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"Development of Telehealth systems and technologies for remote patients' healthcare"

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Abstract

Telemedicine, or *Telehealth*, can be defined as the use of the most modern and up-to-date technologies to provide remote healthcare services and information. Through specially developed devices and thanks to the internet and satellite connections, patients and physicians can communicate virtually from anywhere, reaching places and people that other healthcare systems can't.

Over the years, telemedicine has undergone a notable evolution, successfully supporting ordinary medical practice. Telehealth proved to ensure high-quality medical care, greater possibilities for timely diagnosis, reduction of traveling times – especially for patients living in remote areas, or for elderly and/or invalid patients. The research activity focused mainly on seafarers embarked on commercial ships: generally, in these vessels, there is no doctor or medical staff, and the ship can travel the oceans for a long time, far from ports and health facilities. Healthcare onboard ships represent one of the greatest challenges for modern medicine, and the seafarers are the perfect example of remote patients.

After carefully understanding the problems and health needs of this population, we have proposed strategies, systems, and technologies to promote an improvement in the health care provided, remotely. The final goal was to create standard models of telemedicine solutions based on scientific research and the experience gained over the years, as well as on the regulations and guidelines in force. This to provide standards for the future development of telemedicine systems and technologies, respecting and taking into account the practical and health needs of citizens.

The proposed telehealth services may be effective for remote patients, but even in "non-remote" contexts such as in the ordinary medical/pharmaceutical practice, or in emergencies. The future work can be extended to improve the remote assistance service and explore the services for a larger population, starting from patients living in internal areas, far from health facilities.

Summary

Chapter I - Telemedicine: History and Evolution

Introduction

Telemedicine, or *Telehealth*, can be defined as the use of the most modern and up-to-date medical and computer technologies to provide remote health services and information. [1]–[3]

The prefix "*tele*-" comes from the Greek *τῆλε*, and it means "*far*".

Telemedicine is generally used to connect areas with poor healthcare availability with distant medical centers, to ensure healthcare from afar.

A basic telemedicine system consists of two-way communication between a medical center and satellite stations that could be staffed by physicians, nurses, or other trained personnel.

This allows the patient to be visited by a remote practitioner, who may also provide information and guidance to any staff present on site.

Telemedicine allows the exchange of diagnostic material, vital parameters, medical records, digital images such as X-rays, photographs, electrocardiogram results, resonances, ultrasound scans, etc.

Initially, telemedicine used already existing communication equipment, such as the telegraph and, subsequently, radio and telephone. Today there are specially developed devices that, thanks to the internet and satellite connections, can communicate virtually from anywhere, with impressive speed and computing power.

This is the main benefit of telemedicine*: reaching places and people that other healthcare systems can't: remote* workers, *seafarers in the middle of the ocean, or, even further away, the astronauts in Space.*

Telemedicine can immediately ensure high-quality medical care, greater possibilities for timely diagnosis, **reduction of traveling times – especially for patients** living in remote areas, or for elderly and/or invalid patients.

Over the years, telemedicine has proven to be cost-saving, since it mainly consists of communication, in an exchange of data that is cheaper than the transport and physical movement of people. Generally, the costs of telemedicine are "initial", and consist of the installation of equipment and systems that allow its implementation.

The History of Telemedicine

The exact date of the first use of remote communications for health purposes is unknown. [4]

The first historically reported cases of telecommunication and medical information exchange date back centuries, during the *Black Death* and other similar disasters.

The first instrument to be crucial in the medical field was the **telegraph**. This was already used during the American Civil War, to convey the names of the wounded and to order medical supplies.

With the invention of the **telephone**, doctors were among its first users in the early 1900s. For many decades since the beginning of the twentieth century, the telephone has been the backbone of medical communications, and even today has an important role in it.

Figure 1: *Telegraph, telephone, and radio were the first communication instruments used in telemedicine.*

During the First World War the **radio** came into play, and starting from the 1930s it was used to exchange medical information in remote areas of Alaska and Australia, and it played a crucial role during the Second World War and other conflicts such as the War of Korea and Vietnam.

At the same time, these instruments were used for all those remote workers for whom it was difficult to access healthcare such as, for example, seafarers. [5]

The ad-hoc telemedicine systems available today mainly come from the efforts in space research, together with the early practice of telemedicine among doctors who we may consider as "*pioneers*" of telemedicine.

Historically, distance has always been an issue for medical care. Doctors (*or patients*) had to travel for hours and hours before they could perform the visit in some inland and remote areas. The physician may not be able to acquire all the necessary information, and the help of another specialist could have been essential. Nowadays, there are many areas of highly developed countries without a doctor or medical staff. Some health care facilities do not host all medical specialties, and patient relocation or travel is often unavoidable.

One of the first attempts to break down distances and barriers in healthcare is the so-called Research and Technology Development (R&D) undertaken by the National Aeronautics and Space Administration (NASA), in its space programs.

A major concern of NASA scientists was the effects of zero-gravity on astronauts' health. These concerns resulted in constant monitoring of physiological functions, such as heart rate, blood pressure, body temperature, respiratory rate, etc. This initiative proved that astronauts' vital parameters and health data could be successfully monitored by physicians and scientists on Earth. [6]

From the NASA experience emerged the need to carry out on-board diagnosis, and to promptly treat in-flight emergencies, with practical systems capable of providing effective and quality healthcare. Several research programs were initiated, and the first telemedicine equipment and systems were engineered.

A great boost to telemedicine development was given by television. This device became common in the 1950s, where it took place in citizens' homes and various clinical settings.

The first interactive medical video communication was achieved in 1964, involving the Nebraska Psychiatric Institute in Omaha and Norfolk State Hospital, 112 miles apart.

For the first remote connection between a doctor and a civil patient, we had to wait for 1967, when the medical station of Boston's Logan Airport was put in connection with Massachusetts General Hospital. [7]

These first tests had great importance: the researchers demonstrated the possibility of correct remote diagnoses, thanks to the exchange of medical information, laboratory data, images, X-rays, and health records.

These shreds of evidence prompted the Federal Government of the United States of America to provide funds to support the development and implementation of telemedicine technologies, starting in the late 1960s. The aim was to demonstrate the effectiveness, reliability, and feasibility of telemedicine technologies. Six research programs were initiated, many of them developed in rural areas, where the availability of health personnel was a critical problem.

Thanks to these projects, the importance of establishing the technological base for telemedicine was verified. These demonstrated that telecommunications could be used as a substitute for travel to obtain medical care and to establish a vital link in emergencies where access to a physician is difficult or impossible to achieve.

Early Research on Telemedicine

Telemedicine was conceived to provide health care to people located in remote areas, breaking down the barriers of distance through technology.

The first research projects were developed to evaluate the effectiveness of telemedicine, but also to evaluate the best strategies for its implementation.

In the 1960s, a group of physicians from Massachusetts General Hospital provided remote assistance to patients located 2.7 miles away at Logan International Airport Medical Station, using a two-way audiovisual microwave circuit. [7]

Diagnosis and treatments were evaluated by selected staff. This was one of the first studies showing the reliability and potential of telediagnosis. [7]

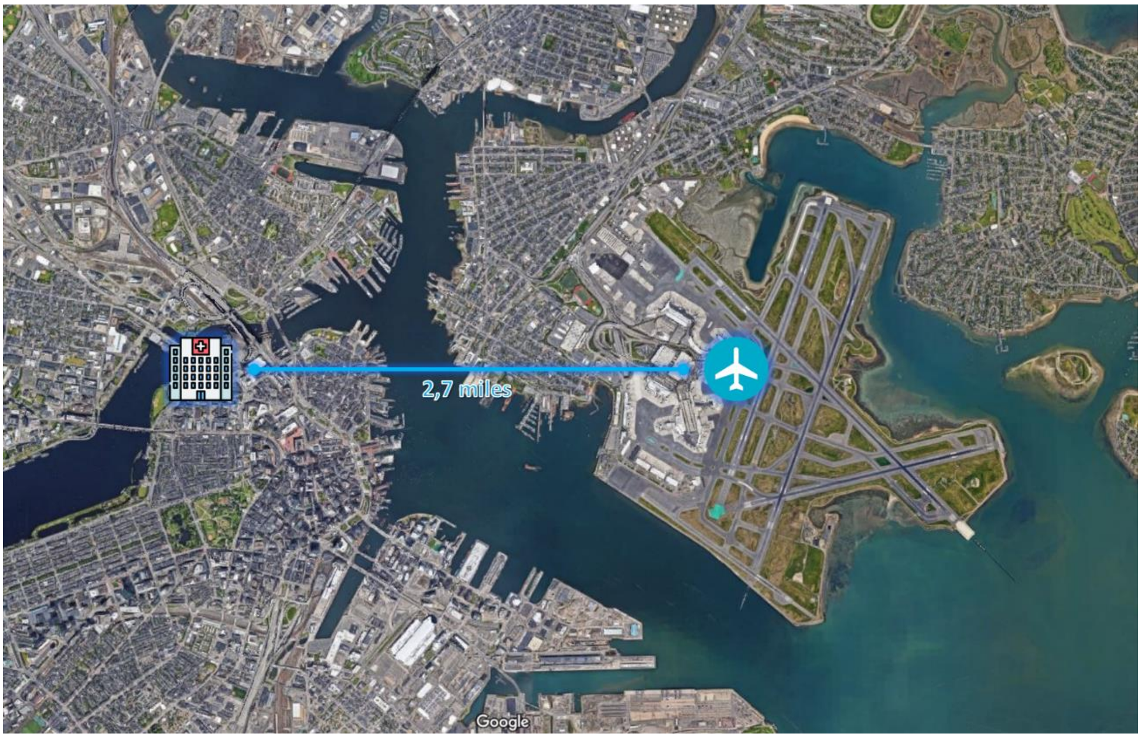


Figure 2: *The connection established between the Massachusetts General Hospital and the Logan International Airport Medical Station represents one of the first practical applications of a telemedicine system.*

The *Space Technology Applied to Rural Papago Advanced Health Care* (STARPAHC) project was approved in 1973 and became operational in 1975. Developed by the Lockheed Missiles and Space Corporation and sponsored by NASA, STARPAHC was unique in its characteristics. [1]

First of all, the most advanced technologies available to the public and private sectors were used, under the guidance of NASA and Lockheed’s vast experience in terms of hardware and human systems.

The target was the Akimel O'odham population (or *Pima people*, also commonly called "*Papago*") living in the remote areas of southern Arizona. The focus was on people with major health problems, and great difficulty in accessing health care.

The Indian Health Service immediately adopted the telemedicine proposal because of its potential and its possibilities to improve healthcare for the Pima people. [8]

The STARPAHC Project was among the "first generation" of telemedicine projects for civilians. The initiative had a short life (from 1973 to 1977) as was no longer economically supported. Nevertheless, it proved the evidence of the reliability of remote consultation, and the clinical effectiveness, training, and education provided by telemedicine. [1], [9], [10]

The importance of including telemedicine in remote areas was highlighted by a 1989 article describing the communication and the collaboration between a medical team operating in a remote area of Queensland, Australia, and hospital facilities located many miles away. The possibility of reducing health care costs in remote areas was also demonstrated. [1]

In 1990, Seattle's Maritime Health Services (MHS) started an occupational medicine service that allowed the crew of a northern Pacific fishing vessel to video-communicate with a doctor ashore. This system was named *Medical Consultation Network* (MedNet) and consisted of a dedicated video communication system allowing the establishment of audio-visual connections between seafarers and doctors on land.

The MedNet system was first tested on the "*Golden Alaska*" fishing ship. The vessel left port in January 1994 for a 3-month voyage to the North Pacific.

Following the experience of *Golden Alaska*, MHS extended the service to similar maritime sectors, such as cruise ships and private yachts, but also land settings, such as mining sites and remote expeditions. [11]

Figure 3: *The "Golden Alaska" is one of the first vessel on which a telemedicine system allowing audio-video connection between crew members and doctors operating ashore was established.*

Specialized Clinical Applications

In the early 1970s, Telemedicine began to be used in specialist settings, such as dermatology, cardiology, psychiatry, radiology, critical care, and oncology. The idea behind it was that the physician's physical presence was not crucial; besides, the transmission of appropriate and accurate information was sufficient.

Anesthesia

In a 1974 study, Gravenstein reported the use of laser-mediated telemedicine in anesthesia. [12]

He demonstrated how the complex maneuvers of clinical anesthesia could be performed by properly trained personnel, under the guidance of a consultant anesthesiologist connected remotely.

The latter, thanks to a video communication system, could observe the operating room, view the patient, and dialog with the operator. The clinical feedback was excellent. [12]

Dermatology

The "*Oregon Teledermatology*" by the National Library of Medicine's (NLM) was designed to improve dermatologic care through the innovative use of high-speed computers, wide-area networks, and full-color digital image storage. The Project guaranteed access to dermatological treatments for citizens of the internal areas of Oregon. [1]

Cardiology

In 1987 an echocardiographic telephone transmission system was established between two hospitals 500km away from each other: the Izaak Walton Killam (I.W.K.) Children's Hospital in Halifax and the Saint John Regional Hospital in New Brunswick. [13]

The experimentation involved 18 patients; complete cardiological examinations were performed in 13 of these, including doppler of all vessels and valves. The transmitted images were classified as "*excellent*" in 16 cases out of 18, while 2 images were considered as "*fair*". New diagnoses were obtained for 8 of 18 patients, while previous diagnoses were confirmed for the remaining 10.

The information was exchanged between the two hospitals in a maximum of 20 minutes. Based on the data obtained, the authors confirmed the reliability of the transmission of specialist cardiological examinations, and the possibility of providing images of the same quality as the originals. [13]

Psychiatry

Video communications systems were established between the communities of Hanover, New Hampshire, and Claremont, 26 miles away.

This consultation service was launched in December 1968 and lasted two years.

The aim was to support family doctors facing the lack of psychiatric staff in certain internal areas, through video-connections with psychiatric doctors. Patient acceptance has been impressively high. Even in patients with a psychotic disorder, the particular video communication system did not create additional anxiety or other psychic problems. [14]

Radiology

The first uses of telemedicine in radiology date back to the 1950s. Gershon and Cohen described X-ray diagnosis obtained from facsimiles transmitted by radio or telephone wires.

Radiology has always been an area of great interest for telemedicine, and it immediately saw the use of wide-area networks (WANs) designed to provide a prompt interpretation of radiologic images for patients in underserved rural areas, but also in those clinics without full-time availability of a radiologist. [15]

In 1994, construction began of a $ 6 million teleradiology facility in Melbourne, Florida. This facility was one of the first ones dedicated to the transfer of X rays, ultrasounds, mammograms, MRIs, and computerized tomography scans via fiber-optic lines, connected to the University of California Medical Center in Los Angeles, where thirteen radiology subspecialists were on staff. [1]

Critical care

Audiovisual communications were used in critical-care medicine since the 1970s as a response to the poor distribution of specialists.

Telemedicine proved to be an excellent educational resource, also improving the quality of health care provided by small and remote health facilities. [16]

Oncology

The implementation of telemedicine in oncology represented a further step forward for medicine. In 1995, the University of Texas Health Sciences Center (UTHSC) in San Antonio initiated a telemedicine project to provide oncology consultations to South Texas Hospital in Harlingen, approximately 250 miles away.

The project was designed to decrease travel expenditures for UTHSC's pediatric oncologists and to increase physical contact with cancer patients.

This telemedicine system allowed for weekly rather than monthly visits to South Texas Hospital, where there was no oncologist on staff. [17]

Other Applications of Telemedicine

Home monitoring

We could say that the home monitoring of patients has existed since the telephone was invented. The simple calls from/to the doctor about the state of health of the citizen represent some of the first rudimentary forms of telemedicine.

Among the first developed home monitoring tools, there were devices equipped with buttons (sometimes called "*panic-buttons*") capable of contacting an emergency service if activated. Pacemakers and devices for monitoring cardiac parameters were adapted or developed to transmit vital information. [18]

Continuing medical education

The possibility of creating video material (videotapes) and the possibility of video communication, allowed to perform Continuing Medical Education (CME) through telemedicine (*the definition of telemedicine includes the exchange of health information, not necessarily healthcare and examinations*).

Numerous potentials and advantages emerged from the first CME programs delivered through telemedicine. First of all, the possibility of following the courses from the comfort of home or the office. Then, the ability to access courses provided by top experts from different countries, to interact and ask questions, to learn about groundbreaking procedures, to discover the latest in diagnostic equipment, and so on. [19]

Today it is possible to access high-level CME courses from home, by participating in virtual classrooms where it is possible to interact via audio/video and via chat. Seminars, in-depth courses, lectures, and University Masters can now be delivered online, guaranteeing the same quality of frontal attendance and the convenience of not having to travel to reach the course venue. [1]

Chapter II - Telemedicine Today

Telemedicine: What do we have?

Nowadays, telehealth services are a stable component of many health systems.

According to the Department of Health and Human Services, 40-50% of US hospitals employ telemedicine technologies. [20] In 2016, the Kaiser Permanente of Northern California reported that remote visits outnumbered face-to-face visits. [20]

The National Business Group on Health expects that all US large employers will ensure coverage of telemedicine services for their workers by the end of 2020. [20]

The Federal Health Program "*Medicaid*" has no state restrictions on the coverage of telemedicine services. Currently, all states cover teleradiology services; 49 states cover telemental health services, and 36 states cover home monitoring and home-based telemedicine services. [21]

The "*Medicare*" program is a bit more restrictive and provides reimbursement only for patients from rural areas. However, the health coverage offered is constantly expanding. [20]

Many healthcare systems integrate telemedicine to bridge the gap in healthcare, reducing patient travel, offering new services, and reducing waiting times for medical visits. A gap that cannot be filled with conventional strategies. [20]

However, regulatory evolution and standardization are required to accelerate the spread of telemedicine and ensure that it advances organically and systematically. [22]

Technology is constantly evolving; with it, telemedicine increases its diffusion, reliability, and accessibility exponentially. Created to assist patients located in remote areas, far from health facilities, today telemedicine is also a part of ordinary medical care. [23]

In an increasingly connected world, today's patient wants to waste less time in the waiting rooms of a hospital and to immediately obtain a medical consultation for all those less serious but still urgent conditions.

Over the years, numerous companies started offering Telemedicine solutions. Some offer 24/7 services through contracted doctors, while others develop and supply only telemedicine software, platforms, and/or devices.

In many hospitals and large clinics, telemedicine is stably included as part of the health service. Several facilities include telemedicine as an integral part of their healthcare offer, integrating it with ordinary treatment methods. [23]

A boost to the rise of telemedicine was given by the spread of smartphones and similar mobile devices. There are now numerous applications (mobile apps) that are easy to use, allowing patients to obtain health information, or to monitor their health.

