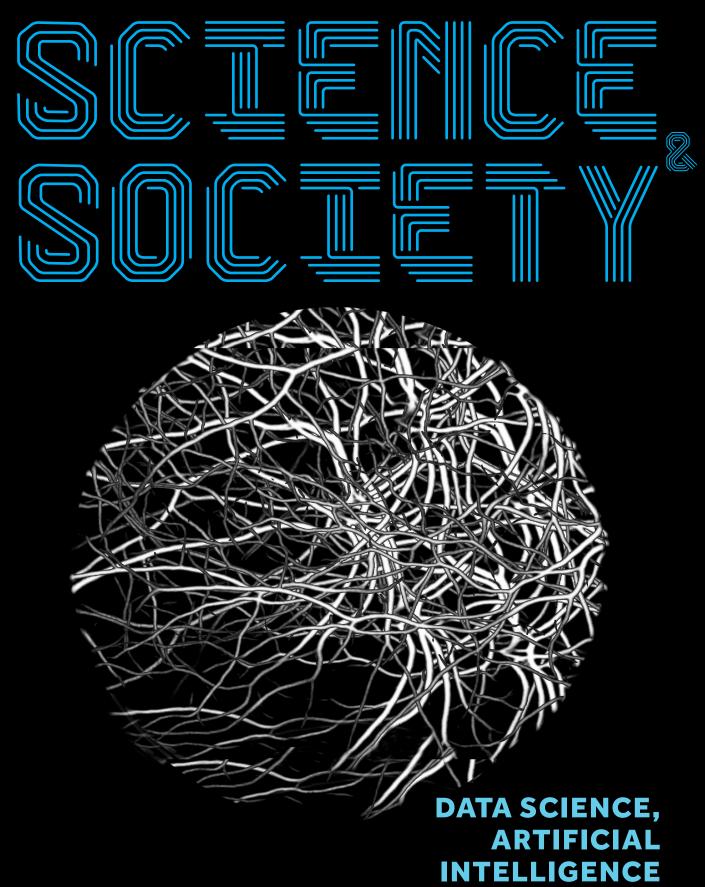
AND HEALTH

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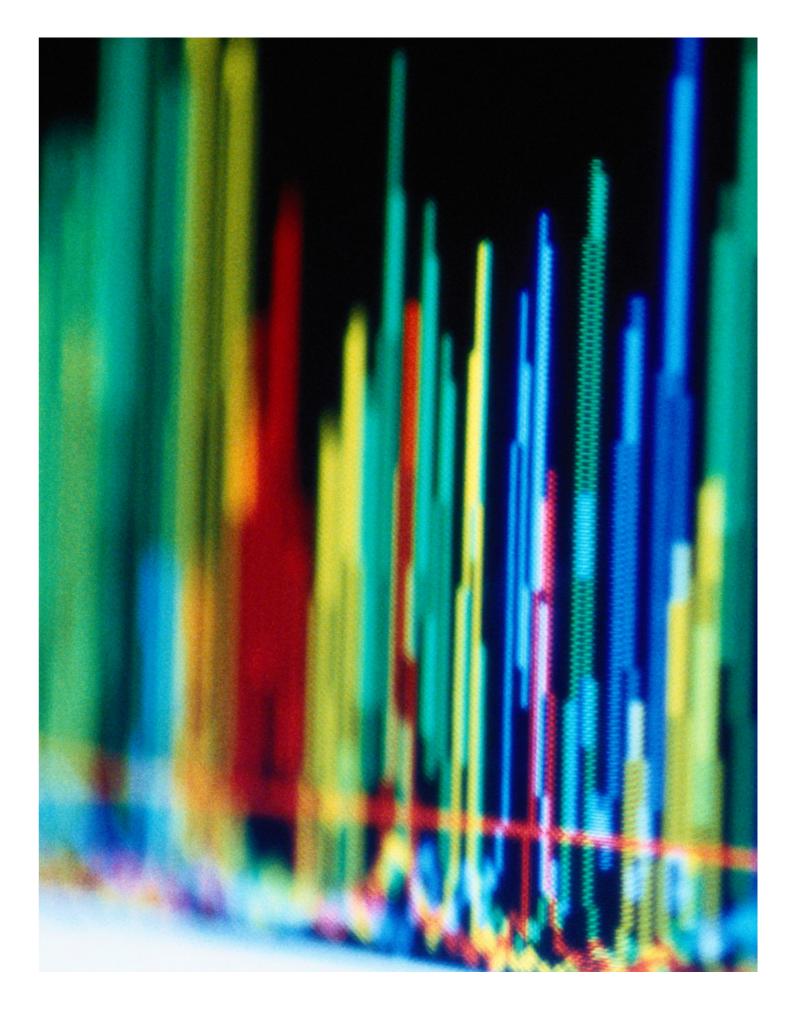
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COVER PHOTO

Self portrait, image obtained from the automatic detection of the retinal vascular network, conceived within the scope of the project Other Portraits and Self-portraits © Renato Roque, 2018, under the SCREEN-DR Project CMUP-ERI/TIC/0028/2014, supported in part by the European Regional Development Fund (ERDF) through the Operational Programme for Competitiveness and Internationalization COMPETE 2020 Programme, and in part by the National Funds through the Fundação para a Ciência e a Tecnologia (FCT).



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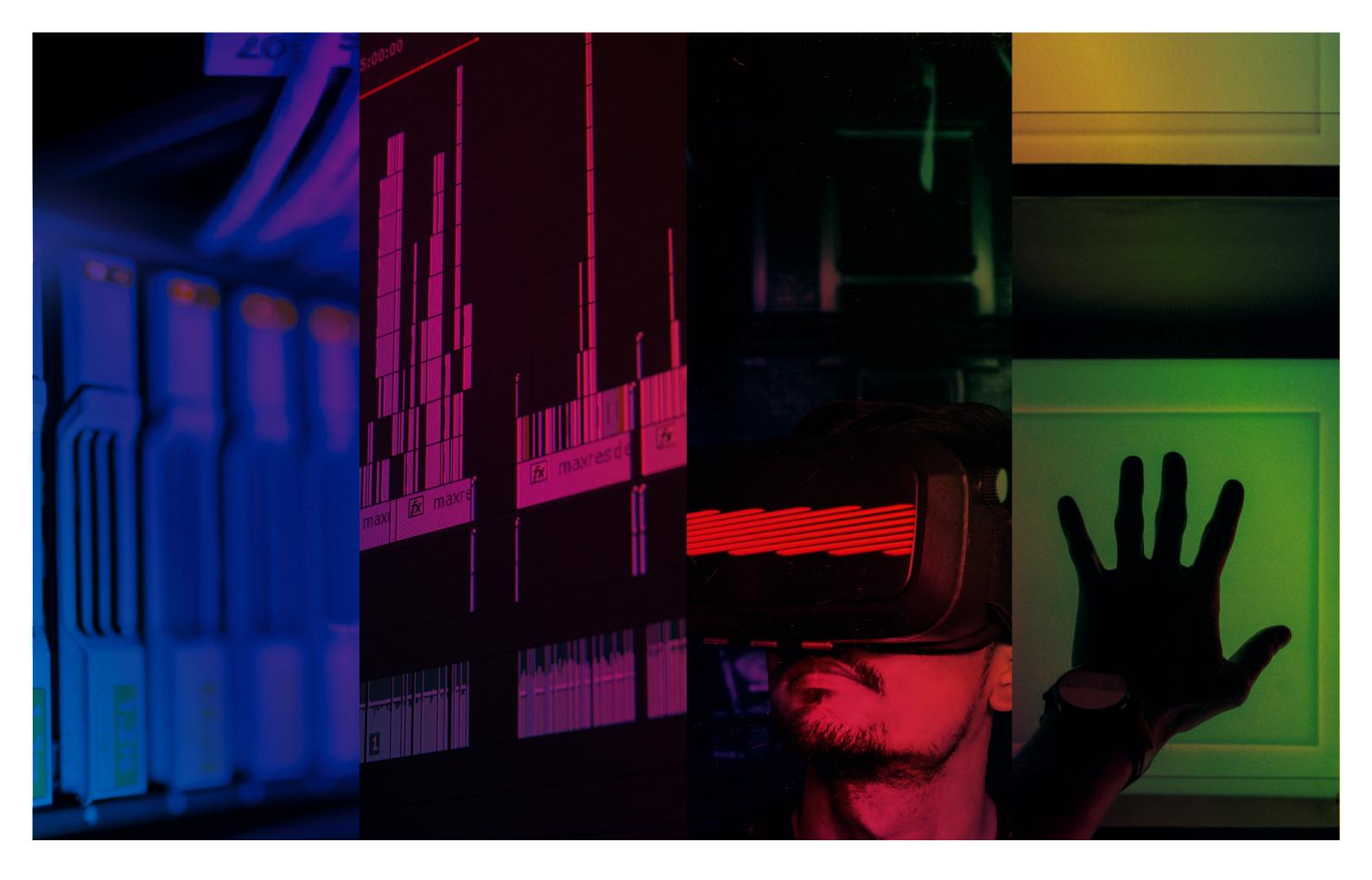
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SCIENCE & SOCIETY

This new magazine "INESC TEC Science & Society" aims to disseminate science to society and to contribute to ongoing debates, aiming in particular at the managers, politicians and technicians of the systems in which the themes discussed are applied. The magazine will have two issues per year, one in the fall and one in the spring. Each issue will address a special topic, without excluding other articles of opportunity, and the autumn issue will have the same theme as the Autumn Forum that INESC TEC has held since 2015.

It was with great satisfaction that I accepted to be the coordinator of the series and I must say that the adhesion of the entire editorial team, the technical and communication services of INESC TEC and all the authors we invited was exceptional. My greatest thanks to all of them.

This first issue has as its special theme the science of data in health, an area of great opportunity in the circumstances that we are going through. We are considering it as a test of our capabilities in which we seek to define the style most suited to our purposes, which is a complex task because it is about implementing a new communication culture and a new way of intervening in the debate of policies most influenced by technology.

We sincerely hope that the result is to your liking.

