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Final Dissertation

A Comprehensive Framework for Healthcare Analytics

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Abstract

In the post-pandemic era, predicting the life of people or a community is the real challenge of the coming years, and it is also the goal of the Health Systems. The doctor-patient relationship has assumed a crucial role in responding to the fragility of health affecting the elderly population, which requires continuous assistance and presents increasing difficulties in accessing health facilities.
The remote management of the patient becomes necessary in protected discharges or any quarantines, and it aims to make the activities currently carried out in the health sector more efficient: first of all, by improving the health services provided by health structures which see the active involvement of various actors (doctors, nurses, health workers, etc.), to increase their productivity and improve the patient's quality of life.
Artificial Intelligence techniques, the Internet of Medical Things and mobile technologies play a fundamental role in supporting patients at home, constantly monitoring vital parameters, assessing a potential deterioration in health conditions and requesting the intervention of medical staff in case of emergency.
This thesis investigates a new technique that combines the computing power of the Edge with Process Mining techniques to provide an accurate analysis of patient behaviours. In particular, I propose a new method that, starting from the bottom, can get to analyse the progress of an entire health system, thus providing greater awareness of the operational context. The main objective is to support doctors in addressing cognitive overhead and make the public decision-maker more reactive in strategic choices. The experimental results analysed and discussed in this thesis synthesise a series of industrial research projects in the Healthcare sector.

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Chapter 1

Introduction

1.1 Motivation

Artificial Intelligence (AI) has emerged as a key element in the technology market in recent years. This success is due to the technological ecosystem: the vast availability of huge data sets (now commonly called Big Data), the evolution of powerful computing architectures and the maturity of languages and libraries to develop scalable algorithms. Cutting-edge artificial intelligence systems can process language, analyze images, manage multiple heterogeneous data sources. Furthermore, artificial intelligence can be used to create decision support tools that are so precise that they sometimes equal or exceed human capabilities, especially when it comes to specific tasks, such as interpreting diagnostic images. However, this interest in AI still finds slow application in industries such as medicine, where misuse without human supervision can lead to serious consequences. Bioengineering has thoroughly researched the application of AI in medicine since the early 1980s. Today, bioengineers are successfully leveraging artificial intelligence methods and algorithms to support the full range of its potential applications, ranging from clinical decisions to the implementation of robotic systems. This thesis work is the result of a path created in synergy between the Polytechnic University of Bari and the Healthcare Research Team of the company Exprivia S.p.A. and wants to analyze state of the art and the perspective of AI in medicine, linking clinical decision support and robotics, showing how a series of applications can converge in a framework for supporting

the health system. Through the framework, it will be possible to understand this developing topic's main aspects and trends. Its interdisciplinary elements are of utmost importance to research stakeholders and public decision-makers.
The thesis work is designed to carefully consider all the aspects mentioned above, tracing a path from the basics, through the building blocks of decision support and artificial intelligence systems, to real-world applications, robotics, and finally embedded intelligence.

1.2 Overview

This thesis is organized as follows:

- **Chapter 1** presents motivation, contributions and publications related to the thesis.
- **Chapter 2** introduces the context of precision medicine and how the approach to therapy has evolved.
- **Chapter 3** provides an overview of the digital twin model approaches for healthcare.
- **Chapter 4** introduces Process Mining and describes the main techniques focusing on the Healthcare sector.
- **Chapter 5** is dedicated to explaining the experiences and use cases achieved in the company during the Ph.D. program.
- **Chapter 6** explains the formalization of the framework and how all the experiences have been organized to provide an overview for strategic support to the Healthcare system.
- **Chapter 7** describes the overall conclusions of the work presented in this thesis and the potential future work.

1.3 List of publications

This thesis is based on the following publications produced during the Ph.D. program:

- Artificial Intelligence on Edge Computing: a Healthcare Scenario in Ambient Assisted Living
  Pazienza, A., Mallardi, G., Fasciano, C. and Vitulano, F.
  Artificial Intelligence for Ambient Assisted Living (AI*AAL.it 2019)

- Adaptive Critical Care Intervention in the Internet of Medical Things
  Pazienza, A., Anglani, R., Mallardi, G., Fasciano, C., Noviello, P., Tatulli, C. and Vitulano, F.
  IEEE Conference on Evolving and Adaptive Intelligent Systems (EAIS 2020)

- A Proposal of Case-Based Approach to Clinical Pathway Modeling Support
  Ardito, C., Bellifemine, F., Di Noia, T., Lofù, D. and Mallardi, G.
  IEEE Conference on Evolving and Adaptive Intelligent Systems (EAIS 2020)

- Towards a Trustworthy Patient Home-Care Thanks to an Edge-Node Infrastructure
  Ardito, C., Di Noia, T., Di Sciascio, E., Lofú, D., Mallardi, G., Pomo, C. and Vitulano, F.
  Human-Centered Software Engineering (HCSE 2020)

- An adaptive architecture for Healthcare Situation Awareness
  Ardito, C., Di Noia, T., Lofú, D. and Mallardi, G.
  6th Italian Conference on ICT for Smart Cities and Communities (I-CiTies 2020)

- Towards a Situation Awareness for eHealth in Ageing Society
  Ardito, C., Di Noia, T., Fasciano, C., Lofú, D., Macchiarulo, N., Mallardi, G.,

Pazienza, A. and Vitulano, F.

Italian Workshop on Artificial Intelligence for an Ageing Society (AIxAS 2020)

- Management at the Edge of Situation Awareness During Patient Telemonitoring

  Ardito, C., Di Noia, T., Fasciano, C., Lofú, D., Macchiarulo, N., Mallardi, G., Pazienza, A. and Vitulano, F.

  20th International Conference of the Italian Association for Artificial Intelligence

- An Edge Ambient Assisted Living Process for Clinical Pathway

  Ardito, C., Di Noia, T., Fasciano, C., Lofú, D., Macchiarulo, N., Mallardi, G., Pazienza, A. and Vitulano, F.

  ForItAAl 2020 – 11° Forum Italiano dell'Ambient Assisted Living

- INSTAMED: an Integrated Platform for the Advanced Automation of Diagnosis in Precision Medicine

  Di Noia, T., Fasciano, C., Lofú, D., Mallardi, G., Pappadà, G., Tatulli, C. and Vitulano, F.

  7th Italian Conference on ICT for Smart Cities and Communities (I-CiTies 2021)

Chapter 2

Health in the Precision-Medicine Era

2.1 Introduction

Personalized and precision medicine is based on the ability to use the most significant number of data, including genetic and morphological ones, to target rehabilitation therapies, treatments, and cures on the individual patient's needs. The rapid development of Information and Communications Technology allows today to integrate many elements and values that are difficult to group with paper resources. Among the specializations that can benefit from this new approach are oncology, neurology, and general, all those areas in which exchanging information and data via networks and IT tools can add value to the therapies administered. Initially born concerning pharmacogenetics, the theme was also developed regarding prostheses and devices of various types, helpful in increasing the current models of care with reference above all to the health problems of elderly, chronic, or disabled people. The invitation of scientific communities worldwide is to constructively develop a debate around precision medicine through research and commit themselves so that patients can benefit from these innovative treatments. The continuous and recent technological developments have allowed a rapid decrease in the costs of the equipment, which until a few years ago, given the high cost, could have been a limit to the spread of these methods. Precision medicine is not based only on innovation, but reviews specify and accurately identify how accurate the guidelines and Evidence Base Medicine are for the needs and characteristics of each patient. The most involved patients are the elderly, in which the incidence of chronic diseases is significantly higher. Clinical sectors and fields recognize different characteristics depending on the multifactorial nature of the disease. For example, by analyzing movement disorders related to neurological diseases such as Parkinson's, the introduction in medicine of precision tools such as inertial movement sensors have provided crucial support for clinical diagnosis, allowing the identification of motor symptoms earlier and better calibrating the clinical path according to the different response and tolerance to drugs of each patient. Symptom control and slowing of disease progression can be improved with personalized care strategies for patients who are constantly monitored as they follow drug therapy. Analyzing the symptoms more precisely than outpatient assessments will allow us to know the individual patient's specific needs, making the result of the treatment objective and identifying the actual effectiveness of the therapy. Recording every behavior and daily data with more accuracy will avoid late diagnosis and have more complete outcomes for the treatments administered.

2.2 Personalized Medicine

For Personalized Medicine, we mean the process that leads to the prescription of therapies about the individualities defined by each individual's genetic and pathophysiological information. The concept of personalization considers the person's general conditions by adapting the different therapies where there is multiple chronicity, studying the interaction and effect of multiple therapies on the general well-being of each individual. The first published works in which the term "personalized medicine" appears in 1999, although some key concepts had already appeared in the early 1960s [1]. Recent discoveries and technological developments have quickly brought this new paradigm to be a concrete reality that can be easily used on a clinical level. Each patient has its own genetic and environmental specificities, which require personalized, predictive, and participatory care. Although personalized medicine is linked to pharmacogenetics and the effects of genetic variability (polymorphism), asking about personalized medicine also means discussing new diagnostic models and the ineffectiveness of some therapies on many patients. Customizing a diagnosis and treatment by having a large number of data collected by bioinformatics and diagnostic tools available translates into better management of chronic diseases. Significant steps forward made in translational medicine allow continuous and new knowledge from basic science is transferred to biomedical one, bringing new tools and diagnostic/therapeutic applications [2]. In some fields, such as stem cell therapies, the result achieved was more effective in cases where the treatment was personalized and adjusted according to the specific profile of the patient. Setting personalized therapies on the patient is also helpful for reducing costs and the number of drugs taken. The potential of artificial intelligence, big data, and new technologies, increasingly used at the clinical level (diagnostic and therapeutic), will revolutionize the medical profession, changing, for example, research models, no longer hypothetical-deductive (cause-effects-feedbacks) but by correlation and interdependencies. The expected change for doctors and patients will involve a "personalization" of assistance starting from the first visit up to diagnostic-therapeutic precision. Although, to date, there are no robots or algorithms capable of carrying out a complex logical-deductive process as a prepared and trained human mind can do, however, it is essential to observe the continuous improvements of these algorithms and software [3]. These systems will probably never replace the doctor's preparation, knowledge, and experience, but they must be considered support to help reduce their cognitive overload.

2.3 Precision Medicine

In medical terminology, precision and personalized medicine are commonly used interchangeably. Many clinicians claim to have continuously practiced individualized and personalized medicines, which is difficult for the versatility of the human being. For this reason, the term precision medicine further clarifies how the new high-tech devices such as sensors from the Internet of Things are fundamental for 360-degree monitoring of the patient and the evaluation of the effectiveness of the therapies provided. While precision medicine identifies itself more and more towards an explicit specialization, personalization, the growth of which is directly proportional to that of precision medicine (as the more significant the progress in the direction of precision, the greater the attention to strengthening the personalization) is placed in a more holistic context of the person [4]. Scientific interest in this topic grew significantly in 2014 when there was an increase in scientific publications relating to the subject of 66%. Although the first article in the NCBI[1] database about precision medicine dates back to 1952, even if going further in time, we observe how the Canadian doctor William Osler introduced the concept starting from the end of the nineteenth-century observation of significant existing variability. In 2016, under the Obama presidency, the US established the Precision Medicine Initiative involving patients, doctors, researchers, lawyers, and pharmaceutical industry leaders. With a grant of $ 215 million (divided between the National Institutes of Health, NIH National Cancer Institute, and Food and Drug Administration), they have set themselves the goal of improving the application of genomics and immense amounts of data with modern methods by combining them with technological knowledge and thus expanding the discoveries in the biomedical field. Over the years, the goal of improving the clinical results of the therapies provided about the different severity of symptoms, minimizing side effects or adverse effects, has been entrusted to evaluation scales with high variability. In the literature, it has also been noted how inaccurate are the home clinical diaries on which patients, especially in complex clinical pictures, are unable to report their symptoms in a detailed and precise manner, making the patient's assessment approximate. However, the novelty is the pace of progress in diagnostic and treatment options. Just think of the management of neurodegenerative diseases, which, as known, is influenced by many external factors

[1]National Center for Biotechnology Information

such as age, personality, lifestyle, pharmacogenetics and comorbidities. Although, following the COVID-19 pandemic, investments in this area have changed and have even been accelerated for some topics.

2.4 Healthcare 4.0

With the name Healthcare 4.0, we identify revolutionary changes due to adopting "disruptive" technologies, similar to those of the fourth manufacturing revolution. Ultimately, the concept is based on intelligent machines that have access to large amounts of data, which allows them to make decisions without human involvement [5]. In the health sector, this concept can be exemplified in the definition of the so-called 4P medicine (participatory, personalized, preventive, predictive). Increasingly widespread chronic diseases and an increasingly elderly population require an epochal transformation from medicine based on diagnosis and treatments to preventive or better "predictive" medicine. The growing diffusion of Information and Communication Technology (ICT) in the health system (medical records and electronic medical records, telemedicine, digital documentation, 3D printing, artificial intelligence, robotics, development of biomedical apps, augmented reality, etc.) requires the overcoming not only structural but above all cultural obstacles and interaction with knowledge systems. Adequate training and continuous updating of health professionals are necessary, and the active involvement of citizens and patients in clinical decisions can only be made thanks to the provision of precise and reliable information. If healthcare cannot be entrusted entirely to automated assistants, medical staff can, however, thanks to such aids, make their services faster and more effective. In this way, it is possible to obtain, in real-time, thanks to the intelligent use of updated knowledge from databases and clinical decision support systems, vital information for the treatment of patients based on the most up-to-date scientific evidence. However, if technology brings significant improvements in the health sector and personalized assistance (precision medicine), there is no shortage of challenges. One of these is to integrate data coming from different information systems. To do what, it is necessary to develop high levels of interoperability that would make it possible to manage the so-called “Big Data”. However, this entails the need to face significant problems, such as confidentiality protection. Furthermore, it requires huge investments, both in terms of time and in terms of costs, also to acquire the professional training necessary to face the new challenges posed by Healthcare 4.0. The investment is necessary for a sustainable health system that avoids waste and rationalizes interventions in the light of the knowledge and application of the best scientific evidence.

Chapter 3

Digital Twin Model

3.1 Introduction

The spread of the Internet of things and distributed computing powers has allowed the concept of a "digital twin" in everyone in many industrial sectors and health-care. The genesis of the term "digital twin" dates back to 2003, in the context of product life cycle management (PLM), when digital representations of physical products were not yet developed. The goal was to optimize business performance by creating virtual replicas of physical objects in near real-time to detect problems earlier, predict results more accurately, and help design better products. It is a virtual copy of a device that is continuously fed with data from integrated sensors and software to provide an accurate real-time status of the physical device dynamically. While virtual models have been around for decades, digital twins represent a huge step forward because they use machine learning and big data technology, leveraging vast amounts of sensor data. Through machine-to-machine communication and automation technologies, digital twins monitor the process dynamically, representing it graphically with advanced techniques. Thus, a system's performance or condition can be monitored while it is running by analyzing changes in digital replication. So it is a replica of a physical object, a "twin", which allows us to monitor the status, diagnose and predict problems or anomalies as well as test solutions remotely, by creating a safe environment in which it is possible to test the impact of potential changes on the performance of the system itself. When the power of computational technologies such as Artificial Intelligence is added, it is also possible to identify potential problems before they occur, allowing for the timely resolution of a malfunction. This technology can be applied to a machine, to a process, or a living body understood in turn as a complex system of interconnected components.

3.2 Digital Twin in Healthcare

It is not difficult to understand how in the health sector, with all the specificities of the case, benefits can be derived from this technology. After all, if digital twins of physical systems offer so many opportunities to keep physical devices healthy, why not apply the same concept to humans? If we had a digital copy of us, could we help doctors diagnose and treat a disease? Moreover, could it help manage our health? There are at least two uses that can be mentioned: hospital design and management on the one hand and patient care on the other. With a digital twin, the hospital can be virtualized to create a safe environment, which verifies the influences of changes on the performance of the organizational and structural system without risk. So, this is extremely important in the healthcare sector, as it enables informed strategic decisions to be made in a highly complex and sensitive environment. However, digital twin technology can represent an individual's lifestyle and physiological characteristics and genetic makeup to personalize medicine. A digital copy of a human body can help doctors discover a condition early, simulate treatments, and possibly surgery. Also, data derived from individuals typically come from costly and time-consuming activities, such as blood tests and scans, DNA sequencing beyond psychological implications, etiopathogenetic factors, and the limitations that molecular biology places. The development of the digital twin of a human body consists, in fact, in a process that is far more advanced and delicate than any other engineering product. There are sectors of medicine that, better than others, could benefit from the use of digital twins, such as chronic diseases affecting specific vital organs, identifying potential anomalies or degenerations before they occur so that therapy can be planned, in a preventive and, hopefully, less invasive manner with shorter recovery times and an overall improvement in economic sustainability. Proactive remote monitoring allows us to solve unexpected problems and plan the intervention of medical staff when necessary. Since the "system" data is analyzed in advance, doctors know exactly what kind of intervention is needed and which therapy to administer, or even make it happen automatically or with the collaboration of the conscious patient. When developing predictive models, it is crucial to bring together data scientists, engineers, and doctors with in-depth knowledge of the field, as some know how a human body works while others know how a device is designed and how it works. Obviously, in all this, the doctor's role is essential since the system that detects an anomaly cannot be left to prescribe a therapy on its own automatically. On balance, a digital twin can be defined as a person's lifelong data set, combined with models powered by artificial intelligence capable of "interrogating" data to provide answers to a series of clinical questions. In some respects, the digital twin in healthcare could be considered as a natural evolution of the Electronic Health Record, which, instead of containing data and numbers, contains the "living" replica of the patient's body in all its functions, also updated with the values deriving from instrumental tests and numerous sources (diet, lifestyle, environmental parameters, familiarity, etc.). A digital twin can play a decisive role in predicting the outcome of an intervention, such as a patient's heart (which uses MRI, ECG, and blood pressure data) can allow cardiologists to accurately determine lead placement resynchronization devices that work best on a specific patient, virtually experimenting with different positioning hypotheses, before an actual surgery begins. Additionally, it can assist in determining the right treatment option for that particular patient. For prostate cancer, for example, treatment options range from surgery and radiation to more minor invasive treatments like hormone therapy. Several subsets of these therapies can also be combined. A digital twin that includes a patient's medical records, laboratory findings, and genetic data, in combination with a clinical path model, helps ensure optimal decision making regarding that particular patient's treatment, aiding healthcare providers in outlining the Clinical Paths in the best possible way. For chronic diseases, lifestyle, residence, and how a patient takes care of himself make a considerable difference in the possible onset of complications or other related diseases. In this scenario, the digital twin should include physiological and behavioral data to help the patient and the doctor effectively manage the evolution of the disease for the benefit of patients and the entire health system. Until a true digital twin is created that encompasses the entire human body, it may be essential to focus on individual organs, such as the kidneys. The prevalence of kidney disease is increasing worldwide (according to some estimates [6], 10-15% of today's world population suffers from some kidney disease). If not managed correctly, kidney disease can lead to much more severe kidney failure, requiring a kidney transplant or dialysis for life at very high costs. A digital twin could help manage kidney disease early to prevent more severe consequences. At present, the knowledge in this field is not yet sufficiently evolved to analyze the human body in its entirety, also due to the innumerable interactions (sometimes unknown) between the various organs and systems, but some experiments have been done, and some first ones have been reached. results.