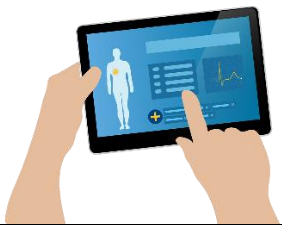
Actors involved	Telemedicine tools	Telemedicine services
Patients-Physician 	Phone, video call, e-mail, chat, remote wireless monitoring, internet	Home monitoring, care for chronic diseases, medication management, counseling, post-discharge follow-up, mental health
Health Professionals 	E-mail, videocall, chat	Information exchange, consultations, emergency, and ICU care
Patients and Mobile Health Technologies 	Wearable monitoring devices, smartphones, mobile apps, e-mail, videos, websites	Health education, monitoring of basic health parameters and physical activity, cognitive fitness, monitoring of diet, medication adherence
Integration with Electronic Health Records (EHR) **Data Analysis** 		

Table 1: *Table showing how the different telemedicine services and different actors can vary and interact with each other, for a 360 ° approach to the patient's health.*

More advanced applications allow contacting, via chat, call, or video call, a doctor through specially developed telemedicine platforms. [23]

These possibilities may be accompanied by the integration with medical devices allowing the patient to monitor its vital parameters, measure its blood pressure, blood glucose levels, etc. and communicate these data to the doctor, or store it in a personal Electronic Health Record, for later consultation (Table 1).

Day after day, the population becomes more and more compliant in using technology to monitor their health and be remotely visited, and telemedicine is destined to change our vision of healthcare forever. [22], [23]

Legal and Ethical Challenges

One of the main concerns today is *privacy*. With telemedicine, delicate, and extremely confidential data is exchanged: *health information*. Strict compliance with privacy regulations must be certified by all the actors taking part in the system, especially by the attending physician and by the company that supplies or develops the devices and/or systems used. [24]

In a systematic review, we highlighted the current state and what should be implemented in Telemedicine regarding ethical and legal standards. From this analysis, entitled "*Telemedicine Practice: Review of the Current Ethical and Legal Challenges*", gaps emerged between current legislation, existing services, providers, and above all in the interactions between patients and their data. [24]

Overcoming the legal challenges in telemedicine can be a long and complicated process, but not impossible. The first step is to know the current status.

Current measures often ignore ethical issues concerning professional conduct and relationships, protection of patient anonymity, patient safety, cultural diversity, and the human value system.

Protection of data and confidentiality always existed for medical information. However, GDPR has further classified and defined data points for easier understanding and managing personal data. For maximum data protection, some authors consider it necessary to uniform guidelines, similar to the GDPR in force in the European Union. The provider has a strong responsibility for the use of devices, which must be safe in order not to make the patient feel "spied", and easy to handle. Instead, the doctor must pay the utmost attention during the patient’s data transmission and in the data storage. There are many hypotheses for maximum data protection such as the anonymity of online data, or encrypted transmissions.

Of critical importance are the fundamental right of the patient and issues concerning medical malpractice. The discussion on malpractice can be classified into two segments: 1) Telemedicine introduces a new form of malpractice or 2) there is no difference with the normal malpractice with the patient in presence.

Some authors proposed interesting concepts such as training of doctors to prevent "*tele-negligence*". Many articles indicate extended insurance coverage or a civil responsibility as a solution to the damage deriving from the exercise of telemedicine, to protect the careers of health care professionals.

The training of professionals carrying out telemedical activities is the responsibility of universities, institutions, and scientific societies. This will greatly help the performance of the remote assistance services.

"*The critical concerns data privacy. Although the guarantees are high, in the future maximum protection of the patient's data must be ensured. This guarantee must be provided first and foremost by those who supply the device, but also by all health professionals*." [24]

The gaps in legislation (for some countries there are no laws regulating telemedicine) represent one of the main obstacles to a correct and safe spread of telemedicine. Governments and authorities should act in this direction, issuing well-defined rules on remote assistance services.

Top Telemedicine Medical Specialties

Telemedicine is used in different medical fields. For some of these, telemedicine is a recent, albeit effective, implementation. For others, its integration dates back to several decades ago, in the 60s and 70s.

From that moment, telemedicine has not stopped improving and evolving.

Below, I reviewed the most popular telemedicine solutions specialties: [23]

- ***Teleradiology*** has been one of the first applications of telemedicine, back in the 1960s. Today it allows to send X-rays and equivalent images to a qualified radiologist located in a different location and to obtain a quick consultation and medical reporting of the material sent.

- ***Telepsychiatry*** allows psychiatrists to follow their patients remotely. It is one of the most widespread telemedicine applications, probably due to the general scarcity of psychiatric doctors. Doctor and patient are put in contact via video call, and can thus converse in front of a screen even from two incredibly distant locations.
- ***Teledermatology*** has developed incredibly in recent years. Today there is equipment capable of capturing high-resolution images and photographs of skin lesions and neoformations. Thanks to these devices it is possible to send photos of moles, rashes, lesions, wounds, and other skin anomalies, for a remote diagnosis. The acquisition of these images can be carried out comfortably by the general practitioner, or in pharmacies equipped with the right equipment. For most cases, a polarizing dermatoscope is sufficient: it is a practical and portable instrument capable of taking high-quality photographs with polarized light. The images are then sent to a dermatologist who will report the documentation remotely. Teledermatology has a great impact on national health systems. First of all, it leads to a significant reduction in waiting times for a dermatological visit. Furthermore, the patient can obtain the diagnosis almost immediately (usually within 24 hours) for any skin lesions transmitted. The competent dermatologist will then assess the possible need for further information and any in-person visits.

- ***Telenephrology*** is an example of an inter-professional application of telemedicine. Generally, it consists of remote communication between the general practitioner and the nephrology specialist.
- ***Teleophthalmology*** also generally proceeds as an inter-professional application. The remote doctor can view the patient's eye in real-time, which is generally located in an outpatient or infirmary without an ophthalmologist. Teleophthalmology finds great application in the field of occupational medicine, in particular in settings where the worker is at risk of injury or infections. Thanks to telemedicine these conditions can be diagnosed and treated immediately.
- ***Teleobstetrics*** could be defined as an enhancement of ordinary obstetrics. It generally consists of providing remote prenatal obstetrics care. The most common example is the transmission of the child's heart rate to an obstetrician operating in another health facility.
- ***Telepathology*** has wide possibilities of application. It generally consists of allowing pathologists to share pathology information, for diagnosis, research, and education. Also, in this case, the exchange of high-resolution images and analytical results is foreseen.
- ***Teleoncology*** generally connects cancer patients with their oncologists. Although many teleoncology technologies offer store-and-forward tools to send images for the diagnosis, it has a strong empathic component to support the patient's mental health.

- ***Telerehabilitation*** allows doctors to provide rehabilitation and physical therapy services remotely. The doctor can view, follow, and guide the patient in each phase of rehabilitation, comfortably from home. [25]
- ***Telenutrition***: food problems, personalized diet plans, weight loss, sport needs; all these can be managed through telemedicine. The nutritionist can talk to and view the patient (via videocall or images/video), access his Electronic Health Record, check his physical characteristics and his vital parameters. He can, therefore, create personalized nutritional plans for the patient, and constantly follow him during his journey, both for health and for aesthetic reasons. Telenutrition is particularly useful for those affected by chronic diseases such as Crohn's disease, diabetes, ulcerative colitis, etc.

Over the years, telemedicine has proved to be both rapid and effective for some fairly common health issues, for which telemedicine successfully replaced the traditional frontal visit.

Among these, we remember (in alphabetical order):

Allergies, Arthritic Pain, Asthma, Bladder Infections, Bronchitis, Cellulitis, Colds and Flu, Conjunctivitis, Diarrhea, Infections, Insect Bites, Nutritional Advices, Pharyngitis, Rashes, Respiratory Infections, Sinusitis, Skin Inflammations, Sore Throats, Sprains & Strains, Sports Injuries, UTIs, Vomiting. [23]

Examples of modern telemedicine consultations

Usually, when we talk about “telemedicine”, the first image that comes to mind is that of the doctor connected in a video call with a patient. In reality, telemedicine can potentially include any clinical service today.

Moreover, the applications of telemedicine are not necessarily relegated to a single specialty. Inter-professional and inter-specialty applications are quite common. This translates into a further increased quality of healthcare, as it allows for a quick exchange of information between professionals operating in different facilities.

There are some types of telemedical consultation that are so advanced and effective to be well rooted in today's medical practice. The main ones are described below. [23]

Store-and-forward telemedicine services

Also called “asynchronous telemedicine”, the “store-and-forward” services consist of the exchange of patient medical data (images, videos, laboratory results, etc.) between practitioners located in different places.

These services use sophisticated, safe, and dedicated platforms that comply with security and privacy regulations in force.

The definition of “*asynchronous*” refers to the fact that the patient, consulting specialist, and primary doctor do not necessarily have to communicate in real-time. On the contrary, medical data are transmitted to be viewed at a later time.

To better understand the concept, we could compare it to the difference between a phone call and an email exchange. The phone call consists of live, real-time communication. The exchange of emails, on the other hand, can take place after a more or less long time.

Store-and-forward telemedicine works well in the case of inter-professional medical services, or where there is no immediate availability of the required specialist doctor.

Let's take another example: a clinic located in a remote internal area has the equipment to perform X-rays but does not have a radiologist. Telemedicine, in its asynchronous form, allows the operator to perform the X-ray, and to send the images to a doctor operating kilometers away, who will proceed with the reporting.

Store-and-forward telemedicine is widely applied today in various branches of medicine, such as teledermatology and teleophthalmology.

Among all the forms of telemedicine, asynchronous telemedicine is probably the first to improve the effectiveness of healthcare, as it allows the provision of specialist health services even where the competent doctor is not available. It reduces patient travel and waiting lists, improves the time organization of doctors, provides health coverage to remote and disadvantaged areas, etc. [23]

Real-time telemedicine

In the collective imagination, when we talk about telemedicine, we imagine a doctor connected in a video call with a patient. This is the case of real-time telemedicine, also known as “synchronous telemedicine”. It consists of real-time communication between doctor and patient. The consultation takes place immediately, just like in an in-person visit.

These are real medical examinations carried out through sophisticated and specially developed platforms, guaranteeing audio-video connections between doctor and patient, or between different health professionals.

Real-time telemedicine is proving to be a valid alternative to frontal visits, capable of boosting work-life balance, and reap the many other time-related issues: reduction of travel, possibility of having disabled patients perform medical examinations without them must travel, etc.

The basic equipment required is incredibly simple: internet connection, a microphone, and a webcam, or more simply, a smartphone. [23]

Remote patient monitoring (RPM)

The first advanced forms of Remote Patient Monitoring (RPM) date back to the first space expeditions. In fact, through RPM it is possible to monitor the patient's vital parameters, and other health information, at a distance.

This makes it possible to identify risk signals and to intervene promptly in case of risk.

Also called *telemonitoring* or *home telehealth*, this form of telemedicine is spreading very quickly, particularly in the area of chronic diseases. It exploits innovative devices able to communicate the data collected in real-time with a central hub; for example, a glucose tracker can monitor the blood glucose levels of the diabetic patient, and transmit them to the treating doctor. In the case of risk values, the devices will send an alert, prompting the doctor to intervene as required.

With the recent spread of wearables and mobile medical devices, remote patient monitoring has undergone an incredible boost. Patients have access to inexpensive, fast, practical tools capable of accurately monitoring their vital signs and collecting health data. [23]

Telemedicine Clinical Guidelines

Although there are no universal rules for telemedicine, the American Telemedicine Association (ATA) - based on more than 600 studies - has put together guidelines for professionals who employ (or are going to employ) telemedicine as an expansion of ordinary health care.

Without going into detail (further information is available on the ATA website), providers should follow the same standards they would for an in-person medical visit.

The practitioner must respect the rules of ethics and privacy, and must adequately inform the patient about methods, pros, and cons, costs, etc.

Telemedicine is a constantly evolving science. Research and continuous updates are essential to keep up with the times and to guarantee an informed, safe and effective use to professionals and patients. [26]

Chapter III - Research Activity

Research Activity of the Ph.D. Candidate

The research activity carried out during my Ph.D. course essentially followed two main paths:

1. **Use of telemedicine and e-Health technologies as epidemiological and pharmacological investigation tools** to discover population health conditions, and to propose ideas for improving healthcare quality.
2. **Studies about telemedicine**, intended as the pure remote application of healthcare: current, possible, and future applications; problems, obstacles, regulations; advantages and disadvantages; challenges, possibilities for improvement and evolution, etc.

The final goal was to create **models** *of* telemedicine *solutions* based on scientific research and the experience gained over the years, as well as on the regulations and guidelines in force.

This to provide ***standards*** for the future development of telemedicine systems and technologies, respecting and taking into account the practical and health needs of citizens.

The proposed telehealth services may be effective for remote patients, but even in "*non-remote*" contexts such as in the ordinary medical/pharmaceutical practice, or in emergencies.

The future work can be extended to improve the remote assistance service and explore the services for a larger population, starting from patients living in internal areas, far from health facilities.

The Seafarer as a “Remote Patient” model

Nowadays, telemedicine allows access to an impressive amount of health information. Medical records are easily accessible, and population health surveys have become easier and faster to carry out.

Since telemedicine's first applications, remote patients have been the main recipients of its technologies.

Today, by "*remote patients*" we mean an important percentage of the population that includes the elderly, the disabled, people with reduced mobility, inhabitants of remote areas, remote workers. People for whom access to ordinary health care is more difficult, impossible, or simply not immediate.

Thanks to a close collaboration between the Telemedicine and Telepharmacy Center of the University of Camerino and the Centro Internazionale Radio Medico (C.I.R.M.) of Rome, I could have performed scientific research on a particular class of remote workers: *seafarers* embarked on commercial ships without a doctor on board.

The choice of the maritime patient as a *research model* was not casual.

Health care aboard commercial ships represents a great challenge for modern medicine: generally, in these vessels, *there is no doctor or medical staff*, and the ship can travel the oceans for a long time, far from ports and health facilities. [27]

Health care comes through Telemedical Maritime Assistance Services (TMAS), which are remote assistance centers capable of providing remote healthcare. [28]

From the vessel, the crew (in the figure of the captain, or a delegated officer) can communicate with the TMAS and connect to a specialized doctor who will provide information remotely.

Conceptually, this kind of remote assistance for ships originated in the early 20th century, when Guglielmo Marconi used the radio to assist ships at sea. On May 30, 1934, in Rome, a group of doctors led by Dr. Guido Guida founded the Centro Internazionale Radio Medico (C.I.RM.), of which Guglielmo Marconi was the first president.

Since those years, the assistance provided onboard has changed considerably. Today, telemedicine tries to "*bring the seafarer closer*" to the mainland, providing health care systems as high as possible. Scientific research proceeds to identify the health needs of sailors, analyzing critical issues, and proposing solutions.

However, one constant has always remained throughout all these years: that is the crucial role of the "**onboard pharmacy**". This is a depot containing all medicaments, tools, and devices to be used in case of need. [29]

It is therefore crucial to keep it always well managed and promptly supplied.

Furthermore, the naval setting is a dangerous environment where the seafarer is exposed to an increased risk of accidents and diseases compared to the general population. [27], [30]

The distance from home and the peculiarities of the naval environment also expose the seafarer to mental health problems, which adds up to the physical health problems mentioned above.

Therefore, in such a complex and potentially dangerous settings, the crucial importance of providing rapid and effective health care emerges - to identify the symptoms of a morbid condition as soon as possible, and to act quickly in the most appropriate manner.

The study of the health conditions and the remote assistance provided to seafarers offers unique possibilities for the improvement of telemedicine globally.

Studying telemedicine applied to a remote population means studying it in its natural "*habitat*".

Once we have identified the improvement possibilities in a remote setting (as well as the criticalities and gaps) we could hypothesize improvements that will be even more effective - not only for the remote patient - but also for the ordinary citizen.

The "Medicine Chest"

In the previous section, I said that the implementation of healthcare in commercial vessels strongly depends on the onboard pharmacy, also known as the "*medicine chest*". [30]

This name derives from the fact that, historically, the first doctors on board carried suitcases containing all the medical and pharmacological instruments that may be needed. Today it is no longer a “*chest*”, but a real deposit containing drugs, medication devices, medical instruments, etc.

Ideally, the medicine chest should contain everything that may be needed to counter or solve health problems. When a request for assistance reaches the TMAS, the doctor must have access to the onboard pharmacy to provide precise instructions on interventions to be performed on board. If medicines or devices are not available, the possibilities for effective intervention may be reduced.

Two crucial needs arise from this:

1. to keep the onboard pharmacy always supplied, and to *integrate* the material used as soon as possible;
2. to provide the onboard pharmacy with medicines and tools that may be needed by seafarers, based on their real epidemiological *needs*.

The captain is responsible for the management of the onboard pharmacy. He has to inventory the medicine chest, check the elapsing dates, proceed with the order of the new material, etc. Many TMAS provide services that facilitate these tasks, but the role of officers always remains central.

With the growth of maritime traffic in the 20th century, many nations began to enact laws and regulations relating to health, safety, and hygiene onboard ships. Most countries provide for an onboard pharmacy, which must contain precise quantities and types of drugs, medicaments, and devices. These are established by national and/or community laws and adapted to the type of vessel.

Non-compliance with the regulation's requirements, the lack of medicinal products, and incorrect management of the onboard pharmacy may entail significant penalties for the shipping company.

Evaluation of medical prescriptions and off-label use of drugs onboard commercial ships

One of the first studies carried out in collaboration with the C.I.R.M. was a pharmaco-epidemiological investigation based on 17,844 Electronic Health Records (EHR) of seafarers assisted by the C.I.R.M. in the period 2011-2015. [30]

This research resulted in the publication of the article "*Evaluation of medical prescriptions and off-label use onboard ships to improve healthcare quality*" [31], and was divided into two phases:

1. **first phase**: we carried out a thorough epidemiological investigation in which all seafarers' symptoms and diagnoses were analyzed; the latter were classified according to the ICD-10 system proposed by the WHO.
2. **second phase**: we assessed the congruence of the pharmacological therapies prescribed by the treating doctors of the TMAS, following the guidelines reported by the MICROMEDEX database, which provides detailed information about medicines and their use.

Epidemiological Results

Table 2 shows the diagnoses, classified according to the International Classification of Diseases 10 (ICD-10) system proposed by the WHO.

Diseases of the digestive system (class XI ICD-10) cover the first place in terms of the number of diagnoses, found in 18.28% of patients (3,261 cases), followed by *injury, poisoning, and certain other consequences of external causes* (class XIX ICD-10), covering 17.97% of patients (3,207 cases); then we have *diseases of the skin and subcutaneous tissue* (class XII ICD-10) covering 9.47% of patients (1,690 cases) and so on (Table 2).