ARTUR PIMENTA ALVES ^(1,2) ⁽¹⁾EMERITUS PROFESSOR OF FEUP

⁽²⁾ASSOCIATE DIRECTOR AT INESC TEC artur.p.alves@inesctec.pt WE ARE INESCIEC WE ARE KNOWLEDGE GENERATION WE ARE SCIENCE-**BASED INNOVATION** WE ARE **NETWORKED INTELLIGENT SYSTEMS** WE ARE **POWER AND ENERGY** WE ARE **INDUSTRIAL AND SYSTEMS ENGINEERING** WE ARE COMPUTER SCIENCE WE ARE INESCIEC WE ARE KNOWLEDGE GENERATION WE ARE SCIENCE-BASED INNOVATION WE ARE NETWORKED INTELLIGENT SYSTEMS WE ARE POWER AND ENERGY WE ARE INDUSTRIAL **AND SYSTEMS ENGINEERING** WE ARE **COMPUTER SCIENCE** WE ARE INESCIEC WE ARE KNOWLEDGE GENERATION WE ARE SCIENCE-BASED INNOVATION WE ARE NETWORKED INTELLIGENT SYSTEMS WE ARE POWER AND ENERGY WE ARE INDUSTRIAL AND SYSTEMS ENGINEERING WE ARE **COMPUTER SCIENCE** WE ARE **INESC TEC** WE ARE **KNOWLEDGE GENERATION** WE ARE SCIENCE-BASED INNOVATION WE ARE NETWORKED INTELLIGENT SYSTEMS WE ARE POWER AND ENERGY WE ARE INDUSTRIAL AND SYSTEMS **ENGINEERING** WE ARE **COMPUTER SCIENCE** WE ARE **INESC TEC** WE ARE **KNOWLEDGE GENERATION** WE ARE **SCIENCE-BASED INNOVATION** WE ARE **NETWORKED INTELLIGENT SYSTEMS** WE ARE **POWER AND ENERGY** WE ARE INDUSTRIAL AND SYSTEMS ENGINEERING WE ARE COMPUTER SCIENCE WE ARE INESCIEC WE ARE KNOWLEDGE GENERATION WE ARE SCIENCE-BASED INNOVATION WE ARE NETWORKED INTELLIGENT SYSTEMS WE ARE POWER AND ENERGY WE ARE INDUSTRIAL AND SYSTEMS ENGINEERING WE ARE COMPUTER SCIENCE WE ARE INESCIEC WE ARE KNOWLEDGE GENERATION







ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

We need you

Hardly anyone will disagree that we need better health policies. In fact, we need better public policies across all sectors. The question is whether the lack of quality of Public Policies is merely the result of the actions by the governments we choose, or a consequence of our limited involvement, since we can help the government making better decisions, but we rarely do so. Interestingly enough, the scientific community was not absent in the actions against the COVID-19 pandemic, and the sense of volunteerism and participation was significant. We have witnessed, not only in Portugal, but also in other places, researchers asking (in the case of Portugal, begging) for access to data that would allow them to study, analyse and, simply put, contribute to improve knowledge about a virus that was, and still is. unknown.

We also observed researchers redeploying their laboratory equipment, particularly 3D printers, to produce Personal Protective Equipment and non-invasive ventilators. The Faculty of Engineering of the University of Porto (FEUP), for instance, collaborated with several hospitals, and there was even a collection of acetates, useful in the design of improvised visors. Several researchers, from different research centres, have also worked on projects focused on the development of mechanical ventilators, thus trying to meet the needs resulting from the huge increase in demand, as well as to address their significantly high cost.

Hospitals and other healthcare facilities have accelerated the use of telemedicine, which was still limited and sporadic, in order to reduce the impact of the pandemic on clinical activity (which still managed to be significantly high). This required the requalification of technological infrastructures and the training of healthcare professionals, which always represent a cost, but will lead to long-term benefits, eventually becoming a way of reducing the disparities and inequities that still exist in the access to healthcare in Portugal, particularly in remote regions.

INESC TEC was also guite active during this pandemic, contributing with solutions in the healthcare sector. This incursion into healthcare is not new, by the way. This field intersects with several INESC TEC's research centres, in multiple scientific areas and in several projects, involving a considerable number of researchers who contributed to the creation of some companies as shown in the diagram on pages 16 and 17. In this special issue of the first edition of the magazine INESC TEC Science and Society, we highlight some relevant activities by INESC TEC researchers, who resorted to technology to innovate in healthcare.

The opening piece is an opinion article about the duty of the scientific community towards society, which translates into its collaboration in the discussion of Public Policies. Several articles involve the use of advanced methods of Artificial Intelligence (AI), so we frame them with an article that presents some of the recent advances in AI, while revisiting Alan Turing and the origins of Al. Moreover and misquoting José Régio -, since we must know where we are heading to, we invite you to read the article that explains the importance of explainable Artificial Intelligence.

The use of AI was also part of a project of recognised practical relevance to address COVID-19, developed at INESC TEC. This work is described in an article that seeks to help detect the presence of lung lesions caused by the virus in X-ray images. To do this, it uses AI algorithms that will help the clinical teams to grade the cases. Concerning another initiative described in an article included in this edition – which has been generating a lot of media coverage -, INESC TEC researchers have joined together to develop a contact tracing application, which allows to identify outbreaks of infection and intervene more quickly, in order to stop or limit contagion. Despite the potential objections to this type of applications, namely with regard to privacy, the truth is that STAYAWAY COVID is working and contributing to stop the spreading of COVID-19.

And since there is life beyond COVID-19, it is important to highlight what has also been done by our researchers in other clinical contexts. This is what you can find in an article describing the MINE4HEALTH project, developed in partnership with The Portuguese Oncology Institute of Porto. This initiative will enable the collection of extremely valuable clinical information from clinical journals, placing it at the

service of science and clinical practice,

from History, we include an article about while assisting doctors in making cancer the sanitary siege during the bubonic decisions. plague epidemic that occurred in Porto, Another article describes how Artificial in 1899. Some of the similarities between what happened more than a century ago Intelligence could help screening for diabetic retinopathy, allowing the and what we are witnessing now, during automatic detection of the presence the pandemic that is deeply affecting us, or staging of this pathology, which can are striking. We should reflect on this. lead to blindness if it is not detected All of these contributions were made possible by three fundamental vectors: and treated in earlier stages. Another INESC TEC project, also described in sheer will, technology and health policies. this magazine, uses AI to support the In this case, sheer will and technology diagnosis of gastric cancer through the preceded the policies, which followed analysis of endoscopic images using the important breakthroughs. There were changes in the legislation that were Artificial Intelligence. This tool can be a valuable resource to oncologists, by changed to allow the use of contact helping them making faster and, hopefully, tracing; Infarmed moderated some more accurate diagnoses. criteria, in order to launch some of the We also highlight the design of a innovative solutions that were being disinfection robot. which allows proposed; and the Public Administration disinfecting healthcare units, particularly hastened certain ponderous formalities, hospitals, through ultraviolet rays. You in order to promote a timely reply. may think its influence is guite limited, The urgent nature of the situation made but it is important to bear in mind that all of this possible; but, and above all, the pressure from the academic community infections in hospital environments are one of the leading causes of death among and society was crucial. Consciously inpatients, especially those who have or unconsciously, we were agents who undergone surgery. You can read more promoted health policies and advocated

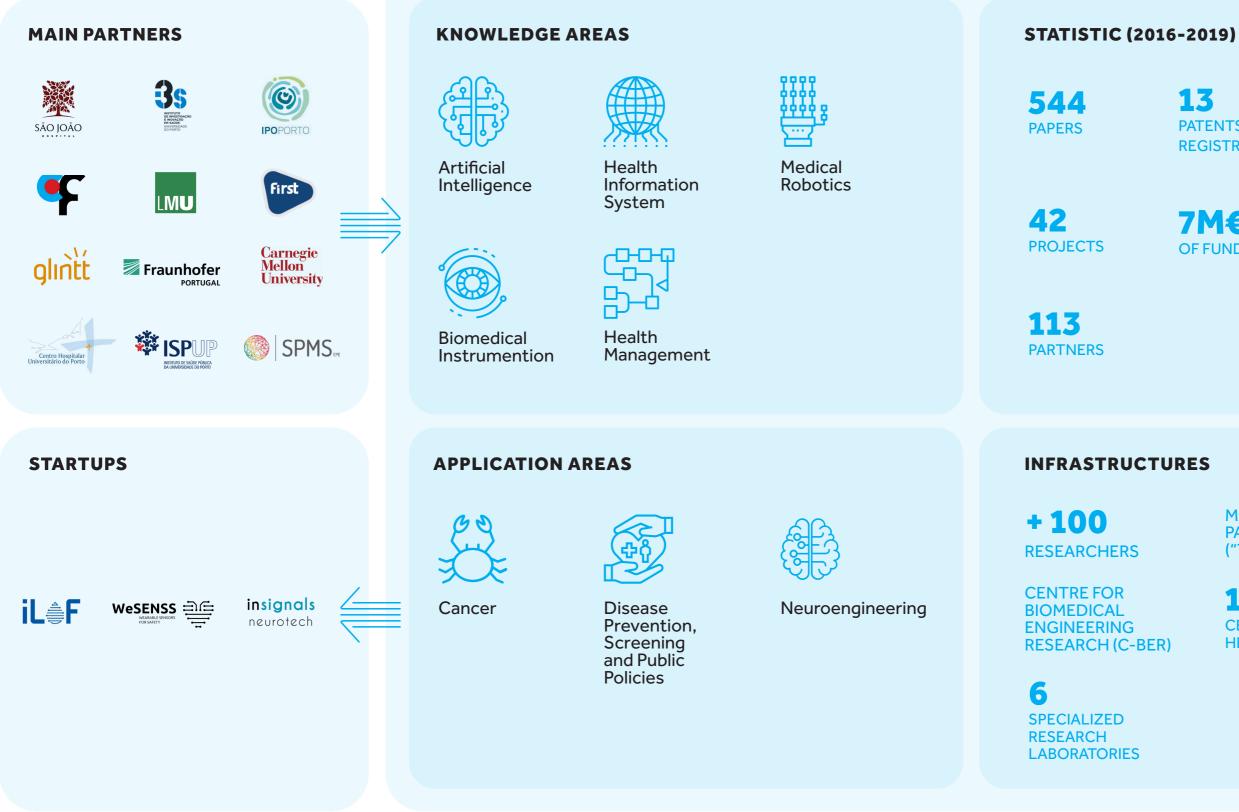
about this in an article describing this disinfection robot.

Finally, and as Hegel once said, what we learn from History is that we learn nothing for change. If we can do it during times of crisis, why shouldn't we be able to do it in times of normality? It is our duty towards society.

