRole":"DOTTORE"},
    "enabled":true,
    "emailValid":true,
    "registrationTime":{"numberLong":"1592242851"},
    "doctorID":"*****",
    "chatNotificationEnabled":false,
    "birthDate":{"date":"******"},
    "birthPlace":"******",
    "patients":[*******],
    "lastLogin":{"date":"2021-03-14T20:11:04.585Z"},
    "usageTime":{"numberLong":"881869"},
    "_class":"com.backend.web.ibdtool.entity.UserEntity"
}
```

- pending questionnaires collection, which stores all the questionnaires that must be compiled

```
{
    "\_id":"30/06/2020-MIAH-CD-*****-****************",
    "uuid":"464653df-2ef2-4506-b643-9fd9c00a0782",
    "type":"MIAH-CD",
    "doctorID":"*****",
    "patientSSN":"****************",
    "date":{"date":"2020-06-30T20:56:12.725Z"},
    "\_class":"com.backend.web.ibdtool.entity.Pending"
}
```

- questionnaires collection, which stores all the already compiled questionnaires

```
{
    "\_id": "***************",
    "type": "PATIENT-SCCAI",
    "doctorID": "*****",
    "patientSSN": "****************",
    "compiled": true,
    "date": {
        "date": "2020-08-14T16:56:42.057Z"
    },
    "results": ["0-3 evacuazioni", "1-3 evacuazioni", "Si", "Si", "No", "Mai",
                "5","No", "No", "Si", "No", "No", "No"],
    "finalScore": 5,
    "read": true,
    "evaluation": false,
    "warning": false,
    "\_class": "com.backend.web.ibdtool.entity.QuestionnairePatientSCCAI"
}
```

- chat-messages collection, which stores all the messages

```
{
    "\_id":"2021-04-22T13:19:48.765642-*******",
    "sender":"****@gmail.com",
    "recipient":"****@gmail.com",
```

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```
    "patientEmail":"*****@gmail.com",
    "patientName":"***",
    "patientSurname":"***",
    "doctorName":"***",
    "doctorSurname":"***",
    "date":{"date":"2021-04-22T13:19:48.765Z"},
    "text":"***************",
    "read":true,
    "\_class":"com.backend.web.ibdtool.entity.ChatMessage"
}
```

- questionnaires to notify collection, which stores all the results of questionnaires that must be send to the doctor

```
{
    "\_id":"07/07/2021-IPAQ-SF-****",
    "type":"IPAQ-SF",
    "score":0,
    "doctorID":"*****",
    "patientSSN":"****************",
    "patientName":"***",
    "patientSurname":"***",
    "ripresaAttivita":false,
    "\_class":"com.backend.web.ibdtool.entity.QuestionnaireToNotify"
}
```

To get the data from the database, all the methods that are defined within the backend *repository* folder are used. These methods perform some specific queries and the various repositories in this folder are interfaces. To modify the database collection fields the *get()* and *set()* methods and the *save()* method must be used.

The database can be easily managed directly from the application or by using *MongoDBCompass*, which is a tool that permits to easily do queries and aggregating data.

4.4 Development support instruments

4.4.1 Gmail

Since IBD Tool is based on the automatic sending of questionnaires that is notified by email, it has been necessary to create a gmail account (with an username and a password) specifically for the web-app and configure an email sending service on the backend using the SMTP protocol (Simple Mail Transfer Protocol).

4.4.2 IDE and GitHub

To develop the code, it has been used as an IDE **IntelliJ IDEA Ultimate**, which permits to import the repositories present on a **GitHub** account to proceed with the development. In fact, a private repository has been created on GitHub, in which there are two main folders representing the backend and the frontend. GitHub is

a platform that facilitates code management in terms of saving, editing and even releasing. The organization on GitHub has foreseen the presence of two branches of code: on the one hand the **dev** branch which is configured to work locally and is connected to a local database, on the other the **main** branch which works officially instead. GitHub is particularly handy when several developers are working on the same application. This is because it is possible to create separate branches to do not interfere with the work of others and then perform a **merge** operation between the various branches to merge the jobs and resolve any conflicts.

Generally, after making the merge between any new branch, created to work on a certain aspect, and the dev branch, which is officially adopted to work locally, doing a test locally on the dev branch is recommended before proceeding with the remote upgrade. Having verified this, it is possible to proceed with the merge between the dev branch and the main branch to transfer the changes to the official application.

Before any merge it is necessary to make sure that the developer is always working with the latest version of a branch, so **pull** actions are always recommended first, as they update the local branch with the latest online version. After merging with main, the developer can move on to the next **commit and push** step, which allows to save the new changes by giving a title to the commit and uploading them to the online repository.

4.4.3   Deploy

Deployment is handled in different ways depending on the backend or the frontend.

The backend repository on GitHub has been directly linked with the Heroku server, which is a cloud computing service. So, each update of the main branch on GitHub causes an automatic restart and update of the application backend as well. In this sense, updating the backend is very easy.

Instead, to deploy the frontend, it is necessary to use Firebase Hosting. Firebase Hosting offers web services hosting, in our case the application is hosted at a specific address which is *https://ibd-tool-mauriziano.web.app/*. To be able to update the front-end as well, it is not enough to simply commit and push from GitHub, but some steps must be performed:

- install from CLI: *npm install -g firebase-tools*

- move to the master branch

- run from CLI: *firebase login*

- enter the Google account credentials created for Mauriziano Hospital of Turin

- move from CLI to the frontend folder

- run from CLI: *ng build –prod –aot –output-hashing = all*

- execute this command from the CLI: *firebase deploy -m "Commit title"*

4.5 Chart.js: the main library for chart rendering

Many features of the application require to display charts. The visualization of information through graphs is advantageous both in terms of the speed which the information is learned, and in terms of readability of the information itself. Graphs are useful in the section where the scores of the questionnaires completed by a patient over time are displayed. In this thesis it has been necessary to deepen the rendering of the graphs, especially for the development of the section concerning the dashboard which summarizes the general status of the application. Charts have been created using a famous library: Chart.js v3.4.0. The implementation of graphs is based on the official documentation of the library [33]. In particular, the main graphic templates used in IBD Tool are:

- Line Chart

- Doughnut Chart

- Bar Chart

- Radar Chart

4.5.1 Graph architecture

To render a graph it is necessary to have a canvas element in the .html file with its own id which is used in the .ts file to define all its properties. Everything is contained in a chart-container type element which is particularly useful for adapting the chart to different screen sizes, especially for switching to a mobile view. Below it is illustrated an example of how the bar chart of active and inactive patients has been created. In the declaration of the .html file bar-chart-inactive-patients-components.html, the key [ngStyle] refers to a particular Angular directive which permits to select the style in base of a define condition (in this case it determines the aspect of the cursor on the graph):

```
<div class = "chart-container"
      [ngStyle]="{'cursor':isActiveInactiveHovered?'pointer':''}">
  <canvas id = "myChartInactivePatients"></canvas>
</div>
```

The following lines of code are used to initialize the graph in the .ts file:

```
import {Chart} from 'chart.js';
canvas: any;
ctx: any;
myChartInactivePatients: Chart;
```

The following lines of code in the .ts file are used, instead, to select the correct canvas element from the .html file:

```
this.canvas = document.getElementById('myChartInactivePatients') as HTMLCanvasElement;
this.ctx = this.canvas.getContext('2d');
```

The following lines of code are used to give the correct configurations to the graph called "myChartInactivePatients", in terms of options, graph type and data:

```
this.myChartInactivePatients = new Chart(this.ctx, {
        type: this.barChartTypeGlobal,
        data: {},
        options: {}
});
```

- The configurations called "type" are the following:

  ```
  this.barChartTypeGlobal = 'bar'
  ```

- The configurations called "data" are the following:

  ```
  data: {
     labels: this.barChartLabelsGlobal,
     datasets: this.barChartDataGlobal,
  }
  ```

  and they are based on:

  ```
  public barChartLabelsGlobal = ['TELEMEDICINA', 'STANDARD'];
  public barChartDataGlobal = [
  {
    data: this.activeGlobalPatientsArray, label: 'Attivi',
    backgroundColor: ['teal', 'teal'],
    hoverBackgroundColor: ['#066', '#066'], barThickness: 70,
  },
  {
    data: this.inactiveGlobalPatientsArray, label: 'Non␣attivi',
    backgroundColor: ['orangered', 'orangered'],
    hoverBackgroundColor: ['#cc3700', '#cc3700'], barThickness: 70,
  }];
  ```

- The configurations called "options" include all those aspects concerning:

  - the onClick() callback which is called when a user clicks on the chart and a certain action follows

  - the onHover() callback that is invoked when the pointer goes over the graph and a certain action follows

  - everything related to the scales and axes of the chart

  - everything about the legend and the callbacks attached to it

  - everything related to the tooltips, that are the writings that appear when the pointer goes on the graph