3.3 Advantages and Disadvantages

An example can be the Dassault company that developed "Living Heart", the first realistic virtual model of a human organ (heart) that represents blood flow, mechanics, and electricity [7]. Dedicated software can generate an accurate high fidelity model of an individual's heart through a scan of a human being. However, parts of the body, such as the brain, are much more complex. The French start-up "Sim & Cure" has progressed in assisting medical researchers in treating the brain while developing a digital patient to treat aneurysms [8]. "Twinning" the human body will have multiple benefits for doctors, such as knowledge of not fully known diseases, experimentation with treatments, and improved preparation for surgery. The precision of the digital twin depends on an accurate, precise, and updatable virtual representation in almost real-time, therefore on the quality and quantity of data processed. For this reason, one of the main factors that can limit the growth and full integration of technology is the system's sensitivity to cyber threats in general, as attackers can potentially have access to highly confidential and immense value data. To address this problem, developers need to be careful to respect the different ethical, legal, and security issues raised by multiple parties. First, using the Internet of Things and cloud computing exposes systems to cyber threats, such as hacking and viruses, allowing attackers to steal highly confidential information. Therefore, in addressing the issues due to the interaction with data from various sources, developers will have to give due weight to compliance with the various regulations that imply the processing of personal and non-personal data and cybersecurity. Likewise, the possibility of considering digital twins as Medical Devices cannot be underestimated based on the prerequisites of the specific legislation (in Europe EU Reg. 745/17 soon to come into force, in the USA, the regulations of the Food and Drug Administration). Secondly, it is a considerable investment within reach of prominent players with the necessary capital and human resources, with the risk of creating monopolies. Third, this technology requires equipment and knowledge not available on a large scale. Therefore, the digital twin technology could increase the health digital divide, exacerbating the one existing between rich and poor areas by geographical location. Finally, doctors and researchers must be involved in using digital twins, and then they must be instructed on how to use them correctly. Therefore, strengthening skills and knowledge is significant to ensure that doctors can use such digital tools. This opens the way for the expansion of precision medicine and improved patient experience, allowing patients themselves to proactively manage their health, perhaps having it at their wrist. Digital twins also help reduce physicians' cognitive burden by providing actionable information with the clinical context to help them make more personalized decisions for each patient [9]. A hypothetical as well as futuristic and evolved digital twin, in fact, through a complex mix of physics, biology, anatomy, chemistry, genetics, and genomics, should be the faithful representation of a living organism in all its components, almost a sort of "Life Simulator" that allows you to predict how aging or a specific pathology evolves on that specific patient [10]. However, making digital twins a disruptive technology is the large-scale implementation: making this approach universally applicable to clinical practice would allow processes to be innovated using digital simulations and medical training. It is evident that the repercussions on the economic aspects are equally significant, cost savings, waste, unnecessary procedures and tests, and in terms of reducing waiting lists and Public Health Management, limiting hospitalization and its negative implications.

Chapter 4

Process Mining

4.1 Introduction

Thanks to the increasingly effective use of information systems and their application in various areas, the amount of data produced to record and analyze all the activities that are stored in the logs has increased. Today the challenge is to transform this data into real value. The volume of information is not enough to identify them, so to interpret them, we must consider criteria that take the name of the *"4 Vs of Big Data"*:

- **Volume**: it concerns the quantity of data that are generated by the systems;
- **Velocity**: the data are constantly updated and constantly changing, and many devices can collect and update data in real-time;
- **Variety**: there are different types of data ranging from text to images, and one needs to combine these various sources of information;
- **Veracity**: refers to the reliability of the data as it is not possible to be entirely sure that what has been recorded is accurate.

Organizations find it difficult to interpret data and derive valuable information for their business. For this reason, a new discipline was born known as ***Process Mining***, which is a helpful tool for companies to interpret data and improve end-to-end processes.

4.2 Definition

Process mining is an innovative discipline whose research studies began in 1999 at the University of Technology of Eindhoven in the Netherlands. Initially, the techniques developed were rarely used due to the lack of data availability. Still, subsequently, thanks to the increase in the amount of data available, there was a marked improvement in the techniques developed.

Process mining desires to model, monitor and enhance processes by extracting facts from event logs. These event logs contain information relating to the execution of operations. This allows you to define strategies to improve the quality of processes, reduce costs, or compare reality with models, so process mining positions itself as a valuable tool in the context of Business Process Management (BPM).

Process mining combines traditional model-based process analysis and data-centered analysis techniques. Process mining can be seen as the link between "data science" and "process science". Specifically, it looks for the comparison between event data representing observed behaviour and hand-made or automatically discovered process models. Data mining and machine learning techniques do not consider end-to-end models. At the same time, "process science" approaches are process-based, focusing primarily on modelling. In contrast, process mining can be seen as a helpful tool to exploit the considerable amount of data available to improve end-to-end processes[11].

Application use cases of process mining include the analysis of patient management processes in hospitals, improving customer-care service processes, understanding the browsing behaviour of customers using an e-commerce site, etc. The use of process mining is extended and should not be restricted to automatic process discovery alone but can be used for compliance checking, deviation diagnostics, bottleneck detection, performance improvement to prevent flow times and recommend actions. For this reason, process mining techniques are not limited to specific application domains

[11].

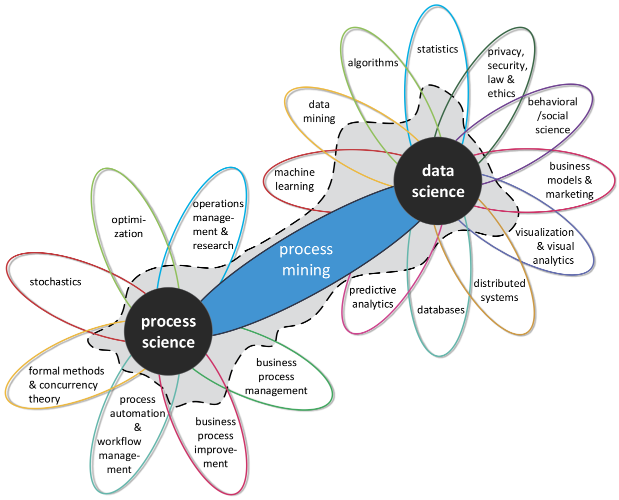


Figure 4.1: *Process mining - a bridge between data science and process science[11].*

4.3 Event Log

The starting point for any process mining technique is an event log, as process analysis is impossible without a good event log. In process mining, the concept is to investigate the event log from a process-oriented point of view. The starting point is "raw" data available in various sources, from a simple file, an Excel sheet, a transaction log or a database table. In real situations, these data are not present in a single well-structured source but are scattered in different sources due to technical or organizational reasons, and therefore it is necessary to collect the relevant data [11].

The data mining process should be driven by inquiries rather than data availability. In the context of Business Intelligence, the expression *"Extract, Transform, and Load" (ETL)* is used to characterise a process that applies extracting data from different sources, processing it to meet operational needs and loading data into the target system such as a data warehouse or a relational database. [11].

Process mining bases its analysis on the use of event logs, i.e. particular logs (sequential files used to record all the operations performed in chronological order) that record all the activities carried out in a given company environment. An **event log** is a collection of process traces, where a trace indicates the execution of the process or a sequence of events. On the other hand, an event represents a step that has been made in the process and contains various information. Among the most important are: the name of the activity, which indicates the activity performed, the case-ID, which allows you to assign each activity to a specific trace in the event log and the timestamp indicating the instant in time in which the activity was performed. Each track contains all activities with the same case-ID, sorted by timestamp. An event may contain further information, in addition to those mentioned above, such as the resource who performed the activity or the execution costs.

Case ID	**Event ID**	**Properties**			
		Timestamp	**Activity**	**Resource**	**Cost**
1	35654423	30/12/2010 11:02	Request registered	Pete	50
	35654424	31/12/2010 10:06	Accurate check	Sue	400
	35654425	05/01/2011 15:12	Ticket check	Mike	100
	35654426	06/01/2011 11:18	Decision	Sara	200
	35654427	07/01/2011 14:24	Request rejected	Pete	200
2	35654483	30/12/2010 11:32	Request registered	Mike	50
	35654485	30/12/2010 12:12	Ticket check	Mike	100
	35654487	30/12/2010 14:16	Random check	Pete	400
	35654488	05/01/2011 11:22	Decision	Sara	200
	35654489	08/01/2011 12:05	Refund of payment	Ellen	200

Table 4.1: Claims event log example [11].

The following table shows a fragment of an event log, where each row corresponds to an event, and each event has different properties.

4.3.1 XES Formalism

In 2011, the IEEE Task Force of Process Mining decided to adopt the XES (eXtensible Event Stream) format, which is a format for storing logs. XES is a standard based on XML (eXtensible Markup Language), whose goal is to standardize a language for transporting, storing and exchanging large amounts of data. The aim is to define a recognized format for exchanging event data between information systems and data analysis tools. The basic hierarchy of an XES document follows the information structure of the event log. It presents three types of log objects to define the document's structure without containing logged information stored in the attributes of each object:

- ***Log***: present at the top level and contains all information about the events of a specific process;
- ***Trace***: each trace describes the execution of a specific case of the recorded process;
- ***Event***: each trace contains several event objects, which represent the activities that have been observed during the execution of a process, characterized by a duration.

4.4 Process Models

Defining a process means specifying the activities and relationships in terms of synchronization and logical dependencies. Process models are models that describe the individual activities that must be carried out within a process. The goal of a process model is to decide which activities must be performed and in what order. Specifically, the activities can be performed sequentially, there may be optional or concurrent activities, or the execution of an activity can be repeated. There are several notations for process modelling. Here are some of the most used notations.

4.4.1 Transition systems

A transition system is a triad TS = (S, A, T) where S represents the set of states, A indicates the set of activities or actions, and T is the set of transitions. A path begins in one of the initial states and successfully ends in one of the final states.

A path is blocked if it reaches a non-final state characterized by the absence of outgoing transitions [11].

The figure below shows a transition system that models the management of a refund request by an airline. There are seven states, represented by black circles, while the transitions are represented by arcs that connect two states, characterized by a label indicating the name of the activity.

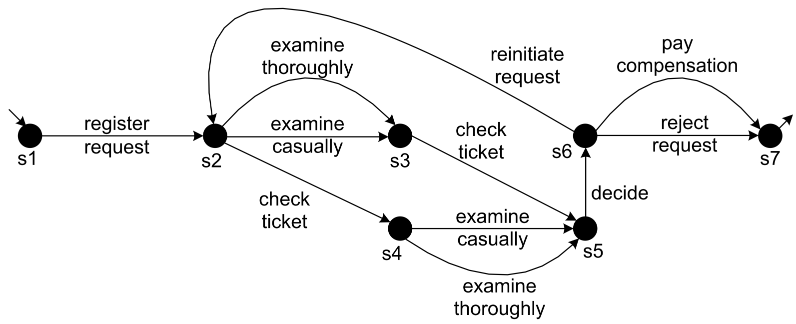


Figure 4.2: *Example of a transition system [11].*

The transition systems are simple but have problems in expressing competition. Due to the concurrent nature of business processes, more expressive models are needed, such as Petri Nets, to adequately represent the results obtained through the use of process mining techniques.

4.4.2 Petri Nets

Petri nets are the oldest process modelling language, introduced in 1962 by Carl Adam Petri, and represent an abstract model helpful in describing the dynamics of a system characterized by synchronous and concurrent activities (activities that can be carried out in parallel). A Petri net is a bipartite, oriented and weighted graph made up of places, transitions and arcs connecting them. The input arcs connect the places to the transitions, while the output arcs connect the transitions to the places. The network structure is static, but tokens can flow through the network; in fact, the state of a Petri net is determined by the distribution of the tokens on the places, which indicates the marking of the Petri net. The marking refers to the fact that each place contains a non-negative integer number of tokens, defines the network's state, and allows to highlight its evolution.

A Petri net is defined by a quadruple $PN = \{P, T, Pre, Post\}$ where P is the finite set of places, T is the finite set of transitions, *Pre* is a pre-incidence matrix specifying the arcs directed from posts to transitions, and *Post* is a post-incidence matrix that specifies the arcs directed from transitions to posts. With Petri nets, it is possible to represent and describe a process. It is also possible to follow the evolution of the process, displaying the state in which the network dynamically is in a specific instant. The status of a Petri net is represented graphically by placing the tokens in the places, which indicates the progress of the operations carried out in the process.

The presence of tokens in places indicates the availability of the resource in question. The dynamic behaviour of a Petri net is defined by the *"firing rule"*: i.e. a transition is enabled if all the places before the transition (pre-set) contain a number of tokens at least equal to the weight of the arc that connects them to the transition. The triggering of a transition causes the removal from each place in the pre-set and the addition of several tokens in the places downstream of the transition (post-set) equal to the weight of the arcs that connect the transition to these places.

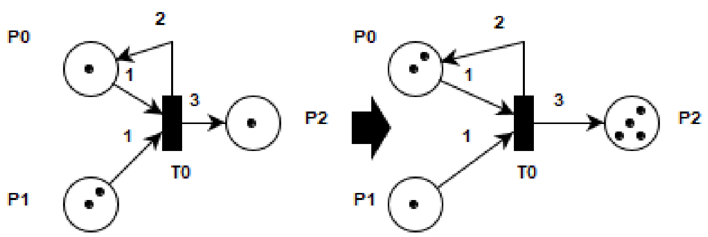


Figure 4.3: *Example of a transition shot.*

Fundamental structures of a Petri net, useful for systems modelling:

- **Sequence**: it is represented as a succession between places and transitions. Two transitions t0 and t are said in sequence if t0 precedes t1.

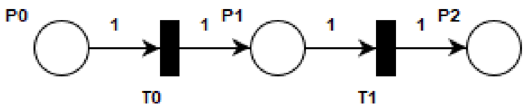


Figure 4.4: Example of transitions in sequence.

- **Concurrency**: an event is triggered and enables different events simultaneously, and then you decide which one to take place first.

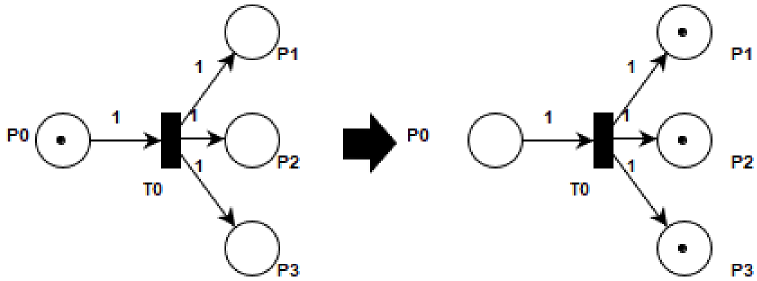


Figure 4.5: Example of parallel transitions.

- **Choice**: unlike the concurrency where everyone can shoot, with the choice, it is possible to enable only one, and there is a different evolution depending on the triggered event.

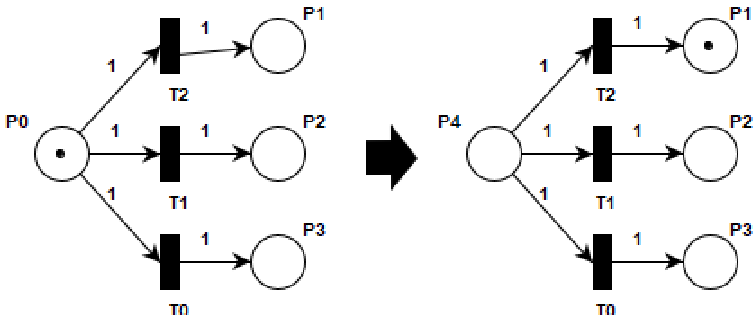


Figure 4.6: Example of a choice situation.

- **Synchronization**: transitions without common entry places, all enabled and followed by exit places which are also entry points for a common transition.

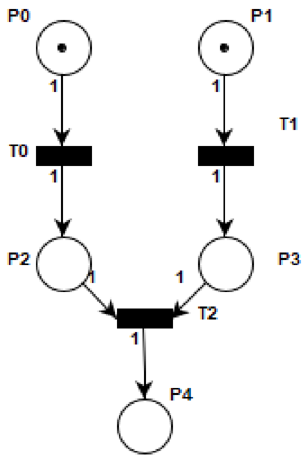


Figure 4.7: *Example of synchronous transitions.*

The basic properties of Petri nets are the following and are called *behavioural properties* as they depend on the structure of the net and the initial marking:

- **Reachability**: indicates the possibility of obtaining a given marking, that is, a specific state, starting from another marking. A marking M is said to be reachable starting from a marking M0 if there is at least one sequence of transitions such that by making them trigger starting from M, M0 is obtained.
- **Limitedness**: a place of a Petri net is called k-limited if, in all the markings reachable by the net, the number of tokens present in the place never exceeds a predetermined value k.
- **Reversibility**: a Petri net with initial marking M0 is said to be reversible if, for each marking M reachable from M0, M0 can be reached from M; therefore, if from each marking, it is possible to return to the initial marking M0.
- **Conservativeness**: a marked Petri net is strictly conservative if the number of tokens that the net contains does not vary for each reachable mark.
- **Vividness**: a transition t is said to be alive if and only if starting from any marking of the graph it is possible to turn on t.

Petri nets have the following advantages:

- The graphical representation of the Petri nets is very compact and concise, allowing an easier understanding of the evolution and functioning of the system;
- Petri nets are a mathematical model, allowing the network analysis using linear algebra;
- The representation of a Petri net is modular, in fact, each part of the system can be considered as an independent subsystem, and it is possible to analyze it independently from the others;
- Petri nets allow you to analyze the activities that take place simultaneously quickly.

4.4.3 BPMN

Business Process Modeling Notation (BPMN) has become one of the most used languages for modelling business processes. It was developed by the *Business Process Management Initiative*. BPMN is used to create easy-to-read flowcharts for modelling business processes, which can be shared among all interested parties, whether technical or not.

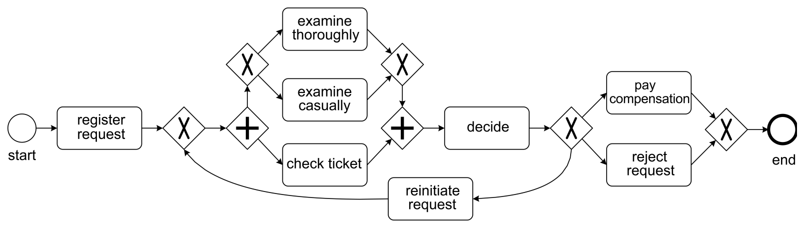


Figure 4.8: *Example of a process model using BPMN notation [11].*

Atomic activities are called tasks, which can be nested. An event is analogous to a place in a Petri net. In BPMN, there is no need to enter events between the activities, and the events cannot have multiple entries or exit arcs. Early events have an arc out, intermediate events have an arc in and arc out, and final events have an arc in. Unlike a Petri Net, it is not possible to have events with multiple incoming or outgoing arcs, so the division (split) or the union (join) are performed through gateways. The figure below shows the most common BPMN notation symbols.

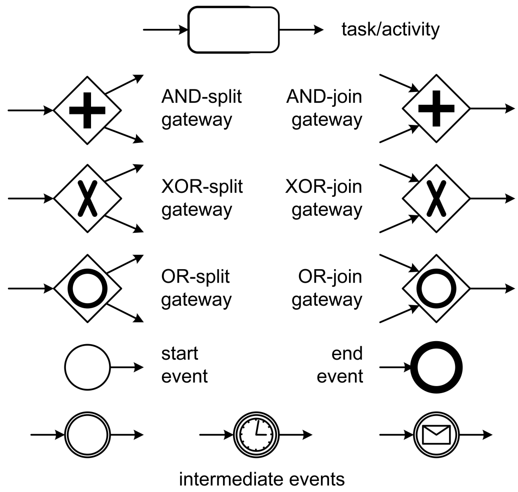


Figure 4.9: *BPMN notation symbols*

4.5 Process Mining Techniques

One of the fundamental aspects of process mining is the emphasis placed on establishing a relationship between the process model and the reality contained in the event log. The terms *play-out*, *play-in*, and *replay* are used to describe this type of relationship.

- **Play – out**: it refers to the traditional use of process models, and it is possible to generate a behaviour starting from a Petri net. It can be used both for analysis and the implementation of business processes, as it allows you to execute operational processes using executable process models. The main idea of the simulation is to run a model and collect statistics and confidence intervals repeatedly.

- **Play – in**: it is the contrary of play-out, that is, the example behaviour recorded in the logs is taken as input. The aim is to build a model based on the recorded data automatically. The Alpha algorithm or other process discovery approaches are examples of play-in techniques.

- **Replay**: it uses an event log and process model as input. The event log is "replayed" on the process model to check for compliance or discrepancies between the event log and the model. By replaying the log, it is possible to see which parts of the model are executed frequently, also identifying the bottlenecks. In addition, it is possible to build predictive models. It is possible to make predictions for the different states of the model. The replay is not limited only to the data of the recorded events. However, it is also possible to reproduce partial traces of events still running in such a way as to detect deviations during the execution of the process.