Pharmacological results: off-label use of drugs

Based on the epidemiological data obtained, for each case, we wanted to verify if the therapy prescribed by the treating physician was consistent with the indications for use of the chosen drugs, according to the Micromedex Database. The results are shown in Figure 4.

International Statistical Classification of Diseases and Health-Related Problems, 10th Revision. ICD-10	2011 NUMBER OF CASES/ PERCENT	2012 NUMBER OF CASES/ PERCENT	2013 NUMBER OF CASES/ PERCENT	2014 NUMBER OF CASES/ PERCENT	2015 NUMBER OF CASES/ PERCENT	TOTAL NUMBER OF CASES/ PERCENT
IX- Diseases of the circulatory system	232 8,72%	226 7,06%	205 5,77%	258 6,31%	268 6,18%	1189 6,66%
XI -Diseases of the digestive system	481 18,07%	634 19,79%	640 18,01%	718 17,57%	788 18,17%	3261 18,28%
XII- Diseases of the skin and subcutaneous tissue	222 8,34%	291 9,09%	323 9,09%	381 9,32%	473 10,90%	1690 9,47%
XIII- Diseases of the musculoskeletal system and connective tissue	152 5,71%	217 6,77%	244 6,87%	337 8,25%	338 7,79%	1288 7,22%
XIV- Diseases of the genitourinary system	252 9,47%	322 10,05%	301 8,47%	342 8,37%	378 8,71%	1595 8,94%
XIX- Injury, poisoning and certain other consequences of external causes	482 18,11%	581 18,14%	657 18,49%	716 17,52%	771 17,77%	3207 17,97%
CASES EXCLUDED	101 3,79%	83 2,59%	126 3,55%	179 4,38%	143 3,30%	632 3,54%
TOTAL CASES	2,662	3,203	3,554	4,087	4,338	17,844

***Table 2**: Number of diagnosis (and their percentage), identified according to the ICD-10 classification system (ICD-10 World Health Organization Version: 2016).*

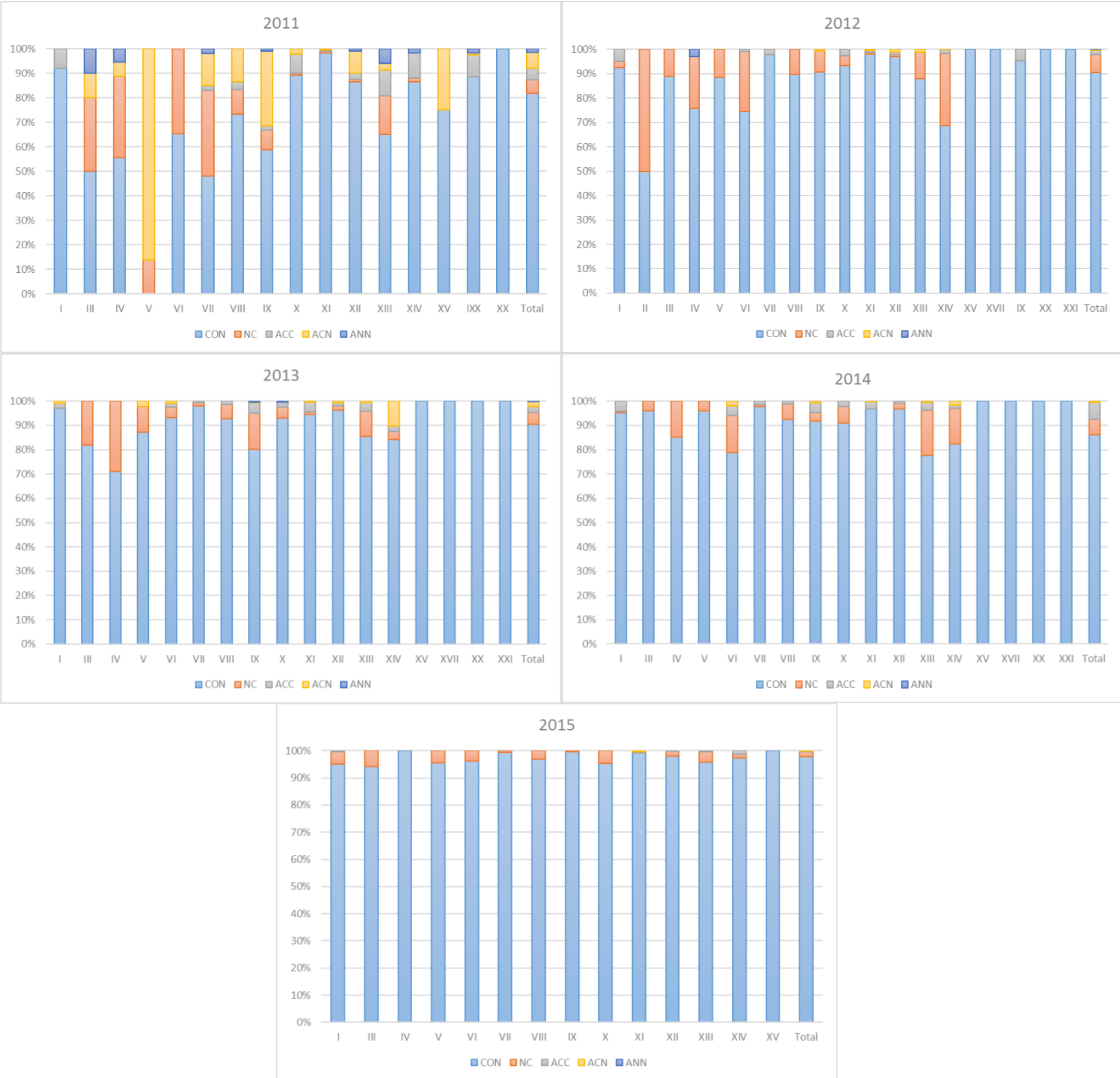


***Figure 4**: Consistent and non-consistent use of drugs in the five analyzed years (2011-2015). Legend: **CON**: consistent use. **NC**: non-consistent use. **ACC**: consistent association. **ACN**: partially consistent association. **ANN**: non-consistent association.*

We defined "consistent" (CON) all the prescriptions complying with the indications of primary use reported in the Micromedex database. Contrariwise, “non-consistent” prescriptions have been defined (NC). In some cases, doctors have prescribed multiple drug therapies. In this case, prescriptions were: completely consistent with the primary indications for use (ACC), partially consistent (ACN) - or at least one of the drugs respected the indications for use, and non-consistent (ANN) if none of the prescribed drugs met the guidelines.

Detailed results are shown in Figures 4 and 5.

Off-label use was different depending on the class of pathology examined. On average, over the years, off-label use covered 10% of all prescriptions, with a slight tendency to decrease.

The lack of certain drugs onboard, as well as the practical, linguistic, and legal difficulties that may involve the purchase of certain medicines in different countries, can significantly undermine the quality of healthcare provided to seafarers.

From the results of the study above described, it was clear that off-label use was motivated by the limited choice of drugs on board. This shortage of first-choice medicines has forced doctors to prescribe off-label therapies. This practice is legal and quite spread in medical practice, but it can lead to ethical and health issues; therefore off-label use should be limited and only be performed if strictly necessary and under direct medical supervision.

Figure 5: *Time-trend of consistent and non-consistent use of drugs in 2011-2015, for the classes of disease with greater non-consistent use.* ***Legend****:* ***CON****: consistent use.* ***NC****: non-consistent use.* ***ACC****: consistent association.* ***ACN****: partially consistent association.* ***ANN****: non-consistent association.*

The possibility that a badly supplied onboard pharmacy could affect the quality of the assistance provided, leading to second-choice therapies, led us to another study, again of a pharmaco-epidemiological nature, entitled "*Benzodiazepine prescriptions on merchant ships without a doctor on board: analysis from medical records of Centro Internazionale Radio Medico (C.I.R.M.)*". [27]

The analysis was performed on the 17,844 electronic medical records analyzed in the previous summarized study.

The choice to focus on benzodiazepines was given for 3 main reasons:

1. They are the most widely administered class of medicines, after cardiovascular drugs. [32]
2. Scientific literature reports a wide use of benzodiazepines in the naval environment as "*off-label*" drugs.
3. Due to their sedative and hypnotic effect, benzodiazepines can have harmful effects on seafarers’ safety, already normally exposed to a greater risk of accidents at work.

The results of the epidemiological investigation are summarized in Table 3.

ICD-10	Total cases assisted	No. of cases with benzodiazepines prescriptions	% of cases
I. Certain infectious and parasitic diseases	**670**	**3**	**0.45**
II. Neoplasms	**2**	**0**	**0**
III. Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	**60**	**0**	**0**
IV. Endocrine, nutritional and metabolic diseases	**172**	**3**	**1.74**
V. Mental and behavioral disorders	**172**	**111**	**64.53***
VI. Diseases of the nervous system	**577**	**110**	**19.06***
VII. Diseases of the eye and adnexa	**639**	**3**	**0.47**
VIII. Diseases of the ear and mastoid process	**231**	**3**	**1.30**
IX. Diseases of the circulatory system	**1,227**	**279**	**22.74***
X. Diseases of the respiratory system	**885**	**15**	**1.70**
XI. Diseases of the digestive system	**3,261**	**43**	**1.32**
XII. Diseases of the skin and subcutaneous tissue	**1,690**	**9**	**0.53**
XIII. Diseases of the musculoskeletal system and connective tissue	**1,243**	**51**	**4.10**
XIV. Diseases of the genitourinary system	**1,595**	**20**	**1.25**
XV. Pregnancy, childbirth and the puerperium	**52**	**0**	**0**

ICD-10	Total cases assisted	No. of cases with benzodiazepines prescriptions	% of cases
XVI. Certain conditions originating in the perinatal period	**0**	**0**	**0**
XVII. Congenital malformations, deformations, and chromosomal abnormalities	**15**	**1**	***Insufficient number of cases***
XVIII. Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	**1,279**	**74**	**5.79***
XIX. Injury, poisoning, and certain other consequences of external causes	**3,207**	**37**	**1.15**
XX. External causes of morbidity and mortality	**58**	**0**	**0**
XXI. Factors influencing health status and contact with health services	**177**	**3**	**1.69**

***Table 3**: Diagnosis and benzodiazepine prescriptions in 2011-2015 (ICD-10). *Asterisk indicates classes of pathologies with the larger use of benzodiazepine prescriptions.*

Benzodiazepines were prescribed for 765 patients (3.29% of all cases analyzed). In 626 cases (81.83%) these were prescribed alone.

Table 4 shows the types and number of registered benzodiazepine prescriptions.

Benzodiazepine molecule prescribed	**N (%)**
Diazepam	622 (81,31%)
Nitrazepam	2 (0,26%)
Alprazolam	1 (0,13%)
Clonazepam	1 (0,13%)
Benzodiazepines in association	
Diazepam + Codeine	123 (16,08%)
Diazepam + Acetylsalicylic Acid	8 (1,05%)
Diazepam + Paracetamol (Acetaminophen)	3 (0,39%)
Diazepam + Ibuprofen	3 (0,39%)
Diazepam + Diclofenac	1 (0,13%)
Diazepam + Nimesulide	1 (0,13%)

***Table 4**: Benzodiazepines prescribed in monotherapy or associated with other active principles.*

Diseases of the cardiovascular system (ICD-10 class IX) were those for which benzodiazepines were more prescribed from a quantitative point of view, followed by mental and behavioral disorders (ICD-10 class V), symptoms, signs, and abnormal clinical and laboratory findings (ICD-10 class XVIII), diseases of the musculoskeletal system (ICD-10 class XIII) and the nervous system (ICD-10 class VI). In terms of percentage of benzodiazepine prescriptions referred to the number of patients suffering from a given class of diseases, benzodiazepines were given more often for mental and behavioral disorders, followed by diseases of the circulatory system, nervous system, symptoms and diseases of the musculoskeletal system. Concerning ICD-10 class IX (diseases of the circulatory system) prescriptions, benzodiazepines have been prescribed as off-label drugs in the treatment of hypertension and precordial pain. From the literature, we know that benzodiazepines have a hypotensive effect that acts on arterial baroreflex or the sympathetic and vagal outflow. Other researchers attribute the hypotensive action of benzodiazepines to their vasodilatory effect or its effect on peripheral benzodiazepine receptors. [27]

Anyway, these are quite evident off-label uses of drugs. While these are mainly due to the qualitative and quantitative lack of drugs on board, on the other hand, doctors must always respect the international guidelines for the use of drugs, taking into account all the possible adverse reactions and interactions. The situation becomes even more worrying if we think about the increased risk of accidents at work that hypnotic/sedative drugs can cause.

Given the widespread off-label use of drugs, follow-up programs allowing constant monitoring of seafarer's health is essential. [27]

In our study, we choose benzodiazepines as a *model*; but these considerations apply to any other category of drugs for which off-label use could be widespread. Based on our pharmaco-epidemiological results, the urgency of standardization of the onboard pharmacy emerges. This should take into account seafarers' real health needs, following actual epidemiological data.

Comparative Analysis of the Medicinal Compounds of the Ship “Medicine Chests” in Maritime European Countries

The lack of standardization between the various onboard pharmacies is a problem that the authorities have been trying to solve for some time.

A first solution attempt was proposed in 1967 by the WHO through the publication of the first edition of the “*International Medical Guide for Ships*”. In this document, the WHO has tried to lay the foundations for a qualitative-quantitative standard of medicinal products to be held on all ships sailing in international waters.

Even today many of these indications have not been fully transposed by many nations, and the difference between the various medicine chest of each country represents a major problem.

The situation becomes even more serious if we think of the diversity of laws relating to the use, distribution, and availability of medicinal products in different countries.

The European Union in 1992 issued a Directive "*On the minimum safety and health requirements for improved medical treatment onboard ships*". This Directive was enacted as a general guideline for the Member States. Despite this, many European countries do not seem to have fully applied these indications. [33]

This significant issue led us to analyze in detail the structure of the main European medical chests, culminating in the publication of the study “*Comparative Analysis* *of the Medicinal Compounds of the Ship "Medicine Chests" in Maritime European Countries. Need for Improvement and Harmonization*". [33]

In it, we took into account and compared each other:

1. the **12 onboard pharmacies** of the main European maritime nations;
2. the **European Directive of 31 March 1992 n.92/23** [34];
3. the **WHO Model List of Essential Medicine** (3rd Edition) [35].

The latter document indicates the drugs considered "*essential*" to ensure a rapid and effective health response in case of illness or injury. The medicine chest analyzed belong to the following countries: Cyprus (CY), Denmark (DK), Finland (FI), France (FR), Germany (DE), Greece (GR), Italy (IT), Malta (ML), Netherlands (NL), Portugal (PT), Spain (SP), United Kingdom (UK).

The main problem that emerged was a considerable lack of harmonization between the various medicine chests analyzed, with disparities also concerning the European Directive of March 31, 1992 n.92/23, and the WHO Model List of Essential Medicine (3rd Edition). [34], [36]

A general overview of the study results is presented in the following tables (Tables 5-9).

DRUGS	**CY**	**DE**	**DK**	**FI**	**FR**	**GR**	**IT**	**ML**	**NL**	**PT**	**SP**	**UK**	**WHO**
1 Cardiovascular													
(a) Cardio-circulatory analeptics – Sympathomimetics	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Anti-angina preparations	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Diuretics	P	P	P	P	P	P	P	P	P	P	P	P	P
(d) Anti-haemorrhagics including uterotonics if there are women on board	P	P	P	P	P	P	P	P	P	P	P	P	P
(e) Anti-hypertensive	P	P	P	P	P	P	P	P	P	P	P	P	P
2 Gastrointestinal system													
(a) Medicines for gastric and duodenal disorders													
- Histamine H2 receptor anti-ulcer antagonists[*]	P	**A**	**A**	**A**	**A**	P	P	P	**A**	P	P	P	P
- Anti-acid mucous dressings	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Anti-emetics	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Lubricant laxatives	P	P	P	P	P	P	P	P	P	P	P	P	P
(d) Anti-diarrhoeals	P	P	P	P	P	P	P	P	P	P	P	P	P
(e) Intestinal antiseptics	P	P	P	P	P	P	P	P	P	P	P	P	P
(f) Haemorrhoid preparations	P	P	P	P	P	P	P	P	P	P	P	P	P
3 Analgesics and anti-spasmodics													
(a) Analgesics, antipyretics, and anti-inflammatory preparations	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Powerful analgesics	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Spasmolytics[*]	P	P	**A**	**A**	P	P	P	P	**A**	P	P	P	P
4 Nervous system													
(a) Anxiolytics	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Neuroleptics	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Seasickness remedies	P	P	P	P	P	P	P	P	P	P	P	P	P
(d) Anti-epileptics	P	P	P	P	P	P	P	P	P	P	P	P	P

***Table 5**: Medicinal products for Cardiovascular system, Gastrointestinal system, Analgesics and antispasmodics, and Nervous system listed in Annex II of the Directive (92/29/EEC) - included (P) or not included (A) in the medicine chests of the 12 European countries examined. Legend: CY: Cyprus, DE: Germany, DK: Denmark, FI: Finland, FR: France, GR: Greece, IT: Italy, ML: Malta, NL: Netherlands, PT: Portugal, SP: Spain, UK: United Kingdom*

DRUGS	CY	DE	DK	FI	FR	GR	IT	ML	NL	PT	SP	UK	WHO
5 Anti-allergic and anti-anaphylactic													
(a) H1 Anti-histaminics	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Injectable glucocorticoids	P	P	P	P	P	P	P	P	P	P	P	P	P
6 Respiratory system													
(a) Bronchiospasm preparations	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Anti-tussives	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Medicines used for colds and sinusitis	P	P	P	P	P	P	P	P	P	P	P	P	P
7 Anti-infection													
(a) Antibiotics (at least two families)	P	P	P	P	P	P	P	P	P	P	P	P	P
*(b) Anti-bacterial sulphonamide**	P	P	P	**A**	**A**	P	P	P	P	P	P	P	P
(c) Urinary antiseptics	P	P	P	P	P	P	P	P	P	P	P	P	P
(d) Anti-parasitics	P	P	P	P	P	P	P	P	P	P	P	P	P
(e) Intestinal anti-infectives	P	P	P	P	P	P	P	P	P	P	P	P	P
(f) Anti-tetanus vaccines and immunoglobulins	P	P	P	P	P	P	P	P	P	P	P	P	P
8 Compounds promoting rehydration, caloric intake, and plasma expansion	P	P	P	P	P	P	P	P	P	P	P	P	P