  - the title and the stylistic aspects attached to it

  Below there are the options of the chart of active and inactive patients:

```
options: {
  maintainAspectRatio: true ,
  responsive: true ,
  onClick: event => {
    if (this.myChartInactivePatients.getElementAtEvent(event).length > 0) {
      if (this.myChartInactivePatients.getElementAtEvent(event)[0]['_model'].datasetLabel
                === 'Non␣attivi') {
        this.showTable();
      }
    }
  },
  onHover: (event) => {
    if (this.myChartInactivePatients.getElementAtEvent(event).length > 0) {
      if (this.myChartInactivePatients.getElementAtEvent(event)[0]['_model'].datasetLabel
                === 'Non␣attivi') {
        this.setHoverActiveInactiveVariable();
      } else {
        this.unsetHoverActiveInactiveVariable();
      }
    }
  },
  scales: {
    xAxes: [{
      display: true ,
      stacked: false ,
      ticks: {
        fontSize: 12,
        fontStyle: 'bold',
        fontFamily: 'Helvetica',
        fontColor: '#006192'
      }
    }],
    yAxes: [{
      display: true ,
      stacked: false ,
      ticks: {
        fontSize: 12,
        fontStyle: 'bold',
        fontFamily: 'Helvetica',
        fontColor: '#006192'
      }
    }],
  },
  legend: {
    onHover: (event: MouseEvent , legendItem: Chart.ChartLegendLabelItem) => {
      if (legendItem.text.length > 0 &&
                (legendItem.text === 'Non␣attivi' || legendItem.text === 'Attivi')) {
        this.setHoverActiveInactiveVariable();
      } else {
        this.unsetHoverActiveInactiveVariable();
      }
    },
    display: true ,
    position: 'top',
    labels: {
      usePointStyle: true ,
      fontColor: '#006192',
      fontSize: 18,
      fontFamily: 'Helvetica',
    }
  },
  tooltips: {
    // content: '{pathology}: {number}',
```

```
      backgroundColor: '#1c1c1c',
      bodyFontSize: 18,
      titleFontSize: 18,
      cornerRadius: 5,
      caretPadding: 10
    },
    title: {
      display: true,
      fontColor: '#006192',
      fontSize: 20,
      fontFamily: 'Helvetica',
    },
    hover: {
      mode: 'nearest',
      intersect: true
    }
}
```

Chapter 5

Results and Discussion

5.1 The introduction of IBDQ

5.1.1 The needs of physicians

Previously in IBD Tool there was, among all the questionnaires concerning the impact of the disease on the quality of life, the SIBDQ questionnaire (Short Inflammatory Bowel Disease Questionnaire), a tool composed of ten total questions for the evaluation of the disease on a seven-point scale. When this questionnaire was selected by the patient for completion, the patient was asked not to complete the questionnaire if he had had a colostomy or ileostomy. This is because it was initially thought to insert a questionnaire specifically for this type of patient, the IBDQ-S questionnaire, where "S" stands for "stomy". In the end, the physicians considered appropriate to replace all these questionnaires with the full version, that is the IBDQ questionnaire, consisting of 32 questions and a seven-point rating scale (Figure 5.1). This replacement served precisely to avoid any discomfort or misunderstanding for the patient and to simplify the assessment.

5.1.2 The solution

The proposed solution was to insert this new questionnaire replacing the previous one, the SIBDQ. The IBDQ questionnaire is a three-month frequent questionnaire, only available for "TELEMEDICINE" patients. The system sends this questionnaire automatically when all the others three-month frequent questionnaire are sent. For the patient it is possible to send a new IBDQ questionnaire also going to the section "contact the center" from the home page of the patient and selecting the questionnaire from the specific list. Also for the physician it is possible to send a new IBDQ questionnaire to a specific patient at any time by going to the questionnaire panel of a specific patient and clicking on the send button. The physician receives the IBDQ and he can consult the results in different ways:

Figure 5.1. IBDQ questionnaire. The compilation view from the patient page.

- in the automatic email that the system sends each day to notify the doctor about the compiled questionnaires in the current day (Figure 5.2)

- in the section related to the compiled questionnaires of a specific patient by consulting each compiled IBDQ (the physician can see each specific given answer) (Figure 5.2, Figure 5.3). In this section there is a chart with the global questionnaire's trend, built with the different IBDQ's scores during time (Figure 5.3).

Figure 5.2. Physician's view of IBDQ. Automatic mail sent to the physician resuming the scores and the results of the compiled questionnaires, including the IBDQ one (a). Physician's view of IBDQ questionnaires related to a specific patient (b).
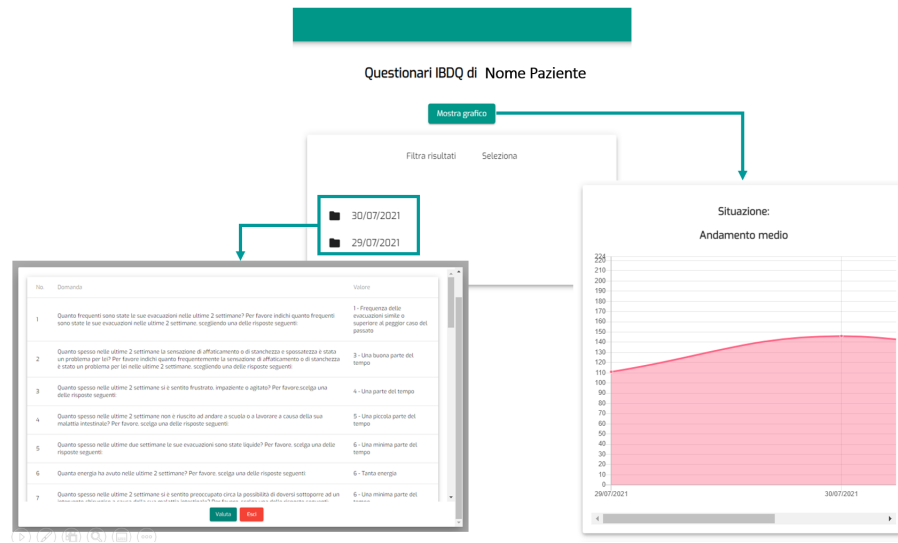
Figure 5.3. Physician's view of IBDQ questionnaires related to a specific patient. It is possible to select and open the IBDQ questionnaire from the patient page, then it is possible to select the questionnaire of interest and visualize all the answers, or select to show the chart and visualize all the results over the time.

5.1.3 Discussion

The replacement of the SIBDQ questionnaire with the full version of IBDQ has led to the revision of all previously existing methods to adapt them to the presence of the new questionnaire. This revision also allowed to carry out maintenance even on what was already present. This phase allowed to become familiar with all the complex architecture of the application.

The IBDQ questionnaire is certainly longer, but also more complete. In the IBDQ questionnaire, patients are asked to answer the questions considering the symptoms of the last two weeks. The questionnaire's topics range from symptoms related to the disease to how the patient has been feeling, and about his mood. To date, patients are completing the questionnaire and about 180 questionnaires have been completed.

Furthermore, this questionnaire returns a final score which allows to have an overview of the state of quality of life related to the activity of the disease. This score is given by the sum of all the scores obtained by the questions. The threshold of 170 used to determine the remission was validated only for Crohn's patients [24], but in IBD Tool it was inserted identical also for patients suffering from ulcerative colitis. The aim is to collect enough data to verify in the future whether it can also be transposed to ulcerative colitis patients and to validate what has already been proposed for Crohn's ones.

5.2   Dashboard

5.2.1   The needs of physicians

Up to now, IBD Tool did not allow to have a broad and clear view of registered, active, or actually healthy patient-users at any given time. Therefore, physicians have expressed an interest in having a control panel from which to view the main values of the application regarding the number of registered patients, the number of active patients, the number of patients divided by category, stable and unstable patients in the last month. Having a dedicated section of the application that allows to see these data clearly represents a turning point in terms of communication. This because, above all, it allows to realize about the status of the app quickly and independently.

5.2.2   The solution

The proposed solution to satisfy the needs of clinicians was, through this thesis, to design and release a dedicated section, accessible from the personal home-page referring to the physician (Figure 5.4). Through this section, called dashboard, it is possible to communicate all the necessary data using interactive charts and tables that are continuously updated based on the latest data entered in the database. The
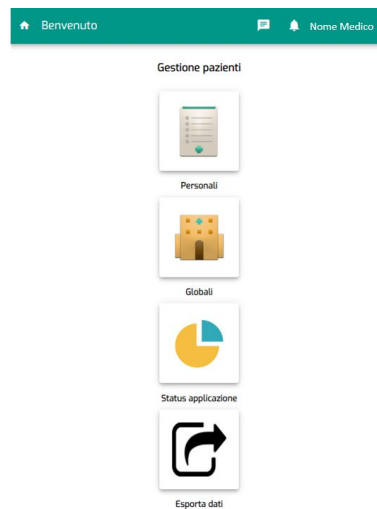
Figure 5.4.   Home page of physician.   The icon called "Status applicazione" redirects to the dashboard section.

dashboard is made up of 6 distinct subsections, each of which has been inserted into a different Angular component, in order to make everything as modular as possible. These sections are:

- the section about the number of global patients of the entire application, divided by pathology and represented through a dedicated doughnut chart and a resuming table (Figure 5.5)

- the section about the number of personal patients (only the patients of the logged physician) of the application, represented through a dedicated doughnut chart and a resuming table (Figure 5.5)

- the section related to the number of patients-users who never logged into the application represented by a horizontal bar chart (Figure 5.6)

- the section related to the number of inactive and active patients, divided by the category "STANDARD" and "TELEMEDICINE", represented by a bar chart (Figure 5.7)

- the section related to the number of stable and unstable ulcerative colitis patients, represented by a stacked bar chart (Figure 5.8)

- the section related to the number of stable and unstable Crohn patients represented by a stacked bar chart (Figure 5.9).

Number of patients

The section about the number of patients is represented by two doughnut charts accompanied by the related table which, respect to the graph, returns the sum of the total number of patients. The number of a single category of patients can be seen both from the table and the tooltip as the mouse moves on the graph. This makes the entire graph interactive (Figure 5.5).