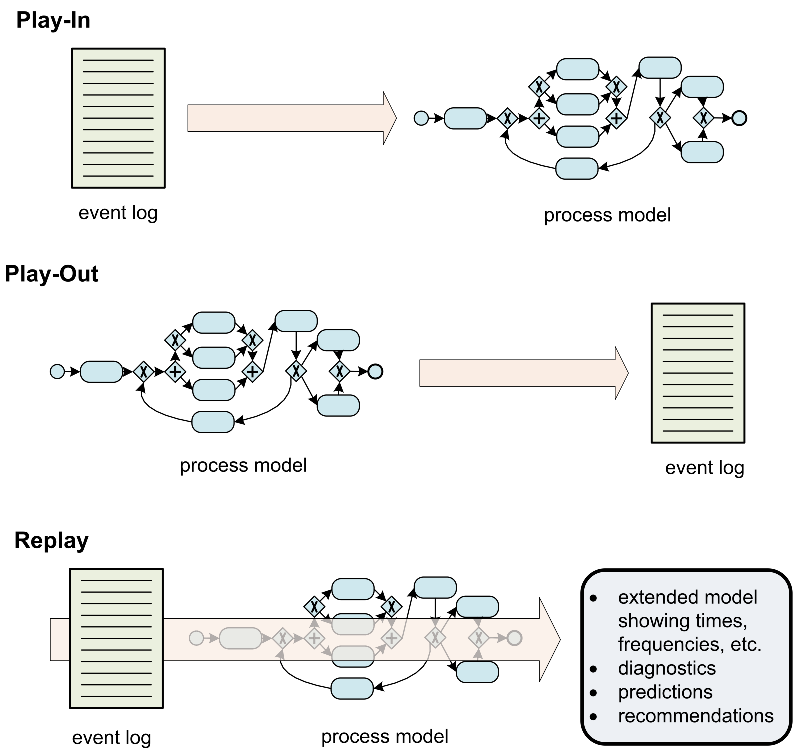


Figure 4.10: *Three ways to relate the event log and process models [11].*

Process mining techniques can be divided into:

1. **Process discovery**: it is a technique that takes an event log as input and produces a model based on the recorded data.

2. **Conformance checking**: a process model, discovered through process discovery or pre-existing, is compared with the information contained in an event

log. This allows us to check if what happens in reality, therefore the information contained in the logs, conforms to the model and vice versa.

3. **Enhancement**: the idea is to enhance an existing process model by using knowledge from the process stored in the logs. Unlike conformance checking, which measures how much a model is aligned with reality, enhancement aims to extend the pre-existing model, showing, for example, bottlenecks, productivity times and frequencies, through the use of stored timestamps in the event log.

4.6 Quality metrics in Process Discovery

Determining the quality of a process model is complicated. For this, there are four quality criteria for evaluating a process model: fitness, simplicity, accuracy and generalization. The four quality criteria often conflict with each other; therefore, it is necessary to make tradeoff decisions to satisfy them [11]:

- **Fitness**: it describes how much of the observed behaviour is allowed by the process model. In particular, a model has perfect fitness (value equal to 1) if the model can play all the tracks in the log from start to finish. Fitness can be defined at the case level, defined on the fraction of tracks that can be fully reproduced on the model, or at the event level, which is the fraction of events in the log that are actually possible according to the model.

- **Simplicity**: a model has good simplicity if it is not complex and is easy to understand for a human. This metric is the only dimension that is not tied to the behaviour of the process model or event log. There are several approaches to measuring the simplicity of a model. Some approaches take the size or diameter of the model into consideration. The size can refer to the number of nodes in the model, while the diameter refers to the length of the shortest path from the start node to the end node. A formula for the calculation of simplicity is the one proposed in the article [12] based on the structural adequacy of the control flow of the process model:

$$\delta_s = \frac{|T| - (|T_{DT}| + |T_{IT}|)}{T}$$

where T is the number of transitions in the model, $T_{DT} \subseteq T$ is the number of duplicate alternate activities, and $T_{IT} \subseteq T$ is the number of invisible redundant activities. Alternate duplicate activities consist of activities that are never repeated together in a sequence, while redundant invisible activities are activities that can be removed without changing the behaviour in the model.

- **Precision**: It refers to how much of the behaviour allowed by the model is present in the register. If the model does not allow behaviours other than those recorded in the log, then the accuracy is high. In contrast, the accuracy is low when the model allows many more behaviours, even if they are not part of the log. A model with poor precision is underfitting because it allows very different behaviours from those seen in the log. A measure of precision can be the one proposed by *Rozinat e Van der Aalst* based on appropriate behaviour, defined as follows:

$$\alpha_B = 1 - \frac{\sum_{i=1}^{k} n_i x_i}{(m-1)\sum_{i=1}^{k} n_i}$$

indicates the number of different tracks in the log. For each log, the trace is $(1 \leq i \leq k)$, n_i is the number of combined process instances in the current trace, and x_i is the average number of transitions enabled during the log replay, while m is the number of tagged activities, not including invisible activities.

$$x_i = \frac{outgoing\_edge_i - used\_edge_i}{outgoing\_edge_i}$$

The accuracy is 100% if the model allows exactly the presence of observed behaviours in the log [12].

- **Generalization**: it describes the probability that the future behaviour of a process is executable on the model. A model with a good generalization aims

to maximize the behaviours supported by the model but which are not part of the system and are not present in the event log. The notion of generalization is linked to the concept of overfitting. Overfitting is a problem that is generated when a model is too specific, that is, the model explains the particular event log but a next sample of the same process can produce a completely different process model; therefore, it only allows the behaviour recorded in the log. Process mining algorithms aim to find a tradeoff between overfitting and underfitting. One approach to measure generalization is to use alignment to see how frequently the model parts are used. If all the parts are used a lot, then most likely all future behaviours are captured, and therefore there will be a very high generalization. On the other hand, if there are parts of the model that are rarely used, it is more likely that there is behavior that has not yet been seen and there is a low generalization.
The generalization can be calculated as follows [12]:

$$Q_g = 1 - \frac{\sum_{nodes}(\sqrt{\#execution})^{-1}}{node\_in\_model} \tag{4.1}$$

Determining the quality of a process model based on the four quality criteria is challenging because some criteria conflict with each other. For example, a process model with good simplicity often lacks precision and/or fitness; or there is a trade-off between precision (underfitting) and generalization (overfitting). Ultimately, it is not possible to meet all four criteria, and depending on the objective of the process discovery, one or two of the four criteria tend to be preferred.

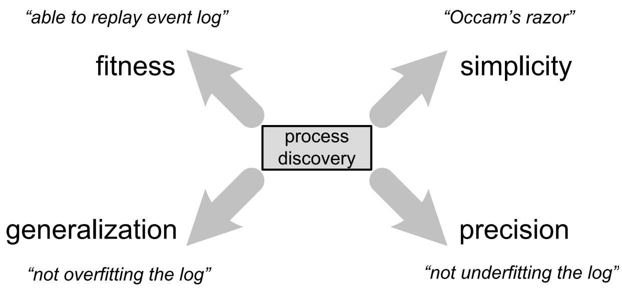


Figure 4.11: *The four dimensions of quality for a model [11].*

4.7 Process Mining in Healthcare

In recent years, process mining has become very popular in the healthcare industry due to its potential to provide a transparent, data-driven view of processes and the growing amount of patient data. Healthcare facilities are constantly working to produce guidelines for various hospital processes; therefore, the common question is whether the procedures performed to comply with the guidelines [13]. The chronological sequences of users' operations are stored in different information systems, according to the type of operation: the booking of an exam will be saved on one system, while its report on another. The data stored in the information systems are extracted to carry out an analysis, producing a single file called the event log, which chronologically tells the patient's history. Healthcare information systems have multiple databases with hundreds of tables with patient event data; therefore, it is natural to exploit this data to improve care processes while reducing costs. Healthcare requires flexibility and variable decision making based on the situation. These characteristics make it impossible to apply standard rules such as those of Business Process Management techniques since a hospital is not an assembly line and patients cannot be treated like machines. However, the large amount of data collected in hospitals can be helpful for making assessments and significantly improving care processes [14]. The primary purpose of process mining is to extract knowledge of processes from event logs that can come from all types of systems. Examples of such systems are the information systems of the hospital ward or those used in an intensive care unit. But even the laboratory systems can store all the tests that have been performed on a blood sample. Typically, these logs contain information on the initiation and completion of process steps along with context data, such as, for example, the actors and costs involved. Health information systems are heterogeneous, as there are heterogeneous databases: medical record data, treatment plan data, emergency room data or medical prescription data. Typically, a data standardization operation is performed, as they are contained in different systems, characterized by different software; therefore, there is no single database, but different data sources present in heterogeneous systems.

4.7.1 Healthcare Process

Healthcare can be represented as the union of the diagnosis, treatment and prevention of diseases to improve well-being. Although healthcare is typically associated with hospitals, there are many care processes in other organizations, and various professionals are involved in these processes, including general practitioners, nurses, and physical therapists. Treatments can be provided in a place other than the hospital: at home, in rehabilitation centres, and nursing homes. There are several types of health processes with different execution features. Regarding the organization of care, there is a distinction between three primary levels of care, where each level corresponds to the patient's specific needs [14].

- **Primary care**: it includes common, possibly minor, health problems that account for about 80% of doctor or health care practitioner visits. Therefore, primary care indicates the first point of consultation for all patients within the health system and is the basis for referral to secondary or tertiary level care.

- **Secondary care**: problems that require more specialized clinical skills are managed within secondary care. In this case, doctors or other professionals provide services who generally do not have first contact with patients. Usually, secondary care involves consulting a specialist for a more in-depth visit or surgery that primary care physicians cannot perform. This can include hospitalization, surgery, consultation with a specialist, and rehabilitation.

- **Tertiary care**: it addresses rare and complex diseases. This care is usually provided to hospitalized patients in a specialized centre. Examples of tertiary care are trauma, intensive care, transplants, and advanced surgery. Tertiary care relies on highly specialized and technology-driven institutions.

- **Emergency care**: is an additional level of care provided by emergency medicine professionals, whose job is to assess, manage, treat and prevent unforeseen illness and injury, providing rapid assessment and treatment of any patient with a medical emergency.

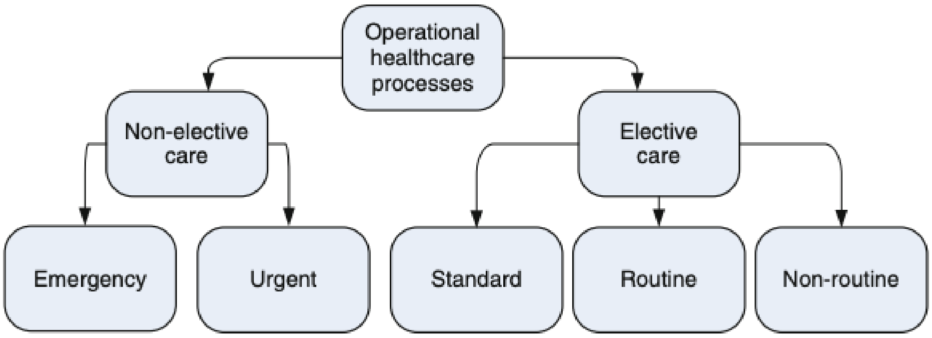


Figure 4.12: *Characterization of health processes [14].*

The previous figure shows a classification of the main types of health processes. The focus is on operational processes, i.e. processes that concern the logistics of work processes, in particular the medical phases that must be performed together with the necessary preparations such as, for example, booking an appointment or a room. Elective treatments refer to treatments for which it is medically correct to postpone treatment for days or weeks, unlike non-elective therapies, which represent patients for whom medical treatment is unexpected and must be planned at short notice. Elective care can range from standardized processes to processes for which variation exists. There is a standardized treatment path for standard processes that define the different activities in the process and their timing. The result of the process is usually known for routine processes, and different process paths can be performed during the treatment. While for non-routine processes, the doctor proceeds gradually, checking the patient's reaction to the single treatment and deciding the next steps each time. When complex care has to be provided, cooperation between various doctors of different medical specialities and departments is required to determine the treatment plan for the individual patient. For non-elective care, emergency care must be performed immediately, and urgent care can be postponed for a few days. For some processes, standard, routine and urgent care, the model discovered can be relatively simple. In contrast, for other processes, the model discovered is much more complicated (emergency and non-routine care).

4.7.2 Challenges in Healthcare

Healthcare faces several challenges, including rising healthcare costs; therefore, one needs to reduce costs. Secondly, people receiving care are getting older, leading to a greater demand for aged care. In addition, long waiting times cause dissatisfaction as the benefits of treatment are postponed, and therefore healthcare organizations need to improve productivity reduce access and waiting times. Understanding what is happening and analyzing deviations from the expected process model is essential to improve processes. Bottlenecks and other inefficiencies can be identified and diagnosed using event timestamps. A process model can be extended with different perspectives: the organizational perspective (*"what are the roles and which human resources perform certain tasks?"*), the case perspective (*which characteristics of a case can influence a particular choice?*), and the time perspective (*"where are the slowdowns in the process?"*).

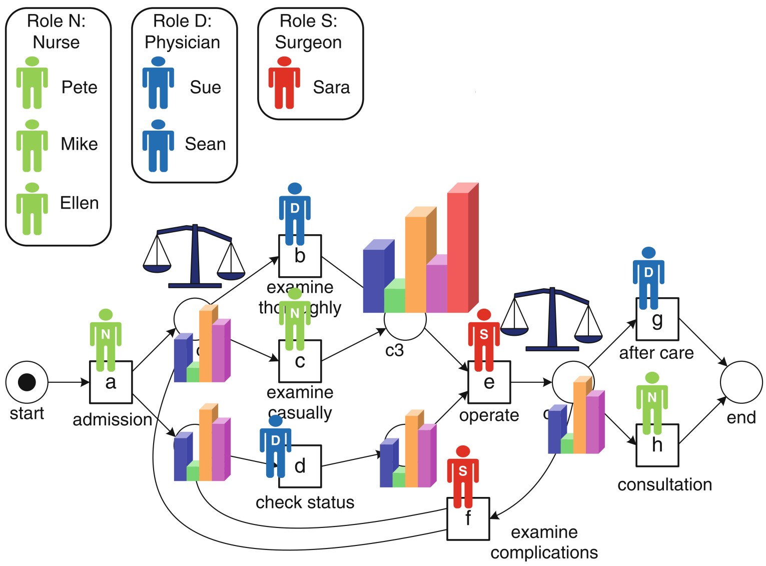


Figure 4.13: *Example of a healthcare process model [14].*

Listed below are various use cases, and examples of possible processes, which can be studied using process mining in the healthcare context:

- The process that is performed by surgery for the treatment of cancer patient;

- The assistance process after the surgery;
- The process of a routine visit in a clinic;
- The process related to the services provided in a ward;
- The process of transporting patients by ambulance.
- The process of continuous monitoring of a patient in the ICU.
- The daily monitoring process of a patient on the ward.
- The daily behavior of a patient at home.

Based on existing work and literature reviews, the following process mining perspectives can be listed for analysis in healthcare:

1. Access to data and data quality remain obstacles for the efficient use of process mining in the healthcare sector;
2. Only data from hospital information systems are considered, thus representing a partial view of the health system;
3. The use of health data requires their understanding, which is not easy due to the complexity of medicine;
4. The data sources are heterogeneous and difficult to use together (patient record, images, vital signs, medical history);
5. Healthcare processes are inherently variable and unstructured due to the diversity of patients and situations;
6. Most process mining methods pay attention only to the start time of the event and the name of an action, but not to the results of the action (example, "Is the patient treated adequately?");
7. Lack of adequate visualization strategies for less structured processes.

Chapter 5

AI Experiences in Healthcare

5.1 Introduction

This chapter will present the experiences gained in the context of the PhD research activities, also carried out within the Exprivia company. Over the three years, I had the opportunity to work on several EU-funded research projects related to the health sector. I was involved in these projects' analysis, design, development, and experimentation phases. The results of the experiences were presented at international conferences and to public decision-makers. These projects have touched on all the crucial points of using Artificial Intelligence in Healthcare to bring the research produced towards industrialization.

This chapter deals with a broad dissertation of the three main dimensions by which health is measured. These are the current challenges that health systems face daily in order to improve their processes, reduce expenses and waste:

- Understand the patient's status and **when** certain events occur
- Understand how the patient journey works and **how** it deviates from the ideal model
- Understanding the situation and **what** allows us to follow an individual patient within a healthcare system.

These three dimensions have been the starting points for the following studies, which will be extensively discussed in this chapter:

- Early Warning Score System
- Clinical Pathway Modelling
- On Edge Remote Patient Monitoring

The first experience led to creating an automatic method for analyzing patients' vital signs and understanding their deterioration. Medical personnel can use this to carry out an automatic assessment of a group of patients. The second experience led to the definition of a framework for formalizing and analyzing the patient's clinical path. This tool wants to be a solution to create the clinical path, even graphically, to know the formal model to follow. The last experience presents a complete architecture for remote patient telemonitoring management. This solution sees a new telemedicine approach based on Edge Computing that comes to create a magnifying glass on patient behaviors.

5.2 Early Warning Score System

The possibility of continuous monitoring of health conditions represents a crucial aspect for the improvement of living conditions, the prevention of potential pathologies and prompt response in critical situations. In particular, in intensive care or emergency situations, the evaluation of illness degree of a clinical risk level can be considered a predictive task in situations where streams of vital signs data are gathered by medical devices and the Internet of Medical Things (IoMT) sensors. In this framework, Early Warning Score (EWS) systems generating an aggregate score based on the measurement of a set of vital signs, such as National Early Warning Score 2 (NEWS2) and Modified Early Warning Score (MEWS), may provide a helpful decision support for the estimation of health state and triggers for critical care intervention. This present work addresses a preliminary analysis to investigate the most suitable Machine Learning (ML) technique for the prediction of clinical risk classes of a continuously monitored patient in a particular condition where a limited number of vital parameters is available. This analysis is then intended to be preparatory for the final goal of designing an edge device connected to one or more wearable medical devices via IoMT, which adaptively exploits the best ML model to predict a reliable EWS.

5.2.1 Introduction

In the healthcare sector, the clinical staff must be able to identify quickly the clinical picture of a patient. Especially in intensive care, in resuscitation, or in the emergency room, many parameters, such as vital signs, can be monitored according to the needs of the patient. In particular, determining the degree of illness or the life risk of a patient may be considered a predictive analysis task, in a framework where serial monitoring is a suitable support tool to prevent the worsening of the clinical picture. Thus, a system of EWS able to indicate the onset of pathological events or severe conditions can be helpful for physicians and caregivers in order to outline a global view of the patient state, and hence to obtain insights for the best care and therapeutic choice.

Thanks to the wide availability of the Web resources, the Internet of Things (IoT) and mobile technologies, the healthcare system has now the possibility of moving a step forward the path of prevention, unleashing the full potential of medical devices. Indeed, we are witnessing at the forthcoming IoMT era, where medical devices and applications are connected to healthcare IT systems via the Web, and Wi-Fi enabled devices can facilitate machine-to-machine (M2M) communication and link to Cloud platforms for data storage. Moreover, the IoMT includes a landscape of wearable devices, remote patient monitoring systems, sensor-enabled hospital beds and infusion pumps, medication-tracking systems, medical supply and equipment inventory tracking, and more. In this scenario, connected wearable devices enabled by the IoMT can improve diagnoses reliability and time performances, while allowing data collection for analytics, and consequently a more responsive adaptivity to the fluctuations of conditions.

However, medical devices must undergo to specific ethical requirements imposed from the medical community, since they need to address the following concerns [15]:

- *reliability*: the potential diagnostic nature of IoMT-based systems mandates reliability of every system component in order to guarantee the correctness of collected information;

- *safety*: a safe medical device must not cause harm to its operating environment;

- *security*: medical devices must be robust to external threats and attacks because of the sensitive and personal information they collect.

A promising approach towards the satisfaction of such mandatory requirements comes from the paradigm of Edge Computing, that pushes computing tasks and services from the network core to the network edge. In the meantime, considering that artificial intelligence (AI) is functionally necessary for quickly analyzing huge volumes of data and extracting insights, the field of Edge Intelligence, or *AI on Edge*, is disruptively emerging. Essentially, the physical proximity between the computing and information-generation sources promises several benefits compared to the traditional cloud-based computing paradigm, including energy-efficiency, reduced bandwidth consumption, and context-awareness [16]. As the level of Edge Intelligence goes closer to the device computational capabilities, the amount and path length of data offloading reduce. As a result, the transmission latency of data decreases and the data privacy increases.

Our goal is to deal with a clinical and operational context to develop integrated solutions for seamless care in which AI and IoMT are used at the Edge, with a people-centered approach that adapt to the needs of healthcare providers and that are embedded into their workflows (recalling a paradigm of “adaptive intelligence”). Adaptivity deals also with training ML models using not only the statistical estimation of data, but combining them with specific domain knowledge. Moreover, several successful applications of ML approaches to healthcare there exist (see Refs. [17, 18] for an overview). Therefore, the final purpose of our work is to design an edge device, connected to one or more wearable medical devices via IoMT, which adaptively exploits the best ML model to predict the best healthcare EWS, according to: (i) the patient vital signs, suitably gathered from one or more available wearable medical devices; and (ii) the patient's conditions and environments, ranging from low-to-high emergency situations, such as the cases of:

- a user monitoring himself while doing a fitness/running session;
- a patient monitoring himself or a physician monitoring a patient to prevent a critical care intervention or a prehospitalization;
- a hospitalized patient continuously monitored to early detect a clinical deterioration and a potential need for higher level of care.