Table 6*: Anti-allergic and anti-anaphylactic, Respiratory system, Anti-infection, Compounds promoting rehydration medicinal products listed in Annex II of the Directive (92/29/EEC) - included (P) or not included (A) in the medicine chests of the 12 European countries examined. Abbreviations are the same as in Table 1.*

DRUGS	**CY**	**DE**	**DK**	**FI**	**FR**	**GR**	**IT**	**ML**	**NL**	**PT**	**SP**	**UK**	**WHO**
9 Medicines for external use													
(a) Skin medicines													
- Antiseptic solutions	P	P	P	P	P	P	P	P	P	P	P	P	P
- Antibiotic ointments[*]	P	P	**A**	P	P	P	P	P	P	P	P	P	P
- Anti-inflammatory and analgesic ointments	P	P	P	P	P	P	P	P	P	P	P	P	P
- Anti-mycotic skin creams	P	P	P	P	P	P	P	P	P	P	P	P	P
- Burn preparations	P	P	P	P	P	P	P	P	P	P	P	P	P
(b) Eye medicines													
- Antibiotic drops	P	P	P	P	P	P	P	P	P	P	P	P	P
- Antibiotic and anti-inflammatory drops[*]	P	P	P	P	P	P	P	P	**A**	P	P	P	P
- Anaesthetic drops	P	P	P	P	P	P	P	P	P	P	P	P	P
- Hypotonic myotic drops	P	P	P	P	P	P	P	P	P	P	P	P	P
(c) Ear medicines													
- Antibiotic solutions[*]	P	**A**	**A**	P	P	P	P	P	P	P	P	P	P
- Anaesthetic and anti-inflammatory solutions	P	P	P	P	P	P	P	P	P	P	P	P	P
(d) Medicines for oral and throat infections													
- Antibiotic or antiseptic mouthwashes[*]	P	P	P	**A**	P	P	P	P	P	P	P	P	P
(e) Local anesthetics													
- Local anesthetics using freezing	P	P	P	P	P	P	P	P	P	P	P	P	P

- Local anesthetics given by subcutaneous injection	P	P	P	P	P	P	P	P	P	P	P	P	P
- Dental anesthetic and antiseptic mixtures	P	P	P	P	P	P	P	P	P	P	P	P	P

Table 7*: Medicines for external use listed in Annex II of the Directive (92/29/EEC) - included (P) or not included (A) in the medicine chests of the 12 European countries examined. Abbreviations are the same as in Table 1.*

WHO Model List of Essential Medicines, 2017	**European Directive 92/29/EEC**
MEDICINES FOR PAIN AND PALLIATIVE CARE	Present
ANTIALLERGICS AND MEDICINES USED IN ANAPHYLAXIS	Present
ANTIDOTES AND OTHER SUBSTANCES USED IN POISONINGS	Present
ANTICONVULSANTS/ANTIEPILEPTICS	Present
ANTI-INFECTIVE MEDICINES	
Antibiotics (at least two families)	Present
Anti-bacterial sulphonamide	Present
Urinary antiseptics	Present
Anti-parasitics	Present
*Anti-malarial**	**Absent**
Intestinal anti-infectives	Present
Anti-tetanus vaccines and immunoglobulins	Present
*Antileprosy medicines**	**Absent**
*Antituberculosis medicines**	**Absent**
*Anthelmintics and Antiprotozoals**	**Absent**
ANTIMIGRAINE MEDICINES	Present

MEDICINES AFFECTING THE BLOOD *Antianaemia medicines** *Medicines affecting coagulation* *Blood coagulation factors** *Plasma-derived medicines and Plasma substitutes**	 **Absent** Present **Absent** **Absent**
CARDIOVASCULAR MEDICINES	Present
DERMATOLOGICAL MEDICINES (topical)	Present
DIAGNOSTIC AGENTS	Present
DISINFECTANTS AND ANTISEPTICS	Present
DIURETICS	Present
GASTROINTESTINAL MEDICINES	Present
HORMONES, OTHER ENDOCRINE MEDICINES, AND CONTRACEPTIVES Adrenal hormones and synthetic substitutes Insulins and other medicines used for diabetes* Thyroid hormones and antithyroid medicines*	 Present **Absent** **Absent**
MUSCLE RELAXANTS (PERIPHERALLY-ACTING) AND CHOLINESTERASE INHIBITORS	Present
OPHTHALMOLOGICAL PREPARATIONS	Present
MEDICINES USED IN MOOD DISORDERS *Anxiolytics* *Neuroleptics* *Medicines used in depressive disorders**	 Present Present **Absent**

Table 8*: Categories of drugs foreseen by the WHO Essential Model List compared with the contents of the "Annex II of the Directive (92/29 / EEC)".* *******: Categories of medicinal products not included in the "Annex II of The Directive (92/29/EEC)".*

DRUGS	CY	DE	DK	FI	FR	GR	IT	ML	NL	PT	SP	UK
Anti-malarial	A	P	P	P	P	P	P	P	P	A	A	A
Antileprosy medicines	A	A	A	A	A	P	A	P	A	A	A	A
Antituberculosis medicines	A	A	A	A	A	A	A	A	A	A	A	A
Anthelminthics and Antiprotozoals	P	P	P	A	P	P	P	P	A	P	P	P
Antianaemia medicines	A	P	A	A	A	A	A	A	A	A	A	A
Blood coagulation factors	P	P	A	P	P	P	A	P	P	A	P	A
Plasma-derived medicines and Plasma substitutes	A	A	P	A	A	P	P	P	P	P	P	P
Insulins and other medicines used for diabetes	A	A	A	P	P	A	P	A	A	A	A	P
Thyroid hormones and antithyroid medicines	A	A	A	A	A	A	A	A	A	A	A	A
Medicines used in depressive disorders	A	A	A	A	A	A	A	A	A	A	A	A

***Table 9**: Drugs listed in the WHO Model List of Essential Medicines, but not included in the European Directive n. 92/29 - compared with the 12 medicine chests investigated.*

Several critical issues emerged from the analysis. For example, drugs such as insulin, metformin, and glucagon, included in the WHO Model List of Essential Medicine, are not included in the European Directive 92/29/EEC of March 31, 1992, and are absent in most of the medicine chest analyzed.

These specialties are considered as "*life-saving drugs*", and should be held regardless of whether or not diabetics or patients with metabolic disorders are present on board. After all, potentially dangerous episodes of hyper/hypoglycemia can also happen to healthy individuals; therefore, having these medicines available can make a difference.

In a high-risk environment such as the naval one, where traveling to high-risk countries is a constant, drugs such as anti-tuberculosis and antimalarials should also be considered mandatory. In particular, about the latter, it would be useful to plan a fairly comprehensive and varied supply of antimalarials, selected based on the travels that the ship is going to undertake.

To summarize, the study revealed some critical issues that should be discussed and solved by the competent authorities as soon as possible:

1. **a lack of standardization** between the various onboard pharmacies;
2. **the overall failure to comply with the main guidelines**;
3. **a lack of some important drugs** that could be crucial for the seafarer's health and first intervention;
4. **a scarce consideration of the real health seafarers' health problems** in the design of onboard pharmacies.

Having a well-supplied onboard pharmacy means guaranteeing quality and first choice health care possibilities. The lack of some medicinal products may force the attending physician to prescribe second-choice or off-label therapies - as we have highlighted.

These 3 studies aiming to lay the foundations for a **standardization process** of the onboard pharmacies of all commercial vessels in the world. Standardization that shall be based on real **epidemiological data**, to meet seafarers' real health needs.

Malaria Among Seafarers

As part of the epidemiological investigation and health surveillance program for seafarers called "*Healthy Ship*", born from the collaboration between the Telemedicine and Telepharmacy Center of the University of Camerino and the C.I.R.M., we carried out a thorough epidemiological investigation of malaria among seafarers.

This research resulted in the publication of the article "*First surveillance of malaria among seafarers: evaluation of incidence and identification of risk areas*". [37]

Despite enormous research advances in recent years, malaria is still the deadliest parasitosis in the world, causing an average of 400,000 deaths per year.

Among the various forms of malaria, the one transmitted by the *Plasmodium falciparum* parasite is the most lethal, and it is mainly found in Sub-Saharan Africa. It has an incubation period of about 7 days and a clinical evolution that depends on the species of the infecting parasite. Initial symptomatology usually starts with *fever, chills, muscle aches, nausea, vomiting, diarrhea*. Subsequently, potentially lethal complications can arise, such as *organ failure, pulmonary edema, generalized convulsions, cardiovascular collapse, coma*, and *death*.

Recent epidemiological investigations have shown a reduction of infectious diseases on board over time, but malaria is still a major threat for seafarers. [38]

In our epidemiological investigation, we analyzed the electronic medical records of seafarers assisted by the C.I.R.M. from 1 January 2011 to 31 December 2015. The diagnoses were classified using the ICD-10 system of the WHO, the same we used in our previous epidemiological research.

The diagnosis of malaria onboard comes from a correct identification of the symptoms and physiological parameters measured directly on the ship. In case the symptoms are ascribable to malaria, confirmation must be given through clinical tests to be carried out as soon as possible at the nearest port. These tests allow confirming the diagnosis of malaria - a diagnosis that cannot be based solely on the symptoms.

In this paper, the diagnoses were divided into:

- "***suspected unconfirmed cases***": cases characterized by malarial-like symptoms, but for which the tests have returned negative results.
- "***cases confirmed by clinical tests***": patients with malaria symptoms for which the tests have returned positive results.

The results of the epidemiological investigation are summarized in Table 10.

Year	*Number of Seafarers assisted by the CIRM*	*Number of ICD-10, category I cases*	*Number of "Suspected unconfirmed" Malaria Cases N(%)*	*Number of Malaria Cases "Confirmed by clinical tests" N(%)*
2011	2,561	80	2 (2,50%)	27 (33,75%)
2012	3,120	84	3 (3,57%)	35 (41,67%)
2013	3,428	152	5 (3,29%)	33 (21,71%)
2014	3,908	200	4 (2,00%)	31 (15,50%)
2015	4,195	154	2 (1,30%)	20 (12,99%)
Total	17,212	670	16 (2,39%)	146 (21,79%)

Table 10*: Number of ICD-10 class I diagnoses, and the number of malaria cases onboard commercial ships assisted by the CIRM in the period 2011-2015.*

In Table 10 malaria diagnoses (confirmed and unconfirmed cases) are compared with the diagnosis of other infectious and parasitic diseases included in the ICD-10 category I (*Certain infectious and parasitic diseases*), and reported in percentages (%).

Of considerable interest were the results of the pharmaco-epidemiological investigation, in which we analyzed the therapies prescribed by the C.I.R.M. doctors. [39]

These therapies can be distinguished into two different phases of treatment:

1. **Phase 1**: pending the results of the laboratory tests, the doctors prescribed medicines to control the symptoms, in particular the feverish ones. In 75% of cases, paracetamol was prescribed, with dosages of *0.5-1g three times a da*y. In the remaining 25% of cases, ibuprofen was prescribed with dosages ranging *from 200mg to 600mg*. These therapeutic regimens were continued even in the case of negative results for malaria in laboratory tests.
2. **Phase 2**: in case of confirmation of malaria, doctors prescribed antimalarial therapies based on the type of malaria contracted and, above all, on the availability of antimalarial drugs on board. Chloroquine was the most prescribed drug (107 prescriptions, corresponding to 73.29% of all cases), followed by artemether (19 prescriptions, 13.01% of all cases), then by mefloquine (13 prescriptions, 8, 90% of all cases) and finally by Malarone (7 prescriptions, 4.80% of all cases).

Although the total number of malaria cases seems quite low when compared to the total number of patients assisted, in reality, the percentage of malaria cases accounts for a significant percentage: we are talking about an average of 21.79% of all cases of infectious diseases. This data is somewhat worrying, as the ICD-10 class I also includes quite common and much less serious infectious diseases, such as fungal or viral infections.

This means that malaria still represents a serious threat to seafarers' health. On the other hand, the reduction of malaria cases between 2013 and 2015 (Table 10) is encouraging, suggesting that if the correct prevention rules are followed, a significant reduction of malaria cases onboard commercial vessels is achievable.

For all the "*cases confirmed by clinical tests*", we have analyzed the coordinates corresponding to the moment in which the request for assistance was received by the C.I.R.M. This allowed us to create a map of the infections (Figure 6, upper).

Furthermore, considering that the onset of symptoms occurs after an average incubation period of about 7 days, we analyzed the ships' routes in the 7 days before the request for assistance was performed. This information allowed us to create a map that highlights malarial infection risk for seafarers, distinguished with different colors (Figure 6, lower).

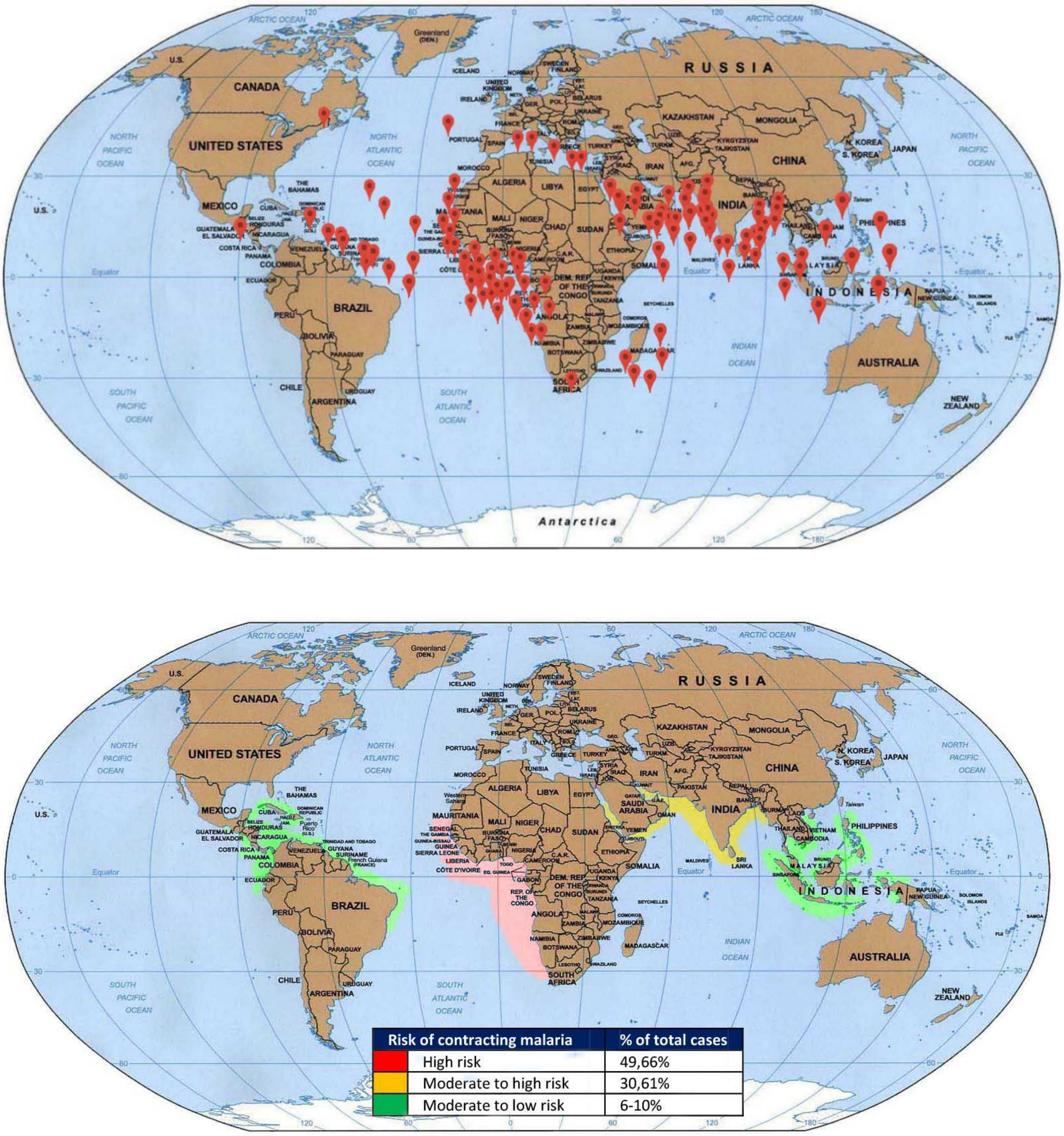


Figure 6: *Upper: coordinates corresponding to the moment in which the request for assistance was received by the C.I.R.M. Lower: malarial risk areas for seafarers according to the obtained data.*

From Figure 6, it is possible to note that the areas we highlighted correspond to the malaria risk areas as indicated by the WHO (Figure 7). What is worrying is the fact that the areas with the highest incidence of infection correspond to the areas with the greatest risk of P. falciparum infection. [40]

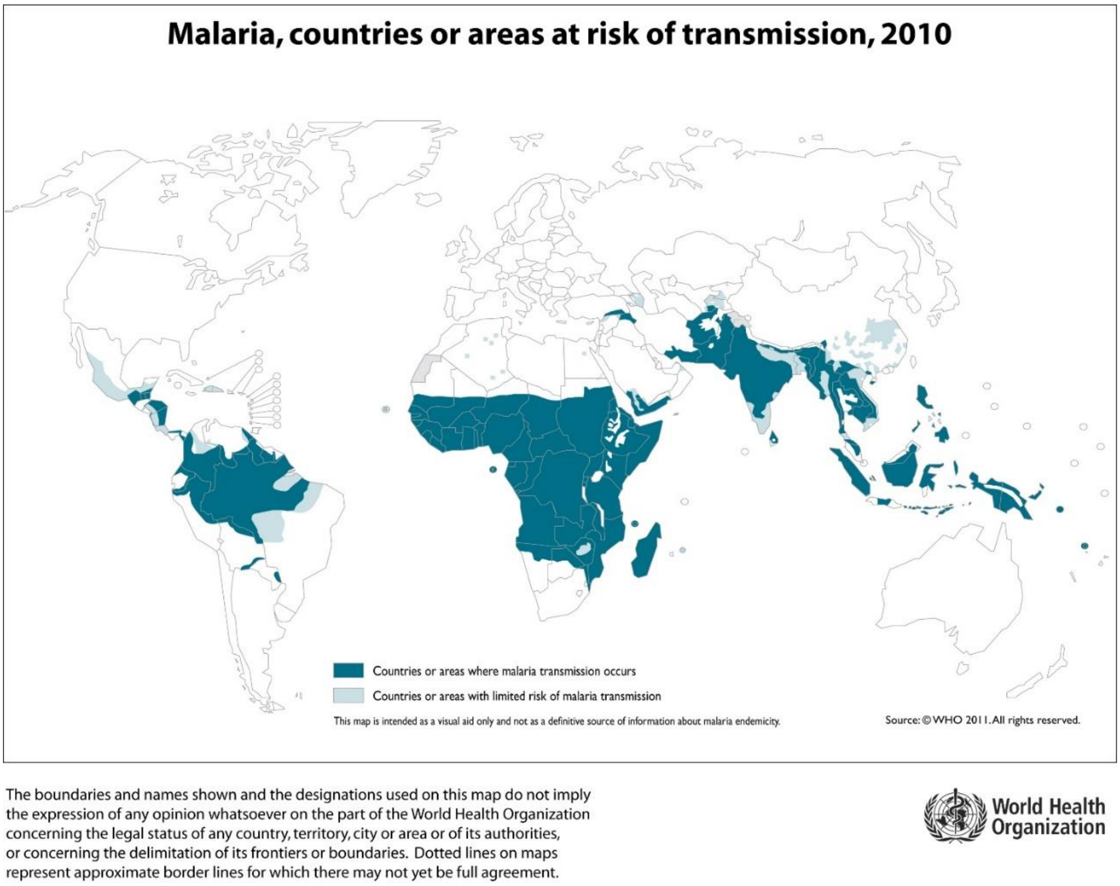


Figure 7*: geographical areas at risk of malaria transmission. Source: WHO, 2010.*

From the literature, we know that Malarone is the most effective drug against P. falciparum to date, as well as against multidrug-resistant Plasmodium. [41]

Despite this, Malarone is one of the least administered drugs on board (4.88% of all antimalarial prescriptions), probably due to its absence in most of the on-board pharmacies. [27], [30], [33]

Therefore, the need to rearrange and standardize the onboard pharmacies emerges again, as described in the previous sections.