Never logged in patients

The section about the number of patients who have never logged into the application is represented by a horizontal stacked bar chart. The red part of the graph represents the number of patients who have never logged in, the grey one represents users who logged in at least once after their registration. The red part of the graph is clickable and clicking on it a table appears. This table contains the name of the patients who have never logged in and there is the possibility to select some or all of them to let the system send an automatic reminder email (Figure 5.6). The text of the automatic email is "Dear user, we encourage you to log into IBD Tool as soon as possible. Log in: https://ibd-tool-mauriziano.web.app//login. Best regards, IBD Tool - Mauritian Hospital".
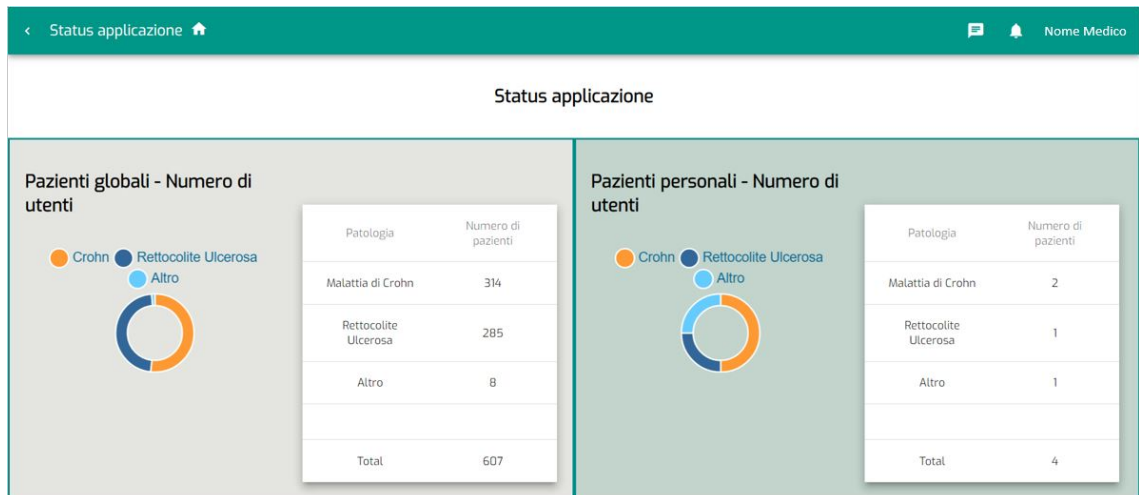
Figure 5.5.   Section about the total number of global patients (the left side) and of personal patients (the right side), divided by pathology.
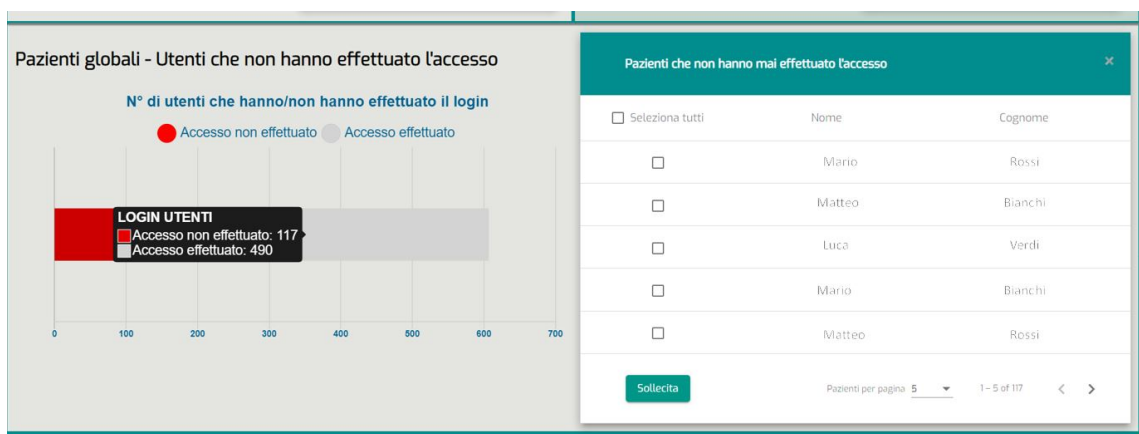
Figure 5.6.   Section about the total number of never logged in patients.

Active and inactive patients

The section about active and inactive patients is represented by a grouped bar chart, where the two main groups are "TELEMEDICINE" and "STANDARD" patients. The orange column represents the inactive patients. "TELEMEDICINE" patients are considered inactive if they do not login from four months or more. "STANDARD" patients are considered inactive if they do not login from seven months or more. Clicking both on the "TELEMEDICINE" inactive or on the "STANDARD" inactive a table appears. This table contains the name of all inactive patients (both telemedicine and standard ones), the date of their last login and there is the possibility to select some or all of them to let the system send an automatic reminder email (Figure 5.7). The text of the automatic email is the same of the previous section.
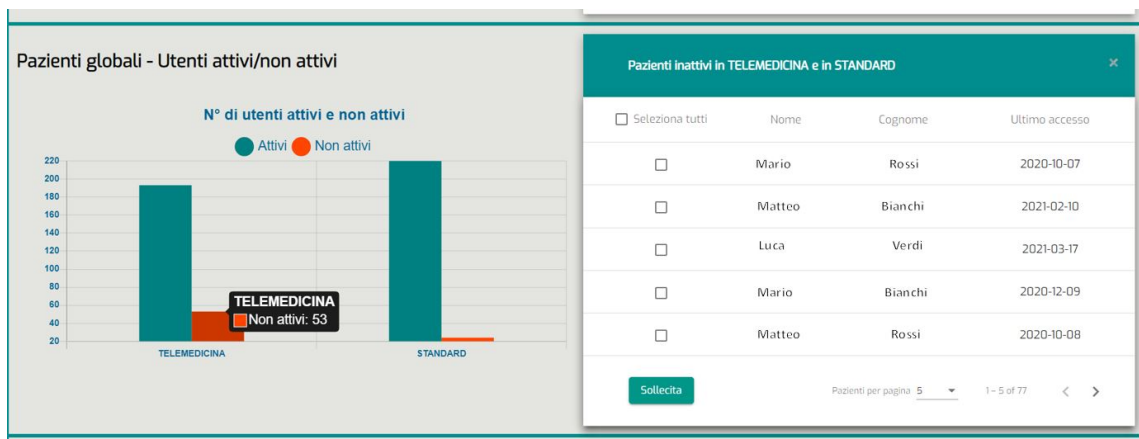
Figure 5.7.   Section about the total number of inactive and active patients in the two categories, TELEMEDICINE and STANDARD

Stable and unstable patients

The section about stable and unstable patients is represented by a stacked bar chart. There are two main graphs: one is related to the ulcerative colitis patients (Figure 5.8) and the other to the Crohn patients (Figure 5.9). The ulcerative colitis chart is composed by three main categories: the improving patients, the worsening patients and the stable patients. A patient is considered improved if, comparing the last two compiled patient-SCCAI questionnaires, he has a better score in the last one, or the last score is less or equal than the previous score minus two points. A patient is considered stable if the variation score is in the range of two points. A patient is considered worse if the last score is greater or equal of the previous score plus two points. Each of these three categories can be divided in two groups:

- patients in remission if the score is less than five (the green group)

- patients in relapse if the score is greater or equal than five (the red group).

The Crohn chart is similar to the previous one, except for the reference score questionnaire which is the patient-HBI and the groups in which each category is divided which are no longer two but four. For each category there are four main groups:

- patients in remission if the last questionnaire score is less than five (the green group)

- patients in mild activity if the last questionnaire score is greater or equal than five and less than eight (the light orange group)

- patients in moderate activity if the last questionnaire score is greater or equal than eight and less than sixteen (the dark orange group)

- patients in severe activity if the last questionnaire score is greater or equal than sixteen (the red group).