The aim of this work is therefore to address a preliminary study and to analyze the general conditions to run the best ML model, both in terms of performances metrics and time efficiency, which is able to predict the clinical risk class of a continuously monitored patient with the real-time recording of his vital signs, in the particular condition where a limited number of vital parameters is available. The work is organized as follows. Section 5.2.3 provides an overview of technologies which were investigated as background knowledge, namely, the EWS clinical protocols. Section 5.2.2 discusses the state-of-art of IoMT and the related work about retrieving an EWS from IoT devices. Section 5.2.4 describes our vision and proposal, and then defines the objectives of our work. In particular, Section 5.2.5 shows the experimental setting and the analytical results about real-data gathered for clinical diagnosis and real-time monitoring. Finally, Section 5.2.6 concludes the research, outlining future perspectives.

5.2.2 Related Work

IoMT is emerging in healthcare industry to face several future challenges such as data privacy, security issue, real-time processing, low power consumption, and need for medical expertise (see Refs. [19, 15] for a first overview with a focus on IoT services and technologies in healthcare). In order to circumvent difficulties of current IoT-based systems to provide continuous and real time patient monitoring due to issues in data analytics, a solution presented in [20] exploits a fog computing architecture enabled by machine learning algorithms to early-detect patient deterioration arrhythmia in ECG signal.

A reinforced self-aware EWS system by using the IoT technologies and the self-awareness concept has been recently proposed by Azimi et al. [21]. This approach provided system adaptability with respect to various situations and system personalization by paying attention to critical parameters of patient condition. Even though most of the existing EWS systems are used in hospital environment, Anzanpour et al. [22] proposed an intelligent early warning method using IoT, to remotely monitor in-home patients and generate alerts in case of different medical emergencies or radical changes in condition of the patient. Moreover, Rahmani et al. [23] focused on the need to use a gateway between sensor infrastructure network and the Internet. The strategic position of such gateways at the edge of the network offer several higher-level services such as local storage, real-time local data processing, embedded data mining, etc., presenting thus a Smart e-Health Gateway. Exploiting the concept of Fog Computing in Healthcare IoT systems was formed a Geo-distributed intermediary layer of intelligence between sensor nodes and cloud. In order to address the management of the sensor network and a remote health center, this fog assisted system architecture can face many challenges in ubiquitous health systems such as mobility, energy efficiency, scalability and reliability.

In Refs. [24, 25] the authors focus on an Ambient Assisted Living scenario, in which a Smart Home Environment is carried out to assist adaptively users at home. Particularly in the latter, the study focuses on elders at home, aiming at performing trustworthy automated complex decisions by means of IoT sensors, smart healthcare devices, and edge nodes, thus, exploiting the proximity between computing and information-generation sources with the help AI-based techniques directly on the Edge would enable a faster, more private, and context-aware Edge Computing empowering.

Another early warning system by integrating IoT, big data, and cloud computing technologies which physically linked personal communication devices of patient/doctor, cloud systems, and hospital medical information systems has been proposed by Hsu et al. [26]. The system collects personal heart rate and metabolic equivalent (MET) features from calibrated fitness devices wore by users, and was successfully validated for coronary artery disease (CAD) patients.

Finally, it is worth mentioning that a Deep Learning approach called Deep Early Warning System (DEWS) has been suggested. This framework take advantage of deep learning model to interpolate historical trends of vital signs and predict the probability of a clinical risk. The evidences of the work has shown that DEWS can perform better than other EWSs like the National Early Warning Score [27].

5.2.3 Pre-requisites

The EWS protocol is based on an aggregate scoring system in which a score is allocated to physiological measurements when patient is monitored. Six simple physiological parameters form the basis of the scoring system:

1. respiratory rate (breaths per minute);
2. oxygen saturation (SpO_2);
3. temperature (°C);
4. systolic blood pressure (mmHg);
5. heart rate (beats per minute);
6. state of consciousness, according to the AVPU scheme.

AVPU (Alert, response to Voice, response to Pain, Unresponsive) is a system by which clinical staff can measure and record patient's level of consciousness. The most known EWS protocols which are currently used are:

- the National Early Warning Score 2 (NEWS2) [28];

- the Modified Early Warning Score (MEWS) [29].

Table 5.1: The Scoring System for NEWS2 Protocol.

NEWS2 Vital Signs	**3**	**2**	**1**	**0**	**1**	**2**	**3**
Respiratory Rate (bpm)	≤ 8		$9-11$	$12-20$		$21-24$	≥ 25
Oxygen Saturation (SpO_2)	≤ 91	$92-93$	$94-95$	≥ 96			
Systolic Blood Pressure (mmHg)	≤ 90	$91-100$	$101-110$	$111-219$			≥ 220
Heart Rate (bpm)	≤ 40		$41-50$	$51-90$	$91-110$	$111-130$	≥ 131
Temperature (°C)	≤ 35.0		$35.1-36.0$	$36.1-38.0$	$38.1-39.0$	≥ 39.1	
State of Consciousness				A			VPU

Table 5.2: The Scoring System for MEWS Protocol.

MEWS Vital Signs	**3**	**2**	**1**	**0**	**1**	**2**	**3**
Respiratory Rate (bpm)		≤ 8		$9-14$	$15-20$	$21-29$	≥ 30
Systolic Vlood Pressure (mmHg)	≤ 70	$71-80$	$81-100$	$101-199$		≥ 200	
Heart Rate (bpm)		≤ 40	$41-50$	$51-100$	$101-1110$	$111-129$	≥ 130
Temperature (°C)		≤ 34.9		$35.0-38.4$		≥ 38.5	
State of Consciousness				A	V	P	U

NEWS2 protocol is actually recommended by the National Health Service (NHS[1]) of UK, and is particularly designed for the determination of a degree of illness of a patient and prompt critical care intervention in the settings:

- *emergency*: for initial assessment, serial monitoring, and assessment for triage;
- *ward*: for initial inpatient assessment and continuous monitoring;
- *prehospital*: for communication of illness severity to receiving hospitals.

Instead, MEWS protocol is used to identify in-hospital patients with declining conditions.

In the former protocol, a score is associated with each detected vital parameter value as shown in Table 5.1. In the latter, instead, the associated score to each vital parameter value is computed as shown in Table 5.2. The sum of those values determines an aggregated final score, which is used to delineate a clinical risk class (low-medium-high) at different thresholds. In particular, only for NEWS2, a weighting score of 2 should be added, in addition, for any patient requiring supplemental oxygen.

For NEWS2, the risk class is:

[1]`https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2`

- *low*: the aggregated score is $0-4$;
- *medium*: if it is $5-6$;
- *high*: if it is ≥ 7 (up to 20).

For MEWS, the risk class is:

- *low*: if the aggregated score is $0-2$;
- *medium*: if it is $3-4$;
- *high*: if it is ≥ 5 (up to 16).

5.2.4 The Healthcare Tool Proposal

In this section, the innovative proposal is firstly presented. Then, the initial objectives of this project are set out, and the preliminary steps that this work intends to accomplish are illustrated.

As depicted in Figure 5.1, our main idea is to develop an integrated solution for healthcare in which AI and the IoMT devices are exploited at the Edge, in order to define a responsive healthcare tool which adapt itself to the needs of patients and caregivers. Adaptivity shows up in a two-fold perspective:

- in terms of trade-off between ML performances and timeliness;
- in terms of availability of vital signs that can be collected in a given situation.

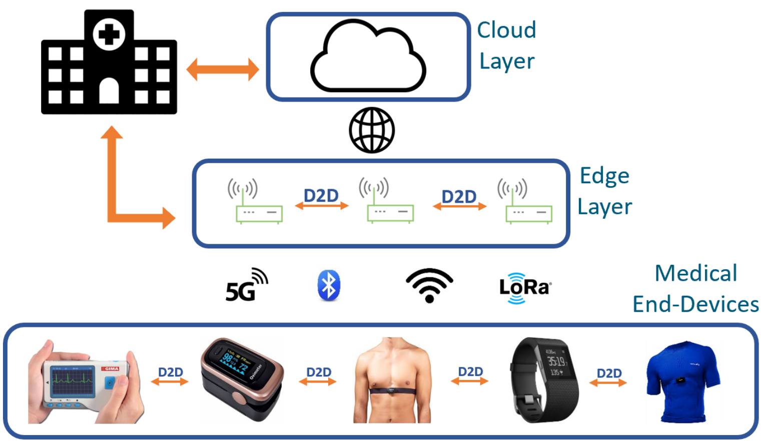


Figure 5.1: *Edge Intelligence Architecture*

In particular, the purpose of our work is to provide an edge device, connected to one or more wearable medical devices via IoMT, which adaptively exploits the best ML model to predict the best healthcare EWS, according to:

- the patient's vital signs, suitably gathered from the available wearable medical devices;
- the patient's conditions and environments, ranging from low-to-high emergency situations.

As shown in Figure 5.1, the Architecture of our proposal has a Medical End-Devices Layer, made up of all the nearby end-devices connectable by device-to-device communications [30]; an Edge Layer which can be a server attached to an access point (e.g., WiFi, router, base station), a network gateway, or even a micro-datacenter available for use by nearby devices; and, finally, a Cloud Layer, in which gathered raw data and processed data (at the Edge) are conveyed to optimize the overall performances. In this way, the Cloud Layer would act as an intermediary, by receiving any request and/or alert sent by the Edge Layer after the measurement of specific vital signs, and by activating specific operating protocol with the hospital, thus supporting a (remote) complex decision making process. With that in mind, this study is focused on investigating the possible medical wearable designs for non-invasive applications. Specifically, the study is still open regarding the front-end hardware components required to design these wearable devices and how they can be used to analyze clinical conditions. Hence, the following scenario is proposed, as shown in Figure 5.2. Consider a patient at home which has monitoring instruments and wearable medical devices, and is constantly monitored from the edge computing infrastructure of heterogeneous multi-IoMT network devices. The edge device coordinates and monitors the patient's care at home through the exploitation of a predictive model which determines the clinical risk of the patient. In this case, the edge device will adopt the trained model for predicting the NEWS2 score class. Such infrastructure may be useful also for in-hospital patients which are continuously monitored to prevent a clinical deterioration.

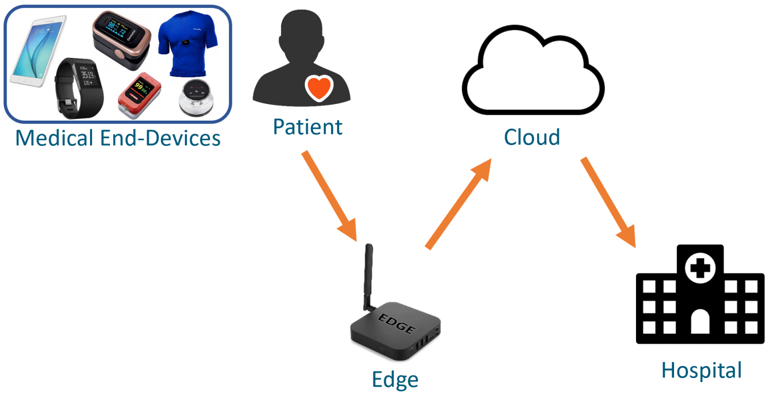


Figure 5.2: *Design Scenario*

Then it also figured out a scenario in which our edge computing tools are adopted for hospitalized patient so that the edge device would adopt the trained model for predicting the MEWS score class. As starting point, we therefore delve in developing the ML toolbox, analyzing which ML model best suits such a scenario. The edge device will then adaptively switch the running ML model according to the user needs and environment, or depending on the available data under monitoring. In this way, an adaptive system of medical devices would be able to provide an exact standard EWS class in presence of all parameters and an approximate but reliable prediction when only some vital signs can be measured at the moment where an intelligent support is needed.

5.2.5 Experiments

Data collection

The data collection activity started with retrieving real-data about vital signs of continuously monitored patients within the project "Progetto Cluster Tecnologici Nazionali - MIUR - Tecnologie per gli Ambienti di Vita: Active Ageing At Home"[2]. Interestingly, the project activities were also oriented towards the design of a hardware/software framework that allows the integration of medical devices for active and real-time monitoring, collecting and tagging data [31]. The gathered data were

[2] Active Aging At Home Project, PON Code CTN01_00128_297061 - http://activeageingathome.eresult.it/

used to develop and improve analysis and transmission systems capable of extracting the key information and of transmitting it to the various healthcare stakeholder (family members, caregivers, service providers) identifying critical situations and allowing efficient monitoring of the well-being level of the user by reducing the cognitive overload.

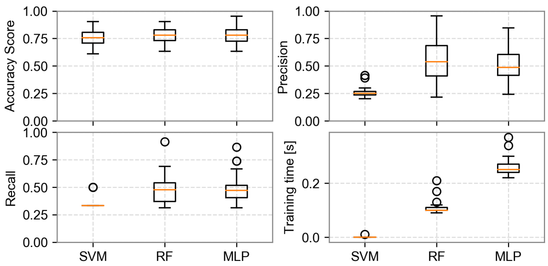
Then, a dataset containing time measurements of a set of 6 vital signs was collected for a cohort of 201 patients. The parameter set includes body temperature (BP), blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen saturation (OS) and state of consciousness (SoC). The measurement session for each patient presents an average duration of $\sim$ 6 hours. Along one session, the observations for each parameter are taken independently with a non-periodic rate. The minimum time interval between two consecutive measures is 60 seconds, while the maximum interval is 53 minutes. The average number of observations for each patient is around 74 in a range between 66 and 82 measures. Even though a not relevant number of measures has been detected as outliers, they have not been treated since NEWS2 and MEWS scores are not affected anyway.

Dataset generation

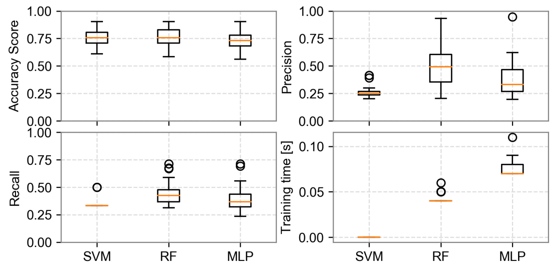
In order to simulate a real-time process of simultaneous measurements of a set of vital signs, the observations were organized according the chronological order of detection along each measurement session. Consequently, an $n \times p$ matrix of records, where n is the number of simultaneous measures, and p is the number of features, was obtained for each patient. Since the numerosity of observations can change among patients and among features for the same patients, the tail of the dataset has been cleaned after the removal of those instants where it was not possible to collect valid measurements of the six vital parameters at the same time. Following this process, the resulting dataset X for each of 201 patients is made of $n = 43$ observations and $p = 6$ features, with a total number of observations equal to 8643 records.

Table 5.3: Range and Percentile of Vital Signs Values in the Dataset.

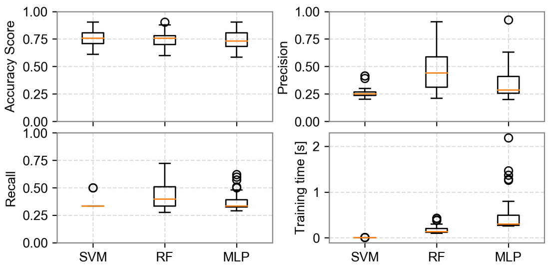
	avg	min	25p	50p	75p	max
BP [mmHg]	110	70	86	115	127	150
HR [bpm]	78	20	52	75	103	150
RR [bpm]	22	5	12	17	30	50
SoC	1	0	0	2	2	3
T [°C]	37	33	35	36	39	45
OS [SpO_2]	95	80	91	95	100	105
NEWS2 Score	9	0	7	9	11	18
NEWS2 Class	high	low	high	high	high	high
MEWS Score	5	0	4	5	7	13
MEWS Class	high	low	medium	high	high	high



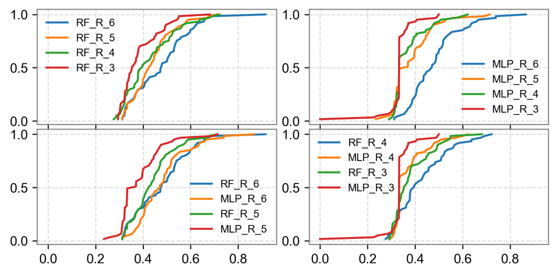
(a) with 6 vital signs



(b) with 5 vital signs



(c) with 4 vital signs



(d) Comparison among CDF of recall performances

Figure 5.3: Performances of classifiers in predicting NEWS2 classes

Learning experiment

As already discussed in previous section, MEWS and NEWS2 scores and classes are evaluated using an additive formula based on specific ranges of values of the six vital signs. The simulation study presented in this work is devoted to a preliminary analysis of the performance of three classification methods in terms of their ability to predict the MEWS and NEWS2 class of a patient, when the six necessary parameters are not available at the same time. The classifiers include Support Vector Machine (SVM) [32], Random Forest (RF) [33] and Multilayer Perceptron (MLP) [34]. These three algorithms are the most popular classifiers dealing with independent observations. Each of them, in particular, respond to the classification problem in a different approach. In particular, SVM can solve nonlinear classification problem projecting linearly inseparable data onto a higher-dimensional space where it becomes linearly separable through a kernel function, such as Radial Basis Function (RBF) and Polynomial Kernel (selecting the proper kernel after a Cross Validation process). On the other hand, RF represents an ensemble of decision trees aim at building a more robust model that has a better generalization performances and is less affected to overfitting. It is also able at handling categorical and continuous features together. Finally, MLP is a type of Artificial Neural Network that use back-propagation supervised algorithm for training and nonlinear computation techniques to deal with features that are not linearly separable.

The learning experiment is divided into three steps:

1. Sampling of training datasets;
2. Hyper-parameters tuning;
3. Models comparison.

Sampling of training datasets

As a first step in performing the learning experiment, it has been extracted from the total dataset X several subsets suitable for the training of the classifiers. Actually, since the 8643 observations (43 measures for 201 patients) are time-dependent, several datasets have been arranged according to the following criteria: (C1) each dataset is made of m independent observations associated with m different patients; (C2) the proportions of the NEWS2 classes are preserved in each drawn; (C3) the union of the drawn datasets should cover at least the 75% of the original dataset. Within these criteria, the result is two large sets of data: one made of 61 datasets,

$D = \{D_1, D_2, \ldots, D_{61}\}$ and one made of 17 datasets $K = \{K_1, K_2, \ldots, K_{17}\}$ obtained from $\{X - \bigcup_{i=1}^{61} D_i\}$. Some remarks about the aforementioned criteria are in order. As a preliminary analysis, condition C1 has been applied in order to avoid the problem of auto-correlation in time series data such that training and test set take into consideration only independent observations of the vital signs. Condition C2 is required in order to replicate the actual conditions of detection and to pave the way for potential re-training session of wearable devices or within experiments provided with limited number of observations. Condition C3 is a way to take into considerations as much as possible the information contained in the population of reference data. Hence, the dataset generation can be summarized in the following steps:

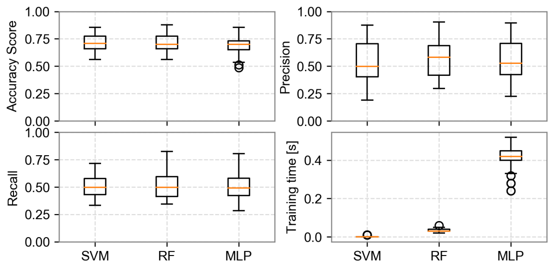
1 From X evaluate the proportion of high, medium and low risk classes. Draw 201 binary samples from a binomial distribution with elementary probability p_1 given by the frequency ratio $p_1 = \#(\text{medium} + \text{low})/\#\text{high}$. Suppose that h is the number of bits 1 (high) and $\bar{h}$ is the number of bits 0 (not high). Then, draw $\bar{h}$ binary samples from a binomial distribution with elementary probability p_2 given by the frequency ratio $p_2 = \#(\text{low})/\#\text{medium}$, such that one has m is the number of bits 1 (medium) and l is the number of bits 0 (low) with $\bar{h} = m + l$.

2 Generate 201 ordered pairs given by the patient ID and one of the risk state drawn in the previous step: $L_1 = \{(I_1, S_1), (I_2, S_2), \ldots, (I_{201}, S_{201})\}$ where patient ID I_i range from 1 to 201 and S_i can be one of the three risk class high (H), medium (M), low (L).

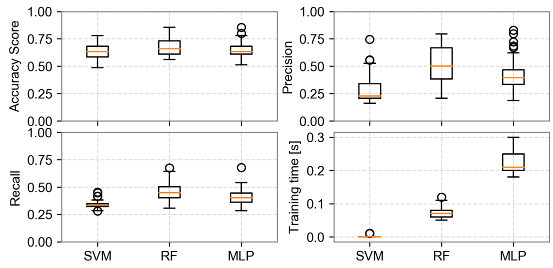
3 Given the entries of L_1, extract randomly the corresponding records from X in order to have a dataset D_1 made of independent observations associated to different patients.