For work reasons, seafarers cannot avoid malaria risk areas. The only way to protect these workers is to pursue an accurate prevention methodology (trying to avoid mosquito bites, and carrying out periodic disinfestation operations) and to equip the vessels with appropriate antimalarial drugs, possibly based on the areas where the ship is traveling to. Particular care must be reserved for the patient's care and follow-up, proceeding immediately to his evacuation or diversion if his health problems cannot be resolved on board. [37]

Mental Health and Psychological Stress of Seafarers

Introduction

The isolation condition of the naval environment can strain seafarers' mental health. Dangerous and complex tasks performed in the same spaces, isolated from the rest of the world can cause a psychological deterioration that may lead to serious disorders and even pathologies. [42]–[46]

Seafarers' mental health issues are not new to the marine industry. In 1993 the World Labor Organization (ILO) formed a study group on the working conditions of maritime crews. [47] Subsequently, the International Maritime Organization (IMO), followed by other authorities and governments, established the first general rules of protection for seafarers. [39], [48], [49]

However, maritime epidemiology has always focused on physical pathologies, accidents, and injuries, sometimes neglecting mental and psychological conditions that can seriously compromise the health of the subject. [39], [50]

The WHO defines health as: "*a complete state of physical, social and mental well-being*", and therefore not just the absence of diseases or infirmities. [51]

Although technology has ensured closer contacts with the mainland thanks to the internet, life on board is still, as centuries ago, a highly penalizing reality. [45]

Several studies agree that the main cause of seafarers' mental health problems is the long absence from home.

Nostalgia for home – the desire to return home, has been documented since ancient times, by Greek mythology, from Homer onwards, and substantiates the individual even when he has returned to his family because he has been completely impregnated and altered by it.

The distance from home does not only compromise life on board. It can ruin relationships at home, separating couples and families; children, especially younger ones, tend to see their parent as a distant relative or, at worst, as a stranger. [52]

As part of the research activity for the protection and safety of seafarers, carried out in collaboration between the Telemedicine and Telepharmacy Center of the University of Camerino and the Centro Internazionale Radio Medico (C.I.R.M.), we carried out two noticeable types of research:

1. A thorough **systematic review** of the scientific literature on "*mental health*" problems onboard ships.
2. An **epidemiological study** on the maritime population, from 2011 to 2019.

The objective of these two studies was to determine whether the mental health of seafarers is a significant problem and to propose solutions and practices aimed at improving the health of this class of workers **-** by providing actual epidemiological information and by properly analyzing the available scientific literature.

Methods: Factors affecting the Mental Health of Commercial Seafarers: a systematic review

We have conducted a systematic review based on the scientific literature published between January 2006 and December 2019, through the search engines PubMed, Web of Science (WoS), and Cumulative Index to Nursing and Allied Health Literature (CINAHL).

The keywords used were "*mental health*", "*behavioural disorder*", "*seafarers's stress*", "*physical training on board*", and "*seafarers's mental status*", or a combination of these.

Previous studies were considered unsuitable for the review because they mainly aimed at identifying the factors considered secondary or indirectly related to seafarers' mental health, and without proposing strategies for improvement.

This systematic review was made to determine whether the problem has acquired the right scientific interest or continues to be still not correctly identified.

This research was carried out in compliance with the Prisma guidelines. [53] Furthermore, to carry out a quality evaluation of filtered papers, the Newcastle-Ottawa Scale (NOS) was employed. [54]

Methods: Psychological stress and mental health of seafarers: an epidemiological study from 2011 to 2019

We have carried out an epidemiological investigation about mental and behavioral disorders among seafarers onboard commercial ships without health personnel. The aim was to identify the main mental health issues diagnosed on board and to propose solutions to improve the quality of life in this difficult working environment.

We examined 38.477 requests of assistance from patients embarked on ships assisted by the CIRM from 1st January 2011 to 31st December 2019.

The diagnoses were classified based on the ICD-10 system by the WHO and confirmed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) published by the American Psychiatric Association. [55], [56]

Epidemiological results

From 2011 to 2019, 376 cases of "*mental and behavioral disorders*" were diagnosed (Table 11), with a slight increase in cases over the years (Figure 8), together with an increased number of patients assisted.

Between 2011-2019, the most diagnosed mental disorder was anxious syndrome (119 cases), followed by depressive disorder (103 cases). Next are insomnia (51 cases), panic attacks (35 cases), psychotic syndrome (21 cases), psychomotor agitation (13 cases), behavioral disorder (13 cases), confusional state (9 cases), spatiotemporal disorientation (6 cases), generalized malaise (6 cases) (Table 11 and Figure 9).

Over the 9 years analyzed, 37 suicides and 4 attempted suicide (*not succeeded*) cases occurred (Table 12). The number of suicides over the years appears fairly constant, and the number of successful suicides is significantly higher than suicide attempts (37 versus 4).

	2011	2012	2013	2014	2015	2016	2017	2018	2019	TOTAL (2011-2019)
ANXIOUS SYDNROME	15	16	14	14	15	13	8	12	12	119
BEHAVIORAL DISORDER	2	1	1	1	1	2	1	2	2	13
CONFUSIONAL STATE	1	1	0	1	2	0	2	1	1	9
DEPRESSIVE DISORDER	4	8	14	7	10	16	12	16	16	103
GENERALIZED MALAISE	1	0	0	1	2	1	0	0	1	6
INSOMNIA	2	1	6	4	6	7	11	6	8	51
PANIC ATTACK	3	2	3	2	9	4	4	3	5	35
PSYCHOMOTOR AGITATION	1	2	1	0	1	2	1	3	2	13
PSYCHOTIC SYNDROME	1	3	3	1	2	3	2	2	4	21
SPATIOTEMPORAL DISORIENTATION	1	1	0	0	1	1	0	1	1	6
TOTAL	**31**	**35**	**42**	**31**	**49**	**49**	**41**	**46**	**52**	**376**

Table 11 Legend: *Specific diagnoses and total cases included in class "V" of the ICD-10 system, sorted by year.*

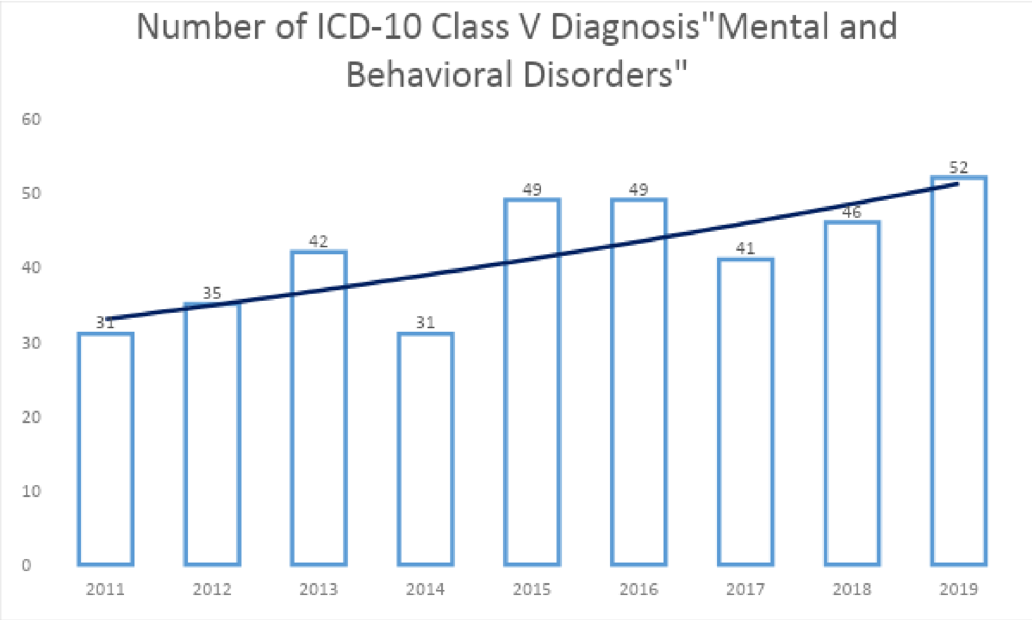


Figure 8: *Number of "Mental and Behavioral Disorders" (ICD-10, WHO) diagnosed, sorted by year from 2011 to 2019. A trend line is represented showing a possible upward trend in the number of mental disorders, due in part to the increase in the total number of patients assisted.*

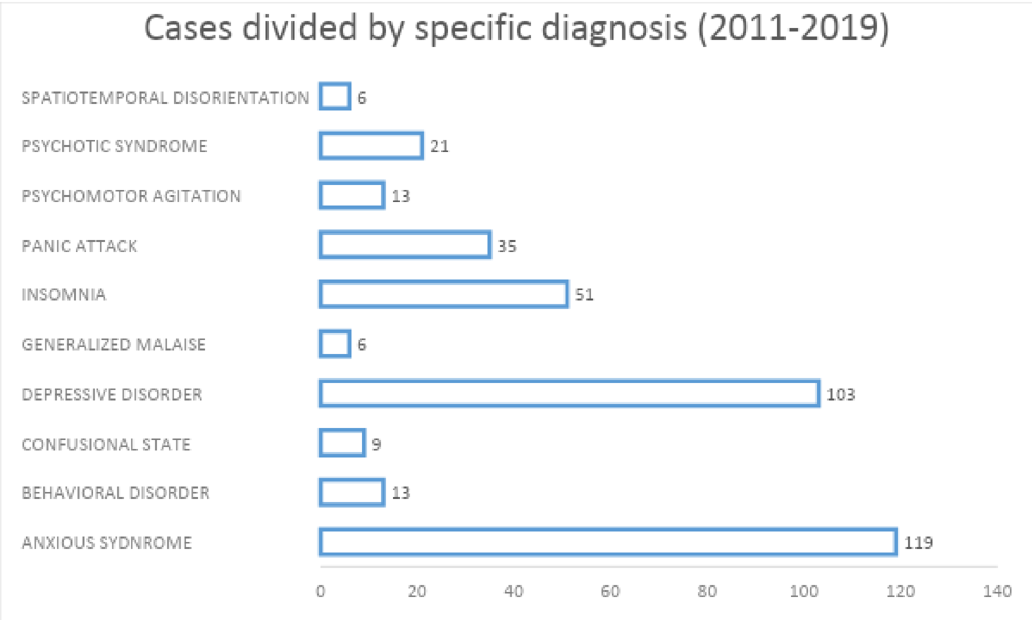


Figure 9: *Total cases of mental disorders recorded in 2011-2019, distinguished according to their specific diagnosis.*

Discussion

Anxious Syndrome and Depressive Disorders

The most diagnosed mental disorders on board from 2011 to 2019 were anxious syndrome (119 cases) and depressive disorder (103 cases).

Anxiety disorders are a set of psychiatric syndromes characterized by *anxiety* and *unjustified fear*. These are often associated with psychosomatic manifestations that create considerable distress for the subject.

The naval environment may trigger these disorders, as suggested by the epidemiological results.

Depression is a complex psychiatric pathological condition characterized by episodes of depressed mood, low self-esteem, loss of interest in life activities, etc. It can compromise the patient's social, physical, and working life.

Although the causes of depression are still being investigated, it seems that both biological and genetic factors, as well as environmental and psychological factors, can induce the onset of depressive disorder. [57]

Among the environmental and social factors that would seem to play a greater role in the etiology of depression, we have: childhood trauma, family problems, bereavements, divorces, serious health problems, poverty, unemployment, social isolation, etc. [58] Work mobbing, bullying, and prolonged work stress are also recognized as triggering causes. [59]

These situations, according to the most recent literature, occur quite frequently on board. [60]

The maritime authorities must act and consider these social issues before these have harmful consequences for seafarers' health. Aggressive, violent behavior, as well as repeated physical and verbal abuse phenomena must be predicted and punished according to the regulations in force.

Suicides onboard

The number of registered suicides onboard is worrying, especially if compared to the number of confirmed deaths per year (Table 12). For example, in 2019, the year with the highest number of deaths (26), 6 suicides occurred (23% of all deaths).

In 2017, 4 of the 27 deaths recorded were suicides (15% of all deaths). The same applies for 2015 where 3 suicides occurred out of 23 total deaths (13% of all deaths). This means that suicides account for an important part of all the deaths occurring on board.

Although the number of mental illnesses diagnosed on board is low, it would be interesting to understand why suicides onboard are such a significant constant in all the years analyzed.

According to recent studies, seafarers seem to prefer suffering in silence, fearing to be diagnosed with a psychic and/or mood disorder which may lead to repatriation and a possible compromise of their career. [60]

This may cause a not negligible underestimation of diagnoses of mental illness and stress on board. Monitoring and support programs aimed at the psychophysical health of the maritime patient are therefore crucial.

Year	Suicide Attempts	Suicides	Total (Suicides + Attempts)
2011	0	4	4
2012	1	2	3
2013	0	5	5
2014	0	3	3
2015	1	3	4
2016	0	4	4
2017	1	4	5
2018	1	6	7
2019	0	6	6
Total	**4**	**37**	**41**

Table 12 Legend: *Number of suicides and suicide attempts reported in the 9 years 2011-2019.*

Factors Compromising Mental Health of Seafarers

According to the most recent literature, numerous factors can compromise the mental and psychological health of seafarers.

In the first place we have the distance from home, followed by the isolation condition, loneliness [61]–[63], too long work contracts [64], poor quality food [60], bad social relationships on board [64], fear of losing the job [65], [66], fear of losing their family [61], [62], [64], [67], [68], etc.

Some authors reported that the different tasks performed onboard can significantly affect the mental stress to which seafarers are subjected. From this point of view, the most affected categories are that of the officers, engineers, and engine crew. [44], [63], [68], [69]

Very important are the social relationships that can be established in the naval environment: strong relationships can improve life on board. On the contrary, enmities, bullying, fights, and bad relationships can significantly deteriorate an already difficult co-existence. [60]

The mental health problems of seafarers are not limited to their time of embarkation. Ashore problems can also be more serious. Separation and divorces are very frequent among seafarers. [70]

The situation is even more serious for couples with children, where the maritime member usually cannot see their child growing up. [60]

Initiatives to improve the mental health of seafarers onboard

The work done by ITF Seafarers Trust and Yale University is probably the best survey carried out to date concerning seafarers' psychological health. This study, thanks to the submission of a special questionnaire, led to the identification of the main needs of seafarers, especially those they think would be useful to make them happier and reduce *stress*. [60]

Since naval isolation and distance from home are the main causes of depression and mood disorders on board, it is crucial to enhance the possibilities of communication and contact with the mainland. Communicating with families and friends must be easier and more immediate. [60]

Besides, there is a need for something that breaks the daily routine and diversifies the working days. Recreational and social activities, sports, better quality food, should be introduced or improved onboard. [60]

Themed events, group activities, customizable and thematic menus (for example "*Monday pizza day*", "*Tuesday Indian dinner*", etc.) are some of the seafarers' wishes to break the monotony of their working life. [60]

These needs could be satisfied with a minimum of organization, and they can guarantee a significant improvement in the working conditions of this particular class of workers.

Conclusions

Epidemiological data concerning the mental health of seafarers has been rather scarce so far. This is mainly due to a historical lack of interest in maritime epidemiology, with a greater emphasis on physical pathologies and injuries. [39], [50]

After all, determining seafarers' mental health is quite difficult.

First, we are talking about remote workers, located far from the land, and difficult to reach. They are selected following specific medical examinations. This determines the immediate elimination of the most fragile and sick subjects, creating a population of workers we could define as "*selected*", and therefore theoretically "*stronger*".

That's why it is difficult to compare maritime workers with other populations, even from a merely statistical point of view.

The mental problems onboard commercial ships are concrete and capable of seriously compromising the seafarer's health, work, and life in general.

Although in terms of numbers the specific cases of maritime patients affected by mental disorders appear low when compared with other classes of pathologies, there is evidence that these health problems may actually be more widespread, and often hidden by the seafarer himself. Based on the epidemiological data and the literature review, we hypothesize that data about mental disorders among seafarers may be underestimated.

The number of suicides occurring onboard every year is concerning, as it represents an important amount of all recorded deaths.

Authorities and shipping companies should take care of seafarers' health more seriously and establish monitoring and supporting programs. Nowadays, only a small group of shipping companies are considering the problem of mental health among seafarers, proposing strategies to improve co-existence onboard commercial vessels.

Scientific research should be expanded to better identify the needs of the seafarers, proposing reactive solutions, and guaranteeing mental well-being on board.

Chapter IV - Development of Telehealth systems and technologies for remote patients' healthcare

Introduction

After analyzing the logistical and health issues onboard commercial vessels (as described in the previous chapters), our goal was to propose solutions aimed at concretely improving the healthcare provided on board.

This objective has materialized through the conception of 3 distinct but *ideally* complementary services:

- the "**C.I.R.M. Medicine Chest**";
- the "**Seafarer's Health Passport**" (SHP);
- the "**TelePharmaSea**" (TPS) software.

The "C.I.R.M. Medicine Chest"

Among the main issues highlighted during my three years as a doctoral student, there is that of the *inadequacy* and *non-standardization* of on-board pharmacies by various countries, as described in Chapter III. This problem can have serious repercussions on the health of the seafarer, by reducing possibilities of on-board care.