Each group of both graphs is clickable, and a table appears when clicked. The table allows to view the patients who belong to a given category, and to visualize the compiled questionnaires of interest (the specific type for classification). On the table there is also the link to the patient card, which contains the personal and clinical data. It is also possible to contact each patient directly by email icon or by opening the dedicated chat through the chat icon on the table.
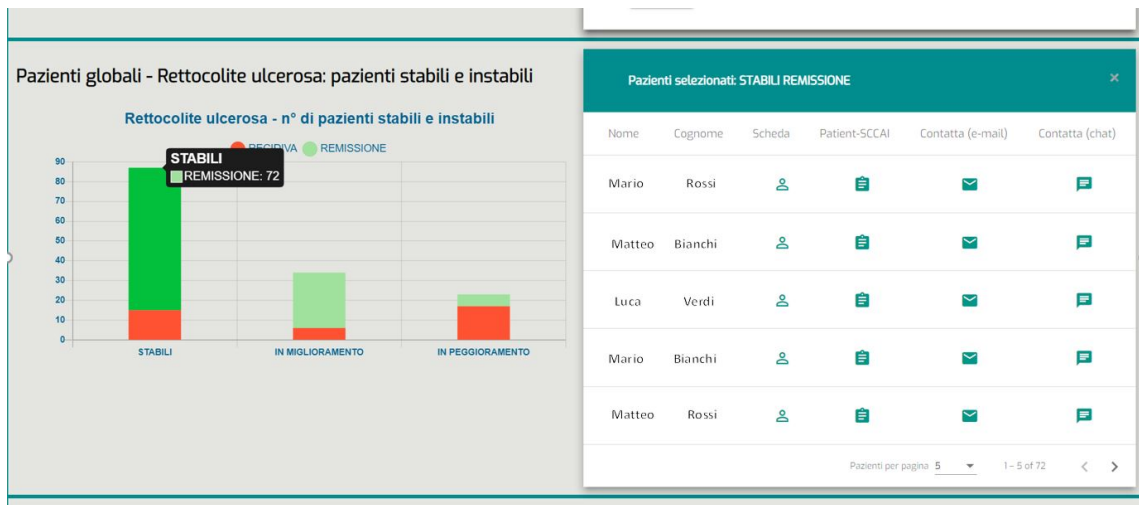
Figure 5.8.   Section about the total number of ulcerative colitis patients, in terms of stable and unstable patients (improving or worsening ones), both in remission or relapse.
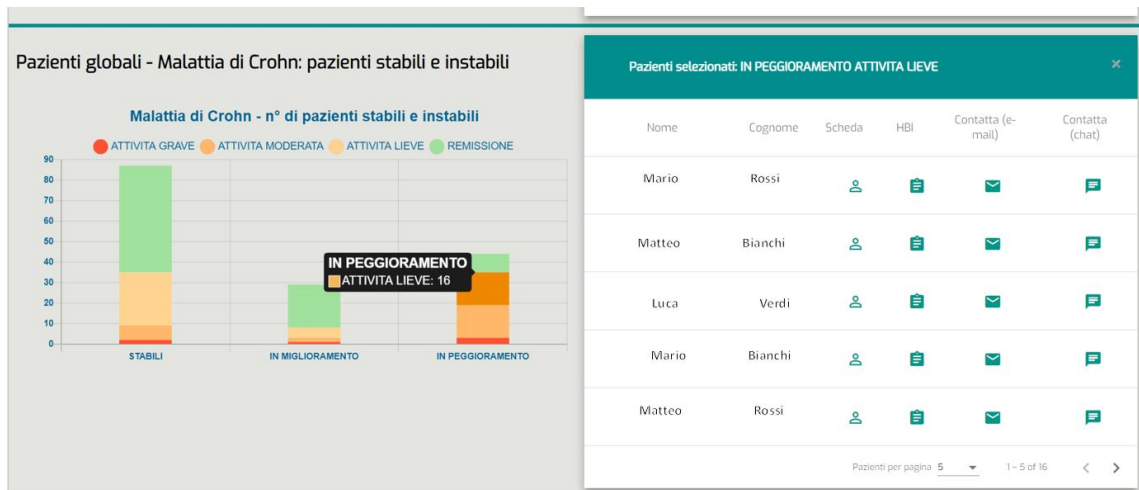
Figure 5.9.   Section about the total number of Crohn patients, in terms of stable and unstable patients (improving or worsening ones), both in remission, mild activity, moderate, or severe activity.

Adaptation and interaction

The entire dashboard, with its graphs and tables, has been designed to adapt to any screen size, both for simple window size reductions (Figure 5.10) and for mobile viewing (Figure 5.11). The latter has been slightly modified to allow for the best performance in the small screens of smartphones.   Another important feature of
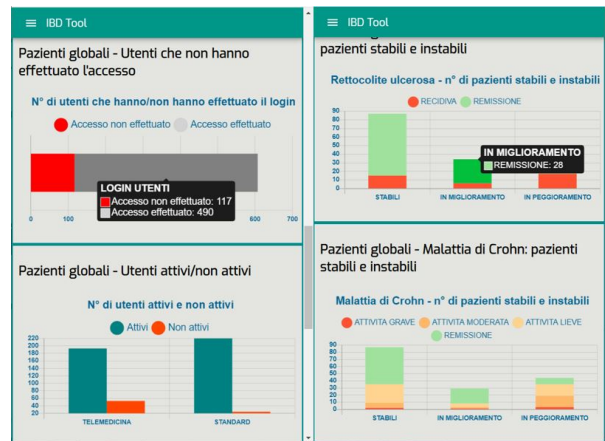
Figure 5.10.   Dashboard visualization if screen size is less than 1500px.

Figure 5.11.   Dashboard visualization if screen size is less than 500px, for mobiles.

the charts is that, thanks to the properties defined using the formalisms of the Chart.js library, it is possible to eliminate from the legend what the user does not want to be displayed on the chart (Figure 5.12).
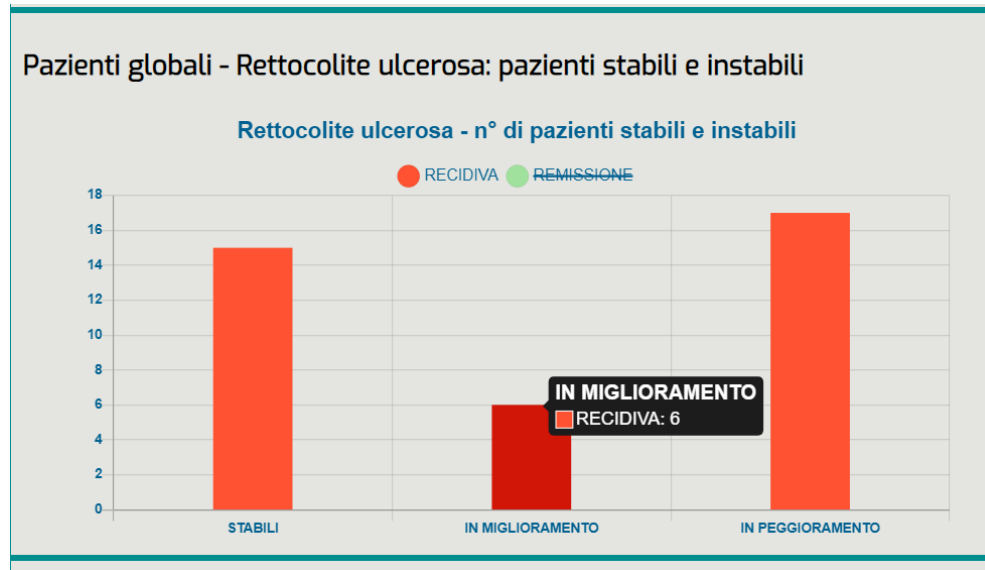
Figure 5.12.   Example of the interaction with the legend.

5.2.3   Discussion

The designed dashboard and all the additional features related to it, such as the ability to send reminder emails to inactive users or users who have never logged in, and the ability to take note of who and how many stable and unstable patients are, it is a section that has found an excellent impact in these months of testing, especially in terms of frequency of use. The main reason is that it permits to see the health state of patients at a glance, and in this way, physicians can get a general idea of disease's evolution.

The dashboard also allows to have some simple but important first overview regarding the use of the application. For example, it is easy to know that more or less 105 above 633 patients have never logged in (the 16,6% of registered patients); among the patients who have logged in, about 40 above 267 in the category "TELEMEDICINE" are inactive, and 24 above 261 in the category "STANDARD" are inactive too. This will surely lead to some future interventions to improve patient involvement.

The first proposed easy solution has been the reminder sending function (through emails) integrated in some of the tables of the dashboard. This function has been particularly useful, allowing some users to start the password recovery procedure and to re-access the application after a long time, modifying a bit the numbers shown before.

Another positive aspect is that the data are not static, but they follow the evolution of registered users and of the completed questionnaires updated at the time the section is opened.

5.3 The data aggregation

5.3.1 The needs of physicians

After about a year of data collection through the compilation of questionnaires by both physicians and patients, physicians expressed the need to compare the results. In order to conduct a concordance study, it has been necessary to reorder all the completed questionnaires and organize them in a way that was functional to the expressed needs. Physicians specifically requested that the system will reorganize only the data from the PRISM, CLINICAL-SCCAI and PATIENT-SCCAI questionnaires for patients with ulcerative colitis and PRISM, CLINICAL-HBI, and HBI for patients with Crohn's disease. In fact, the physician's score of these questionnaires only can be compared with that of the patient. Furthermore, another request was that the concordance not only will be studied between clinician and patient, but also it has to take into consideration the comparation between physicians called "senior" and those called "junior" with less experience.