MÁRIO AMORIM LOPES^(1,2) AURÉLIO CAMPILHO^(1,2)

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ACTIVITY **FROM INESC TEC IN HEALTH**



13 PATENTS/SOFTWARE REGISTRATION



MARKET PULL AND PARTNERSHIPS ("TEC4HEALTH")

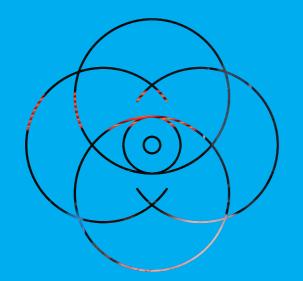
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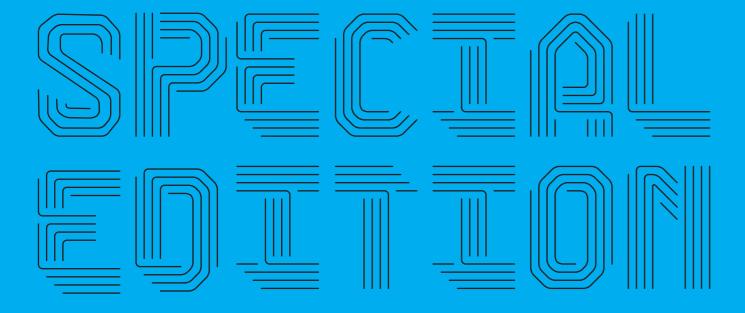
Bottles to store syrup, pills and other medicines

© Renato Roque – Faculty of Pharmacy of the University of Porto, 2016





DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH



OUR DUTY TOWARDS SOCIETY

Science serves or should serve a greater duty — that of improving the economic and social conditions of humanity. To achieve this, science and scientists, most of all, need to have a voice in the discussion of Public Policies, which carry decisions that influence the economic and social outcomes. Public Policies based on the best evidence available and in an open and rich discussion are our best assurance to a more prosperous society — but for this to be possible, the scientific community must join the discussion.

MÁRIO AMORIM LOPES^(1,2)

⁽¹⁾INESC TEC; ⁽²⁾FACULTY OF ENGINEERING OF THE UNIVERSITY OF PORTO mario.a.lopes@inesctec.pt Benoit Mandelbrot once said that science would be doomed if it worked in narrowly defined specialties, causing scholars to debate only with their closest peers. This echo chamber would then amplify only to the insiders. Mandelbrot compared it to sports: soccer players play soccer; tennis players play tennis; and basketball players play basketball. There is no linkage between the different sports; there is no interdisciplinarity. There is no common ground, except by the very few who enjoy several sports. While this worked well in sports, said Mandelbrot, it can

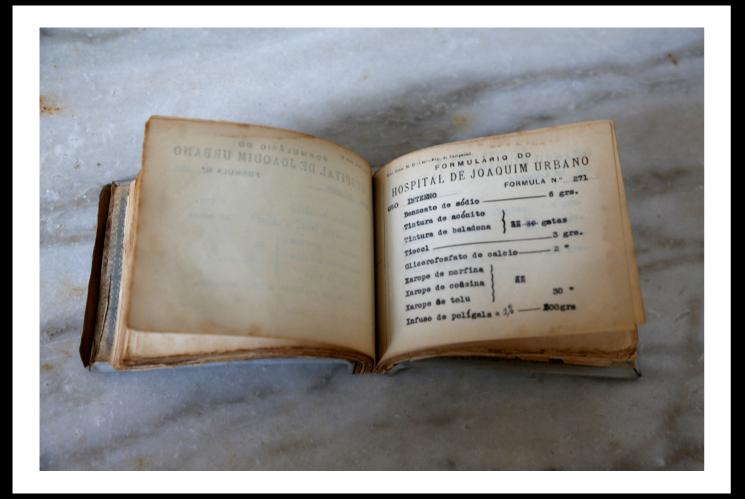
endanger science. Science benefits from intellectual nomads who can cross disciplines. And perhaps more importantly, science, but above all society, benefits from resolute scientists who want their research to have an impact on society.

By impact, we mean all that may generate prosperity, material or not, to society, contributing to its economic and social development. For many scientists, this means knowledge transfer, usually done through the means of patents or copyrights, but we may also accomplish this objective through other means - through influence. Positively influencing society and its stakeholders, in particular policymakers, to be rigorous with their analysis, to not be immune to acclaimed evidence, to discuss overtly, and to accept discord and pluralism. Such endeavour can be done through Public Policies, a matter from which we have been puzzlingly absent. Our continued absence from the public policy arena has the effects we all know: precarious public policies that are a burden on taxpayers and do a disservice to society. This does not mean that our participation is a guarantee to infallible public policies — after all, scientists are also (very) fallible. It is my conviction, however, that we can contribute to more rigorous public policies, and rigor is, after all, the crux of science. We may contribute to cogent decision-making and to better-informed policymakers, letting them know that their decisions have an impact well beyond their legislature and that it will be us, citizens, who will bear the costs. We may contribute by informing

society in a rigorous and structured way.

This is much more than a prerogative — it is a duty to those who make science, especially those who have reached excellency in doing science. INESC TEC and its Associates have some of the most brilliant minds in the country, but also in the world, which heightens on our duty to be an active and participative actor in the public policy arena.

However, this doesn't mean that we speak with a single voice. There is no such thing in Public Policies. What this means is that we can and should provide meaningful contributions to an overt and amenable discussion, even if our stances are sometimes contradicting. It would be very detrimental to an open society if a research institute which should be plural, heterogeneous and intellectually free had only single thoughts and abiding researchers. Healthcare, in particular, is in desperate need of these contributions. Many decisions that are made rest only on ideological prejudice and bear a cost to society, especially to those who are most vulnerable, a fact to which we cannot remain indifferent. Bad decisions and deficient policy-making impact directly millions of people. Our mission, as scholars, is also to these people — our fellow citizens. Even if everyone is absent from this debate, it will have to be us, scholars, the last people standing to defend the Enlightenment, reason, facts and science. It is not an option. It is our duty.



Photographs of a Medicines Form used at Hospital Joaquim Urbano, in 1934, which contains a prescription for the preparation of medicines. As of today, almost 100 years after this photographic record, there is still ample recourse to paper in Portuguese hospitals, although on a much smaller scale.

Although information systems have contributed to the dematerialization and digitization of many of these records, the fact that they are still stored in text, although digital, makes it difficult to use for other purposes, such as clinical research, which could greatly contribute to better health care.

© Renato Roque – Joaquim Urbano hospital, Porto, 2016



FORMULÁRIO HOSPITAL JOAQUIM URBANO Redicamentos aso Interno

ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

THE NEW SPRING FOR ARTIFICIAL INTELLIGENCE

We interact with AI systems for a long time. Most of the time, the interaction was silent: we were not aware of the interaction. Nowadays, AI comes to the front page of journals: Watson won Jeopardy, AlphaGO won the world championship, an accident with an autonomous car, etc. In this article, we argue that the yeast of this vigorous AI Spring is machine learning and data sciences.

JOÃO GAMA^{(1, 2),} ALÍPIO JORGE^(1, 3) ⁽¹⁾ INESC TEC; ⁽²⁾ FACULTY OF ECONOMICS OF THE UNIVERSITY OF PORTO; ⁽³⁾ FACULTY OF SCIENCES OF THE UNIVERSITY OF PORTO joao.gama@inesctec.pt alipio.jorge@inesctec.pt The idea of Artificial Intelligence as we conceive it today has existed since the 1940s. Around 1940, Alan Turing, suggested that machines, like humans, could also think. In 1950, Turing wrote an article on the topic proposing to answer the question "Can machines think?" The term Artificial Intelligence was first used in 1956, at a conference at Dartmouth College, organized by Marvin Minsky, John McCarthy, with the participation of Claude Shannon, Arthur Samuel, Allen Newell and Herbert A. Simon among others. All these scientists have played a very relevant role for decades in Al research. As we conceive it today, artificial intelligence is a branch of computer science that aims to develop computational models that simulate the human ability to reason, make decisions and solve problems. These capabilities are defined by: ability to link reasoning, apply logical rules and derive conclusions; learning from facts and observations, making future actions more effective; recognizing patterns; applying reasoning to everyday situations. The 60s and 70s were years of inflated expectations. Or relative advances in areas such as automatic theorem demonstration, robotics, automatic translation, development of logic programming languages, etc. The initial success is well illustrated by the GPS - General Problem Solver, developed by Newell and Simon [1], capable of solving problems automatically. In the 1980s, Japan launched a 10-year project for the Fifth Generation of Computer Systems, to create computers using massive parallel computing and logical programming.

Since the 1970s, there has been an effort to use Artificial Intelligence to solve real problems. Initially, the problems were treated by Al through the acquisition of knowledge from specialists in any given domain. These systems, known as expert systems, were modular with the inference engine being independent of the knowledge base. For each specific domain, a knowledge base was built through interviews with experts in the field to discover the rules used by the expert to make decisions. In the late 1980s, early 1990s, expectations were followed by a period of marked disillusionment, leading to disinvestment in the area. AI had entered its winter. In 1997, IBM's DeepBlue computer won over world chess champion G. Kasparov. IBM stressed that the victory was due to the machine's processing capacity and not to the use of AI technologies!

In the 1980s, more sophisticated and autonomous computational tools for extracting knowledge from facts and data began to gain popularity. In the 90s, these tools gained maturity, beginning to be used in companies. These tools had great impetus with the development of computer networks and the WWW, associated with the ability to collect, store and process large amounts of digital information.

Al appeared on headlines of the newspapers when, in October 2005, the DARPA Grand Challenge took place in the Nevada desert. It was the first time that an autonomous car successfully completed the challenge. Sebastian Thrun said that "The robot's software system relied predominately on state-of-the-art Al technologies, such as machine learning and probabilistic reasoning" [2]. It is the beginning of a new spring of Al, which will be reinforced when machine learning is used in other Al areas such as Knowledge Representation, Computer Vision, Natural Language Processing. Al has developed algorithms and technologies capable of solving difficult problems, and which have come to be widely used in the most diverse sectors. In 2011, the Mackinsey Institute published the report "Big data: The next frontier for innovation, competition, and productivity" [3] which relaunched public and private investment in AI technologies, machine learning and data science.