From this arose the intention to create a highly recommended list of drugs and medicaments to be carried onboard.

This list comes from a collaboration between the Centro Internazionale Radio Medico (C.I.R.M.) and the Telemedicine and Telepharmacy Center of the University of Camerino, Italy.

This list is called: "*C.I.R.M. Medicine Chest: Recommended medicinal products to be carried on board ships to provide high-quality telemedical assistance*".

These recommendations come from:

- accurate **epidemiological investigations** that have allowed us to identify the criticalities and pathologies that can seriously impact seafarers' health, especially concerning the potential lack of the proper medicines on board;
- in-depth **study of national, community, and international guidelines**;
- **comparative analysis of the medical equipment to be kept on board**, according to the WHO International Medical Guide for Ships (3rd Edition) and to the regulations of 25 different relevant maritime countries: *Antigua and Barbuda, Australia, Bahamas, Belgium, Bermuda, Cyprus, Denmark, Finland, France, Germany, Gibraltar, Hong-Kong, India, Isle of Man, Italy, Liberia, Malta, Marshall Islands, Netherlands, Norway, Panama, Portugal, Singapore, Spain, United Kingdom*;
- accurate **analysis of the scientific literature** about remote care, on-board assistance, and new frontiers of pharmacology.

In summary, the "*C.I.R.M. Medicine Chest*" is an all-encompassing list that allows having onboard:

1) all the drugs and medicaments **required by the regulations in force** (and therefore allowing to avoid unpleasant legal issues);
2) the drugs and medicaments recommended based on the **real health needs of seafarers** – according to epidemiological data and the experience gained by C.I.R.M. over the decades.

A personalized "*C.I.R.M. Medicine Chest*" is created by analyzing 1) the vessel's flag, 2) the type of vessel (and consequently also the type of cargo transported) and 3) the planned geographical destinations.

The Seafarer's Health Passport (SHP)

Overview

Concerning the concrete applications of telemedicine services, the "Seafarer's Health Passport" (SHP) project was born, which is described in detail in the publication "*Design and Evolution of a Seafarer's Health Passport (SHP) for supporting (Tele)-Medical Assistance to Seafarers*". [71]

The project (born from a collaboration between UNICAM, C.I.R.M., CIRM Servizi s.r.l. and 3Cube Ltd.) led to the creation of an Electronic Health Record (EHR) for seafarers, associated with specific hardware and software.

This SHP is defined as a "*device-system*" dedicated to the storage and collection of seafarers' medical data, which can be accessed in case of health needs.

The information contained in the SHP starts from the so-called "*minimum information*" (Table 13) that the SHP must necessarily have for each patient, namely:

- ***personal information***: essential for correct identification of the seafarer.
- ***basic health information***: basic physical data, such as height, weight, BMI, as well as measurements that can be carried out periodically and constantly updated, such as blood pressure, glycemia, laboratory results, etc.
- ***crucial health information***: allergies, intolerances, drug therapies, pre-existing pathologies, etc.

Type of Information	**Details**
Personal Information	*Name, Rank, Age, Nationality*
Medical History	*Family and Personal Medical History*
Medical Data – Vitals	*Height, Weight, BMI*
	Blood Pressure, Blood Glucose, and other essential vitals
Medical Data – Lab Results	*Any previous lab results if available*
Medical Notes	*Any Notes on Allergies, Prescriptions, Medicines taken chronically, etc.*

Table 13: *Minimum health information of a seafarer that should be included and updated in the SHP.*

Furthermore, the SHP must store the results of any diagnostic tests, screenings, medical examinations performed over the years, as well as all requests for assistance received by the TMAS, including symptoms, outcomes, and prescriptions.

In this way, the SHP will be able to play its role as a complete database of patient health information.

Thus, in the case of health needs, the treating doctor will have access to comprehensive and precise health information. This may allow intervening better, sometimes in a personalized way according to the specifics patient's needs - even if the subject cannot provide information to the caregiver himself. After all, the seafarer may not be able - or simply cannot remember - to tell some details about his health (e.g. drug therapies, test results, etc.).

Let see a practical example: *a patient presents a severe bacterial infection but is allergic to a specific antibiotic. The doctor knows this information and prescribes the best antibiotic to fight the infection, without risking dangerous adverse reactions which, onboard, could have fatal consequences.*

Structure and Functionalities

The SHP consists of two basic elements:

- **Physical Device**;
- **Software Platform**.

The physical component consists of a water-proof personalized USB drive provided to each seafarer, containing his electronic health records. The seafarer can always carry this pen-drive with him, keep it around his neck, in his pocket, or his set of keys.

Having the SHP in physical form allows to access the patient's health information even in case of a lack of internet connection. In this particular circumstance, the captain may communicate the seafarer’s health information to the attending physician, or send it to him with the instruments at his disposal (eg by telephone/radio).

Figure 10: *The Seafarer’s Health Passport (SHP) USB device.*

On the other hand, the software component consists of a specially created cloud platform, which can operate without the USB-drive mentioned above. The physician can access patient information remotely at any time, and update (if necessary) his health information.

The software allows to automatically update the pen-drive content when it is plugged into an internet-connected device.

Medical information is highly sensitive. For this reason, the main objective of the system was to comply with the regulations in force, classifying the information provided into two categories:

- Freely accessible information;
- Password-protected information.

"*Freely accessible information*" includes name and surname, place and date of birth, residence, blood group, any allergies, date of the "fitting certificate" (essential document for the seafarer, as it certifies suitability for the job). Even for the "*freely accessible information*" the user must provide his consent.

All other data are password-protected, according to the General Data Protection Regulations (GDPR), and the information transmitted is protected throughout its travel.

The aesthetic-practical aspects of the SHP are shown in detail in the *Appendix, Section 1*.

Access to Health Information

The seafarer has access to his health data. As part of the enhanced crew care program, the SHP guarantees access to this information also to the TMAS doctors when needed.

According to the GDPR requirements, the user can request the deletion of his data at any time. He can also continue using the SHP when he is not on board, as an *ordinary* Electronic Health Record (EHR).

Evolution and Future Perspectives

Although it was originally developed for seafarers, the SHP aims to be **a model of "advanced EHR"** that can be used in the future by other classes of workers or by all those citizens who may benefit from it. Among these, people living in remote areas, chronically ill patients, patients with handicaps, etc.

After all, telemedicine should meet healthcare challenges for remote patients. Having quick access to all the patient's known health information means not neglecting any detail in establishing a therapeutic regimen, and therefore providing high-level and safe health care.

The information stored on cloud servers reduces the risk of lost paperwork; besides, according to the literature, the risk of misdiagnosis (which represents 10% of the deaths of patients under treatment) is decreased.

The SHP could lead the way to a new perspective of crew-care which, for the reasons described above, could be extended to a much larger population in the future.

For example, through the SHP it is possible to carry out periodic health inspections and questionnaires, mental health surveys, to provide personalized care by analyzing health data, to provide the possibility of preventive and proactive measures, to propose questionnaires on service satisfaction to improve it further over time, etc.

The potential and possible implementations of SHP make it a promising tool, capable of laying the foundations for a solid protocol for the creation of electronic health records for workers and citizens.

The SHP has been introduced as a form of trial to seafarers working for *Marnavi* (Italy) and *CMA CGM* (France) shipping companies. No issues or difficulties were raised by approximately 600 seafarers using it voluntarily. [71]

The initiative was immediately appreciated, and the willingness of many to join the initiative was remarkable. By using the SHP, seafarers said they perceived "*a greater sense of safety and protection*". [71]

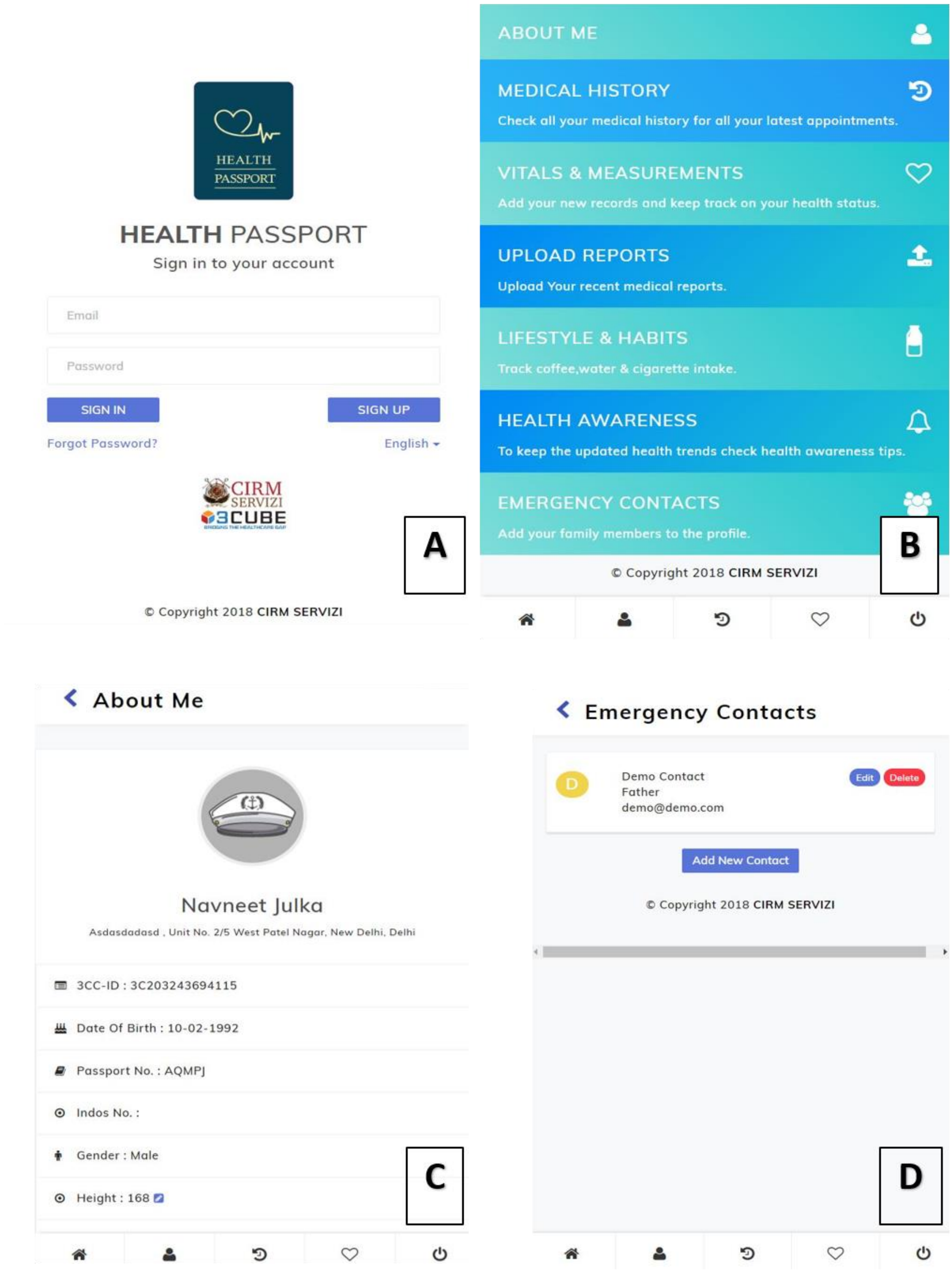


Figure 11: *Screenshots of the Seafarer's Health Passport (SHP): Home page (A), main sections menu (B), basic seafarer personal data (C), and emergency contacts (D).*

Challenges in the onboard pharmacy management

In the previous chapters, we have seen how the quality, safety, and efficacy of on-board care strongly depend on the qualitative and quantitative availability of drugs and medicaments on board.

The on-board pharmacy plays a crucial role in the health care provided to seafarers. But an improper organization can lead to very serious consequences.

Numerous factors can lead to complicated management of the onboard pharmacy.

Commercial ships navigate the oceans visiting different countries, with different cultures, traditions, and languages. The need to supply the medicine chest can occur anywhere in the world.

The captain is directly responsible for the supply and management of the onboard pharmacy. His pharmacological knowledge may be insufficient to always acting in the best way, and avoiding unpleasant misunderstandings.

Language barriers represent one of the main obstacles: just think that "*paracetamol*" in English can be called as such, or "*acetaminophen*".

Furthermore, certain drugs are not commercially available in some countries, and a correct substitution is necessary in order not to face sanctions and health problems.

The general organization of the onboard pharmacy, its periodic control, supplies, etc. can be very complicated.

Once we understood the challenges, we decided to create an application that had the potential to solve problems related to onboard pharmacy management.

Thus, the idea of "TelePharmaSea" (TPS) software was born. It is a specially developed application to optimize the management of the medicine chest of commercial ships without medical personnel onboard. [72]

All thanks to automated procedures that, by reducing the actions that are still carried out manually, can reduce the possibility of risk, accelerate the management of the onboard pharmacy, and thus improve the quality of health care on board.

Methods: Realization of TelePharmaSea

To overcome the linguistic barriers, the drugs identified in TPS are classified based on the **ATC (Anatomical Therapeutic Chemical) system** proposed and used by the WHO for decades. [73]–[75]

According to this classification system, the active ingredients are identified by an *alphanumeric code* that distinguishes them based on the organ or system on which they act, and on their specific therapeutic, pharmacological, and chemical properties (Figure 12).

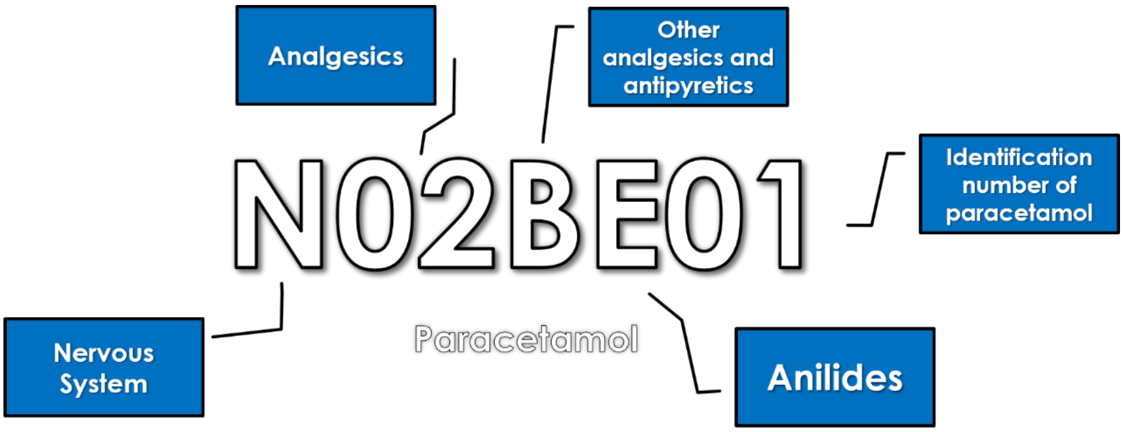


Figure 12: *Explanation and schematic representation of the ATC code of paracetamol.*

For those products that do not have an ATC code, a unique identification code has been assigned.

The lack of standardization among the various regulations and the differences between the several medicine chests are some of the main obstacles for proper and easy management of the onboard pharmacy.

For many fleets, the mandatory list of drugs and medicines to be kept on board is provided in paper or electronic format (usually in PDF or Microsoft Excel format). Captains therefore often have to "*manually*" consult these documents and to compare the ship supply with the current legislation. Some more advanced solutions provide special software for inventory management (similar to what happens in a warehouse, or a pharmacy) or more or less elaborate Excel sheets.

All of these solutions, while potentially effective, have a quite high margin of error.

In creating TPS we have analyzed the Medical Scales of different countries whose maritime activity is significant - regarding commercial vessels without a doctor on board.

These have been converted into a standardized format that can be easily interpreted and accessed from any device (computer, smartphone, tablet, paper format, etc.).

The first realization step consisted of identifying every possible medicine or medical instrument included in the various national and international regulations (*including the C.I.R.M. Medicine Chest, previously described*). Therefore, we cataloged every single item using the ATC system (or alternative specific identification code).

Thereafter a detailed database structure with several master tables was created to document the following:

1. *Active Ingredient*
2. *ATC Code / Unique System Code*
3. *Pharmaceutical Forms*
4. *Similar Active Ingredients*
5. *Special Notes*

Another master table was created to save Flag State Details:

1. *Flag State*
2. *Flag Icon*
3. *Country Associated*

Corresponding tables were thereafter structured to link the Active Ingredients and the Flag States as well as record the additional information:

1. *Flag State*
2. *ATC Code / Unique System Code*
3. *Type of Vessel**
4. *Minimum Quantity*
5. *Special Notes*

The data entry was performed by a team of computer scientists and approved by a team of pharmacists, who subsequently double-checked the entered information.

Each vessel is provided with credentials for a secure login that guarantees access to the platform.

More detailed information about the development of TPS in purely IT terms are available in the publication: "*TelepharmaSea: Proposing A novel approach to Automate, Organize and Simplify Management of Medical Chest Onboard Commercial Vessels*". [72]

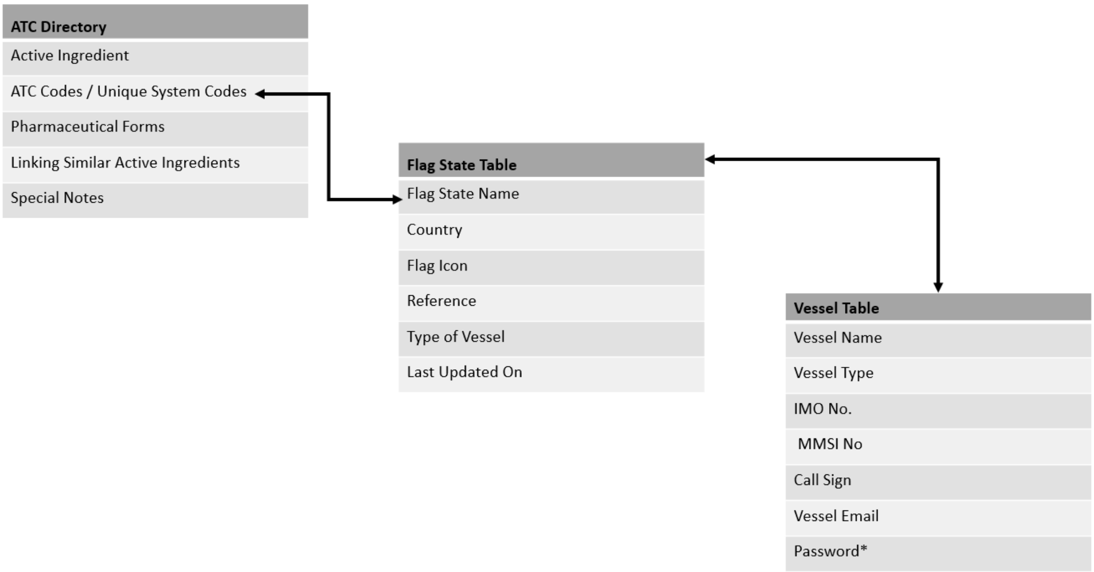


Figure 13: *Simplified relation of some of the various master tables.*

New management possibilities for the Commander

The management of the onboard pharmacy is made easier for the commander from several points of view: automation, alerts, notifications, etc.