5.3.2 The solution

The proposed solution is a new section accessible from the landing page of the physician (Figure 5.13) which lead to a page with two expandable panels (Figure 5.14). The first panel contains all the data of ulcerative colitis patients, the second all the data of Crohn patients; in the description of the panel there is the indication about the reference questionnaires. Opening the panel a table appears. The table contains: name, surname, and the birthdate of the patient; then, there are all the scores with the associated compilation date of the patient, clinical senior/s and clinical junior/s questionnaires; at the end of the row there are some columns which indicate the total number of clinical questionnaires of each type (PRISM and one between CLINICAL-HBI and CLINICAL-SCCAI in base of the disease) and the logical columns which indicate if there are or not both the type of questionnaires scores (PRISM and one between HBI and SCCAI in base of the disease). Data are easily consultable directly from the table (Figure 5.15), from which there is also the possibility to download the table in the excel format (Figure 5.16).
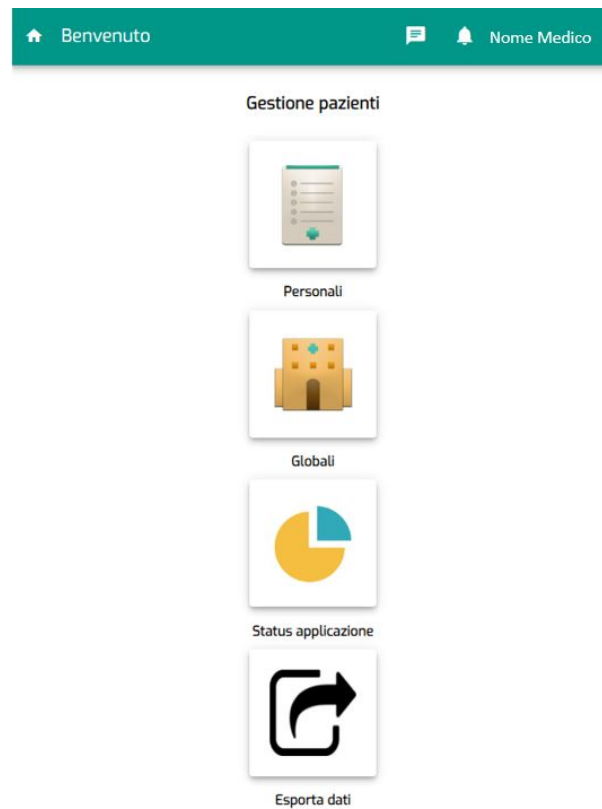
Figure 5.13. Home page of physician. The icon called "Esporta dati" redirects to the data aggregation section.

Figure 5.14. Data aggregation section with two expandible panels, each related to a specific pathology.

Figure 5.15. Table of aggregated data. The table shows all the aggregated data and in the pagination row there is the download symbol which permits to download the data in the excel format.

Figure 5.16. Aggregated data in excel format.

5.3.3   Discussion

The designed section allows the consultation and comparison of the scores of the questionnaires that have been completed by patients and physicians in the same period (i.e. in the same month). The way in which the data have been entered into the table and the contents of the table itself are aimed precisely at facilitating the subsequent concordance study that will be conducted by clinicians.

The ability to download the table allows the work on the data directly in Excel. Keeping the date on which the table has been downloaded in the title of the document is particularly useful because the data are updated every time the section is accessed.

The most critical part of the work was to correctly associate the questionnaires, to decide the cases in which the scores of the questionnaires could or could not be inserted in the table. In the end, the base criterion used was to form a new line every time there were at least two questionnaires that could be associated, of which at least one belonging to a clinician to guarantee a comparison.

5.4   The clinical data

5.4.1   The needs of physicians

Another request from the physicians was to further expand the platform, trying to recreate a real medical record of the patient. Therefore, it has been requested to expand the section relating to the patient card, including not only the patient's personal data, but also further information regarding the disease which will be particularly useful for some medical studies. In particular the request was to insert the following information:

- group of control (TELEMEDICINE or STANDARD), sex, date of birth, age, date of diagnosis, age of diagnosis, pathology duration, familiarity (expressed as 0 for no and 1 for yes), type of pathology (expressed as 1 for Crohn, 2 for ulcerative colitis and 3 for IBD) for all patients

- information about inflammatory state, stenosing state, penetrating state, perianal disease, colon localization, ileum localization, and upper gastrointestinal tract localization (all expressed as 0 for no and 1 for yes) only for Crohn's patients

- information about the UC localization (expressed as 1 for proctitis, 2 for left colitis, and 3 for pancolitis) only for ulcerative colitis patients and generic IBDs

- information about extraintestinal manifestations in the patient's history or active (both expressed as 0 for no and 1 for yes) and information about the

number of resections (expressed as a number), ostomy and major operations (both expressed as 0 for no and 1 for yes) for all patients

- data about past and ongoing therapies, particularly the 5-ASA therapy, the topic therapy, the oral steroid therapy GCS (Glucocorticoids), therapy with immunosuppressants, and therapy with biological drugs for all patients.

5.4.2 The solution

Visualization

Trying to satisfy the requests of physicians, the following solution was proposed. Accessing to the patient card, the previous section of clinical data (Figure 5.17) has been completely overturned and expanded by giving a new aspect (Figure 5.18).

Figure 5.17.   The patient card before this thesis work.

In the clinical data view it was decided to group the variables in three columns to make the view more organized: the first related to basic clinical data, the second

Figure 5.18.   The new clinical data section in the patient card. The section related to the clinical data has been expanded by adding new variables and including the possibility to insert new data from the "+" symbol under the title "Dati clinici".

related to all data regarding interventions and therapies, and the third concerning disease-specific data. Furthermore, the main dynamic variables have been inserted into small panels so that the information remains hidden unless the user opens the panel. This approach is particularly advantageous because the data can increase significantly over time and having it all visible can make the visualization confusing and cluttered (Figure 5.19).

In the panels relating to the therapies there is also the possibility to see graphs that summarize the progress of the therapy over time clicking on the graph symbol (Figure 5.18). In particular, the date on which the data was entered is shown on the abscissas and on the ordinates the information is binary, i.e. it indicates whether or not therapy was in progress. In the case of therapy in progress, the start date of the therapy is indicated in the tooltip as soon as the mouse passes over the data (Figure 5.20 and Figure 5.21). Any notes or annotations on the therapies inserted on the same date of the therapy variable, are also reported in the tooltip in a preview type view and in the lower part of the dialog window (Figure 5.22).

The visualization of clinical data is also adapted to different screen sizes and on mobiles. If the screen size decreases, the three columns scroll all below each other, both on the browser (Figure 5.23) and on the mobile (Figure 5.24).
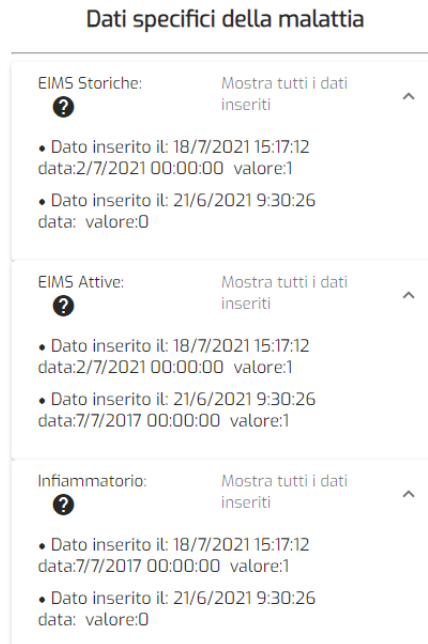
Figure 5.19.   Example of visualization of dynamic clinical variables by expanding panels. The data is always saved keeping the information of the variable (generally with a logical value 0 or 1), of the insertion date of the variable and of the date which the value refers to. This last date can be either the date of the diagnosis or any other date.
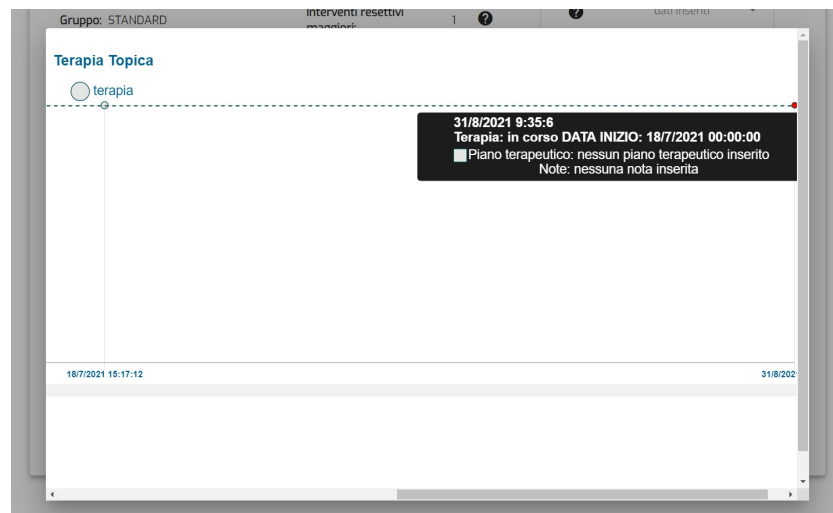

Figure 5.20.   Therapy evolution over the time. Example of ongoing therapy.

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Figure 5.21. Therapy evolution over the time. Example of not ongoing therapy.
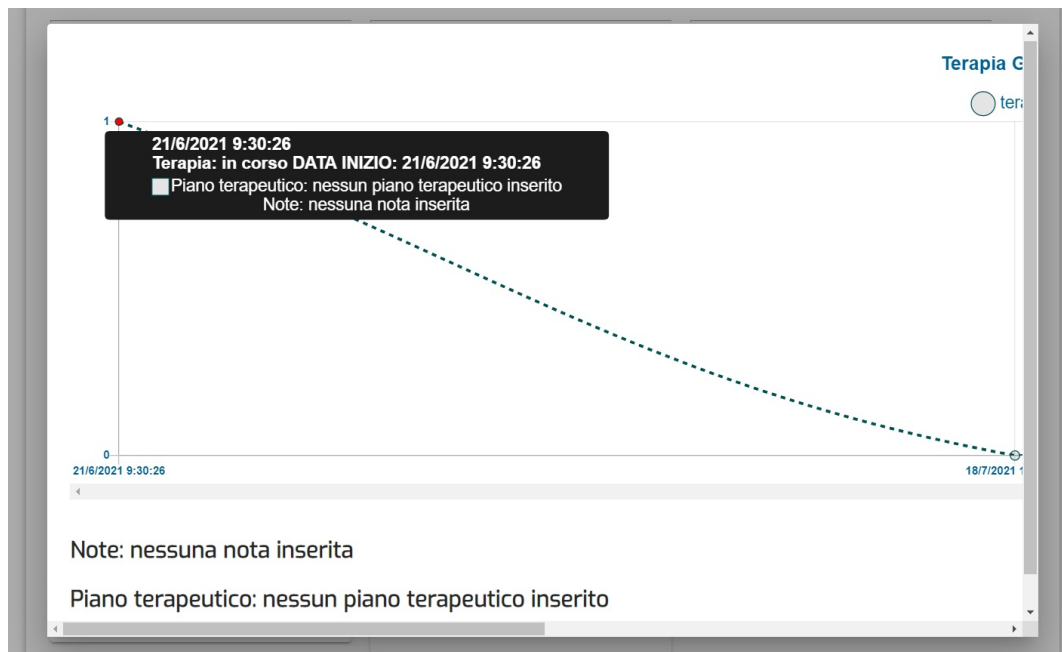
Figure 5.22. Therapy evolution over the time. Notes and therapy's notes visualization in the tooltip and in the lower part of the dialog window.