The greatest growth occurs in companies, where the use of Al is used as a business strategy, as is the case of Google and Facebook, even for the development of marginal business applications, such as the automatic assistants common in apps and websites of several banks. Netflix, for example, uses Al in its recommendation system and to identify the patterns of preferences of its users. Some examples in which Google employs AI, and which are already part of the daily lives of its users, we can mention: organization of photos in Google Photos, in which ML is used to identify the elements of the photos or to group the photos by standards among other uses. Automatic captions for videos on YouTube. Recommendation for quick responses to email messages in Gmail. Use of artificial neural networks, more specifically Deep Learning, to improve the effectiveness of translations in Google Translate.

Examples of successful applications of ML techniques to real problems include: interfaces that use natural language (written or spoken), facial recognition, spam filtering in emails, fraud detection by banks and credit card operators, decision support on medical diagnosis through analysis of clinical data, from images and/ or genetic data, recommendation of products based on the consumer's profile and consumption history, intelligent behavior in game characters, playing Chess and Go with a performance comparable to that of human champions. An application with intensive use of Al and ML that is currently very popular is that of autonomous cars. Several manufacturers. such as Tesla. Volvo. BMW. Mercedes-Benz, Ford and Land Rover, have autonomous vehicle designs. Several commercial models already integrate technologies for partial autonomy. In these models, ML is used diversely in several tasks, such as the detection and recognition of objects and plates, object classification, location, prediction and tracking of moving objects.

The Internet of Things (IoT), counts on millions of devices sensing the environment, processing that information, and forwarding it to other machines. IoT is at the origin of technologies smart-cities, smart-grids, smart-farms, etc. The creation of a level of information about the production process gave rise to Industry 4.0, where decision processes involve people and machines. The machines' ability to explain how they came to a decision is critical to a climate of trust. On the other hand, a large part of the economy is developed in a virtual universe. Any company has a website, and some large companies, such as Facebook, Netflix, Airbnb, Uber, etc. only exist on the web. All companies are accessible 24/7 on our smartphones. Interactions with users are monitored in order to create user profiles: likes, preferences, fears, etc. These profiles can be used for marketing, recommendation or influencing choices. In the digital universe, where there are no borders, concepts such as privacy, the "public" and the "private", and ethics need to be rethought [4].

Figure 1 - Autonomous Stanley Touareg.



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Bottles to store tinctures and other formulae

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ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

ARTIFICIAL INTELLIGENCE AND THE WHY STAGE

The recent remarkable performance of Artificial Intelligence (AI), supported by Deep Learning techniques, has created expectations about its positive transforming potential in society. However, ethical and moral issues have also reappeared with great intensity. Interpretable AI emerges as a partial response to these concerns and the necessary continuous improvement.

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The so-called "why stage" is a classic and usual period in children's development. The child, eager to know the world around him, begins to question the adult about everything he wants to understand; the adult, with patience and respect, helps her to clarify her doubts, thus contributing to her learning process.

It will be exciting when Artificial Intelligence (AI) plays this role of the adult and us, the child who wants to learn. When artificial intelligence is sufficiently developed, it can, by explaining its decisions, contribute to our intellectual growth.

Until then, there is still a long way to go. Al still fails. Therefore, much of the current work in interpreting the automatic decision aims to understand the error to improve the decision algorithm and increase our trust in the machine. It is interesting to note that, in some 'closed' domains, despite deciding globally well, very well, the machine makes 'childish' mistakes and is easily manipulated. This statistically positive behaviour but with individual aberrant cases raises doubts about the concepts that the algorithm integrated; these are doubts that must be dispelled and overcome.

Much of the current work in AI deals with the so-called Deep Learning algorithms. Deep Learning is a specific area of Machine Learning, where learning algorithms generate models from the patterns found in the examples that are processed. One of the most evident differences in Deep Learning is that, in addition to learning decision models, data representation models are also learned. In other words, a model is learned that transforms the input data, for example, an image, into an abstract representation of concepts representative of that image. The performance achieved by these algorithms is remarkable, being state of the art in several domains, for example, in medical image analysis, challenging specialists in their areas. However, there is an obstacle in the interpretation of the decision process of these models - their opacity. In other words, its high complexity and high abstraction make the automatic decision challenging to interpret by humans, whether these are specialists or laypeople in medicine or Al. In an attempt to overcome this difficulty, interpretable Al tries to justify a decision based on supplementary information. For example, it can highlight the most relevant regions of the image for decision making. The 'interpretation' algorithms provide a map of relevance (represented by an image) where the zones that conditioned the decision are identified. The calculation of these maps can be done in different ways, but always trying to assign the responsibility of the decision to the various inputs of the model. For example, suppose the model predicted cancer with an 80% confidence based

on a mammogram. In that case, the interpretation models will try to assign responsibility for this decision to the different regions of the image. Which regions have contributed most significantly to cancer prediction? There are several stakeholders interested in answering this question, namely: the AI specialists who develop and train the models and the end-users of the model, for example, radiologists. The same interpretation of the decision is not always equally useful for all stakeholders. Therefore, it is necessary to adapt the techniques of interpretable AI to those who will take advantage of this information. For example, visual information may not be sufficient, and other forms of explanation are useful for a better understanding of the decision-making process, such as a descriptive text or a set of similar examples. Currently, these interpretations, although still relatively basic, are already useful for diagnosing and improving the Al algorithm itself. If the interpretation highlights areas outside the lung in the image as relevant to a diagnosis of pneumonia based on an x-ray, probably the Al algorithm, even if it has decided well, will have "reasoned" poorly. If the analysis of an Al algorithm to support the recruitment of staff reveals that it is favouring men over women, there is a bias that needs to be removed.

The Workshop on "iMIMIC - Interpretability of Machine Intelligence in Medical Image Computing", which we organized last October 4th as part of the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI) revealed the dynamics of the area, the potential and the virtues of these approaches. However, it also revealed the limitations and the much that remains to be done. The explanations/ interpretations themselves are generated by an automatic Al algorithm, which has its own limitations and flaws. Explanations can also be manipulated. For example, an algorithm can use the customer's origin as a characteristic that conditions the granting of credit, but not use it to explain the decision. In another direction, it is essential to generalize explanations to cases beyond classification. How to explain that the estimated value for the sale value of the house is 437.52 and not just any other value? What is the proper explanation in this case? In yet another direction, how to explain a decision supported simultaneously by multiple sources of information (audio, text, video)?

The area of Al interpretability is taking its first steps. We still have a long way to go, to be followed with optimism, step by step. This joint progress, either focused on improving the decision, either on explaining the decision, is allowing for mutual growth of solutions for both tasks, in which we all win. It is not utopian to want to learn from the machine.

ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

ARTIFICIAL INTELLIGENCE FOR COVID-19 DETECTION IN X-RAY IMAGES

Artificial Intelligence can aid in the front line to fight COVID-19. This innovative technology allows the automatic detection of Covid-19 findings in X-ray images, supporting the decision making process of the clinicians and being an excellent follow-up tool of the patients.

GUILHERME ARESTA^{(1),} CARLOS FERREIRA^{(1),}

JOÃO PEDROSA⁽¹⁾ ⁽¹⁾INESC TEC guilherme.m.aresta@inesctec.pt carlos.a.ferreira@inesctec.pt joao.m.pedrosa@inesctec.pt The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had devastating effects in our daily lives, public health and the economy. The SARS-CoV-2 virus is easily transmittable, causing cough, fever and fatigue and it can, in some cases, evolve to a severe pulmonary infection and even cause death. Chest radiography (commonly known as x-ray) can help in the assessment of the development of the pulmonary infection caused by SARS-CoV-2 and thus aid in determining follow-up and therapy. Given the complexity of chest radiography reading, radiologists play a fundamental role. However, radiologists often have to deal with a high number of exams to assess and often do not have enough to analyse the X-ray images. Also the number of radiologists is scarce, and as result the images are analysed by clinicians or interns with less experience. Artificial intelligence technology could thus contribute to reduce the workload for radiologists by proposing an objective second opinion and help in obtaining the correct diagnosis regarding COVID-19.

X-ray as a complementary COVID-19 diagnosis method

Chest radiography is a medical imaging method that allows to visualize the inside of a patient's body in a painless and non-invasive way. In the particular case of COVID-19 screening and patient management, it is naturally important to analyse the lungs given the pulmonary infection associated with the disease. The goal of imaging the thorax is thus to assess the degree of pulmonary infection and understand the development of the disease, determining the follow-up and therapy of a given patient. Nevertheless, many COVID-19 patients have a normal X-ray in the early stages of the disease, which means that X-ray can only be used as a complementary diagnosis method to the traditional COVID-19 swab test.

Artificial Intelligence as a second opinion

he analysis of X-ray images should always be performed by trained staff and preferentially by a radiologist. In the case of COVID-19 patients, this is even more important as COVID-19 radiological features can be particularly subtle and difficult to distinguish from pulmonary infections caused by bacteria or other viruses. However, trained radiologists often have to deal with a high number of exams to assess and the resulting fatigue, human error and uncertainty could lead to misdiagnosis. Artificial Intelligence technology could thus contribute to improve the analysis of x-ray images by proposing an objective second opinion and help in obtaining the correct diagnosis regarding COVID-19. These

techniques are based on the extraction of features associated to COVID-19 (one simple example could be the difference between the right and left lung volumes), which are then analysed with the goal of predicting the risk of the subject having COVID-19.

How does CXR_AI4COVID-19 actually work?

The algorithm developed by INESC TEC, named CXR_ Al4COVID-19, is based on a set of techniques known as Deep Learning methods. These techniques have been used successfully to solve problems which depend on automatic image analysis (such as number plate identification or autonomous driving) and has recently been used in the development of decision support systems in clinical settings.

One of the greatest advantages of Deep Learning when compared to other image analysis techniques is that the most relevant features for the diagnosis are automatically learned by the system. In order to do this, a large number of images (typically in the thousands) have to be analysed. These images must be representative of the different ways that COVID-19 appears in patients but also of normal subjects and patients with other pathologies. The learning process is done by incentivizing the system to predict the correct diagnosis for as many images as possible (COVID-19, normal and other pathologies). As the system sees and compares images, it tries to predict which ones have COVID-19 (and which ones don't) and receives information on how many correct predictions it made, and on which images. In this way, the system can learn which features are contributing to a correct diagnosis and reinforce the importance of those features. On the other hand, if more incorrect diagnoses occur, the features that were extracted are not useful and the system looks for different solutions. Given enough images, the features learned by the system become representative of the pathology, allowing for automatic diagnosis.