The detailed workflow of officers' activity is shown in Table 14.

Add New Inventory (Batch numbers)	The officer responsible for the medical chest on the vessel can easily update the inventory and manage stocks with different expiry dates. This allows for more accurate analysis of the medical chest and timely restocking alerts.
Update Inventory	With the system being pre-setup as soon as the vessel logs in, the work of the officer responsible is reduced to ensuring the stock is routinely updated.
Complete Checklist	Ideally, it is recommended for the vessel to complete the checklist every quarter. This is also the frequency for the E-certification. However, the officer responsible can run through the checklist at any time to document medical management. These records are synced to the Pharmacist.
View Certificate of Compliance	Once the certificates are issued by the Pharmacist, the Officer responsible can view the same on the platform ensuring an automated digitalized archive of the records.

Table 14: *Workflow of officers' activity.*

Role of the Tele-pharmacist

In parallel, a trained pharmacist assists the commander, controls the information in the master tables as well as completes the certification protocol to generate an E-Certificate of conformity/non-conformity for the vessel.

The detailed workflow of the pharmacist's activity is shown in Table 15.

Add / Edit Item to Master Database	The Pharmacist can Add an item to the Master Tables. For this, the Pharmacist must mention the globally accepted ATC code or if not available ask the system to generate a Unique System Code.
Add / Edit Flag State	Flag State Medical Scales are not routinely updated. However, if there will be updates, the system permits the Pharmacist to make changes which will automatically sync across and intimate the vessels and companies.
Add / Edit Pharmaceutical Forms	Over time medicines may be made available in multiple pharmaceutical forms or be available for different purposes. It is essential to mention the Pharmaceutical form as the use and indications can vary. Should there be a need to update or add, the Pharmacist is permitted to make the required change.
Add / Edit Company & Vessel	To be able to perform E-Inspection and E-Certifications it is important to link the system with the vessel/company. This allows for a 2-way flow of information required.
Digital Review of Checklist from Vessel	The Checklist which was initially completed and shared using more conventional digital formats such as word or excels now has a more secure and easier way of sending this information directly through the platform. No additional email and attachments would be required. The secure system can only be accessed by authorized personnel.
Digital Review of Inventory from Vessel	The updated inventory of the vessel is synced periodically with the checklist which allows the Pharmacist to easily review the quantities. The system provides automated alerts to the Vessel and the Pharmacist thereby allowing them to easily review the same.
Assisted E-Certificate Generation **(2-Step Verification)**	The automated system assists the Pharmacist to quickly review the inventory based on required minimum quantities and the responses from the

	checklist to authorize the compliance certificate or alert the vessel of any incomplete measures.
Assisted Order Form Generation (2-Step Verification)	Order Forms generally take the longest time and can be confusing with the correct Pharmaceutical form, Active ingredient, etc. should be mentioned for it to be correctly supplied to the vessel. Therefore, to mitigate the challenges, the system allows the Pharmacist to auto-generate an Order form by automatically calculating the minimum quantities required. This saves time and prevents manual errors that could arise using the conventional forms of order forms.

Table 15: *Workflow of pharmacist's activity.*

A wider look and future perspectives

The management possibilities of TPS may offer unique possibilities not only to the shipping company but also to TMAS called upon to assist the vessels.

For example, the company can:

- reduce the costs related to incorrect or excessive supplies of drugs;
- not to face penalties due to improper management of the onboard pharmacy;
- achieve a general reduction of costs due to the improvement of the healthcare offer provided to crews, with a consequent reduction in hospitalizations, diversions, medevac requests, etc.

At the same time, the TMAS will have quick access to the on-board pharmacy, without delays due to the request and subsequent communication of the most recent inventory by the ship.

The system is complemented by a telepharmacy service allowing communication and interaction with a team of pharmacists helping the captain and his company towards better management of the onboard pharmacy: easy compliance tracking, remote inspections, and guidelines for smart re-stocking and disposal of medicines onboard.

Continued efforts can lead to a smart re-stocking effort for the industry bringing huge savings if correctly implemented.

The platform will also provide useful statistical data, such as trends of consumptions of medicines, which can be easily linked with the type of Medical Event. The effectiveness of drugs and general prescription patterns could also be investigated. This can lead to several insightful studies and a collaborative approach on highlighting the use of Medical Chest onboard.

TelePharmaSea seeks to be a solution to the problems afflicting the on-board pharmacy, starting from an accurate understanding and referencing the challenges that currently exist in achieving the same.

Chapter V - Conclusions

Health care onboard commercial vessels is a great challenge for modern medicine. Seafarers are exposed to a greater risk of illness, injury, and stress than the population ashore. In a context of high risk and maximum alert, healthcare comes *remotely*, thanks to modern telehealth technologies.

As described in the previous chapters, much of my research activity investigated the main health problems of seafarers, as well as the challenges and obstacles that medicine has to overcome to provide appropriate assistance to this class of workers. Seafarers have been chosen as a "*remote patient model*" - far from health facilities, for whom assistance and solutions to health problems can be solved remotely thanks to telehealth.

Improving the services provided to a distant and difficult to reach population may improve the assistance provided to the rest of the community. Telemedicine systems could be effective for remote patients as well as for “*non-remote*" contexts, such as in the ordinary medical and pharmaceutical practice, or during emergencies.

Future research can be carried out to improve remote assistance platforms and explore the service for a larger population, starting from patients living in internal areas, far from health facilities. Even in the most developed countries, part of the population lives in inland or remote areas. For these people, access to care can be difficult; the situation becomes even more complicated for elderly, disabled, and/or chronically ill patients.

Thanks to telemedicine, these populations can have access to healthcare services, and be visited remotely by a doctor.

Telemedicine Corners

The lack of infrastructure and the shortage of qualified health personnel are problems that affect any country, albeit with different modalities and gravity.

In small inner settlements, where individual doctors' surgeries and pharmacies may represent the unique access point to care, the installation of a *telemedicine corner* could represent a big step forward for the healthcare offer provided to citizens.

Once installed, this corner will guarantee access to advanced diagnostic tests, as well as contact with a remote-connected specialist doctor. [76]

Telemedicine corners (also called *telemedicine points*, or *telemedicine cabins*) are rapidly spreading around the world. They usually consist of a cabin where the patient can sit and find various diagnostic instruments, as well as a screen and a system allowing video calls with a remote-connected physician.

The advantages that these structures can bring are different:

1. the possibility of conducting independent health checks close to home, with considerably reduced waiting times;

2. quick access to care close to home - especially useful for patients with reduced mobility, or in an emergency context;
3. to provide access to specialist exams otherwise not present in the area;
4. considerable possibilities of constant monitoring for the chronically ill (e.g. diabetics or cardiovascular patients);
5. to provide an access point to care in contexts where this is traditionally not available, such as workplaces, factories, schools, universities, etc.

The patient enters the *cabin* and follows the instructions on the screen, eventually under the guidance of an operator present on site. [76] Each telemedicine corner can have a different composition, and allowing different diagnostic exams and checkups. Normally, the cabins can be customized according to their planned location and according to the final user population. Commonly, it is possible to measure blood pressure and oxygen saturation, as well as body weight, height, and temperature, test visual and hearing acuity, perform an electrocardiogram, and, last but not least, have a teleconsultation with a doctor. [76]

The whole operation takes a few minutes, and the test results are sent immediately to the doctor connected with the patient. Based on the data obtained, the physician can provide further information to the citizen, such as asking to perform a given test in the cabin. [76]

Citizens can use the service in different contexts. For example, when the doctor is not available, or if the patient has limited mobility, or during an emergency, or simply to reduce waiting times. There are no limits on where a telemedicine corner can be installed: health centers, pharmacies, universities, public places, workplaces, etc. The Centro Internazionale Radio Medico (C.I.RM.) has started installing telemedicine corners onboard commercial ships, and the same is being done by privates and agencies as a form of protection for their employees. [77]

According to the latest literature, the benefits and accessibility guaranteed by the service determined a high degree of satisfaction of the population, especially among young people. The potential availability of telemedicine cabins (*anywhere and at any time*) is a natural consequence of the modern tendency to consume and act without limits in terms of time and location. [76]

In summary, they represent one of the telemedicine's possibilities to reach people and places where health care is not present or difficult to perform.

As the Telemedicine and Telepharmacy Center of the University of Camerino, we have launched projects aimed at introducing telemedicine corners in different settings to enhance the healthcare offered to the population. Since 2018 we have been studying and introducing telemedicine solutions (in the form of telemedicine cabins) in contexts such as:

1. retirement homes and "RSA" (in Italian "*Residenze Sanitarie Assistenziali*");
2. rural and inland area pharmacies (in particular the Marche region pharmacies located in the areas affected by the 2016 Earthquake) [78];
3. campus and University residences.

Future research should assess the degree of user satisfaction, compliance with regulations and guidelines, and to evaluate the impact of these initiatives on healthcare systems.

Key Aspects of Telehealth Services Delivery

The research activity carried out in these 3 years of doctoral course has allowed me to identify 6 key factors that must always be respected and that scientific research must constantly monitor to optimize telemedicine services and give a positive boost to the evolution of Telehealth.

1. **Physician Guidance:** the role of the physician must be preponderant in telemedicine research and development. The creation of e-Health devices and platforms must be carried out under the guidance of a doctor; it is, in fact, the first user of this technology, and the professional with the greatest experience in the healthcare field. According to the American Medical Association (AMA): "*physicians should support the ongoing refinement of technologies and the development of clinical standards for telehealth and telemedicine*". [79], [80]
2. **Effectiveness of Telehealth Services:** The effectiveness of telemedicine solutions must be demonstrated to guarantee a quality service and above all, patient safety. According to recent literature, telemedicine proved in most cases to be equivalent to in-person care. Perfectly comparable results were

reported, in particular, in the mental health, teleconsultation, and telerehabilitation sectors. [20]

However, due to a large number of variables involved, the diversity of each medical branch, and the wide variety of conditions that patients can present, telemedicine practice services must be continuously monitored and evaluated.

Evaluating the performance of new technologies is also essential from an *economic* point of view, as final buyers and investors are concerned about the return on investment. Therefore, continued demonstration of value in actual clinical experience is required. Several national medical societies are developing guidelines addressing telehealth. [20], [81]

The American Telemedicine Association (ATA) established an accreditation program evaluating the quality of real-time assistance, patient satisfaction, transparency of pricing and operation, and strict adherence to regulations. [20]

The performance and effectiveness of telehealth services are a critical priority that must be continuously addressed.

3. **Privacy and Security:** Telemedicine systems are becoming more and more complex and integrated; data travels and accumulates. Health information is no longer just paper, and file storage can take place on cloud services, and be accessible from anywhere.

   This upward trend means that *privacy* and *security* become increasingly important and complex to manage. In the United States, for example, federal and state guidelines on privacy and security in telemedicine are not standardized, potentially leaving some regulatory gaps [82]

In Europe, the General Data Protection Regulation (GDPR, EU 2016/679) has tried to standardize EU laws to guarantee citizens greater control of their data. But there is still a long way to go for univocal legislation recognizing telemedicine in all its nuances. [20]

Standardized regulations are crucial and should be based on scientific evidence and best practice, guaranteeing appropriate safeguards. Research proposing solutions in this area is a priority.

4. **Patient-physician relationship:** Technology has evolved the perception of healthcare and has led to a change in the doctor-patient relationship. The latter now has access to a large amount of health information, it is much more independent, and the possibilities of communication with the doctor are greater. At the same time, the distance and communication through devices could make this relationship quite cold and detached, especially in the case of not very young users.

   We must not forget that although new models of care continue to emerge, the role of the doctor and his ethical responsibility always remain the same. Following the Guidelines proposed by the AMA Council on Ethical and Judicial Affairs, doctors must inform patients about the characteristics of telemedicine, its pros, and cons, guide them in the use of these new technologies, and support its diffusion especially among patients who could benefit greatly. [80]

5. **Human Factors:** User-centered design that allows the patient to use these technologies with simplicity and perceive their advantages is essential. [20] Both physicians and patients must be able to access intuitive, easy-to-use equipment, and software. [83], [84]

   This ease of use must be constantly checked, perhaps by creating a feedback system, or by proposing periodic service satisfaction questionnaires. Knowing what the end-user thinks is essential to find the right direction to move.

6. **Electronic Health Records and Data Integration:** One of the greatest possibilities offered by telemedicine is the implementation of Electronic Health Records (EHRs). These are electronic medical records in which all information on the patient's health is collected. Both information acquired through telemedicine and in frontal visits can be stored. The EHR is also a database of all patient reports and laboratory results.

   Access to these EHRs, in compliance with current privacy regulations, can be guaranteed to general practitioners, medical specialists, and hospital, ensuring quick access to crucial information on the patient's health - information that citizens often may not provide and may not remember (such as complex ongoing pharmacological therapies). [85], [86]

   A well-structured and accessible EHR may improve the quality, safety, and productivity of provided healthcare, guaranteeing more medical specialists access to a greater number of certified and documented information. [85], [86] The EHR gives immediate access to the patient's health information even when the latter is unable to provide it, e.g. in case of an emergency or first aid intervention, or in case of loss of consciousness. [87]

It will be crucial for the immediate future to ensure that all telemedicine tools and platforms work seamlessly together. [20]

To date, the various telemedical devices tend to work exclusively with their platform and are unable to integrate patient-generated data from other monitoring devices. [20], [88]

This will be essential to prevent the pieces of information acquired from being fragmented and scattered across different platforms.

To meet this challenge, the American Telemedicine Association (ATA) has encouraged unique EHRs being incorporated for patient-generated data from telemonitoring apps and devices. [20]

A promising initiative is given by the SMART Health IT platform, in which standardized and open-source Application Programming Interfaces (APIs) allow clinical Apps to operate jointly and integrate health data into a single EHR. [89]

Despite numerous potential benefits of EHRs, their implementation collides with barriers and issues, such as *technical limitations, attitudinal constraints-behavior of individuals, organizational constraints, standardization and regulations limits, etc*.

However, according to several authors, the biggest barrier to the spread of EHRs is *resistance to change*.

Finally, the EHR could be an excellent tool for concrete public health and occupational health investigations.

Figure 14: *key factors that must be respected and that scientific research should constantly monitor to optimize telemedicine services and give a positive boost to the evolution of Telehealth.*

Practical proposals for future research

Although randomized controlled trials represent the standard for evaluating the efficacy and safety of healthcare delivery, this type of study may not be applicable in all telemedicine contexts.

The evolution of scientific research has led to the development of new rigorous study methodologies, capable of carrying out assessments even in complex and variable contexts such as those of eHealth. [90]

Among these, we have *pragmatic trials, cluster randomization, large, simple trials, factorial designs, and stepped-wedge designs*. [20]

New techniques and tools are gradually becoming available to evaluate healthcare interventions, in particular systems providing for the integration of data such as EHRs, laboratory results, diagnostic images, drug therapies, etc. [91], [92]

The growing interest from scientific research towards telemedicine, the increasing number of researchers employed by health systems are promising factors for faster and more effective research on telemedicine. [93]

Telemedicine and the SARS-CoV-2 Pandemic

With more than 70 million confirmed cases and more than 1,600,000 deaths worldwide in January 2021 [94] the SARS-CoV-2 pandemic shattered the Health Systems of the major world countries, many of which were unprepared, without methods and infrastructures to guarantee complete health coverage.

The COVID-19 emergency required urgent action to transform the provision of health care by freeing the power of digital technologies.

In the United States, there has been some considerable progress, particularly in the past few years, through federal and state laws promoting the integration of telemedicine into the National Health System. [95]

Legislative changes have also been carried out by some Asian and European countries, such as the United Kingdom and France. [96]

As the COVID-19 pandemic progressed, the telemedicine platforms have been subject to major investments. In China, the Miaoshou Doctor platform, which provides advanced telemedicine, tele-pharmacy, and insurance services via an online hospital, proprietary applications, and software, as well as direct drug distribution, is currently valued at more than $ 1 billion. [97]

BestDoctor is a Russian private health insurance offering 24/7 telemedical assistance and it has recently secured $ 4.5 million in funding. In the United States, Gyant, a platform that works with numerous hospitals and health insurers, has closed a $ 13.6 million financing round. [97]

Remote assistance systems proved to be one of the greatest opportunities of the moment. However, the emergency made it clear that in most contexts, current implementations were insufficient. Those who have been provident and far-sighted have been successful, simply operating in the "*traditional*" way, that is remote consultation with real doctors behind it. [97]

Through remote care platforms, the doctor can monitor the patient using essential diagnostic equipment (blood pressure, heart frequency, temperature, blood oxygenation).

Although Italy has been the second COVID-19 outbreak of infection in the world and the legislation on telemedicine was enacted in 2012, the latter is not yet included in the essential care guaranteed to all citizens by the National Health System. As the pandemic got worse and worse, on 24th March 2020 the Italian Ministry for Technological Innovation and Digitization and the Ministry of Health, together with the National Institute of Health and WHO have finally published an open call for bids for "telemedicine and monitoring system technologies". [96]

Despite this, telemedicine has not seen an appreciable spread and improvement, unlike what has happened in other countries. In France for example, the Minister of Health promulgated a decree on March 9th, 2020, which envisaged the reimbursement of the costs of teleassistance services and tele-expertise by the National Health Insurance (NHI) for all COVID-19 positive patients.

There are legal and ethical challenges that telemedicine still has to face before it can finally become an ordinary integrated assistance system. [22], [98] The SARS-CoV-2 pandemic has pushed some authorities in one direction, that of promoting the use of digital technologies, so far way too neglected and underestimated.

Implementing telemedicine systems to monitor asymptomatic patients or with mild symptoms can reduce hospital overcrowding, and therefore the chance of gathering of people, with an increased risk of contagion of both patients and health personnel.