Figure 5.23.   Visualization on small screen size on browser.

Figure 5.24.   Visualization on mobile.

Data entry

It has been created a new dedicated section to insert clinical data. This section is accessible from the patient card, clicking at the "+" symbol below the title in the patient page (Figure 5.18). After pressing this symbol, a form appears. There are two main situations: the first time data are compiled for a new registered user and subsequent times.

The times following the first in which the form is filled, as soon as the form appears, it is already pre-filled with the values already entered the last time (Figure 5.25, Figure 5.26, Figure 5.27, Figure 5.28). It was decided to have a pre-filled form to facilitate and speed up the procedure of subsequent visits.

Figure 5.25. First two parts of the pre-filled form.

Figure 5.26.   Second two parts of the pre-filled form.

Figure 5.27.   Third two parts of the pre-filled form.

Figure 5.28.   Last part of the pre-filled form.

The first time the form is compiled, these things happen:

- the field "age" is automatically calculated from the birth date, so this field is not editable

- the field "pathology" is taken from data that have been entered during the registration phase, but it is still editable

- after choosing the date of diagnosis, fields like "age of diagnosis" and "pathology duration" are automatically compiled

- all the other fields like familiarity, inflammatory state, stenosing state, penetrating state, perianal disease, colon localization, ileum localization, and upper gastrointestinal tract localization, extraintestinal manifestations in the patient's history or active, ostomy and major operations are by default set on "yes" answer and by default the reference date is set equal to the diagnosis date, but they must be modified by real values referred to the patient

- therapies fields are empty; the user must choose if a therapy has ever been done, if the answer is "yes" another question appears that wants to know if a therapy is still ongoing; if the selection to this last question is "yes", the starting therapy date must be compiled (Figure 5.29).

Figure 5.29. Example of therapies' data entry. There are three possibilities: a therapy which has been done in the past but it is not ongoing (a), a therapy which has never been done (b), and a therapy which has been done and it is still ongoing (c).

- at the end of the form there is a section which permits to insert some general annotations or specific annotations regarding therapies (Figure 5.28)

- the last action to do is the possibility to confirm or cancel the data entry procedure (Figure 5.28). If the user confirms, a dialog window appears, with a summary of inserted data (Figure 5.30). If all data are correct, the user can confirm again or cancel definitely. After this second confirmation, a message of success appears (Figure 5.31), the window is reloaded, and data are inserted in the database. If any problem occurs, a message of alert appears, and the page is refreshed (Figure 5.31).

It has been also inserted a functionality which permits to speed up the data entering of users who do not have clinical data saved yet. Through a simple check box in the table of personal or global patients it is possible to show only users with no clinical data (Figure 5.32). In addition, it is also possible to scroll through the list of patients and a warning triangle indicates whether clinical data have been completed at least once or are missing (Figure 5.33).

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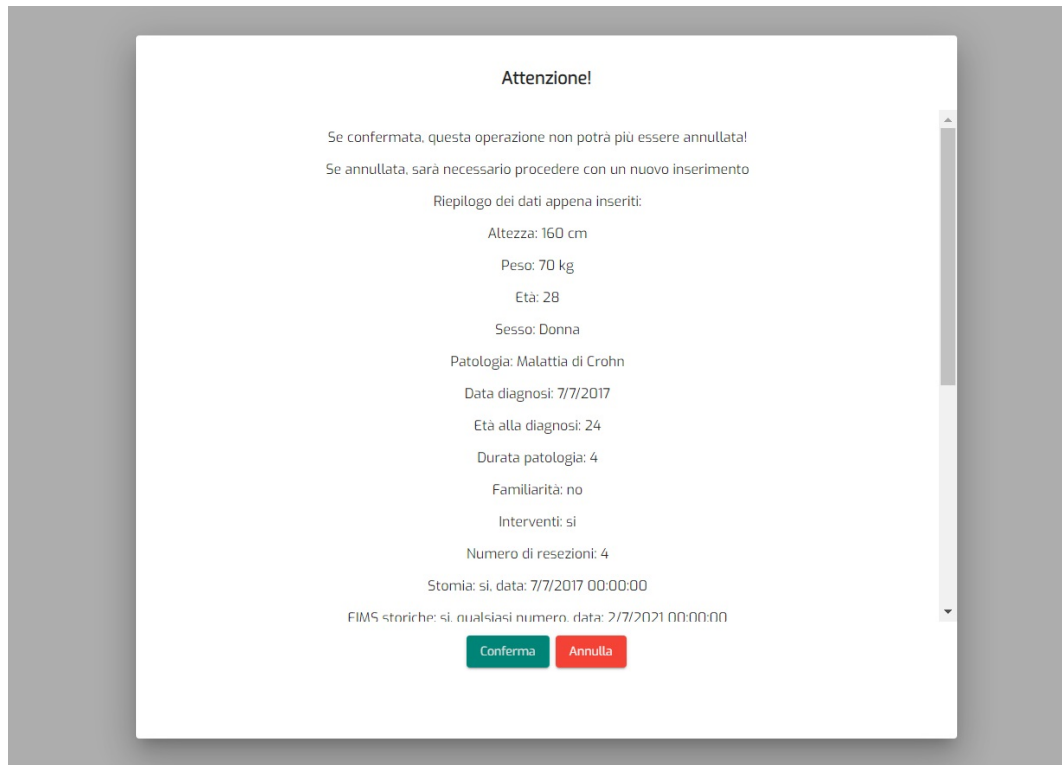
Figure 5.30.   Confirmation and summary dialog window.
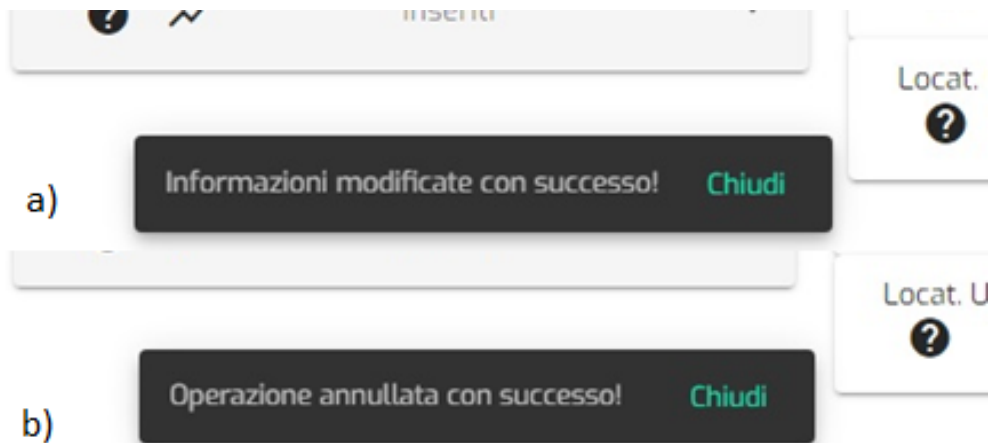
Figure 5.31.   Feedback about the status of the operation. If data have been saved, a success message appears (a); in any case of failure a cancellation message appears (b).
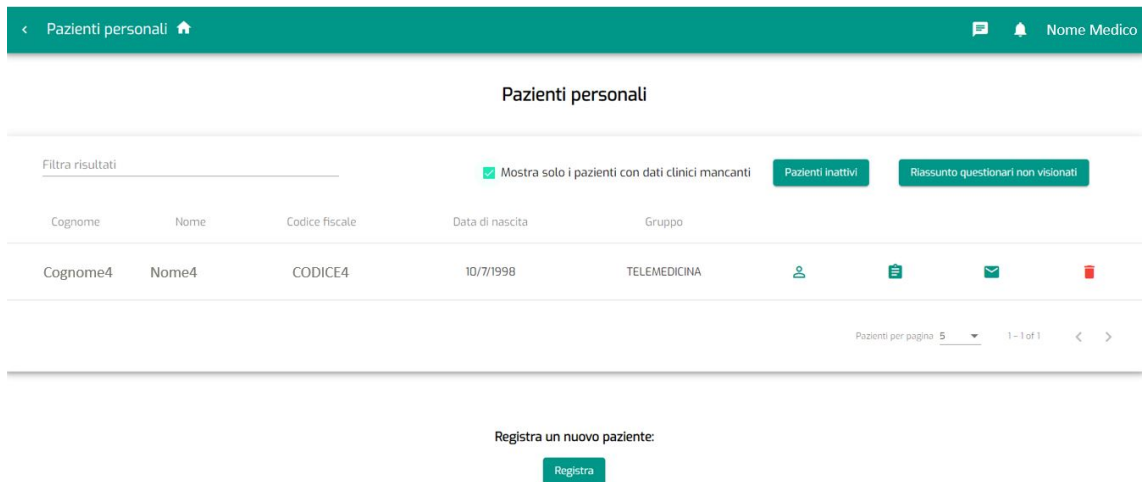
Figure 5.32. Check box showing only patients with missing clinical data.
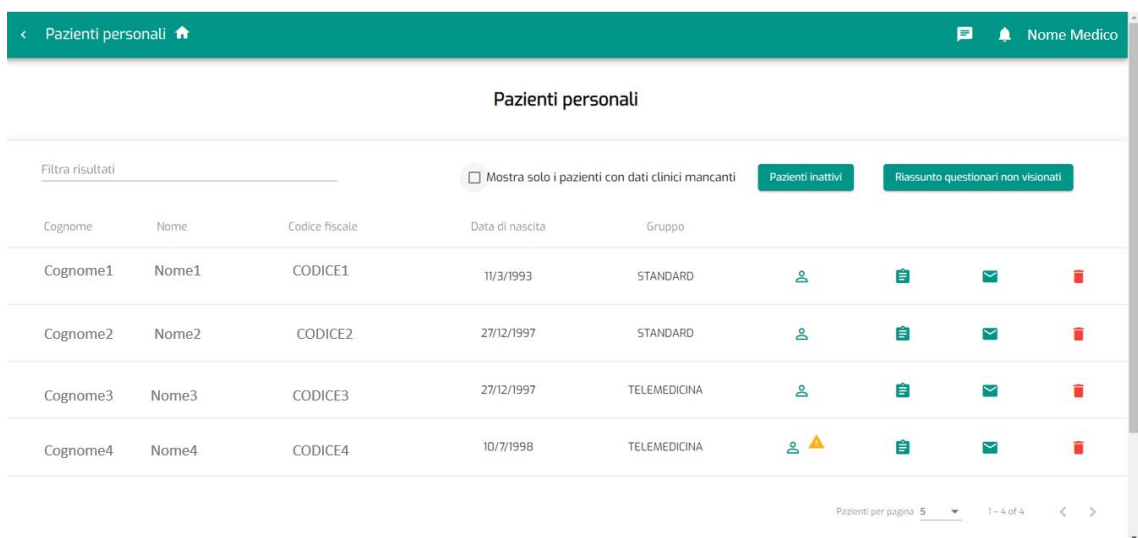
Figure 5.33. Warning icon to warn about the lack of clinical data for a given patient.