4 Repeat Step 1→3 until $|(\bigcup_i D_i)| \geq 0.75|(X)|$ such that one obtains $D = \{D_1, D_2, \ldots, D_m\}$.

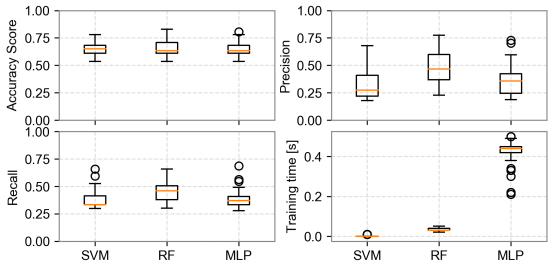
5 From $G = \{X - \bigcup_{i=1}^{m} D_i\}$ repeat Step 1→3 in order to get $K = \{K_1, K_2, \ldots, K_r\}$



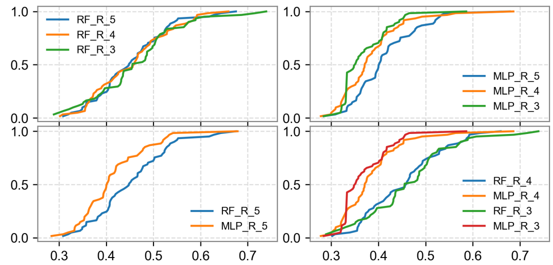
(a) *with 5 vital signs*



(b) *with 4 vital signs*



(c) *with 3 vital signs*



(d) *Comparison among CDF of recall performances*

Figure 5.4: *Performances of classifiers in predicting MEWS classes*

Hyper-parameters tuning

For each dataset of $K = \{K_1, K_2, \ldots, K_{17}\}$ and for each classification method, a 5-fold cross validation (CV) has been performed in order to tune the parameters that maximize the precision of the classifiers (micro-averaged over all classes), obtaining a set of ordered triples ($\mathrm{SVM}_b^{(i)}$, $\mathrm{RF}_b^{(i)}$, $\mathrm{MLP}_b^{(i)}$).

Table 5.4: Example of triples of best classifiers from Cross Validation.

Dataset	5-fold best	5-fold best	5-fold best
K_1	$\mathrm{SVM}_b^{(1)}$	$\mathrm{RF}_b^{(1)}$	$\mathrm{MLP}_b^{(1)}$
K_2	$\mathrm{SVM}_b^{(2)}$	$\mathrm{RF}_b^{(2)}$	$\mathrm{MLP}_b^{(2)}$
...	...	...	...
K_{17}	$\mathrm{SVM}_b^{(17)}$	$\mathrm{RF}_b^{(17)}$	$\mathrm{MLP}_b^{(17)}$
Best Overall	SVM_{best}	RF_{best}	MLP_{best}

Hence, the final classifiers with tuned parameters, namely SVM_{best}, RF_{best} and MLP_{best} are chosen as the best performers over all validation runs (see Table 5.4).

Model comparison

A model comparison was performed among the best classifiers in terms of prediction accuracy, precision (positive predictive value), recall (sensitivity) and execution time for training. Time performances refer to an Intel Core i7-7700HQ machine with 2.80GHz and x64 operating system, while fit algorithms and performance metrics refer to Python `Scikit-learn` library [35]. As a preliminary study, the comparison involved the performances of the models in predicting both the risk classes NEWS2 and MEWS with, respectively, 6, 5, 4 and 3 vital signs, and 5, 4 and 3 vital signs as features.

In particular, the reduced sets of, respectively, 5, 4 and 3 vital signs for NEWS2, and 4 and 3 vital signs for MEWS, aim to reproduce the situation where {'state of consciousness'}, {'state of consciousness', 'blood pressure'} and {'state of consciousness', 'blood pressure', saturation}, respectively, are not available or not promptly measurable as other vital parameters. The performance metrics have been evaluated for every dataset in $D = \{D_1, D_2, \ldots, D_{61}\}$ after a 80/20 random split in a training and a test set. A remark is in order. Even though the EWS score under examination can be exactly evaluated in presence of all vital signs (see Tables 5.1 and 5.2), the idea of testing a prediction in the case of 6 parameters is to provide a benchmark when the number of vital signs is reduced to a limited set.

In the present work, as a preliminary test, systolic pressure and state of consciousness have been removed from the features set. The choice is motivated by the evidence that the detection of systolic pressure or the determination of the state of consciousness require the use a sphygmomanometer or the decision of an expert which are not promptly embeddable in a IoMT edge device.

Results

The performance results for the prediction of NEWS2 and MEWS classes with the specific number of vital signs are reported in Figures 5.3, 5.4 as boxplot associated to the metrics evaluated for all the 61 datasets $\{D_1, D_2, \ldots, D_{61}\}$. Panels (d) of each figure represent a comparison among empirical cumulative distribution functions of recall performances evaluated over $\{D_1, D_2, \ldots, D_{61}\}$. In the case of NEWS2 prediction (Figure 5.3), the median accuracy scores are above 75% and substantially comparable for all the three classifiers. Random Forest apparently is the best in positive predictive values rates (median $\geq$ 50% with $75p$ close to 75%, while the sensitivity is comparable with the one of the multilayer perceptron.

For all classifiers the training time range from fractions of seconds to 0.4s. The significant delay of the MLP is due to the high size (100 hidden neurons) of hidden layers. The apparent outperforming time of SVM is due to the behaviour of the classifier in presence of unbalanced multinomial classes, that starts to be responsive with trade-off term C larger than 10^3 with the dataset under examination. Similar performances are reported in Figure 5.4 in the case of prediction of MEWS score, with the only exception of precision that seems to be comparable for all classifiers. The reduction of number of features clearly lowers precision and recall performances overall. For NEWS2 prediction the median positive predictive value lowers from 53% to 44% for RF and from 48% to 41% for MLP.

This evidence is also confirmed by one-sided Kolmogorov-Smirnov tests (KS2) performed between the recall measurements samples for the same method between different numbers of vital signs. Here, the null hypothesis that the two samples s_1, s_2 are drawn from the same distribution has been tested against the alternative hypothesis that the empirical cumulative distribution function (ECDF) $F(x)$ of s_1 is "less" than ECDF $G(x)$ of s_2. For instance, the KS2 test performed between the sample s_1 recall measures for RF with 6 vital signs and the samples s_2 for RF recall with 5 and 4 parameters provided p-values $p = 0.008$ and $p = 0.015$, respectively, hence rejecting the null hypothesis, with a 95% confidence level. The same happens for the median sensitivity that lowers from 47% to 40% for RF and from 47% to 33% for MLP. The KS2 test performed between sample s_1 of recall measures for MLP with 5 vital signs and the samples s_2 for MLP recall with 3 parameters provided $p < 10^{-4}$. Then, time performances slightly but not significantly reduce for RF and MLP with some not relevant outliers and this is due to a variation in hyper-parameters that increased the number of estimators for RF and the number of nodes in hidden layers.

Upper panels of (d) in Figure 5.4 show that empirical cumulative distribution functions of recall measurements with different number of vital signs are not significantly distinct within the same classifier. This may suggest that MEWS score is less sensitive to the reduction of vital signs and hence it may represent a more efficient score in the condition where not all vital signs are available in real-time mode.

Finally, a comparison of performances between RF and the other classifiers under examination suggest that Random Forest is the most suitable classifier that can support the reduction of vital parameters providing reasonable performance levels for a correct classification of clinical risk class. As a matter of fact, given the same number of vital signs, RF performs significantly better than MLP in terms of recall measurement. For instance, one-side KS test between RF and MLP recall measures for 5 vital signs gives a p-value $p = 0.0013$, confirming the visual evidence of ECDF plots in Figures 5.3 and 5.4.

5.2.6 Conclusion and future work

The wide availability of the Web resources and the progress of the IoT and mobile technologies can push the healthcare systems a step forward in the path of prevention, early diagnosis and care, unleashing the full potential of medical devices. The forthcoming Internet of Medical Things (IoMT) era will connect a landscape of wearable devices, remote patient monitoring systems to healthcare systems via the Web, and Wi-Fi enabled devices will facilitate M2M communication and link to Cloud platforms for data storage. This perspective will allow a continuous monitoring of health conditions of human beings promoting the improvement of living conditions, the prevention of severe disease and a prompt response in critical situations. Consequently, the availability of streams of data collecting information from vital signs can be helpful especially in intensive care or emergency situations, where data-driven risk measures can be crucial as decision support for physicians. Actually, well established early warning score systems, such as NEWS2 and MEWS, are already exploited in UK National Health Service to provide scores associated to different degrees of illness and to trigger critical care interventions. The evaluation of these scores requires the observation of a set of vital parameters, including body temperature (BP), blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen saturation (OS) and state of consciousness (SoC). However, some measurements like blood pressure and state of consciousness are not promptly embeddable in a IoMT edge device, thereby imposing a constraint in terms of responsiveness and design of an edge device. Motivated by these arguments, a ML-based framework has been proposed to address the problem of predicting Early Warning Scores in the particular condition where a limited number of vital signs is available. In particular, a comparative analysis of classification methods has been presented for the prediction of NEWS2 and MEWS clinical risk classes with different sets of vital parameters. A learning experiment based on real physiological data has been set up within project "Progetto Cluster Tecnologici Nazionali - MIUR - Tecnologie per gli Ambienti di Vita: Active Ageing At Home" to perform the analysis. The evidences show that Random Forest is the best classifier in terms of precision and sensitivity in predicting EWS classes with a reduced number of vital signs.

However, the experiment presented here needs to be extended and refined in forthcoming works in order to test other classifiers, to impose different constraints on set of vital signs and to improve the general performances of the algorithms. This work is intended to be preparatory for the final goal of designing an edge device connecting wearable medical devices, which adaptively provide anyway a risk assessment according the number and quality of available data streams.

5.3 Clinical Pathway Modelling

In this work, the formalization and the role of the Clinical Pathway (CP) have been analyzed): it is growing up as a main instrument for the implementation of clinical guidelines and evidence-based medicine. Its primary objective is the improvement of the care process monitoring the unjustified variations in clinical practices to reach faster the best fit care and to reduce the costs of the health system. In a generalized context of an ageing population and the ever-increasing diffusion of chronic diseases, a CP methodological and technological approach has been introduced to improve the way patients are monitored during their pathway, to help physicians to read the clinical picture in the best and fast way and to reduce the general clinical complexity.

5.3.1 Introduction

In the development of digital services for supporting clinical-health and care processes, it is possible to identify some areas of innovation in charge of the Regional Health Services. The one that is attracting the most attention is related to the digital management of Clinical Pathways (CPs)[36].

CPs are emerging as a main tool for the implementation of clinical guidelines and evidence-based medicine. Their primary objective is the optimization of care, reducing unjustified variations in clinical practice and the costs of the health system, thanks to its interfunctional and multidisciplinary nature, and its integrated and cooperative coverage of the hospital and extra-hospital settings[37] [38].

CPs are also functional to containing clinical complexity, in a generalized context of an aging population and the ever-greater diffusion of chronic diseases linked to unhealthy lifestyles and improper eating habits: the elderly and/or chronic patient typically presents a difficult to read clinical picture and a high diagnostic and therapeutic complexity.

New ways to mitigate the cognitive overload for the clinician have to be investigated. Starting from decision support to medical prescription using predictive analysis, it is possible to guide the clinicians in dealing with complex pathology cases as depicted in Figure 5.5. Providing clinicians a guide that helps them to follow the best care pathway can reduce variations from the ideal pathway, which affects medical spending.

Despite the development of CPs offers increasingly broad and qualitatively satisfying coverage of clinical cases (both in the diagnostic and therapeutic fields, as well as in the treatment of chronic diseases), their adoption in treatment centers is still slowed down by human, cognitive, organizational and technological barriers.

The increasing computerization of clinical/health workflows and medical records offers a significant opportunity to reduce these barriers. However, the same computerization of clinical practices has generated new problems - mainly due to a large technological and informative fragmentation - that generally make the progress in the dissemination of evidence-based medical practice sub-optimal, and reduce the contribution of information technology to this progress.

In many sectors, ICT is gaining momentum due to the consolidation of technologies and methods for process automation and the availability of very large transactional and historical data and tools able to exploit its volume and heterogeneity for creating a prescriptive and predictive value. These techniques, which go under the name of predictive analytics, are successfully applied in areas such as marketing, customer relations, fraud or financial risk. Unfortunately, especially in Italy, they are weakly exploited in the clinical-health context, although characterized by the presence of enormous amounts of information, both structured and textual.

The progressive computerization of clinical practice processes in care centers is in fact, leading to the accumulation of an extraordinary amount of data whose value in terms of support to medical decision (both for care and secondary uses - such as health administration/government and scientific research) is huge and, to a large extent, unexpressed.

The exploitation of these broad masses of health data is promoted by another strategic area of the healthcare sector: the development of models and solutions for Clinical Governance that boost interoperability between various databases, also to improve resource management and for evidence-based governance.

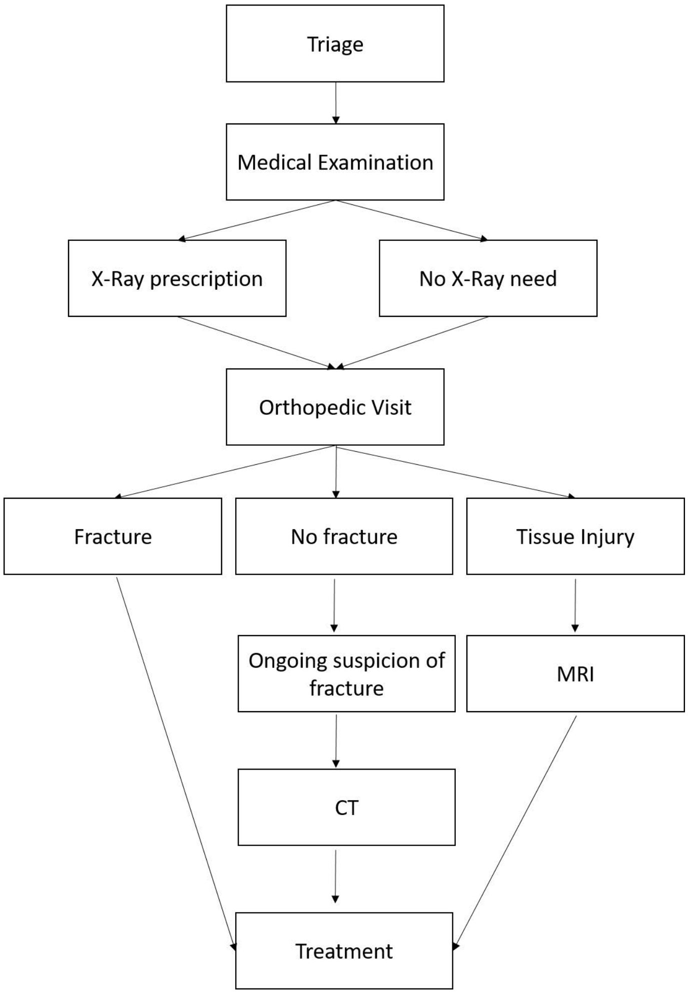


Figure 5.5: *Example of Clinical Pathway*

In summary, the current scenario offers wide space for creating value to support clinical trials and health governance, in response to the urgent need to:

1. design interventions and policies to optimize treatment, improve prevention, epidemiological surveillance and expenditure restructuring, especially with reference to the growing incidence of high-risk and high-cost patients;

2. accelerate the diffusion of CPs, so exploiting its benefits in terms of quality and continuity of care, of prescriptive appropriateness and containment of health spending;

3. mitigate the cognitive and managerial overload of the healthcare staff in the treatment of highly complex patients.

5.3.2 Related Work

In the health sector, significant efforts are made to create a level of interoperability and exchange of information between different systems. Furthermore, the biggest challenge is to represent information streams to try to extract clinical path information from this scattered dataset.

An integrated clinical pathway management has been proposed by Li et al. [39]. This approach is based on a semiotically inspired system architecture which aims to embed pathway knowledge into treatment processes and existing hospital information systems. With the aim of supporting later analysis, Caron et al. [40] proposed a process mining-based approach that enables the extraction of valuable organisational and medical information on past CP executions from the event logs of healthcare information systems.

A contribution to the possibility of managing in a personalized and dynamic way comes from Schlieter et al. [41], who proposed personalized dynamic pathways and a reference architecture for integrating them into existing inter-organizational healthcare information systems. In all the works cited above, the authors's aim is to extract information from a series of heterogeneous systems to build a chain of events that, in a second phase, will be formalized as a concrete pathway.

5.3.3 Addressed Problems

The main problems that this work wants to face are related to the fragmentary nature of the care system, to the inadequacy of the notations for the formal definition of CPs, to the information overload of clinicians and to the limited possibility of using many of the available clinical data (especially those recorded on paper forms). Thus, we can identify four main problems:

1. fragmentation of IT support in healthcare;

2. expressive limitations of formalisms;

3. information overload for physicians and care managers;

4. low exploitation of clinical data.

Fragmentation of IT support in healthcare

The adoption of CPs in health facilities and health districts is experiencing rapid diffusion in Italy as a tool for rationalizing clinical guidelines and organizing the treatment of complex pathologies and chronic diseases such as diabetes, Chronic Obstructive Pulmonary Disease (COPD), rheumatoid arthritis and heart failure. Some regions are implementing CPs as an extension of the Electronic Health Record, and there are many CP automation initiatives by individual local health agencies.

The prevailing direction is a "low automation" approach of the CP, e.g. a support in the form of an "open" electronic document (Care Coordination)[42] shared among the clinicians involved in the patient's journey, and coordinated/managed by the so-called case manager. From this point of view, the electronic tracking document of a CP arises as an additional "informational debt" along with the traditional clinical documents such as the specialist report, the first aid report and the hospital discharge letter.

However, the real potential of CPs, compared to clinical guidelines (which have a substantially descriptive/narrative nature), is in the wider possibilities offered by "high automation". This work aims to lay the foundations for the next evolutionary step of CP automation, with a broad integration with the well-established IT support tools such as document repositories, electronic medical records, electronic prescription systems, booking systems and with the overall hospital context.

The main technological barriers limiting the diffusion of IT tools for care continuity are the plurality of poorly interoperable software tools supporting clinical workflows, as well as the need of involving multi-disciplinary specialists and having many contacts with the patients when developing the systems assisting in the treatment of diseases[43] [44].

Expressive limits of formalisms

According to the definition of Edward Shortliffe, a learning health system is a system that *"is capable both of assuring that every decision is made with complete information and ensuring that every care instance can contribute a deeper understanding of care for individuals and populations"*[45].

Clinical/health workflows in general, and CP in particular, show a reduced level of causality. They do not guarantee to obtain the same outcome from the identical repetition of a very complex scheme of actions, but on the contrary they are based on a principle of specificity of each individual "case", the uniqueness of the symptomatic, diagnostic, prognostic, etiological and therapeutic response of each patient[46][47].

A critical success factor for CP automation is the availability of a CP expression notation that overcomes the rigidity of process automation formalisms such as Business Process Model and Notation (BPMN)[48], incorporating by design uncertainty, late choice, exception and non-motivated adherence, as we can see in Figure 5.6.

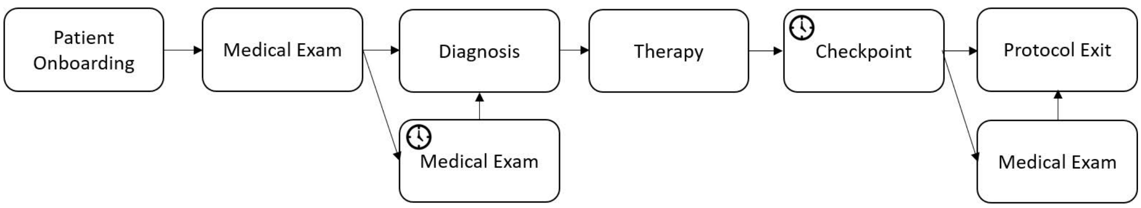


Figure 5.6: *Healthcare process in BPMN*

Information overload for physicians

The management of patients with high clinical complexity (meaning not only patients with complex pathologies and chronicity but also patients in comorbid conditions) and the increasing availability of data entail new problems of information overload for the clinicians.

Computer Science and in particular, the recent machine learning research line, known as data-driven phenotyping or computational phenotyping[49], offers interesting possibilities of development of risk stratification techniques and their application to the clinical domain. For risk stratification we mean the process of statistical determination of detectable characteristics associated with an increase in the occurrence probability of a pathology[50], and of similarity with other patients and therefore of prognostic prediction. This, together with the possibility to elaborate highly visual and interactive patient syntheses, constitutes an excellent opportunity to create a technological tool for mitigating the clinicians and managers cognitive overhead.