Telemedicine solutions shall be used to check the health of people suffering from pre-existing and/or chronic diseases, reducing the number of frontal visits in clinics and hospitals. A digitized care strategy should be applied in situations of lockdown and limitation of movements, especially in those areas where healthcare facilities are far away, or for those patients whose mobility is reduced. The validity of telehealth solutions is confirmed by the example of some remote areas of China, where coronavirus mortality was significantly higher than in more populated ones and with more health care facilities or telemonitoring systems. [95]

The aforementioned telemedical solutions may include the monitoring of hospitalized patients: through tested telemonitoring devices and systems the patient can communicate and be video-monitored by the doctor in an adjacent room or another wing of the structure, or even from home. This would eliminate any risk of infection for both individuals. [95]

The entire system should be managed by specially designed software, which guarantees stable connections, maximum security of information exchange, and respect for privacy. The devices must communicate automatically, letting the doctor read the results, without the patient having to enter them manually, with the risk of making mistakes. [99]

The sick patient in home isolation could be video-monitored and have basic analysis devices, such as a thermometer and wireless pulse-oximeter.

Patients affected by chronic diseases should get even more attention; therefore, it will be up to the physician to decide what equipment should be included (e.g. glucometer for diabetics). The system should also have an "*emergency*" function that the patient can use to contact the doctor or nurse for help.

Video communication is a crucial part of the whole system, as it allows the doctor to guide the patient in the measurement operation, monitor his condition, speak and listen to his problems, etc. The practice of medicine is an intrinsically moral activity, founded on a "pact of trust" between patient and doctor and it must remain the same, even in the digitalized context of telemedicine.

I am proposing a framework for the application of Telemedicine and Telemonitoring technologies (Figure 15). This integrated system may guarantee controlled management not only of positive patients but also of asymptomatic and chronically ill patients, in the novel coronavirus outbreak and/or in similar emergencies. [99]

Telemedicine has already been proved to be effective in the past, during SARS-CoV (Severe Acute Respiratory Syndrome-Associated Coronavirus) and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) emergencies, as well as Ebola and Zika. [96]

Numerous efforts are required from all countries to ensure that epidemics can be faced effectively. In this perspective, if telemedicine were fully integrated into a national health system, it could prove itself to be a valid instrument to guarantee continuity of care, reducing the risk of contagion, especially among health professionals. It would also translate into a reduced overcrowding of health facilities and a minor depletion of doctors and nurses. [99]

The COVID-19 pandemic is a call for action: the political response of nations should include clear provisions for the assessment of these emergency measures. As a second step, when the emergency phase will be over, it will be important to understand if these new telemedical approaches can help increase clinical efficiency. This information will be crucial in evaluating whether such a health model should be permanently integrated into the traditional health system.

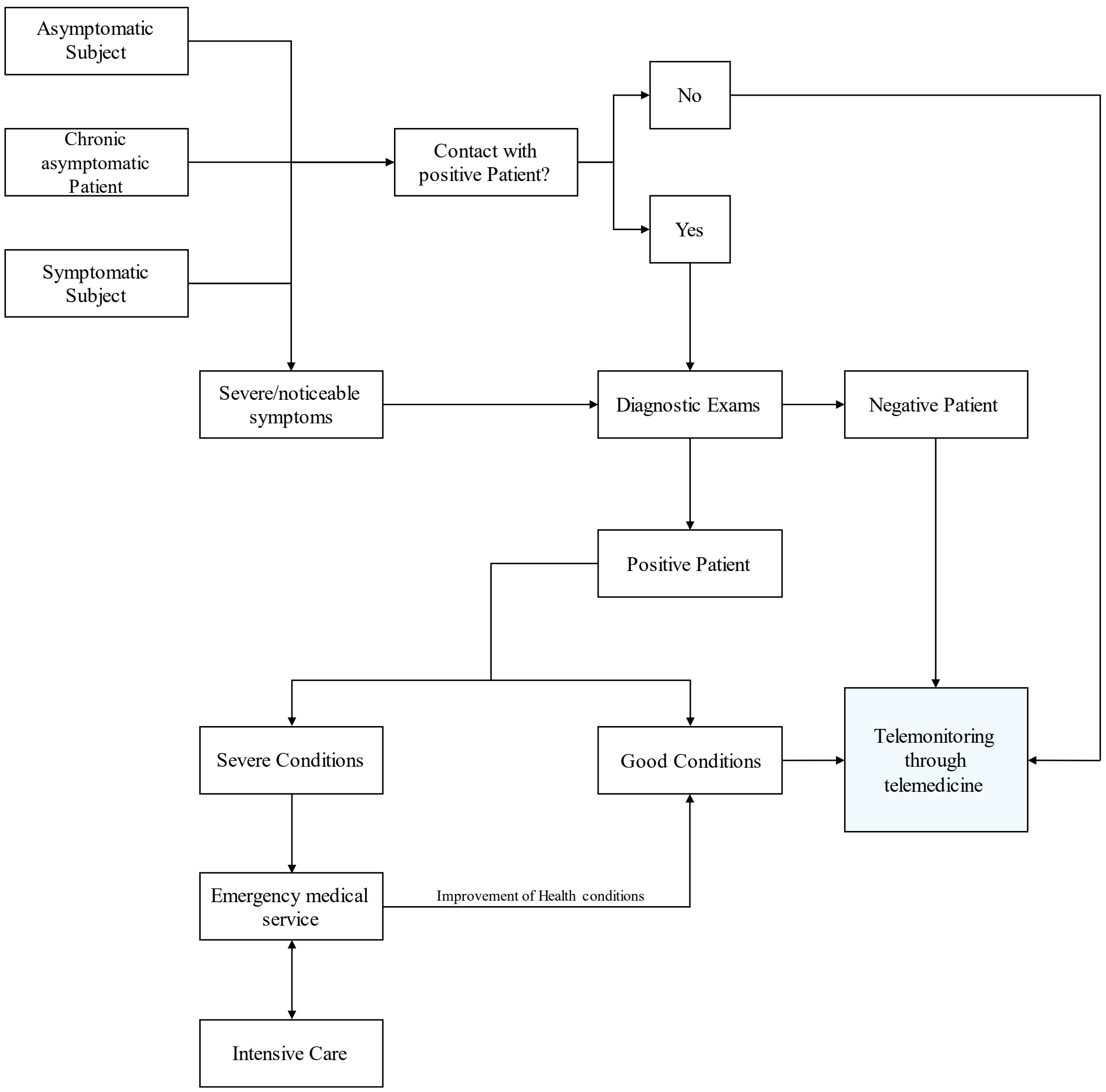


Figure 15*: proposed telemedicine framework for the COVID-19 pandemic and similar emergencies.*

Final Thoughts

SARS-CoV-2 has forced the world's health systems to react abruptly. In many countries, the pandemic has changed the way patients receive care from their doctors. Modern technologies allow being visited by health professionals without being in the same room, thanks to telemedicine or telehealth.

Over the years, scientific research and analytical work have highlighted the potential benefits of telemedicine, in particular concerning the management and monitoring of chronic health conditions, such as asthma, diabetes, and heart diseases. Despite this, before the novel coronavirus outbreak, the situation worldwide was quite "patchy".

In the USA, telemedicine was not yet so widespread mainly due to insurance issues. Most states required insurers to cover remote services but didn’t stipulate payment parity. This means that reimbursements for a telemedical visit could be less than 50% of the cost of a frontal visit. Doctors had no incentive to offer telehealth services, and therefore many didn’t bother.

With SARS-CoV-2 made its appearance, everything changed. The pandemic has disrupted the health systems of the world's leading nations. Immediately, the usefulness - and above all - the need to offer remote medical consultations emerged clearly. Performing preliminary remote examinations made it possible to determine whether or not a patient required a *face-to-face* visit. This has led to the diversion of many non-urgent cases from hospitals, reducing overcrowding, and leaving only the most serious and really necessary cases to frontal examination.

Furthermore, delicate and at-risk patients, such as the elderly, the immunosuppressed, or the chronically ill, could get advice from a doctor without entering a healthcare facility. The number of patients in waiting rooms has also been reduced, reducing the risk of nosocomial infections.

We have moved from a reality where telemedicine was not fully supported by the medical community and insurance companies but, once faced the critical need, it was suddenly embraced by both.

In the US, many health insurers waived *out-of-pocket* costs for telehealth services, allowing more patients to access telehealth care. At the same time, the federal government and several states enacted emergency laws to raise reimbursement rates for remote healthcare providers.

Certainly, telemedicine has some limitations - as we have discussed in previous chapters. However, in most cases, it should be better to have a "*virtual*" visit rather than not having one at all.

Telemedicine can help reduce gaps in healthcare coverage. To date, there are not enough providers able to reach the most distant and vulnerable communities. Simply by using a smartphone and/or an internet connection, we could reduce these distance-related disparities.

But what will happen once the COVID-19 emergency is over? Will telemedicine retain its importance or will it once again be considered of secondary importance, and perhaps resorted only in an emergency?

Currently, we have only a few certainties, other than the fact that keeping access to remote care is essential, as social distancing will likely have to last a while. Hopefully, as patients and doctors get more used to the technology, more benefits of telehealth will emerge.

In Italy, even today, telemedicine has not occupied the place it deserves. Not even the novel coronavirus has provided the hoped *boost* that we have seen in other countries.

The situation is very different from other European countries, where the potentials and advantages of telemedicine have been understood.

From the most recent data, and according to a study we recently carried out, telemedicine and tele-pharmacy services are quite uncommon among pharmacies, although a certain timid diffusion is slightly appreciable. [100] Besides, telemedicine is completely absent in many healthcare facilities, such as retirement homes, rehabilitation centers, etc.

In Italy, although there are still regulatory and legal challenges, these gaps would seem to come mainly from a "*conservative*" mentality typical of some health professionals who, with skepticism and scarce information, see these services as an attempt to supplant the “ordinary” healthcare practice.

Telemedicine is something else.

It is the natural evolution of medicine which - thanks to research and technology - manages to extend, translate, and reach those citizens who, under normal conditions, are not easily accessible.

“Ordinary” medical practice undoubtedly represents the highest form of care: speaking face-to-face, and not through a device, can favor a positive development and evolution of the doctor-patient relationship. A machine or artificial intelligence can never replace the doctor as a social, human, and empathic figure.

However, there are complex situations in which the doctor cannot be present or available; and just like him, the instruments necessary to provide the right care may be absent. Yet, the patient cannot be physically visited for different reasons, such as in the case of reduced mobility, severe infectious disease, and quarantine.

In these settings, telemedicine should be firmly introduced, as an extension of the traditional medical practice, like a virtual bridge connecting doctor and patient, overcoming the obstacles given by the distance, both physical and technological.

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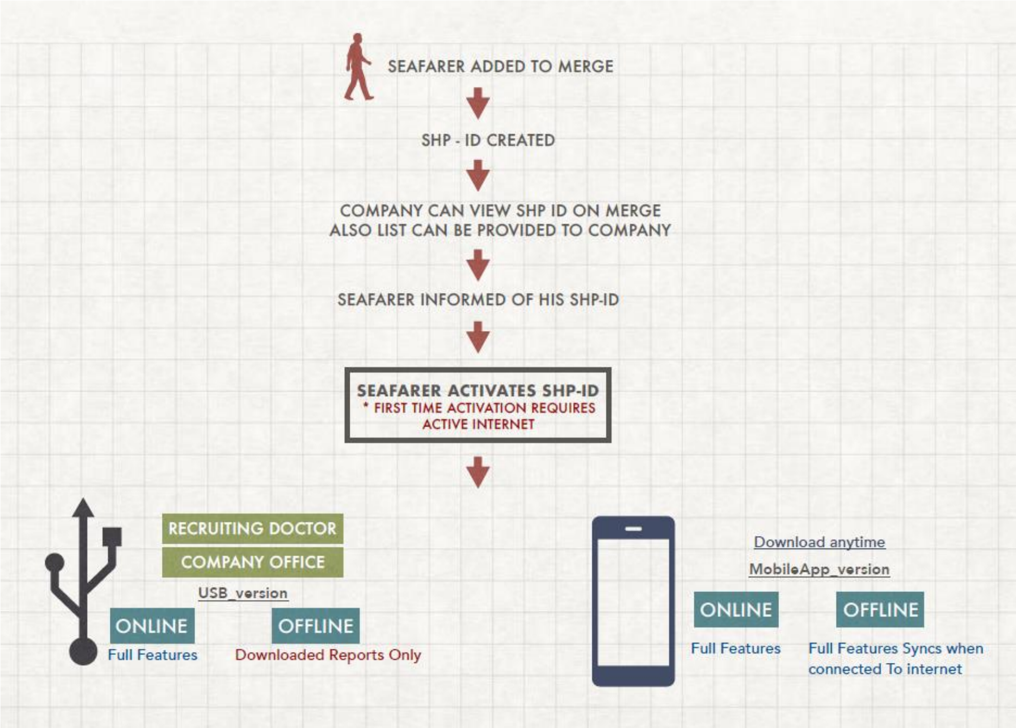
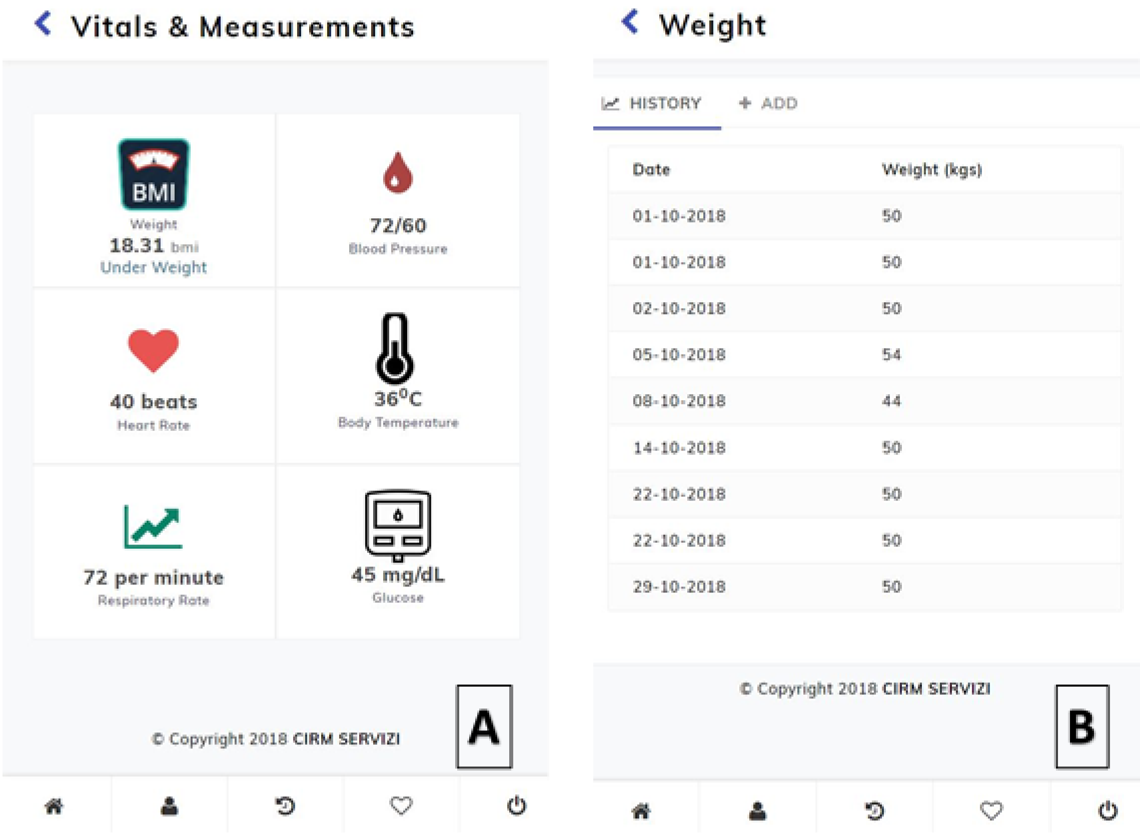
Appendix

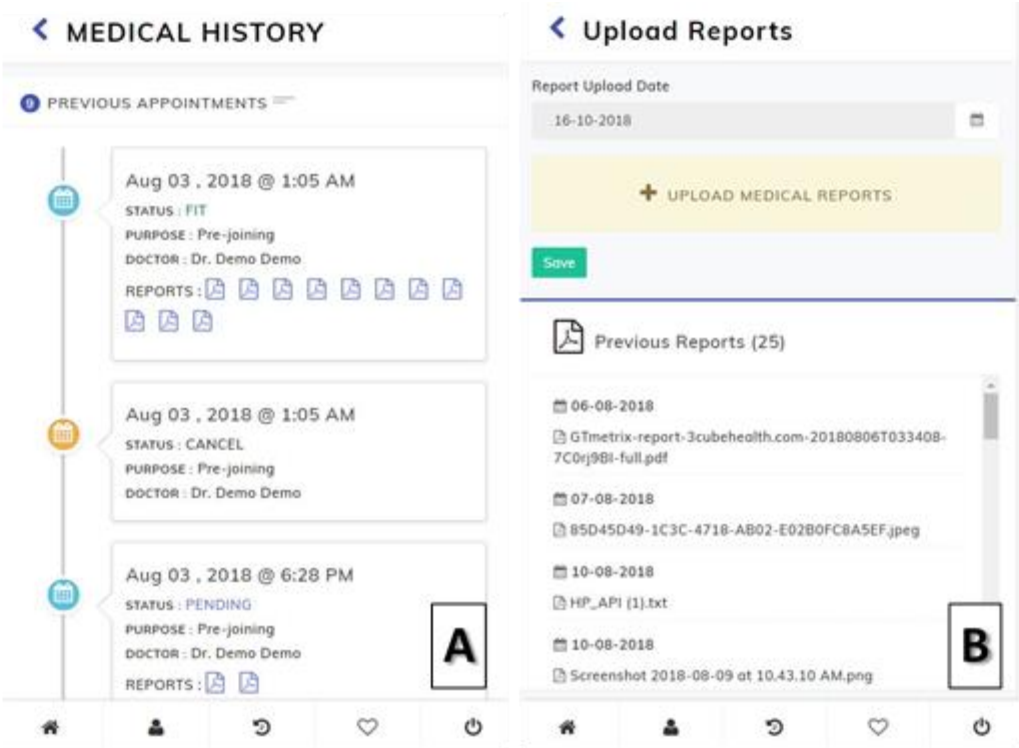
Section 1 – Seafarer's Health Passport (SHP)



Appendix, Figure 1: *Workflow of the Seafarer's Health Passport (SHP).*



Appendix, Figure 2*: The medical history section of the Seafarer's Health Passport. The seafarer can find in this section the files of the reports of his medical examinations uploaded by recruiting clinics and shared with Telemedical Assistance Services (A). Updated reports of the results of new clinical tests that can be downloaded by the seafarers through the section shown in panel B.*



***Appendix, Figure 3**: Screenshots of Vitals and Measurements section of the Seafarer's Health Passport. At any time, the seafarer can review his basic vital data (A) stored in the SHP, and other health information (B). These data constitute a diary that the seafarer is free to consult.*