Data saving

To save the data, it was necessary to use a certain formalism. Most of the values has been saved as logical values, replaced by "0" or "1" or by simple numbers, having a very specific meaning (Figure 5.34). In the database all the clinical variables are saved in a field called "bodyStat" of any patient-user in the "users" collection on MongoDB. All the Yes/No variables and the Ulcerative colitis localization are saved as an object with three fields: "value", "dateInput" and "date" (Figure 5.35).

VARIABLE	PATHOLOGY	MEANING
Sex	All	1. Women 2. Man
Birthdate	All	DD/MM/YYYY
Age	All	Years
Date of diagnosis	All	DD/MM/YYYY
Age of diagnosis	All	Years
Pathology duration	All	Years
Familiarity	All	0. No 1. Yes
Pathology	All	Name of pathology
Inflammatory state	Crohn	0. No 1. Yes
Stenosing state	Crohn	0. No 1. Yes
Penetrating state	Crohn	0. No 1. Yes
Perianal disease	Crohn	0. No 1. Yes
Colon localization	Crohn	0. No 1. Yes
Ileum localization	Crohn	0. No 1. Yes
Upper gastrointestinal tract localization	Crohn	0. No 1. Yes
Extraintestinal manifestations in the patient's history	All	0. No 1. Yes
Active extraintestinal manifestations	All	0. No 1. Yes
Ostomy	All	0. No 1. Yes
Major operations	All	0. No 1. Yes
Ulcerative colitis localization	Ulcerative colitis	1. Proctitis 2. Left colitis 3. Pancolitis
Number of resections	All	Number

5-ASA-OS therapy	All	Done:
		  0. No
		  1. Yes
		Ongoing:
		  0. No
		  1. Yes

GCS-OS therapy	All	Done:
		  0. No
		  1. Yes
		Ongoing:
		  0. No
		  1. Yes

Imm. therapy	All	Done:
		  0. No
		  1. Yes
		Ongoing:
		  0. No
		  1. Yes

Bio. therapy	All	Done:
		  0. No
		  1. Yes
		Ongoing:
		  0. No
		  1. Yes

Topic therapy	All	Done:
		  0. No
		  1. Yes
		Ongoing:
		  0. No
		  1. Yes

Group	All	TELEMEDICINE/STANDARD
Weight	All	kg
Height	All	cm

Figure 5.34. Conversion table of values of all the variables inserted in the database.

"DateInput" is the date of the form submission, while "date" is the reference date of the feature. This last date can be equal to the date of diagnosis, or a different one. Instead, all the data referred to the therapies are saved as an object of four main fields: "done", "onGoing", "dateOfStart" and "dateInput" (Figure 5.36). These fields can be compiled in the following ways:

- if the therapy has been done in the past, but it is not still ongoing: "done" = 1, "onGoing" = 0, "dateOfStart" = null, "dateInput" = date of submission

- if the therapy has never been done: "done" = 0, "onGoing" = null, "dateOfStart" = null, "dateInput" = date of submission

- if the therapy has been done in the past, and it is still ongoing: "done" = 1, "onGoing" = 1, "dateOfStart" = date of start, "dateInput" = date of

submission.

```
∨ localizzazioneUC: Array
   ∨ 0: Object
        date: "30/09/2020 00:00:00"
        value: "2"
        dateInput: "30/09/2020 00:00:00"
```

Figure 5.35.   Example of a saved clinical variable on MongoDB.

```
∨ therapy5ASAOS: Array
   ∨ 0: Object
        done: "1"
        onGoing: "1"
        dateOfStart: "30/09/2020 00:00:00"
        dateInput: "30/09/2020 00:00:00"
```

Figure 5.36.   Example of a saved clinical variable about therapy on MongoDB.

5.4.3   Discussion

After the introduction of this section, physicians entered clinical data of 600 patients. The patient cards, thanks to the clinical data, are much more complete, almost comparable to a virtual medical record. The real usefulness of this section is that through the reading of the present data it is possible to immediately get an idea of the patient's clinical status, of the disease, of the evolution, of the carried out interventions, and of past and ongoing therapies. From a graphic point of view, the way in which clinical data is displayed has been designed not to overload the physician with information, but it allows to choose which information to see by opening the corresponding panel. This design choice was made thinking about a future growth of each user's data. In addition, the functionality of signalling clinical data missing was particularly useful, because it permitted to speed up the first compilation phase of users with no clinical data.

One of the most critical aspects to overcome was deciding how to save the data and how to insert them to do not make the form too complicated and elaborate in its compilation. Finally, the proposed solution has been approved by the physicians, but this does not deny the possibility of future interventions, improvements, or new features to be added based on new needs. In fact, from year to year it could be useful to insert new variables to be used for new clinical studies or it could be the need to insert new therapies because medicine is not a static science. Therefore, the real advantage is that a virtual medical record, thus created, can be easily adapted to new requirements.

Chapter 6

Conclusion and future developments

IBD Tool is nowadays a monitoring tool used on an experimental basis by some physicians of the Mauriziano Hospital in Turin and it counts about 633 registered patients. Through this thesis work it has been possible to retrieve some first numbers on the web app. Among the 633 patients, the 52,3% is suffering of Crohn's disease, the 46,4% is suffering of ulcerative colitis and the 1,3% of other patholigies. The 83,4% (528 patients) has used his own credentials to login at least once, and 64 patients over 528 are inactive (the 12,1% against the 87,9% who regulary uses the application by answering the questionnaires) (Figure 6.1).
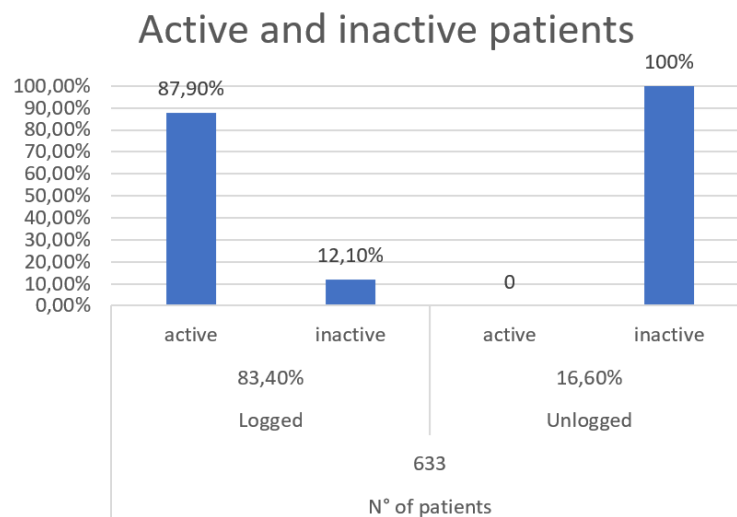

Figure 6.1. Percentage about IBD Tool usage among patients-users.