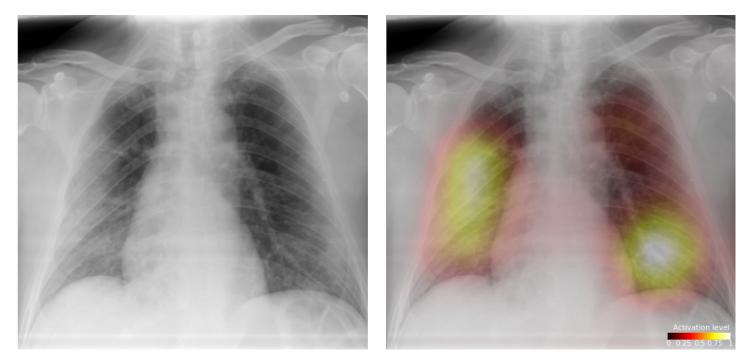
In spite of the extraordinary ability of Deep Learning techniques, its application also has downsides when compared to simpler technology. For one, a large amount of images is needed, which can be complicated in new or rare pathologies. Secondly, most Deep Learning techniques receive an image as input and give as output the probability of having a certain pathology. This behaviour means that it is not immediately possible to determine which features the system has learned and why they are important to determine the diagnosis. This means that one must be extremely careful in the analysis of the results - for example, is the system actually learning the radiological features of COVID-19 or only that intubated patients are more likely to have COVID-19? In fact, this kind of shortcuts learned by the system often lead to unfounded promises of superhuman performance which then fall apart when testing begins in a clinical setting.

The approach used for the development of CXR_ Al4COVID-19 was designed so that these limitations are avoided, making the system more robust and transparent. As such, the radiologist receives not only the diagnosis predicted by the system but also which regions in the image were most important for the decision made by the system (Figure 1), allowing the radiologist to determine whether the prediction is based on clinical principles.

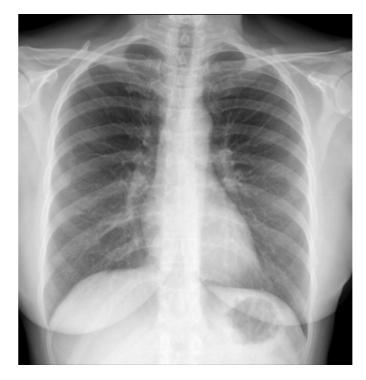
In conversation with the radiologists involved in the developed of CXR_AI4COVID-19, they consider that this project "where Medicine and Engineering walk side by side" there is true potential for "the creation of a diagnostic tool which can have a useful and powerful application in a clinical setting by aiding clinicians in detecting COVID-19 in chest radiography". Furthermore, they stated that these kinds of systems are, more and more, the "Radiology of the future".

In order to understand if CXR_AI4COVID-19 is prepared for testing in a clinical setting, an initial validation of the system in X-ray images from both national and international hospitals was performed, in which images from the Centro Hospitalar de Vila Nova de Gaia e Espinho (CHVNGE) were also tested. To compare with typical human performance, two radiologists were asked to read and make a diagnosis in 1861 X-ray images. On these images, the system showed a similar performance to the radiologists, showing that relevant features for COVID-19 were learned. As such, plans are now underway to test CXR_AI4COVID-19 in a real clinical setting in CHVNGE, where it can contribute with an easily interpretable second opinion regarding the presence of COVID-19 in chest radiography, and hopefully help in the fight against the COVID-19 pandemic.

SYSTEM INPUT IMAGE



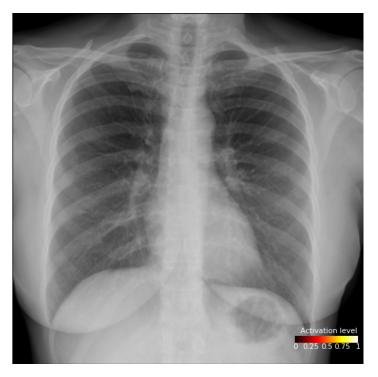
Diagnosis: COVID-19



Diagnosis: Without COVID-19

SYSTEM EXPLANATION

System prediction: COVID-19



System prediction: Without COVID-19



Glass beakers, volumetric flasks and other lab equipment

© Renato Roque – Joaquim Urbano hospital, Porto, 2016 **Glass beaker**

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ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

DATA SCIENCE AND MACHINE LEARNING AT THE SERVICE OF CLINICAL DECISION-MAKING IN ONCOLOGY

Health institutions, and hospitals in particular, deal on a daily basis with an object of immense value: data. If these data could be extracted out of the textual clinical records and fed into machine learning models developed for assisting physicians in clinical decision-making, new opportunities would arise to clinical practice, clinical research, but above all to patients.

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Despite the constant evolution in oncology, shown through the emergence and availability of new therapeutic options, cancer remains one of the most prevalent diseases (affecting, in 2017, around 233 million people worldwide) and one of the leading causes of death in developed countries, which creates enormous social and economic burdens. In fact, with an annual cost of more than 199 billion Euros in Europe alone – and with a significant portion of that amount being spent exclusively on medication –, finding a cure for cancer has proved to be an extremely complex, time-consuming and expensive process.

As part of the procedures to diagnose and treat patients with cancer, massive amounts of data need to be collected by clinicians. This information is stored in the patient's clinical process, and it includes indicators of his/ her general health status, history, exams and diagnoses, follow-up notes, among many others. This information, which has an enormous clinical – but also scientific –value, is generally kept in free text, hampering its use in diverse purposes, including statistical treatment or clinical decision making. Even worse, it is an addition to the physician's tasks, as he/she has to analyze huge volumes of text, and leads to errors, such as exam duplications.

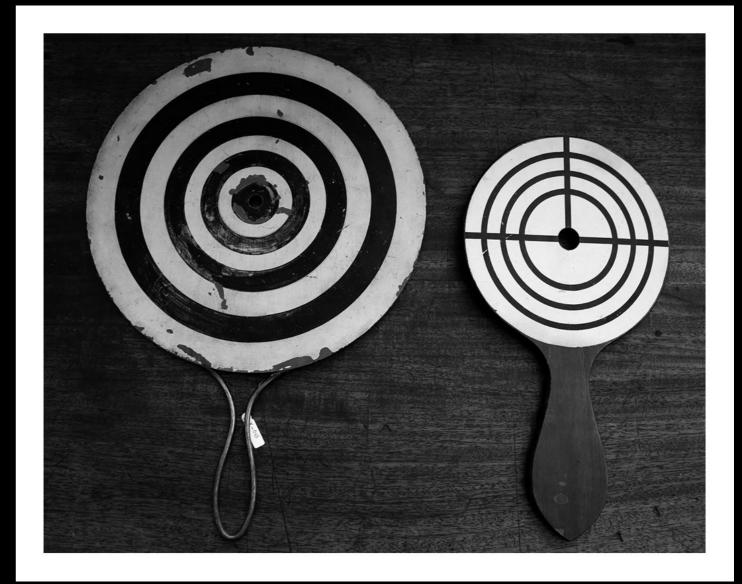
The objective of the Mine4Health investigation project is to help solve, or at least ease, the aforementioned problems, through two main contributions. First, using a Natural Language Processing approach, it aims to convert the free text present in clinical records into structured and chronologically organized blocks stored in a database, so that they can become each patient's clinical narrative and later be retrieved for clinical, research and management purposes. Figure 1 illustrates this idea.

The second contribution is more ambitious. The goal is to use the systematized results from the previous step, to develop and improve machine learning and artificially intelligent models so that they can be used to support clinical decision-making, particularly to predict treatment responses (predictive models) or to suggest procedures and actions (prescriptive models), considering each patient's individual characteristics, including their age, gender, ethnicity, comorbidities, previous conditions and biological profile. In this context, the development of new models can become an important ally in the fight against cancer – provided data exists and can be used.



The Plácido disk - an instrument designed by <u>António Plácido Costa</u> (1848-1916) to analyze the curvature of the cornea.

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Although previous scientific work devoted to this topic already exists, it is scarce at a national level, and it tends to resort to small datasets, limiting the applicability of its results. Hence, the main advantage of this project is the partnership with IPO Porto – Portugal's largest oncological hospital, and one of the largest in Europe -, which allowed obtaining over 10 years of duly protected medical records, containing information about over 795 808 unique patients and 7 791 918 clinical episodes, and with 2000 records created or updated on a daily basis. As a contribution to society, we expect the methods developed in the context of this project to be able to help healthcare professionals in the decision-making process, thus exploring the potential of the clinical experience of IPO Porto, and assisting decision making with specific recommendations and guidelines for each patient. Among many other possible applications, this tool can assist in performing patient stratification according to the risk of relapsing, developing metastases or undergoing a certain treatment or intervention, and reduce the need for invasive exploratory procedures.

By being based on all relevant information and providing up-to-date recommendations – that is, according to the most recent and scientifically validated oncological techniques - this tool will have the potential to avoid unnecessary expenses by significantly reducing the number of misdiagnoses and misprescriptions, to reduce the workload suffered by clinicians and even detect subtle markers that might not typically be considered by physicians. The products of this work can also be transferred to other oncological facilities, as well as to generalist hospitals with medical oncology services, national and international, which will encourage sharing practices between centers and facilitate future cancer research.

Finally, and despite all the efficiency gains, this tool can be translated into faster and more accurate diagnoses, personalized treatments according to the patient's biological characteristics and his/her specific cancer, a better understanding of his/her diagnosis and therapeutic options, and better health care for the population as a whole.

ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

ARTIFICIAL INTELLIGENCE AND THF SCREENING OF DIABETIC RETINOPATHY

Artificial Intelligence can be useful in scenarios where skill labour fails to meet needs. This article describes the challenges and solutions found to face the diagnosis of diabetic retinopathy considering the increasing prevalence of diabetes in the Portuguese population.

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Registo clínico (dashboard)

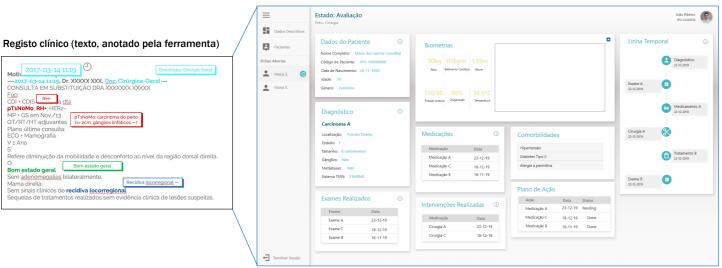


Figure 1. Example of the extraction of structured data to be used for building dashboards.