Low usage of clinical data

The progressive spread of high-risk and high-cost populations is creating new challenges for the health government, both locally and regionally, in an already difficult scenario of a constant reduction of public funding for health spending.

In this scenario, it would help the availability of data-driven clinical intelligence tools that allow statistical analyses, based not only on the services provided and hospitalization, but which can go into the details of the single treatment or clinical observation. This allows putting in evidence and performing more detailed analyses of, for example, latent patterns in the demographic and / or temporal distribution of a pathology, or spotting the emergence of hidden risk factors corresponding to syndromes or pathological conditions of high social significance[51].

Although much of the data-generating streams are already digitized, and despite the existence of technological and regulatory devices of standardization and centralized storage, such as the Electronic Health Record (EHR) and Pathology Networks, the population's clinical and health data are often confined to heterogeneous silos and in forms that limit their aggregability, prompt availability and analysability.

In particular, a substantial portion of the data digitally available is documentary or narrative. In order to make the information contained in a report or a hospital-discharge letter useful in an analytical context that also includes patient-structured data (such as hemato-chemistry, reports of pathological anatomy, structured anamnesis and measurements taken from diagnostics for images). It is essential that text documents are treated with semantic classifiers, i.e., with techniques that recognize and extract information, such as diagnoses, measurements, observations, and therapeutic indications.

On the other hand, the wide availability of clinical data relating to a sample of patients (considering all the clinical specialties and the temporal dimension) identifies new problems of:

- conceptual modelling of the person (in the clinical sense);
- population (in epidemiological and health governance);
- technological management of masses of data that exceed the storage and processing capacity of traditional computer architectures.

5.3.4 Approach

The research presented in this work aims at developing a tool that supports the definition, the management and implementation of a broader meaning of CP called Diagnostic Therapeutic Care Pathway (DTCP). This tool is intended for care and assistance centers according to a highly-automated and highly-integrated model capable of transforming the body of available data in the knowledge that can be used to support physicians and health authorities.

Specifically, this research aims at creating value for the following perspective:

1. support to design and maintenance of DTCP schemas, by developing a formal notation and a specific process automation platform for the clinical/health domain;
2. support to medical diagnostic, by developing a tool recommending clinically similar cases;
3. operative and cooperative support to the implementation of DTCP in care and assistance points, by developing a platform for application integration, which uniforms the operational management of the patient under DTCP.

The architecture proposed to reach these goals is composed of two main layers: the *Patient Engagement Layer* and the *Medical Supervisor Layer*.

The Patient Engagement Layer includes all the software systems used in healthcare facilities. One of the components of this layer is the Healthcare Information System (HIS) where it is possible to acquire information regarding flows in a hospital, such as accesses to the emergency room. The main component is the Electronic Medical Record (EMR), which contains all the information related to a patient's care and to his overall clinical picture, such as drug therapies or vital signs. Another important component is the booking system: it allows us to know the tests that the patient has to carry out, the timing and the related waiting lists. Other pieces of the system are represented by RIS/PACS, where reports and imaging are stored, and by telemedicine systems that allow patient management at home as if they are inside a hospital ward. Accesses to the emergency room, vital parameters, therapies, exam booking, reports, are all outputs of heterogeneous systems that put together feed a system capable of tracking the patient during the clinical pathway.

To reduce the fragmentation of information in healthcare, it is necessary to introduce an integration layer. This level must necessarily have a high degree of flexibility to guarantee interoperability with all the different types of possible systems located in the different places with different levels of granularity and goals. The Medical Supervisor Layer "consumes" the information collected in the Patient Engagement Layer.

Among the elements in this level, the Notation Layer manages notations and formalisms in a mixed and hybrid way, thus solving the limitations related to using only one formalism.

A process mining module in the architecture enable it building a clinical pathway. Moreover, this module is also responsible of conformance check and calculate the performance of clinical pathway.

From the doctor's point of view, the presence of a Recommender System module makes it possible to analyze clinical pictures of patients and receive clinical recommendations in the drug prescription task and compare similar cases. This part can be consider an entry point of a more complex Clinical Decision Support System (CDSS).

Finally, the Predictive Analytics module enables predicting if and when patients will undergo significant changes in their health conditions, which is a challenging task for the medical staff but that would avoid the consequences of a late intervention. The system, therefore, is able to identify in advance the patient's health decline, allowing physicians to intervene in a timely and systematic way.

All the module in the Medical Supervisor Layer work together to verify the patient journey and helps doctors keep a high number of patients under control in every step of their care path and gives the patient the perception of being followed and guided towards the best care.

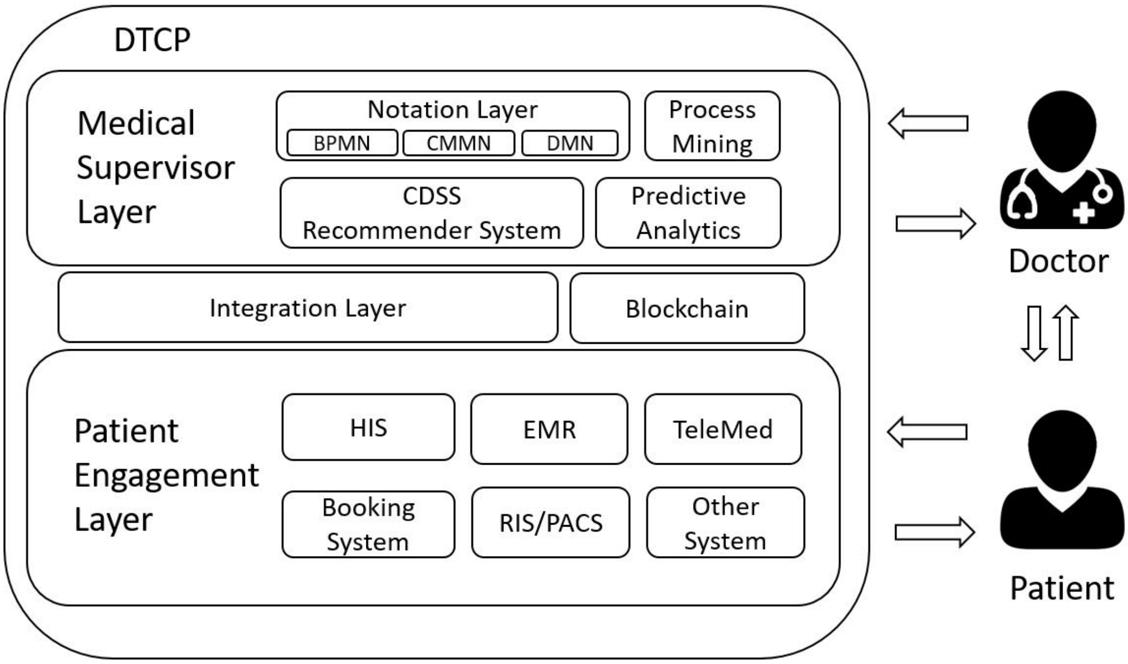


Figure 5.7: *Architecture of DTCP*

The proposed approach is based on using Case Management Model And Notation (CMMN) or Decision Model And Notation (DMN), specializing them for clinical/health domains, noting that they are suitable to shaping human uncertainty and arbitrariness during the implementation of a path[52]. These formalisms will be extended with new syntactic constructs through which DTCP models can be expressed in terms of both procedures and goals. The two notations are partially integrated by some already available engines, in which some discretional fragments of a model case are procedural in nature, namely, they obey specific and non-discretionary dependencies between tasks. This is a model of clinical cases in which a decision period is followed by a specific examination.

The declarative nature of CMMN and its ability to incorporate procedural portions in BPMN make it a very good candidate formalism for modelling and running DTCP. The extensibility of CMMN with domain-specific constructs and the availability of an open-source engine are further advantages in terms of integrity, flexibility, and opportunities for research and innovation, as we can see in Figure 5.8.

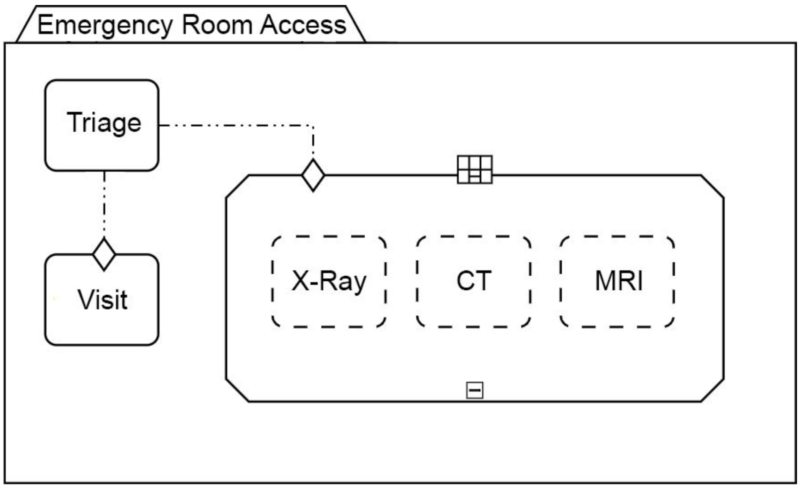


Figure 5.8: *Healthcare process in CMMN*

In order to enrich the support to the execution of DTCP, it is also necessary to develop techniques to aid repair, realignment, suspension, recovery, and abortion of DTCP. This will provide an additional environment of "motivated violation", by the doctor, of the DTCP in place.

Furthermore, the system uses Blockchain technology to verify the patient's identity, track prescriptions, or to address the correct application of protocols. This technology combines widespread peer-to-peer control with the most advanced encryption to make information collection and tracking extremely secure [53] [54].
One of its possible uses in DCTP is to verify the patient's digital identity, keep track of prescription history, drug administration and treatment history more safely and reliably.

5.3.5 Conclusion and future work

One of the possible future implementations that aim to make the clinical path management system safer and more reliable lies in introducing a Blockchain system. As far as the use of Blockchain in DCTP is concerned, an evolution of the system may concern the application of therapeutic protocols and certified medical devices. In this way, by introducing the use of the smart contract, healthcare organizations have the opportunity to strengthen the system, as smart contracts are performed automatically when certain conditions are met and allow the safe and unchangeable tracking of information, while at the same time being able to track the correct functioning of medical devices. The use of the Blockchain can serve as the basis for more elaborate healthcare applications, including prior authorization and automatic data processing. This technology uses algorithms to fully customize the conditions that determine when to exchange value, transfer information or trigger events, recording them in a secure and unchangeable way.

Big data processing platforms are born to manage huge quantities of data, without requiring a radical reconstruction of existing IT architectures. At the same time, big data processing times allow transformations, modelling, and processing that are also very sophisticated, including both historical data (batch ingest) and the most recent clinical inputs (event ingest).

The clinical analytics architecture proposed in this work aims at bringing the fundamental principles of big data processing into the health domain, offering an open and scalable tool of ingestion, metabolization and data analysis. This tool would be able to integrate, through connectors, a multitude of existing software components already available in healthcare organizations. Furthermore, it would produce a series of advanced, interconnected, extensible and integrable tools to support clinical care and governance. This suite is organized into three functional areas:

1. the management of clinical big data;

2. the implementation of DTCP;

3. predictive analysis for preventive, diagnostic, prognostic, therapeutic, epidemiological and health governance.

The system will be deployed, under strict clinical supervision, in the context of two cardiovascular diseases with a high social impact: ischemic heart disease and heart failure. For both the considered pathologies, the diagnostic, prescriptive, prognostic and analytical characteristics will be developed through the automation of the DTCP, the automatic stratification of the cardiovascular risk and the therapeutic recommendations, the search for epidemiological correlations and the retrospective monitoring/validation of the clinical adequacy in the cardiovascular context. The development of greater skills in the modelling of welfare processes at a local level, with advanced techniques and tools that use innovative machine learning, big data, and multichannel technologies, enable obtaining a significant competitive advantage through a better understanding of the functioning of these processes and the exploration of opportunities to improve the effectiveness of their execution. By intervening in the processes and thanks to the adoption of specific DTCP, it is possible to obtain a reduction in associated costs and an improvement in quality for chronic patients, creating further opportunities for using technologies and greater advantages.

5.4 On Edge Remote Patient Monitoring

The SARS-CoV-2 pandemic has brought unexpected new scenarios in patient-care journeys and has accelerated this innovative process in the healthcare sector, demonstrating the importance of a systemic rethinking of remote care, mostly when patients are discharged from the hospital and continue their therapies at home in autonomy. The possibility to remotely monitor patients at home by means of smart sensors and medical devices has a dramatic impact on the quality of health services. Situation awareness plays an essential role in the decision-making process about the users, patients in this case, and their behaviors. Leveraging an Edge Computing framework, with embedded Artificial Intelligence capabilities to process near real-time data gathered from connected smart devices, would provide automatic decision support, thus improving the physicians' course of action. This work introduces a dedicated module called Clinical Pathway Adherence Checker (CPAC) within an Edge AI framework, which identifies the discrepancies between the modelled clinical pathway and the observed one using process mining techniques and, hence, detecting early detection of clinical deterioration of patient conditions. Also, further analyses are conducted in the anomaly detection at the Edge that may occur during the health data transmission process.

5.4.1 Introduction

Situation Awareness (SA), already known as Situational Awareness, is an acclaimed decision process to maintain and understand what is happening in a certain situation and leverage this information to avoid or mitigate eventual risks. In the recent years, this trend is gaining strong interest in the eHealth sector [55, 17], since several stakeholders, including domain experts, investors, and researchers, started to leverage awareness and clinical decision-making. One of the objectives of SA in eHealth is to personalize for every patient the therapeutic path, often referred as Clinical Pathway [56, 57], including both the biological characteristics of the pathology, and the aspects of the clinical history, along with the characteristic elements, and the living environment. Despite the advantages given by its applicability, several studies relating to SA in eHealth, and in particular to the Clinical Pathway, offers several lines of research for still unsolved problems. The clinical path, in fact, is manifold and complex [58]:it is not limited only to the moment of the medical consultation or diagnostic examination, but it includes a series of tasks that can be carried out independently by the patient without being monitored by the healthcare staff.

Over the last year, the national health services of different countries have been affected by a substantial and dynamic downsizing of resources and, despite this, they have managed to withstand, albeit with difficulty, the impact of the health emergency related to SARS-CoV-2 [59]. In this scenario, Telemedicine –a particular sub-field of eHealth– arises as a necessary alternative form of care pathways management, allowing remote monitoring of the patient at home. In this perspective, individual patients are encouraged to handle their activities to be managed autonomously, that is, without the medical supervision until a follow-up, in the form of an in-hospital visit or a televisit, which determines an conceptual check-point. Considering the clinical path in the phase not supervised by a doctor, autonomous supervision of patient care is envisaged to be delegated to an intelligent multi-agent system whose architecture can deal with the specific clinical sub-path for the discharged patient, also verifying its validation by a doctor or nurse, and ensuring compliance with effective prescriptions. This proposal would bring numerous benefits not only to patients but also especially to caregivers,as telemonitoring-related activities deal with mitigating challenging problems in the Healthcare sector.

This challenging goal recalls the theme known as “domiciliary hospitalization”, addressed with Ambient Assisted Living (AAL), a branch of Artificial Intelligence (AI), in which mobile technologies support patients at home with a continuous telemonitoring of their health conditions, addressing the case of clinical worsening which may require the backing of health personnel. Intelligent medical devices and sensors from the world of the Internet of Medical Things (IoMT), along with ambient and interactive devices with limited processing and storage capabilities, make it possible to say that each device connected to a smart home can transmit data that is useful for being aggregated, analyzed and processed. In this way, ML algorithms can be leveraged to provide predictive diagnostics that promote, adapt, and validate to the in-home patient's normal activities. Thus, the patient's tasks would be validated to her attached clinical path, that can be managed as a workflow in an evaluation phase of the Process Mining activity, such as [60]. Faced with this complex task, however, data security must not be overlooked. A reliable SA system in the eHealth and AAL scenario would be able to avoid the processing of false or inconsistent data, which could be life-threatening for a patient.

Therefore, in this work, starting from the Edge Computing architecture, already proposed in [61], it extends the work presenting a new intelligent software

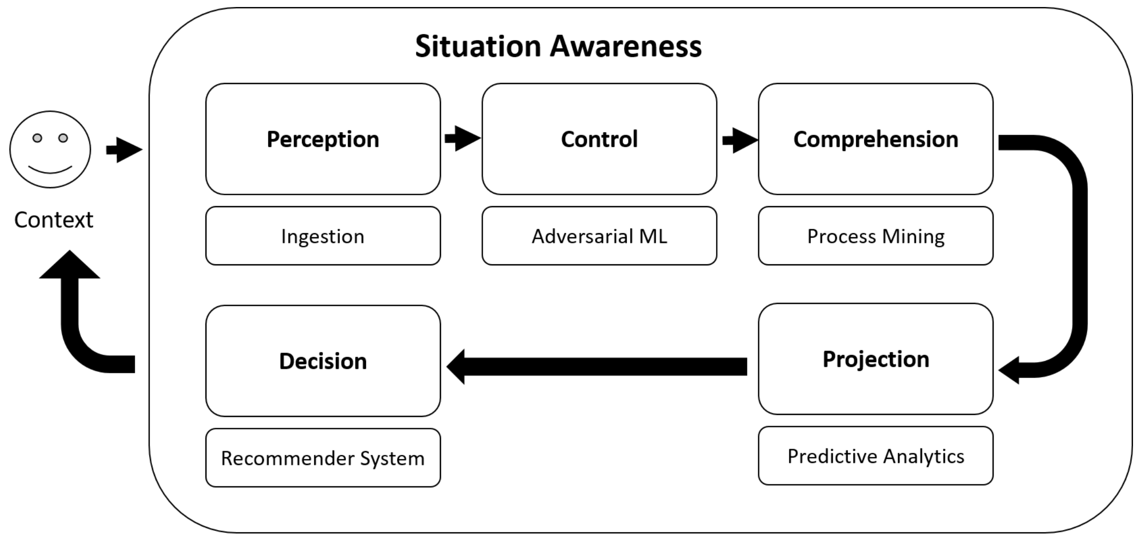


Figure 5.9: *An Overview of technical model of SA in eHealth.*

module aimed at checking the adherence to the clinical pathway assigned to a patient at home being remotely monitored, named CPAC: Clinical Pathway Adherence Checker.

The remainder of the research is structured as follows Section 5.4.2 provides an overview of related work and technologies which were investigated as background knowledge. Similarities, distinctions, and advancements of our approach in a comparison to them are briefly discussed. Section 5.4.3 recalls the Edge architecture which leverages on cloud, edge nodes and medical end-devices to perform AI tasks such as Process Mining and Machine Learning. Section 5.4.4 describes a possible scenario of a patient with SARS-CoV-2 symptoms that has to manage her clinical path in her home. Finally, Section 5.2.6 concludes the research, with an outline of future work.

5.4.2 Related Work

A desirable condition for providing digital support for strategic decisions during critical situations can be achieved through an SA approach. This is evidenced by the recent health crisis due to the COVID-19 pandemic [62]. Specifically, SA provides a series of techniques and tools to ensure a correct perception, in real time, of what happens in operational scenarios through the punctual analysis of information from a multitude of heterogeneous sources. In Figure 5.9, we can see the chain of SA. In the clinical setting, the methods of intervention are always conditioned by the following parameters [63]:

1. *Perception* is related to data that comes from the context: in this sense, *Data Ingestion*, as a first step, collects data from all health information systems and standardizes it into a single formalism.

2. *Control* acts on the reliability of perceived data: *Adversarial Machine Learning* is an important area of Machine Learning that can help improve the reliability of systems and protect ingested data from fraudulent attacks in the healthcare sector where disinformation could endanger and compromise the health of patients [64].

3. *Comprehension* is related to the ability to understand the situation: this is why *Process Mining* for healthcare is an appropriate method to extract information from event logs that are scattered throughout the health system and to define (work-)flows to be analyzed.

4. *Projection* is the ability to prevent future events: for this reason *Predictive Analytics*, by means of Supervised Machine Learning techniques, is a good candidate to predict the flow trend in the system in order to monitor the growth likelihood of critical conditions.

5. *Decision* is the reasoned choice of one of the various possibilities of action or behavior in the face of a situation: *Recommender Systems* may help in personalizing the decision according to previous choices or any similar choices made by others, regardless that the choice is made by a human or an agent.