These first statistics, which emerge from the dashboard, encourage to do better. The results of this first year and a half of use of IBD Tool have shown that patients are well disposed towards telemedicine, but only if telemedicine is not a complete replacement for traditional treatments. In fact, tele-care does not aim to replace the traditional visit, but to offer additional tools that can help physicians and patients. Anyway, there is a need for more effective communication in this regard. Numbers that emerge from the use of the IBD Tool are very significant because they are a clear mirror of the patient's need to feel more and more involved in his health.

IBD Tool's work is far to be finished. In fact, it has already been thought about how to improve the applicationto to give voice to these considerations and to make the platform even more usable and captivating. Through this thesis work the physycian's section has been increased with a lot of funcionalities, but some future projects also for patient's section are listed below.

- After the indroduction of a lot of new data (new users, clinical variables, etc.), it could be good to provide a better organization of data in the database to facilitate and speed up the access procedure to the database itself and to avoid any kind of slowdown.

- Clinicians manifestated the need to implement a section, similar to a notice board, from which communicate to all patients any kind of advice.

- Clinicians also expressed the need to increase the data export section with new tables including all the data on the clinical variables that have been collected in recent months.

- On the patient side, it was decided to create a dashboard similar to that of physicians, but all made up of personal data, focusing on information regarding the evolution of his disease over time based on the scores of the questionnaires. Introducing such a section, the patient's involvement and empowerment could increase.

References

[1] O. Stefano, "Telemedicine during the covid-19 in italy: A missed opportunity?," *Telemedicine journal and e-health : the official journal of the American Telemedicine Association*, vol. 26, pp. 973–975, 2020.

[2] Mann, D. M. and Chen, J. and Chunara, R. and Testa, P. A. and Nov, O. , "COVID-19 transforms health care through telemedicine: Evidence from the field," *J Am Med Inform Assoc*, vol. 27, pp. 1132–1135, 07 2020.

[3] "Use of telemedicine among general practitioners pre- and post-covid-19 in italy in 2020." `https://www.statista.com/statistics/1128317/use-of-telemedicine-among-gps-pre-and-post-covid-19-in-italy/`, 2020. Accessed: 2021-06-18.

[4] "Malattie croniche intestinali, la gestione ai tempi del covid." `https://www.ansa.it/canale_saluteebenessere/notizie/medicina/2020/11/30/malattie-croniche-intestinali-esordio-tra-15-e-30-anni_bb59914d-5b58-4482-bb4c-65332091ca00.html`, 2020. Accessed: 2021-06-18.

[5] "Malattie infiammatorie croniche intestinali. creato registro nazionale pazienti. siglato un accordo tra amici onlus e iss." `http://www.quotidianosanita.it/scienza-e-farmaci/articolo.php?articolo_id=73590`, 2019. Accessed: 2021-06-18.

[6] S. Danese, M. Cecconi, and A. Spinelli, "Management of IBD during the COVID-19 outbreak: resetting clinical priorities," *Nat Rev Gastroenterol Hepatol*, vol. 17, pp. 253–255, 05 2020.

[7] E. M. Strehle and N. Shabde, "One hundred years of telemedicine: does this new technology have a place in paediatrics?," *Arch Dis Child*, vol. 91, pp. 956–959, Dec 2006.

[8] W. G. O. for eHealth, "Telemedicine: opportunities and developments in member states: report on the second global survey on ehealth," p. 93 p., 2010.

[9] M. Aguas Peris, J. Del Hoyo, P. Bebia, R. Faubel, A. Barrios, G. Bastida, B. Valdivieso, and P. Nos, "Telemedicine in inflammatory bowel disease: opportunities and approaches," *Inflamm Bowel Dis*, vol. 21, pp. 392–399, Feb 2015.

[10] R. Latifi and C. R. Doarn, "Perspective on COVID-19: Finally, Telemedicine

at Center Stage," *Telemed J E Health*, vol. 26, pp. 1106–1109, 09 2020.

[11] L. Y. Zhang YZ, "Inflammatory bowel disease: pathogenesis," *World journal of gastroenterology*, vol. 20, pp. 91–9, 2014.

[12] "Malattie infiammatorie croniche intestinali." `https://www.humanitas.it/malattie/malattie-infiammatorie-croniche-intestinali/`. Accessed: 2021-06-18.

[13] G. E. Tontini, M. Vecchi, L. Pastorelli, M. F. Neurath, and H. Neumann, "Differential diagnosis in inflammatory bowel disease colitis: state of the art and future perspectives," *World J Gastroenterol*, vol. 21, pp. 21–46, 2015.

[14] A. B. Pithadia and S. Jain, "Treatment of inflammatory bowel disease (ibd)," *Pharmacological Reports*, vol. 63, pp. 629–642, 2011.

[15] M. de Jong, A. van der Meulen-de Jong, M. Romberg-Camps, J. Degens, M. Becx, T. Markus, H. Tomlow, M. Cilissen, N. Ipenburg, M. Verwey, L. Colautti-Duijsens, W. Hameeteman, A. Masclee, D. Jonkers, and M. Pierik, "Development and Feasibility Study of a Telemedicine Tool for All Patients with IBD: MyIBDcoach," *Inflamm Bowel Dis*, vol. 23, pp. 485–493, 04 2017.

[16] "Hbi harvey-bradshaw index." `https://www.igibdscores.it/it/info-hbi.html`. Accessed: 2021-06-21.

[17] Bennebroek Evertsz', F. and Nieuwkerk, P. T. and Stokkers, P. C. and Ponsioen, C. Y. and Bockting, C. L. and Sanderman, R. and Sprangers, M. A., "The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC) disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological markers," *J Crohns Colitis*, vol. 7, pp. 890–900, Dec 2013.

[18] M. J. de Jong, D. Roosen, J. H. R. J. Degens, T. R. A. van den Heuvel, M. Romberg-Camps, W. Hameeteman, A. G. L. Bodelier, I. Romanko, M. Lukas, B. Winkens, T. Markus, A. A. M. Masclee, A. van Tubergen, D. M. A. E. Jonkers, and M. J. Pierik, "Development and Validation of a Patient-reported Score to Screen for Mucosal Inflammation in Inflammatory Bowel Disease," *J Crohns Colitis*, vol. 13, pp. 555–563, Apr 2019.

[19] Ghosh, S. and Sensky, T. and Casellas, F. and Rioux, L. C. and Ahmad, T. and Márquez, J. R. and Vanasek, T. and Gubonina, I. and Sezgin, O. and Ardizzone, S. and Kligys, K. and Petersson, J. and Suzuki, Y. and Peyrin-Biroulet, L., "A Global, Prospective, Observational Study Measuring Disease Burden and Suffering in Patients with Ulcerative Colitis Using the Pictorial Representation of Illness and Self-Measure Tool," *J Crohns Colitis*, Jul 2020.

[20] Ghosh S, Louis E, Beaugerie L, et al., "Development of the IBD Disk: A Visual Self-administered Tool for Assessing Disability in Inflammatory Bowel Diseases.," *Inflamm Bowel Dis.*, Mar 2017.

[21] R. L. Spitzer, K. Kroenke, and J. B. Williams, "Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire," *JAMA*,

vol. 282, pp. 1737–1744, Nov 1999.

[22] G. Curcio, D. Tempesta, S. Scarlata, C. Marzano, F. Moroni, P. M. Rossini, M. Ferrara, and L. De Gennaro, "Validity of the Italian version of the Pittsburgh Sleep Quality Index (PSQI)," *Neurol Sci*, vol. 34, pp. 511–519, Apr 2013.

[23] R. Ciccocioppo, C. Klersy, M. L. Russo, M. Valli, V. Boccaccio, V. Imbesi, S. Ardizzone, G. B. Porro, and G. R. Corazza, "Validation of the Italian translation of the Inflammatory Bowel Disease Questionnaire," *Dig Liver Dis*, vol. 43, pp. 535–541, Jul 2011.

[24] T. Hlavaty, P. Persoons, S. Vermeire, M. Ferrante, M. Pierik, G. Van Assche, and P. Rutgeerts, "Evaluation of Short-term Responsiveness and Cutoff Values of Inflammatory Bowel Disease Questionnaire in Crohn's Disease," *Inflammatory Bowel Diseases*, vol. 12, pp. 199–204, 03 2006.

[25] "The modern web developer's platform." `https://angular.io/`. Accessed: 2021-06-10.

[26] "Spring." `https://spring.io/`. Accessed: 2021-07-04.

[27] T. Berners-Lee, R. T. Fielding, and L. M. Masinter, "Uniform Resource Identifier (URI): Generic Syntax," Jan. 2005.

[28] "The HTTP protocol." `https://www.ibm.com/docs/en/cics-ts/5.6?topic=concepts-http-protocol`. Accessed: 2021-07-07.

[29] H. Nielsen, R. T. Fielding, and T. Berners-Lee, "Hypertext Transfer Protocol – HTTP/1.0," May 1996.

[30] R. Fielding, D. Software, and R. Taylor, "Principled design of the modern web architecture," *Proceedings - International Conference on Software Engineering*, vol. 2, 10 2002.

[31] "HTTP Methods." `https://restfulapi.net/http-methods/`. Accessed: 2021-07-09.

[32] "Introduction to MongoDB." `https://docs.mongodb.com/manual/introduction/`. Accessed: 2021-07-13.

[33] "Chart.js - Simple yet flexible JavaScript charting for designers & developers." `https://www.chartjs.org/`. Accessed: 2021-04-10.