P**44** INESC TEC SCIENCE & SOCIETY

The diabetes and the diabetic retinopathy

Diabetes is a metabolic disease characterized by the presence of high levels of glucose in the blood over long periods of time. It is one of the diseases with the highest growth rates, affecting over 415 million people worldwide. Recent estimations point out that by 2040 there will be over 642 million people affected by such diseases. Portugal has one of the highest prevalence rates of diabetes among European countries, with 13.3% of Portuguese people aged between 20 and 79 years old having diabetes, which corresponds to more than 1 million people.

Diabetic retinopathy (DR) is a complication of diabetes, which affects more than 25% of the diabetic population, and which is characterized by damage to the blood vessels in the retina (layer of the eye where the images we see are formed). It is a silent pathology that gradually decreases the patients' visual acuity, being the main cause of blindness in the working age population. However, it can be successfully treated if diagnosed at an early stage. Current DR screenings implemented across the country are essential to identify cases of this disease in a timely manner and prevent its progression.

Screening for diabetic retinopathy

During the screening of DR, photographs of the fundus of the patient's eyes are captured. The procedure is noninvasive and, since the eyes are windows to the body, such photographs allow a direct observation of the blood vessels and the detection of diseases such as DR. The diagnosis of DR is made by detecting various lesions in the retina, such as microaneurysms, hemorrhages, exudates and neovessels (Figure 1). The diagnosis of DR is made by detecting various lesions in the retina, such as microaneurysms, hemorrhages, exudates and neovessels (Figure 1). Depending on the presence and number of different types of lesions, a degree of severity of DR can be associated with the patient.

Annually, an appreciable portion of the diabetic population is examined in primary health care units. In the north of Portugal, the Northern Regional Health Administration (ARSN) is the entity responsible for managing and implementing the DR screening process. The acquired images (retinographies) are stored in the ARSN archive, being the first medical decision taken at the Reading Center, where ophthalmologists analyze the retinography and conclude about their normality. If the retinography is normal, a re-screening of the patient is recommended after one year. If it is abnormal, the ophthalmologist determines the severity of the condition and the patient is referred for treatment. Current screening practice implies that ophthalmologists at the Reading Center analyze all images, including those of poor quality, impossible to diagnose, and images without signs of pathology, which represent about 80% of the total number of acquired images.

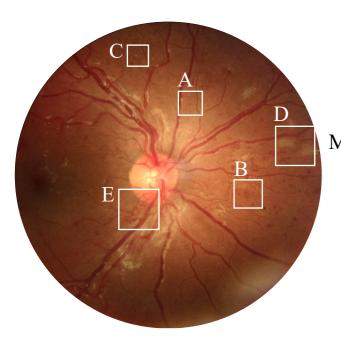
The SCREEN-DR platform: Artificial Intelligence for diagnosing DR

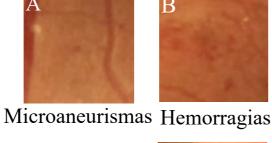
O aumento da prevalência de diabetes coloca alguns desafios aos processos de rastreio da RD visto que têm de estar preparados para acomodar uma população em constante crescimento. Para ajudar os oftalmologistas neste processo, automatizando parte dele e reduzindo a carga de trabalho dos especialistas e a subjetividade do diagnóstico de RD, o INESC TEC desenvolveu a plataforma SCREEN-DR (Figura 2).

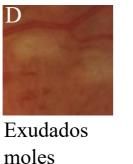
The increase in the prevalence of diabetes poses some challenges to the screening processes for DR since they have to be prepared to accommodate a constantly growing population. To help ophthalmologists in this process, automating part of the process, thus reducing the workload of specialists and the subjectivity of RD diagnosis, INESC TEC developed the SCREEN-DR platform (Figure 2).

SCREEN-DR offers two advanced artificial intelligence (AI) solutions: one for the evaluation of image quality (EyeQualDR) and another for the detection of normality (EyeDetectDR). Besides this, a tool that allows to classify pathological images according to the DR severity is provided (EyeCadDR). This tool assists the ophthalmologist in the decision making, working as a second opinion.

When the acquired images display insufficient quality, EyeQualDR advises the technician to perform a new image capture. By its turn, the good quality images are stored in the ARSN and processed by EyeDetectDR, which distinguishes normal from pathological images.

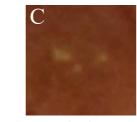






Neovascu-

larizações



Exudados duros



Figure 1 - Most common lesions associated with diabetic retinopathy found in the fundus photographs. Image taken from https://doi.org/10.1016/j.media.2020.101715.

The pathological images are classified a posteriori by an ophthalmologist, with the help of EyeCadDR. By removing from the pool of images to analyse the ones that correspond to non-pathological situations, the SCREEN-DR platform makes the screening and diagnosis process more efficient.

The advances in the Al area, namely in Deep Learning techniques, allowed to obtain truly promising results in the automatic diagnosis of medical images. These techniques "learn", like humans, through experience and trial and error. For that, the algorithm observes a large quantity of ophthalmological exams with the respective medical diagnosis. The algorithm tries to imitate the specialist's decision, learning to identify the patterns in the images which are signs of pathology.

Following these approaches, it was possible to obtain a system capable of identifying simultaneously which images have enough quality for diagnosis and, from these, which should be forwarded to a medical doctor since they show signs of DR. This system learned from a large quantity of past screening data performed by ARSN, contemplating images from a large variety of patients and acquired by different machines, allowing the algorithm to obtain a quite complete experience.

Intuitively, the more experience a medical doctor has, potentially more accurate will be his decisions, and the same logic may be applied to this type of IA techniques. The solution proposed for the grading of the severity of the disease allows to obtain a DR grade, an explanation associated with the grade and an uncertainty of the diagnosis. This system was trained solely with the eye fundus images and the associated DR grade, attributed by the ophthalmologists. The association of an uncertainty to the system's prediction is of special relevance in computer assisted diagnosis, since it allows to establish which are the cases that need additional analysis by specialists. The explanation of the system's decision through the highlighting of the image regions which contributed the most for that decision allows to mitigate the "black-box" (term commonly used for a system that allows the access to the input and output, without any access to the inner information) behaviour associated with deep neural networks, which commonly

hinders the adoption of these automatic systems in clinical contexts.

To evaluate this solution, the predictions of the Al systems were compared with the diagnosis from several medical doctors in past exams. We verified that the system is capable of identifying patients that need treatment with a level of reliability similar to the medical doctors, disagreeing with the specialists to the same degree in which they disagree between themselves. Additionally, as the system utilizes data generated during DR screening, it can continue to improve as more exams are performed.

These results suggest that the implementation of this system in the process of DR screening could reduce the number of exams that the specialists need to analyse, allowing them to spend more time in the treatment of the most severe cases.

Considering that only around 10% of the screened patients require treatment, this system could reduce in,

potentially, 90% the number of cases that the specialists need to analyse. Systems like this are of special importance to ensure that the DR screenings continue to be viable in the future, since our diabetic population is in constant growth. The final goal is to save the sight of the largest number of people possible, ensuring that they can maintain their jobs, which translates in economic benefits to the country but, more importantly, allowing them to maintain their quality of life.

The ophthalmologists who collaborated during the development of this project consider that "the implementation of the SCREEN-DR project, which aims at optimizing and simplifying the diagnosis and identification of at risk DR patients, through screening solutions using Al techniques, could have a very positive impact in the quality of life of several diabetic patients. Software like this greatly facilitate the medical doctors' task of identifying at early stages a greater number of patients at risk, thus accelerating their access to treatment."

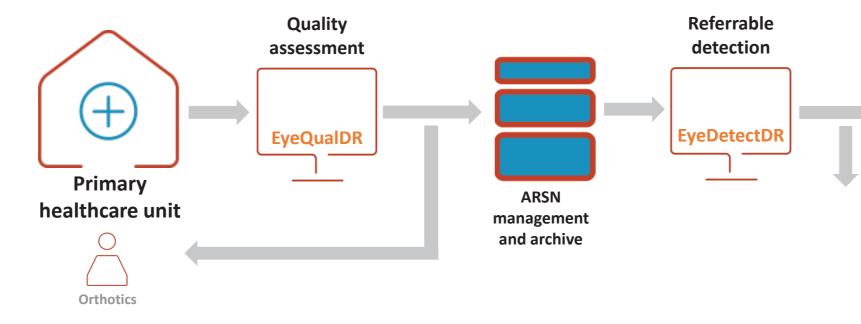
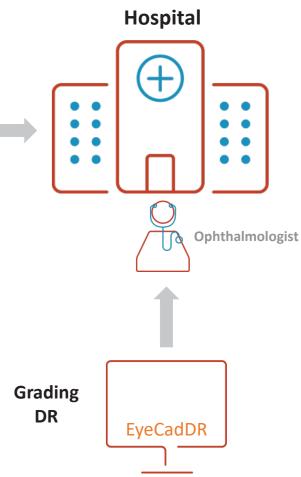
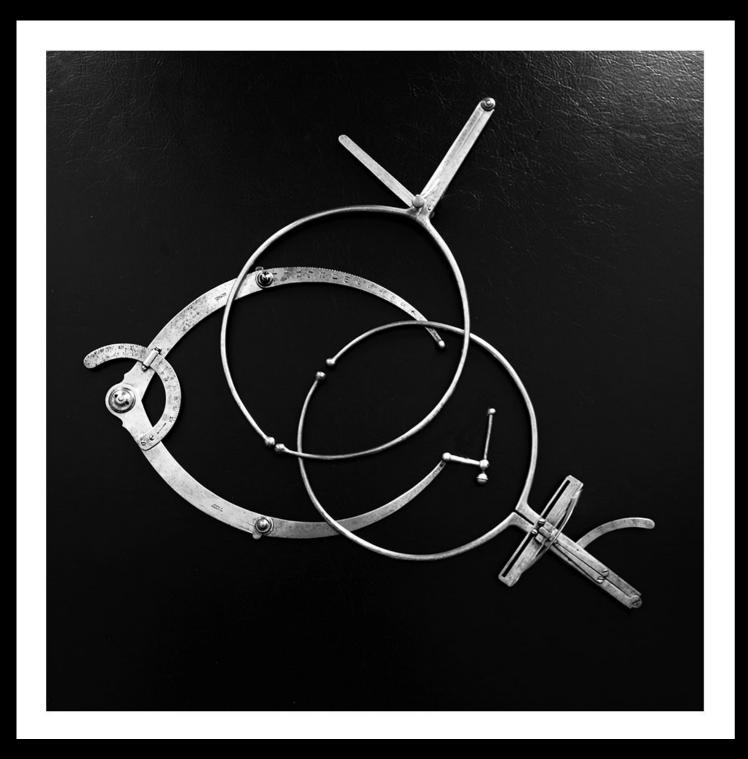


Figure 2 - SCREEN-DR platform for the diagnosis of diabetic retinopathy.