To achieve greater awareness, it is necessary to monitor the situation rigorously and continuously, through an evaluation process capable of detecting successes and possible bottlenecks of a system. Telemedicine, in this case, allows us to complete this task. On the other hand, data is only useful when analyzed. Therefore, the AI techniques, previously described at a high level, can help to perform an SA of the health system, returning an accurate overview. Process Mining techniques are particularly important in eHealth as they are particularly rich in sequential data, even if unexplored. It would become essential to root process management in the organization, accompanying the health facility towards real and in-depth knowledge of its operating mechanisms, through efficient techniques, with low economic impact, in rapid analysis times and guaranteeing the objectivity of the result. In general, workflows are used to support processes. To understand what it is, some brief notions are provided:

- A *process* is a sequence of elementary activities carried out by agents to achieve a goal.
- A *task* is a piece of work defined to be performed in many cases of the same type.
- An *activity* is the actual execution of tasks.
- A *workflow* (or process model) is therefore a formal specification of how a task sequence can be composed and can end in a valid process.
- A *case* is a specific execution of activities in a determined order, as described by a given workflow along an ordered set of steps (time points).
- *Case traces* are lists of events associated to steps.

Health process records can be referred to both patient and healthcare facilities, can be extracted from different sources, and can have different types. For example, the patient's vital parameters, the events associated with her (hospitalizations, rehabilitation, etc.) or even drug therapy, allow to define the treatment processes associated with the individual patient. To this information can be added data from administrative systems, clinical decision support systems, ERP or medical devices, which can be combined in different views: from patient to ward, up to the whole structure.

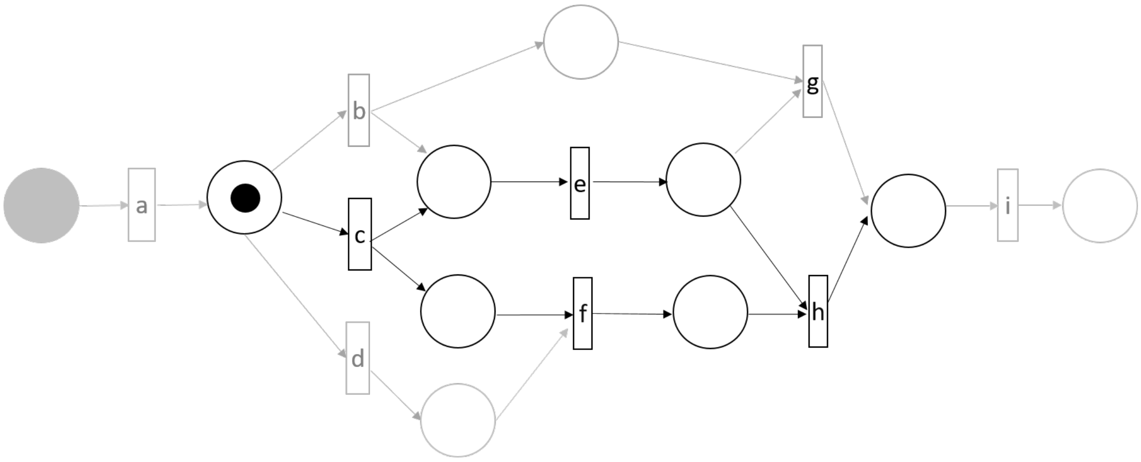


Figure 5.10: *Petri Net example describing a process in a Clinical Pathway.*

The term "compliance" is referred, in the medical field, to the behavioral rigor of a patient in following the prescriptions, defining the level at which the patient's actions (drug intake, adherence to diets, physical activity) are in line with the doctor's instructions. Failure to comply with best practice behavior could have repercussions on the quality of care and on the entire health system. For this reason, the Compliance Checking technique used in Process Mining would help discover the similarities and deviations between modeled behavior (the workflow) and detected behavior (the case traces).

In this regard, AAL systems should adapt to user needs and enable activities independently, using information derived from the context. In the operations of modelling human routines, particularly in the case of clinical pathways, it is necessary to understand the sequences of human activities. Therefore, routine depiction can be done using workflows. A workflow can be managed like a Petri net [65], an expressive formalism that can represent activities and their flow, and the competition between them. Workflows are important for describing human behavior, showing the chronological sequences of user activities. In smart contexts or intelligent environments, this allows us to understand events and build a series of services capable of responding to situations. Therefore, having identified the analogy between the workflow and the clinical path as the succession of events that are performed by a patient, this can be evaluated with process mining techniques to ensure adherence to the doctor's prescriptions and compliance with the clinical guidelines.

To improve system performance, at this stage, the evaluation component of the process must be brought on board the Edge module.

The paper [66] discusses an example of eHealth process analysis. A solid basis for the management and improvement of processes within hospitals is provided. By combining event data and process mining techniques, it is possible to analyse fact-based processes within a hospital. In the paper [67], an ontological model is presented for auditing the clinical process to improve the quality of services and reduce hospital costs. Binti *et al.* [68] provide a methodology for the development of a clinical treatment pathway to facilitate the diagnosis and treatment of patients. This work is particularly contextualised in the treatment of patients with heart failure and makes use of machine learning techniques. Interestingly, the work in [69] is more focused on a well define condition like suffering from aftereffects of a stroke event, however, it does not account for monitoring the patient at home.

Aspland *et al.* [70] propose a literature review on taxonomies of problems related to clinical pathways. The authors explored the combination of this with Information Systems (IS), Operations Research (OR), and industrial engineering. The work [71] highlights in an AAL scenario, the context-awareness, and adaptability of a care pathway in the daily life of the patient. A review of process mining techniques used to manage clinical pathways is carried out in the papers [72, 73]. Ardito *et al.* [74] provide a formalisation of the Clinical Pathway management method. Through the application of this, it is evident how patient monitoring is increasingly improved. Edge Computing is an architectural solution whereby the processing and storage of resource data are moved to the edge of the network. Thanks to the use of AI in the Edge, it is also possible to make a significant contribution to telemonitoring solutions in eHealth. Thanks to this combination, medical devices connected to the remote hospital information system (HIS) can be exploited even more efficiently. The combination of these has led to a massive deployment of smart and wearable devices and Internet of Things (IoT) communication technologies in the healthcare sector. The authors of the papers [75, 76] highlight the potential of the IoT in integrating and harmonising the data produced by Cyber-Physical Systems (CPS) with those already present and generated by classical information systems. In this way, it is possible to unite people, processes, data, and things. The clinical domain is addressed in the work [25, 77] in which the development of integrated solutions for seamless care is contextualised. AI and IoMT techniques at the Edge are used. The work emphasises a people-centered approach, which continuously adapts to the needs of caregivers and is embedded in their workflows.

Finally, Ardito *et al.* in [78] present an approach to bring together IoT technologies with End-User Development (EUD) tools and paradigms. This integration is aimed at identifying innovative scenarios in which end-users are directly involved in the creation and customisation of the AAL systems they use.

5.4.3 Edge Computing Cognitive Architecture

This section presents the Edge Computing architecture that permits to process data on devices (i.e. end-nodes) or gateways (i.e. Edge nodes). This would reduce unnecessary processing latency and data traffic, which is a valuable benefit for applications like analyzing and monitoring critically ill patients. Afterwards, it shows two intelligent modules that leverage data collected from sensors and devices connected to Edge nodes, and perform predictive analyzes preventing the worsening of the patient's clinical condition. In particular, the Clinical Pathway Adherence Checker (CPAC) module is introduced, aimed at verifying that the patient follows her therapeutic path correctly.

System Architecture

The system architecture is depicted in Figure 5.11. The Edge architecture results quite general to be configured in an AAL typical scenario, specifically in the case of a Smart Home Environment. Here, we deal with an high number of heterogeneous devices which differ from one another in storage, computational, and communication capabilities. Therefore, the architecture, at the bottom of its pyramidal topology, presents three types of end-devices:

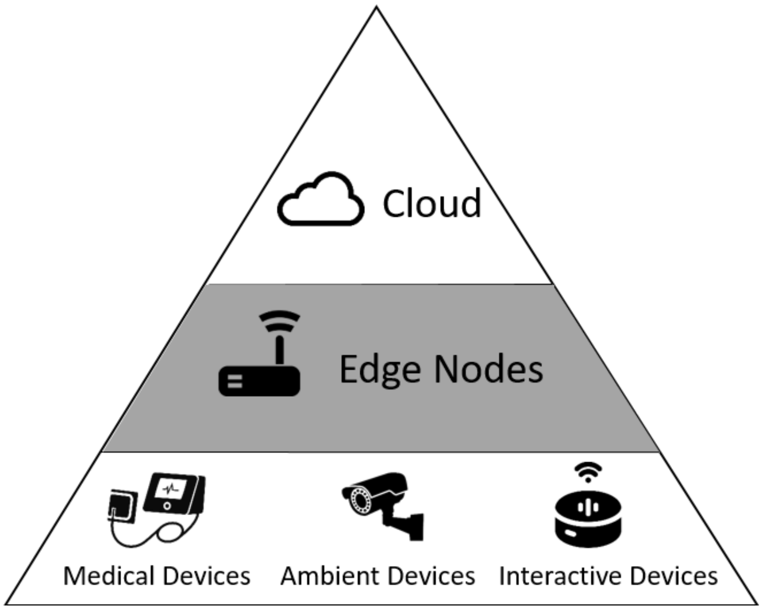


Figure 5.11: *Edge Computing Cognitive Architecture.*

1. *Medical Devices*: any device adopted for medical purposes, such as the treatment, prevention, diagnosis, monitoring, alleviation or compensation of an illness.

2. *Ambient Devices*: any kind of consumer electronics that brings smartness to living environments, such as cameras, motion sensors, smoke sensors, smart appliances, etc.

3. *Interactive Devices*: any mobile or fixed hardware component which favors interaction between human users and an interactive application, such as wearable devices, smartphones, speech recognition devices, etc.

Above the end-devices, there is the Edge Layer, which is composed of one or more Edge nodes which can be an adjacent connectable device through a device-to-device (D2D) communication [30], a server attached to an access point (e.g. router, WiFi, base station), a network gateway or even a micro-datacenter available for neighboring devices. As shown in Figure 5.11, Edge nodes can communicate with each other and exchange the results of a preliminary Edge processing phase. A typical Edge node adopted by the proposed architecture is a *Raspberry Pi 3 Model*

B (RPi for short) with a 1.2 GHz quad-core 64-bit ARMv8 CPU and 1 GB of RAM. In order to implement a scalable, adaptable and general-purpose architecture, the maximum number of devices that can interact via Bluetooth Low Energy (BLE) connectivity simultaneously with RPi and the width of the time window in which the vital signs are collected have been set in a configuration file, parameterized as desired by the user. If, during the time window, the same information is updated several times, at the time of the final acquisition, the system considers the most updated value.

Lastly, the architecture presents a Cloud Layer in which collected raw data and processed data at the Edge are transmitted to enhance the general performances and supply a refinement of the clinical pathway just in case of patient's condition degradation. Consequently, the Cloud Layer would act as an intermediary, by receiving any alert and/or request sent by the Edge Layer after the collection of specific vital parameters, and by activating specific operating protocol with the hospital or the health personnel, hence supporting a remote adaptive and complex decision making process.

In this architecture, an Edge node can gather useful information from, ambient, interactive, and medical end-devices, and process them for a specific purpose. As shown in Figure 5.12, a node in the Edge Layer is designed to run *Conformance Checking* on a predefined sub-process of the Clinical Pathway, another node would be exploited to be an *Anomaly Detection Module* which is able to address the security risks that may occur during the transmission process for the gathered data. Eventually, as already addressed in [77], a further node may be adopted as *Adaptive ML Module* for predicting the clinical risk of a patient, constantly monitored even where a limited number of vital parameters is readily measurable. Hence, introducing an Edge architecture to Healthcare would be beneficial to physician's workload by removing less critical tasks, such as collecting and managing patient data. Moreover, a major benefit would make healthcare more affordable and accessible, especially for remote areas where medical care is limited.

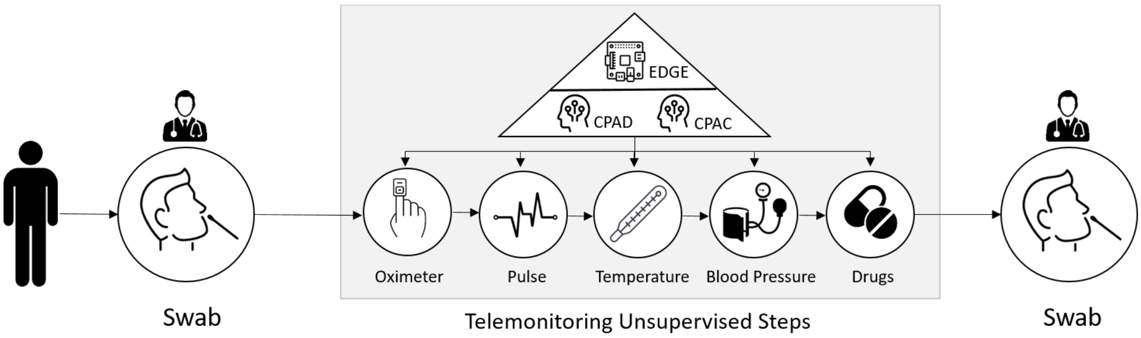


Figure 5.12: *Steps of a Clinical Pathway.*

CPAC: The Clinical Pathway Adherence Checker Module

This section introduces the approach to performing process mining tasks in the eHealth domain. This would foster the intelligent software modules characterizing the Edge nodes in applying AI techniques to perform an automatic decision, and proactively support the patient at home. Within the clinical course, we can distinguish between the intervention made by health personnel, and the ones made by medical instruments. Considering the clinical pathway as a workflow, each activity is therefore represented as a node in the Petri Net. These nodes can, in turn, be sub-processes. Giving a formal notation, the following definition is formulated.

Definition 1 *The execution of a process σ is described as a sequence of actions $\sigma = \langle a_1, \ldots, a_n \rangle$, where $a_1, \ldots, a_n$ is the sequence of the single activities carried out by the user in a specific and strict order. $l_\sigma = n$ denotes the length of σ.*

When the patient is discharged from the hospital and returned at home, she has the task of following the doctor's prescription, to maintain stable or improve the clinical situation. The prescription can be processed in a series of steps that make up the patient's clinical journey and must be performed by the patient at home without supervision. To manage this home monitoring, a new level of control has been introduced that can replace medical personnel, as shown in the Figure 5.12. Patients are endowed with one or more Edge devices that can process their activities at home aware of being constantly monitored. The part of the clinical pathway that has to be managed at home can be thought of as a specified subset of activities that the Edge node will be responsible for validation. In a formal way:

Definition 2 *Given an execution process σ, an execution of a sub-process τ, managed without supervision, is described as a sequence of actions $\tau = \langle b_1, \ldots, b_m \rangle$, with $l_\tau = m$, $\tau \subseteq \sigma$ and $l_\tau \leq l_\sigma$, and where $b_1, \ldots, b_m$ is the sequence of single activities, arbitrarily carried out by the user.*

A translation of these steps becomes a prescription to follow that cannot be verified except in the patient's level of rigor. Our idea is to introduce a control level, based on Edge computing, which can supervise and manage the phases of the Clinical Pathway that the patient must carry out independently at home to avert the worsening of the clinical picture and guide her towards a prompt healing. As a first step, we have to perform a process model, to which an instance of patient activities must adhere. In this context, logs of general patient enrollment are fed into the process mining task to generate the process model. Once the reference model has been defined, the Edge component will be able to verify in real-time the correctness of the operations performed by the patient in the home concerning the clinical pathway. Thus, the Edge architecture will receive from the Cloud layer the process model to be stored. In particular, the Edge framework identifies the most suitable clinical path model for the type of patient by connecting to the cloud and downloading the portion of the clinical pathway as a validated process model. The development of the monitoring phase involves the activation of a series of medical devices that allow the collection of clinical data. These are collected by the Edge module which preprocesses them in log in a standard format (for example, eXtensible Event Stream, XES), with which the process model stored in our Edge node is represented. Logs analysis can be performed immediately for each individual step run (e.g. blood pressure measurement, medication intake, etc.) to verify model compliance. As a matter of choice, in less severe clinical pathways, it can be generated at the end of the period (e.g., a day), in order to appraise the discrepancy on individual activities or on the full pathway. Translating activities into formal notation is a first step to enable the use of algorithms that verify compliance and detect gaps from the process model. Based on the deviation, it is possible to evaluate the discrepancy (e.g., missing to take pills) and also to define the corrective actions to bring back the executions towards the correct pathway model. In order to accomplish

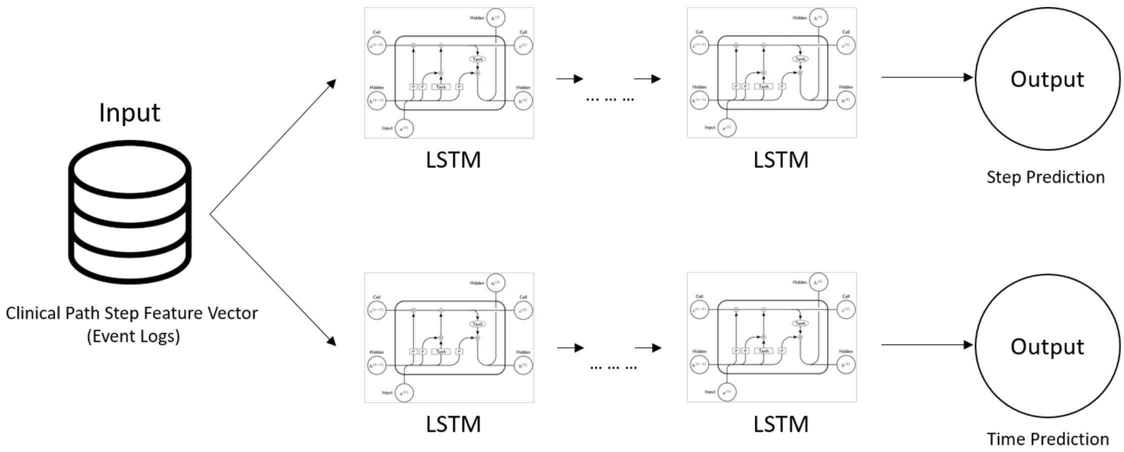


Figure 5.13: *Logs processing towards Conformance Checking predictions.*

this task, a new module called Clinical Pathway Adherence Checker (CPAC) has been introduced. The strategy exploited in this module involves a Deep Learning approach. A Recurrent Neural Network would be able to suitably process sequences of observations to predict a probability of variation of the pathway. Therefore, a Long Short-Term Memory (LSTM) is the candidate deep architecture to perform the Conformance Checking task. The idea behind the approach is to consider the sequences of actions performed by a patient (stored in the logs) and analyze them as characterizing elements of a pattern. Each pattern can be compared with the ideal process model defined by the clinical staff and, through the use of the LSTM, it will be classified according to the level of compliance. Starting from event logs collected by the Edge node, it is possible to give in input and infer the discrepancy from two different models: the first one for clinical pathway step prediction, and the second one for time prediction. A representation of this conceptual strategy is depicted in Figure 5.13. At a later stage, in the event of non-compliance between the current execution and the model, the CPAC module autonomously discloses the specific incident to the medical personnel, sending reports to the Cloud layer of our Edge infrastructure.

CPAD: The Clinical Pathway Anomaly Detection Module

Supervised Machine Learning techniques can be used to predict when a clinical deterioration of vital parameters will occur. These techniques, which are also used in AAL scenarios, are able to understand whether the communication between the patient's devices in the care state is correct or compromised. Such methods, used to detect intrusions in the communication between devices (and the related data exchange between these and the Edge node) have traditionally been developed under the assumption that the environment is not harmful.

In a hospital or home care context, it is reasonable to assume that there are no attackers who want to circumvent data monitoring systems. To avoid this issue, it is useful to equip the system with an anomaly detection module. This approach intends to define a system that is able to monitor several vital parameters of the patient (e.g. blood pressure, heart rate, and respiratory rate). Compromising the data collected by a sensor worn by the patient would risk compromising the clinical course, the doctor's diagnosis, and the patient's health. In order to verify the correct transmission of data and prevent the system from intrusions, the system is equipped with a module called Clinical Path Anomaly Detection (CPAD) [79].

Using Machine Learning techniques, the CPAD manages the security problems that may occur during the data transmission process, analysing them and, if necessary, notifying the anomalies detected. Using a Cognitive Security approach, thanks to advanced AI techniques, the system will be able to learn and analyse at each interaction any threats that are detected. By doing so, it will be able to provide the healthcare provider with an explanation of the intrusion and thanks to this, the patient's clinical course can be corrected immediately. In design terms, the data collected in the node can be viewed as a queue and organized into several sub-processes. Each sub-process represents the phase of detecting a vital parameter from a single device worn by the patient. Using a recurrent sequential autoencoder Long Short Term Memory (LSTM), the CPAD module analyzes the various sub-processes of the chain to perform anomaly detection on the steps of the chain [80, 81]. In fact, the advantage of using sequential LSTM autoencoders is twofold: firstly, it takes advantage of the reduced dimensionality and extraction capabilities of the autoencoder to efficiently perform the data reconstruction process and then detect the anomaly, and secondly, it uses the networks to handle the sequential nature of the data detected by the sensors.