Acknowledgements

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Head circumference measuring device

© Renato Roque – History of Medicine Museum Maximiano Lemos – Faculty of Medicine of the University of Porto, 2016 A E NVFEM PFER U 3 DLRFP 3 WE TLOFOP M 3 WE FRISH MARK Keratoscope (Placido's Disk) – device designed by António Plácido Costa (1848-1916) to assess the shape of the surface of the cornea

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ESPECIAL EDITION - DATA SCIENCE, ARTIFICIAL INTELLIGENCE AND HEALTH

ARTIFICIAL INTELLIGENCE FOR THE DIAGNOSIS OF GASTRIC CANCER

The detection of neoplastic gastric lesions, mainly early lesions, may reduce mortality associated with gastric cancer. Artificial Intelligence algorithms today already present a high accuracy in supporting this diagnosis, motivating its integration in systems to support clinical practice in the near future.

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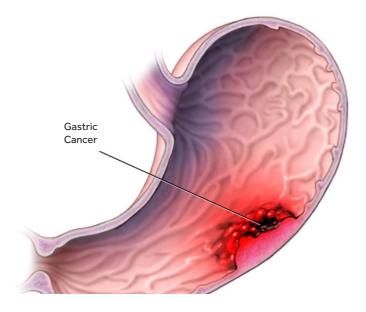


Figure 1 - Gastric Cancer Formation (Adapted from [2]).

Gastric cancer is the third deadliest type of cancer in the world (860,000 deaths in 2017) and in Portugal (2,800 deaths in 2017) [1]. A 20% increase in the incidence and mortality of this type of cancer is expected in 2035, mainly due to demographic effects and late diagnosis. Minimally invasive screening and gastrointestinal endoscopy (GIE) play a key role for an early diagnosis, which is crucial for improving survival rates. However, due to technical and cognitive factors, the risk of diagnostic errors caused by human error is significant, well-illustrated in examples such as Pimenta-Melo [3], a meta-analysis of 22 studies where an error rate of 9.0% is reported in the diagnosis of these lesions. This happens even with the existence of well-defined stomach mapping protocols, such as those of ESGE (European Society of Gastrointestinal Endoscopy) - 10 images - or Japan – 22 images.

Artificial Intelligence, and more specifically Computer Vision, has the potential to mitigate these limitations, especially in two well-defined areas that have been identified as relevant sources of diagnostic errors, and which largely result from the observation and analysis of visual data:

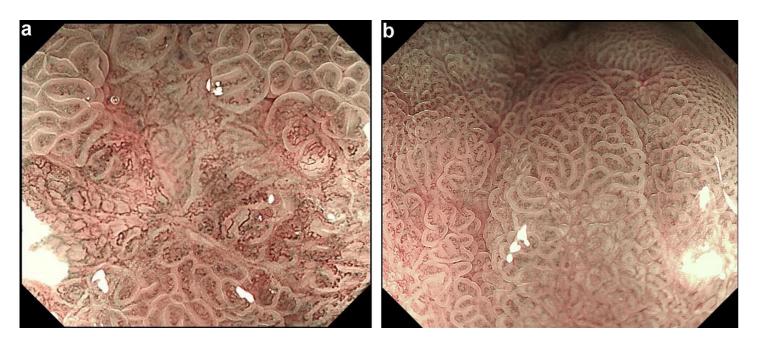
• Detection of gastric reference points – The stomach is a difficult organ to visualize in its fullness. An expert must remotely manipulate a device that illuminates, films, and interacts with a bag-shaped organ, with deformable walls, and with few identifying visual marks. Even for an experienced gastroenterologist, it is not easy to guarantee that 100% of all gastric tissue has been visualized, and it is possible that the lesions to be identified (Figure 2) are precisely in the regions that have not been observed. As reported by Pimenta-Melo [3], this failure rate can reach 9%, which is a very relevant factor for survival rates associated with this disease. What if an artificial intelligence-based system could accurately report to the expert the percentage of gastric tissue visualized during an examination and could guide him to the regions not yet observed?

• Detection of gastric cancer lesions – Although upper digestive endoscopy is a standard and wellestablished procedure, it is possible, as mentioned above, to fail the task of detecting all relevant lesions. As an example, and for physicians still in their learning period, or in regions of the globe where this specialty is not so well developed, we may even think that in the future, systems based on artificial intelligence may enable the optimization of this procedure as it happens for colonoscopy. What if an artificial intelligence-based system allowed the expert to be accurately informed that examined tissues have visual patterns consistent with neoplastic lesions?

To better understand the maturity and current effectiveness of Artificial Intelligence algorithms to support the screening and diagnosis of gastric cancer,

an analysis of this state-of-the-art was made via the research of scientific articles indexed by PubMed, EMBASE and Scopus as of July 2020. In this analysis, we included studies that reported the diagnostic accuracy of artificial intelligence algorithms for the detection and characterization of lesions of the upper gastrointestinal tract, including the stomach, taking into account several performance measures. For more details, we refer to the article where this study was published [5]. The results obtained were positive and promising for the future use of these technologies in clinical environments. From an initial query that resulted in 1678 studies found, 19 met all the criteria for a quantitative analysis, showing already very high values of sensitivity (90%) and specificity (89%). In simpler words, approximately 9 out of 10 neoplastic lesions present were correctly detected and identified in all images analyzed by the algorithm, and approximately 9 out of 10 lesions classified as neoplastic by the algorithms were correctly classified. From a more technical perspective, the vast majority of algorithms were based on the latest deep neuronal network structures, with a wide variety of architectures. Although these results still lack validation in clinical environments, and the problem of the detection of gastric reference points is less developed than that of the presence of gastric cancer lesions, it is unequivocal that the research activity in this field, associated with the very promising results already obtained, outlines a very positive future for the transformative influence that artificial intelligence will most likely have in the screening and management of a growing health problem that is gastric cancer.

Figure 2 - Representative images of lesions of the gastric mucosa, using Narrow-Band Imaging. A) Image diagnosed as gastric cancer; B) image diagnosed as a non-cancerous lesion. (Adapted from [4]).



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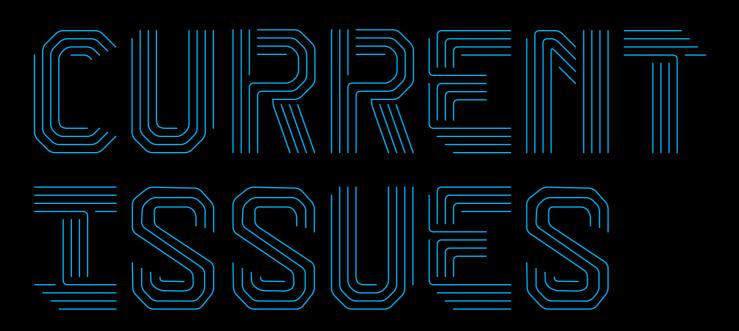
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STAYAWAY COVID. CONTACT TRACING FOR COVID-19

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In a pandemic, contact tracing is crucial to interrupt transmission chains. However, the traditional way of doing this has limitations that can be overcome by a digital tool if properly adopted by the population and integrated with health services. STAYAWAY COVID is the INESC TEC's response to this challenge.

A virus is a parasite whose sole purpose is to multiply and dominate the world. To do so, it depends on seizing the cells from living beings, the hosts, which provide the necessary conditions to copy its genetic material and continue its path of infection and replication. In order to conquer to world, a single host - regardless of how vulnerable and collaborative it is - is not enough; the virus needs to infect more and more hosts. Defeating the virus means preventing its replication. This battle is fought by the immune system of each host; however, and until we are totally immune to it, we can only minimise its transmission. In this sense, and in order to avoid yet another indiscriminate lockdown nationwide, the contact tracing performed by healthcare services in any infectious outbreak is crucial, in addition to all the other individual prevention measures we adopt. In the case of COVID-19, and since the virus is particularly tricky - it renders us silently infectious for a few days, before any symptoms appear, and even though we never feel anything, it can keep us that way for a couple of weeks - and we still don't have the capacity to test the entire population on a regular basis, the fast detection of those who have been exposed to infected individuals is quite important.

Traditional contact tracing relies on the experience of infectious and contagious patients, in order to identify people who have been exposed to them recently.

Based on this identification, the teams of healthcare professionals contact people individually, and carry out their clinical follow-up. The process is demanding and time consuming, so it is difficult to scale up. The goal of the STAYAWAY COVID is to complement traditional contact tracing, thus making it independent of our experience, and allowing each one of us to assess our own risk of exposure to those infected with COVID-19. Each day, the application installed on the users' smartphones assesses their risk of contact with people whose infection has been confirmed by the National Health Service. At the moment, a contact lasting more than 15 minutes, and at a distance of less than two meters, is considered a close contact. After identifying a close contact over the previous 14 days, the application suggests the user to self-isolate and contact the healthcare authorities.

Conceptually, it is guite simple to explain how STAYAWAY COVID works. Each mobile phone generates a random numeric code without any relation to the device or the user. These codes are all different. Each mobile phone broadcasts its code several times a second, which is then received by other devices that have the application, within a range of a few dozen meters. The mobile phone that receives the code is able to estimate, with reasonable precision, whether the devices that broadcast the code were less than two meters away.