The anomaly could also result in an attack on the monitoring of the patient's clinical parameters. In doing so, it causes a dysfunction in the Clinical Pathway which in turn has a direct impact on the patient's health. The anomaly may represent a direct attack on the monitoring of vital parameters in order to modify the expected behaviour of the detection or to compromise it completely, with related tampering of the clinical pathway. Using intrusion detection techniques, the system is able to prevent attacks at various stages of the clinical pathway. It also provides intelligent information to the treating physician and allows domain experts (system IT administrators) to isolate the security breach and reschedule the clinical path together with the physician.

5.4.4 SARS-CoV-2 Patient Monitoring Scenario

This section proposes a usage scenario for clinical pathway handling on Edge related to SARS-CoV-2 patients management. With the help of telemedicine, the traditional treatment scenarios have changed profoundly during the pandemic, bringing beyond its physical boundaries. Thanks to telemedicine, even patients who are distant and isolated can be reached, such as the ones undergoing quarantine measures as they test positive for SARS-CoV-2. In this context, the control setting provides the use of a monitoring and control kit, based on a telemedicine platform [44]. The patient's clinical pathway is downloaded on the Edge node from the aforementioned telemedicine platform, which acts as our Cloud layer, and enables the steps that must be activated at patient's home. The most suitable medical devices are involved, on the basis of the types of the activities to be performed by the patient, in order to detect and monitor the relevant vital parameters.

For example, a pill dispenser can be used to provide information on taking medications to follow the therapy, while the use of the blood pressure monitor can provide the clinical status of the patient. In the specific case of SARS-CoV-2, a subset of relevant vital parameters, such as heart rate, body temperature, and oxygen saturation, must be gathered several times in a day. With the interaction with the medical devices, Edge nodes can monitor the status related to Adherence and Anomalies with the CPAC and CPAD modules. If dangerous situations are detected, alerts can be sent in real-time to an operations center. Detecting simple vital signs can transform radically the lives of many people during a pandemic, while allowing them to monitor and contain the contagion. The crucial role of the health personnel was highlighted during the pandemic emergency. They need to perform their work in safety conditions. The usage of intelligent techniques at the Edge would help to ensure the required safety, thus making digitally viable the relationship between the hospital and the patients, and hence placing the whole monitoring process in a safer place. Providing continuously monitoring and information about the disease, possible complications, and the activities to be carried out can make patients feel more protected. The health personnel of the Medical Control Room, receive the monitoring data through the monitoring system, check the progress of the clinical path and evaluate any anomalies in the state of health that could require a change of therapy or a possible hospitalization. The Edge infrastructure ensure a high level of continuous surveillance and proactive collaboration, making the patient and his relatives more relaxed and making the experience discharge from the hospital more peacefully.

5.4.5 Conclusion and future work

The need for more healthcare choices for SA technologies is reflected in the pursue of established practices related to Telemedicine, allowing teleconsultations with specialists and a more flexible monitoring of the patients at home. In fact, SARS-CoV-2 has accelerated this innovative process in the healthcare sector, demonstrating the importance of a systemic rethinking of remote care.

Based on Edge Computing and AI techniques, this work presented a level of unmanned supervision which can somehow control the steps of the Clinical Pathway that the patient should follow autonomously in his/her living environment to deflect worsening of clinical conditions.

This research shed light on formal aspects of executing process mining tasks in an Edge infrastructure, in which activity logs are collected by data coming from medical, mobile, and interactive devices, in the spirit of IoMT perspective. The core proposal presented an intelligent module which is applied to check patient behavior by means of their adherence to their clinical pathway. This module, called CPAC (Clinical Pathway Adherence Checker) helps patients to follow medical prescriptions (i.e. therapies) and provides physicians actions to induce them to exclude a clinical deterioration.

The present work adds further conceptualization to the aim of designing and developing a full-Edge platform architecture, in which several AI modules cooperates towards a big conjunct goal or more little objectives related to the world of healthcare. The benefits are various: firstly by lightening the physician's workload by removing less critical tasks, secondly by making telemonitoring more affordable and accessible, especially for remote areas where medical care is limited, and lastly by stimulating the advancement of medical technology through Big Data. Definitively, Edge computing will make it easier to manage and classify data in a uniform, efficient, and secure way.

Conscious of the intrinsic vulnerability of AI techniques, the anomaly detection module, called CPAD (Clinical Pathway Anomaly Detection), was also detailed. Interestingly, the detection system may act as an Explainable Security module, which allows receiving an exhaustive explanation of the attack reports that can be easily interpreted even by non Machine Learning experts and therefore in this case by the physician and the user who is undergoing treatment. In fact, the Explainability of AI, which aims to make people understand how ML models work, is essential to promote trust and reliability in AI systems. It will also allow the patient in care to have an overview of the decision-making process of the system. Another scenario will involve this technology to explain other types of alarms that can emerge from the analysis of sensor data, providing explanations both to patients and, remotely, to physicians. Interestingly, one would think about the Petri Net representation to be exploited as an explanatory tool of the clinical pathway executed by the patients.

Future works will concern the many opportunities the Edge module could offer in healthcare. The research will continue in Robotic Process Automation (RPA) to automate the activities performed by physicians in interacting with patients (e.g. notification of therapy changes and acknowledgment). Also, recommender systems will be explored to support physicians more directly guiding the treatment path. In particular, the fundamental aspects of data security at the Edge level will be focused on: by combining the strengths of AI and human intelligence, it is possible to ensure a reliable level of privacy. Finally, while providing efficient and cost-effective monitoring action to gain situational awareness, the proposed study has laid the groundwork for improving the quality of action that can be taken by stakeholders with decision support systems. Equipping humans with the ability to make better decisions thanks to AI, and in particular AI on Edge, defines a process in which AI can be seen as a tool capable of strengthening and increasing human capabilities, thus approaching a Digital Twin model of the physician.

Chapter 6

Healthcare Analytics Framework

This chapter will present an example of a Framework for Healthcare Analytics. This results from synthesizing the experiences described in the previous chapter and highlighting the results obtained to convey them to a single tool for industrial purposes.

6.1 Introduction

The SARS-CoV-2 pandemic has called into question a part of the equilibrium of everyday life at the individual and national system levels. The challenge of COVID-19 and the effectiveness and accessibility of public health are especially putting a strain on its resilience. This feature is essential to sustain an emergency that could extend overtime or recur in the future [82].

As the emergency has spread throughout the world, health systems have dealt with the emergency structure on two parallel levels, dealing, on the one hand, with managing patients affected by COVID-19 and, on the other, continuing to respond to health needs not related to the pandemic. The health systems engaged in this unprecedented stress test have adopted a series of measures to deal with the pandemic (capacity to strengthen staff, beds, territorial planning for the management of people at home, the stocks of health facilities, etc.), without neglecting how to restore the qualitative and quantitative levels of services for Non-COVID patients[83][84].

At the end of 2021, the SARS-CoV-2 virus infected an estimated 300 million people, causing 5 million deaths worldwide. On average, 5-15% of SARS-CoV-2 infected patients required hospitalization, causing a massive overhead on the healthcare system in nearly all countries [85].

Telemedicine is considered one of the essential services for strengthening health systems' response to COVID-19, indispensable for improving the care and assistance of people in isolation. In the emergency period, governments have provided operational reference models for the construction of telemedicine services active in the affected territories with the idea of quickly and for a limited period covering the needs due to the quarantine of large areas [86].

In this scenario, e-health and well-being became two of the more relevant application fields for innovative technologies, for which in literature, many scientific works and projects can be found [87][88]. Still, more activities are asked, especially for grounded methods that systematically design user experience on IoMT-based ecosystems, fostering improvements in the healthcare system.

6.2 Enhancing Situation Awareness in Healthcare

6.2.1 Early Warning Score System

The possibility of continuous monitoring of health conditions is crucial for improving living conditions, preventing potential diseases, and prompt response in critical situations. In critical care or emergencies, assessment of disease and clinical risk level can be considered a predictive task in situations where streams of vital signs data are collected from medical devices and Internet of Medical Things (IoMT) sensors. In order to lighten the burden of doctors, the Early Warning Score (EWS) systems that generate an aggregate score based on the measurement of a set of vital signs, such as the National Early Warning Score 2 (NEWS2) and the Modified

Early Warning Score (MEWS), can provide valuable decision support for health status estimation and triggers for intensive care interventions. Through Machine Learning (ML) techniques, this approach predicts the clinical risk classes of a patient monitored continuously in a particular condition in which a limited number of vital parameters are available, thus creating a clinical digital twin embryo [77].

6.2.2 Clinical Pathway Modelling

Clinical Pathway is growing up as the main instrument for implementing clinical guidelines and evidence-based medicine. Its primary objective is to improve the care process by monitoring the unjustified variations in clinical practices to reach faster the best fit care and reduce the health system's costs. In a generalized context of an ageing population and the ever-increasing diffusion of chronic diseases, a Clinical Pathway methodological and technological approach has been introduced to improve the way patients are monitored during their pathway, to help physicians to read the clinical picture in the best and fast way and to reduce the general clinical complexity. The development of better skills in the modelling of processes, with advanced techniques and tools that use Machine Learning, Big Data, and integration technologies, enable obtaining a significant competitive advantage through a better understanding of the functioning of these processes and the exploration of opportunities to improve the effectiveness of their execution. By intervening in the processes and thanks to the adoption of a specific Clinical Pathway, it is possible to reduce associated costs and improve quality for chronic patients, creating further opportunities for using technologies and more significant advantages [74].

6.2.3 On Edge Remote Patient Monitoring

The possibility of remotely monitoring patients at home using intelligent sensors and medical devices has a significant impact on the quality of health services. Situation awareness plays an essential role in the decision-making process about the users, patients in this case, and their behaviours. Leveraging an Edge Computing framework with embedded Artificial Intelligence capabilities to process near real-time data gathered from connected smart devices would provide automatic decision support, thus improving the physicians' course of action. Designing and developing a full-edge platform architecture, in which different AI modules cooperate towards a significant joint goal or smaller goals related to the world of healthcare, is the missing link to the patient-doctor relationship. The benefits are varied: firstly, easing the physician's workload by eliminating less critical tasks. Secondly, by making telemonitoring more convenient and accessible, especially for remote areas where medical care is limited, and finally by stimulating the advancement of technology medicine through Big Data. Ultimately, Edge Computing will simplify data management and classification in a uniform, efficient and secure way [89].

6.3 Theoretical Framework

This work aims to design an AI end-to-end healthcare framework capable of supporting patients from their homes to give a broad vision to doctors and public decision-makers, as depicted in Figure 6.1.

6.3.1 Edge

The Edge component is the first component of the framework. It plays a key role because it becomes the gateway to the patient's home. Therefore, the Edge becomes a constant presence in the subject's life to be monitored, such as to be active 24 hours a day. Onboard it, there are two modules for monitoring: NEWS and CPAC [77] [89]. The first module analyzes the patient's vital parameters and schedules re-evaluations throughout the day. On the other hand, the second is responsible for monitoring their behaviour and adherence to the therapeutic plan. The two modules, intervening jointly, certainly give a preview of the patient's situation and can take the place of figures such as the caregiver or the home nurse.

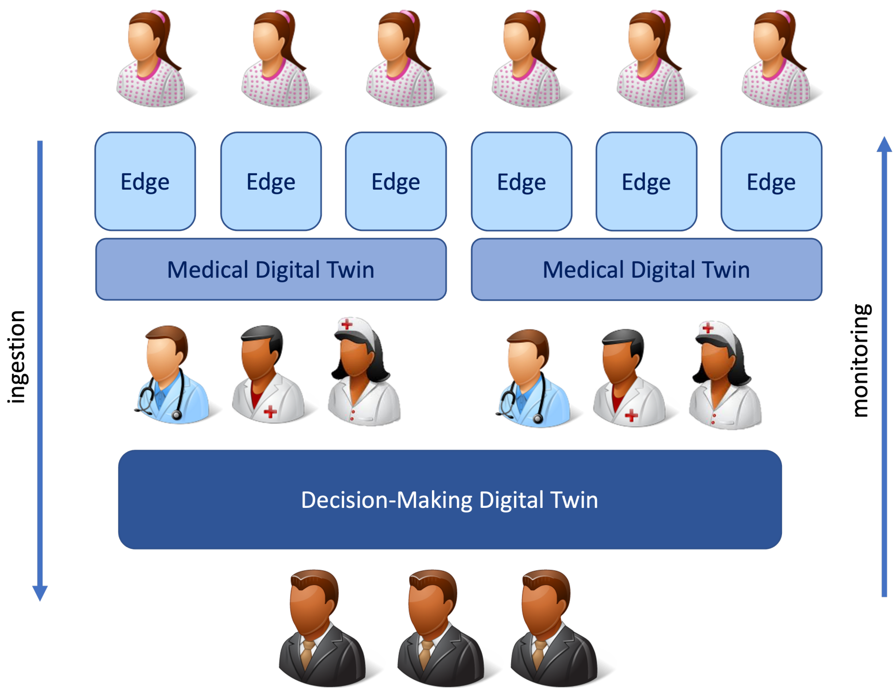


Figure 6.1: *Theoretical Framework for Healthcare Analytics*

6.3.2 Medical Digital Twin

The second level of the architecture is composed of the Medical Digital Twin. It is a level of support for medical personnel as it aggregates the Edge modules of multiple patients. This allows you to create a true digital twin capable of overcoming the limitations of medical personnel: to constantly monitor a multitude of patients from the point of view of vital parameters and behaviours. Figure 6.2 shows how a patient control dashboard works. The doctor-patient relationship in this way, even if unbalanced, becomes continuous as anomalous situations are brought to light quickly. In the traditional scenario, the patient would go to the doctor or contact him in case of symptoms. So, the doctor would not be aware of all the different behaviours of the patients in the taking of drugs or of parameters that could vary slightly even in a single day. Thanks to the digital twin, the doctor could take advantage of having a magnifying glass in the patient's daily life, but the latter could also benefit from an entity capable of highlighting what he would not be able to monitor to the doctor.

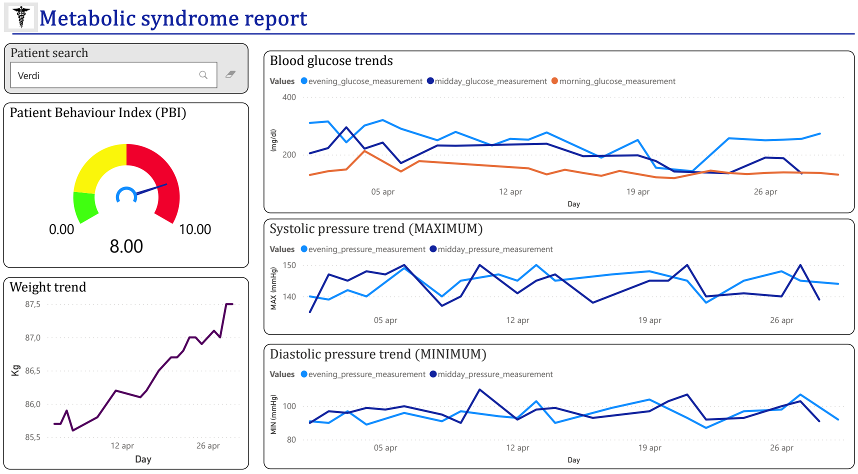


Figure 6.2: *Medical Digital Twin Dashboard*

6.3.3 Decision-Making Digital Twin

The highest level of the architecture is represented by the maximum degree of data aggregation, where the data of all healthcare stakeholders are concentrated. At this level, the public decision-maker can monitor the global trend, analyzing various dimensions: chronic pathologies, drug use, worsening of clinical pictures, and hospitalizations. Figure 6.3 shows how a health system control dashboard works from the public decision-maker point of view. Based on this last data, it will be possible to monitor the capacity of the beds in the departments and, therefore, the pressure on the system. These factors have become vital in response to the epidemic and allocating money for investments.

Therefore, the pandemic has clarified the essential usefulness of digital tools, the development of organisational models, and the integration between the territorial and hospital systems. It is thanks to digital medicine and, in particular, telemedicine that in the height of the emergency, it was possible to follow remote patients affected by COVID-19. At the same time, with telemedicine, it was possible to continue to follow up on chronic fragile patients, evaluate them and possibly adjust their therapy without having them move from home, thus reducing the risk of contagion.
The study pushes the boundaries of the traditional context to design and develop a

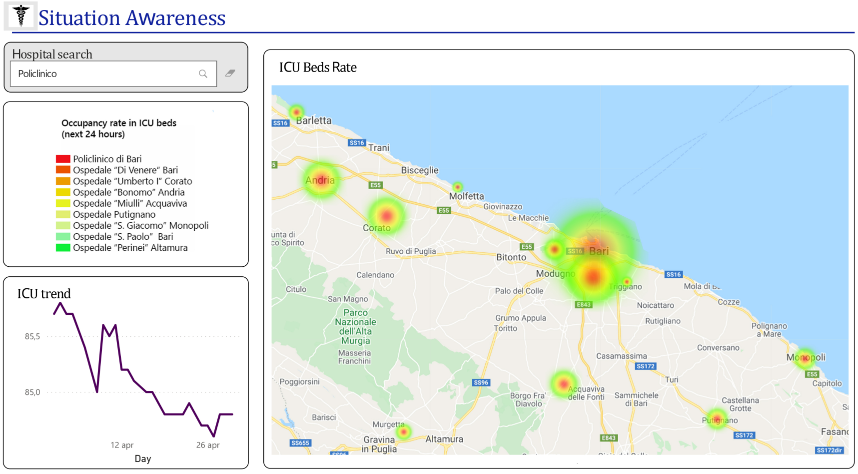


Figure 6.3: Decision-Making Digital Twin Dashboard

Full-Edge framework in which different AI modules cooperate towards one significant shared goal or various smaller goals connected to the world of healthcare.
The framework aims to be a tool capable of automating these processes and improving the monitoring of patients' health status.
There are multiple benefits:

1. The doctor's workload is lightened with less critical tasks taken away from them
2. Remote monitoring is more economical and accessible, particularly in remote areas where medical assistance is limited
3. The progress of medical technology is incentivised through Big Data

In a nutshell, the introduction of Edge Computing to healthcare will simplify the management and classification of data in a uniform, efficient and secure way but also it is a first step toward creating a digital twin of medical staff.

Chapter 7

Conclusions and Future Works

The final result of this thesis is an intense investigation of the methodologies to automate the analysis of patients in a healthcare system, exploiting the potential of Artificial Intelligence. In the last period, the evolution of the SARS-CoV-2 pandemic has accelerated the healthcare sector's innovation processes, demonstrating the importance of redesigning remote care. The introduction of an Edge architecture in the home environment has many advantages: supervising the environment and managing the devices on-site allows for more reactive patient monitoring. Furthermore, this type of architecture extends the limits of the hospital ward, transforming domestic environments into branches of it. Understanding the patient's actions and assessing the clinical picture change can be considered the first step towards a "Digital Twin" model for healthcare personnel to reduce unnecessary travel. This allows, firstly, to lighten the doctor's workload, and secondly, it makes telemonitoring more affordable and accessible, especially for remote locations where medical assistance is limited. Let us think of general practitioners who manage thousands of patients daily: it is difficult for them to know if all their clients are correctly respecting the prescribed therapy. Thanks to the proposed framework, the doctor has a general overview of his patients, lightening their workload. They will be able to focus more on patients who are not compliant with therapy, to understand any problems that do not allow the patient to follow the treatment correctly. This is very important as if patients comply with the treatment, they will most likely not worsen. They will not be hospitalized, and therefore there will not be an occupation of the beds in the hospitals, thus avoiding saturating the health facilities thus containing costs. Furthermore, the doctor can constantly be updated on the adherence to his clients' therapy and call these patients back. For example, an older person forgets to take a pill every day: the doctor can propose more detailed analyses to find a correlation, explain why he fails to perform certain activities, and perhaps discover the onset of new pathologies. (e.g. Alzheimer's disease). However, not only that, it will be possible to analyze the trend of an entire health system and give the public decision-maker the ability to make assessments based on objective and timely data. Future work may concern the implementation of a "Healthcare Supervisor" agent who, by monitoring the patient, invites him to take the right actions proactively, following the therapeutic plan, sending messages if the patient makes a mistake or forgets to perform specific actions. The same direction could concern the public decision-maker who could receive speaking suggestions on the steps to enhance the system under pressure. In conclusion, this work has traced a small path toward what will be the medicine that will characterize the near future in a world that has recently been completely revolutionized.

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