A step ahead of the virus

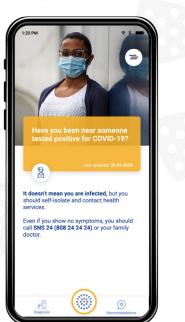
A radar attached to your mobile phone





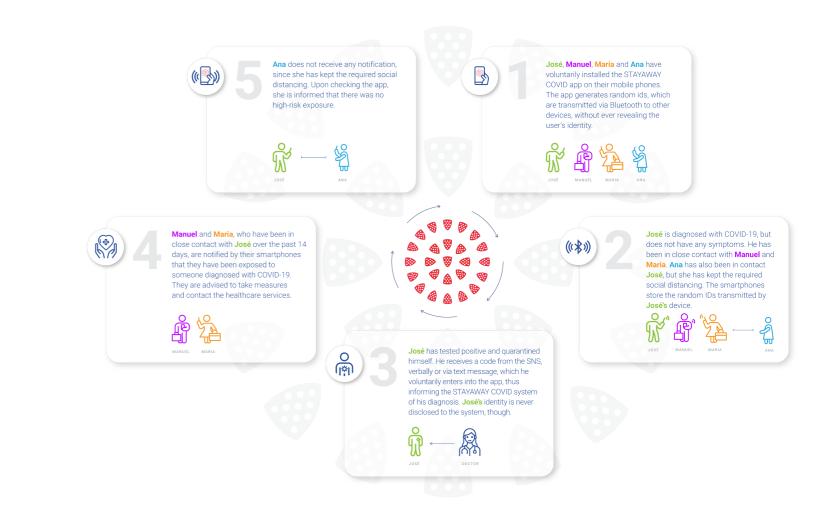


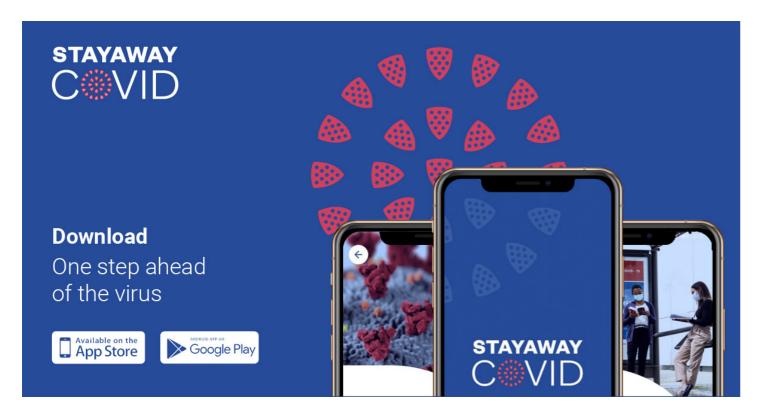
Contact tracing beyond your memory



In this case, it keeps the codes of devices that were close for more than 15 minutes; the other codes are discarded. At the end of the day, each mobile phone identifies the codes issued by devices that were close. In this sense, if the application determines that one of the codes saved is associated with a mobile phone whose user was diagnosed with COVID-19, it immediately displays an alert message. For everything to work correctly, the user diagnosed with COVID-19 must allow the application to broadcast the code issued by his/her device over the previous weeks, so it becomes available to all. All of these codes are anonymous and unintelligible, and do not reveal the identity or any other information about the user. In practical terms, STAYAWAY COVID's architecture, development and operation are much more elaborate. The biggest challenges in the implementation of the system were the analysis and decision-making regarding different trade-offs. It became necessary to find a balance between available technology, usability and "digital inclusion", as well as the various aspects of system security and data involved. In terms of architecture, INESC TEC's solution adopts a distributed computing and storage model that aims to store and

process data partially on each mobile phone, instead of enabling data processing in a global way. Although it is an important way to ensure data privacy, this option hinders scientific, epidemiological and other types of analyses that are equally essential. Regarding security, in addition to following the best development and implementation practices, the team responsible for developing the app adopted specific techniques to address this question. An example is the frequent changes in the code that each mobile phone broadcasts. In fact, this code is not always the same, it changes every 10 minutes. This way, it is possible to mitigate the risk of having someone maliciously observing the code, which could lead to the user-code pair identification. Usability is a constant element in the various parts of the system design. A procedure that reflects this is the way the system seeks to ensure that only users who have been diagnosed with COVID-19 share their codes. The process of validating that the shared codes actually correspond to an infected user is done through a code, which the patient receives from the healthcare authorities, and voluntarily introduces in the application. It is a simple process, but somehow prone to issues concerning





security against fraud. Technically, the team could resort to several options to make this process more secure, but the impact on the users' usability and freedom did not justify them. The development of STAYAWAY COVID has been directed by a constant cost-benefit analysis by all stakeholders.

Unlike traditional tracing, in which healthcare services actively seek high-risk cases, STAYAWAY COVID allows high-risk cases to seek help in a timelier manner. Digital contact tracing is being used for the first time in a pandemic, influenced by the still limited knowledge about the disease, and the only technology that can be used massively and free of charge to estimate how close two people were, in the broadest and wide-ranging situations - Bluetooth. We are only starting to evaluate the app's accuracy and effectiveness, despite the scarce operational information provided by the system. If the results follow the current good indicators, this tool could actually enable (on the short-run) a selective lockdown that promotes a tolerable coexistence with the virus, until we eradicate it. The future will certainly redefine traditional contact tracing.

HOSPITAL CLEANING ROBOT

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The purpose of this robot is to prevent and reduce in-hospital acquired infections, especially those caused by virus and bacteria, to make available a cleaning procedure that can be executed in a systematic and uninterrupted way, and to allow gains in quality and productivity that may let human resources for health focus on other tasks.

Millions of patients are hospitalized worldwide every year. In Europe, for example, it is estimated that around two million will contract infections caused by bacteria gram-negative symptoms present in hospitals, with high mortality. In the United States, infections acquired in hospitals are the sixth leading cause of death in the country, resulting in annual costs between 5 and 10 billion dollars. The elimination of viruses and bacteria thus appears to be of crucial importance, especially now with the pandemic situation in which we find ourselves. Ultraviolet C (UVC) light technology is already well known, and has been used for over 40 years in hospital and pharmaceutical environments, with the purpose of cleaning out the air, water, equipment, materials, among others. This type of radiation damages the genetic structure of the microorganisms, inactivating any virus or microorganism. The key variable is the dose of radiation, that is, the time of exposition to the UVC light. This is well documented in the literature, and therefore, it is possible to calculate both the power and distance that is required for all the microorganisms to be deactivated. Not long ago, this type of systems needed to be operated manually, which implied having an operator deciding where to put the lights and programming the timer. After a while, the operator needs to return to

the site in order to change the location of the lamps and repeat the process. Depending on the furniture (beds, chairs, among others), this procedure may have to be repeated for each room, dorm or ward, becoming burdensome and taking too much time of the operators. By the means of this autonomous robot, it is possible to perform, in a fully automated way, this sequence of operations, freeing human resources to other tasks. After obtaining the map for the site, which is obtained by the robot, it is possible to specify locations to be cleaned, how long should the UVC lights be on, and have it return to the base station, where it will charge the batteries (Figure 1). The robot is also equipped with a module, based on motion and thermal sensors, that is able to detect the presence of human beings, immediately turning off the UVC lights, since this radiation causes harm to any organism. The time during which it is deactivated will be taken into consideration in order to ensure that enough UVC light is emitted to sterilize the site. The inclusion of thermal sensors, aside from the motion sensors, is capable of detecting people (or any hot-blood organisms), even if they are standing still, for instance while in their sleep. This is a failsafe mechanism, as the motion sensors would fail to detect the presence of human beings.



Figure 1 - Hospital cleaning robot.

After the initial programming and configuration, the robot's interface is easy to setup and use, allowing any person to operate the robot, provided they receive a quick training or read the instructor's manual.

In the near future, further work will be developed in order to make the robot more intelligent and autonomous. The idea is for the robot to decide, in an optimal and intelligent way, which routes to take, pit stops, how long it should stay with the UVC lights activated, or if it should continue moving at a constant speed and with the lights on. All will be calculated and decided based on the site to clean. To be able to do this, the robot will first have to draw a 3D layout of the room, using a 3D laser sensor, and with that information decide in an optimal way how to proceed. The main contribution of this Project is then to reduce the transmission of infectious diseases caused by virus and bacteria that live in hospital settings, providing a systematic and uninterrupted cleaning procedure that will generate gains in terms of quality and productivity, freeing human resources to perform other tasks. In addition, health care professionals will be less exposed to toxic or corrosive material that is typically used in traditional cleaning procedures.

The validation tests were performed at the Hospital of S. Martinho, in Valongo. According to João Sobral, member of the hospital, this robot is extremely interesting, since it is a way to reduce in-hospital acquired infections.

Acknowledgements

We would like to thank the participation of everybody who contributed to the success of this project, namely M. Petry, C. Rocha, P. Costa, M. Silva, J. Lima, A. Amorim, A. Baltazar, J. Sobral and J. Teixeira, among others, who dedicated, some in a gracious and voluntary way, their time to this project.











THE SIEGE - ON THE 1899 BUBONIC PLAGUE EPIDEMIC IN PORTO

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Can we learn something from the 1899 bubonic plague epidemic that led to the siege of Porto, isolating the town for a few months? Ricardo Jorge, responsible for identifying the infectious agent, coordinated the medical research and the actions to fight against the epidemic. Considering how serious the disease was, the **Government authorities in Lisbon** decided to isolate the city, forbidding the circulation of people and goods, which led to fierce reactions by Porto's inhabitants. This epidemic was also the first public health crisis, and photography played a relevant role in documenting it, mainly due to two photographers from Porto: Aurélio da Paz dos Reis and Guedes de Oliveira.

The first case of bubonic plague in Porto, considered the third major global plague epidemic, was recorded on July 9 1899, by Ricardo Jorge. At the time, Ricardo Jorge was the physician in charge of the Municipal Health and Hygiene Services, which he established in 1892. He was a physician and academic of great status, dedicating himself to public health issues for quite a long time. Ricardo Jorge would become a major reformer, after starting to work at the Directorate-General of Public Health in Lisbon.

It was the first major epidemic with a remarkable photographic record. There are plenty of photos by the amazing Porto photographer Aurélio da Paz dos Reis, and others by Photographia Guedes, a photography shop that was famous in the city, at that time. The pictures show the actions carried out to address the epidemic, by health brigades and firefighters, as well as the backstage work at the laboratories, performed by medical personnel, under Ricardo Jorge's guidance. They also document several protests by the city's population and living forces.

It was the end of the 19th century, a period of deep social and economic changes in the city, with the arrival of industrialisation, new technologies and photography.

Porto's intellect... belonged to the Positivism generation. The generation that came after the Romantic generation of Café Guichard and Águia de Ouro. In 1878, the magazine O Positivismo emerged, produced by Teófilo Braga and the doctor Júlio de Matos, director of the Conde Ferreira hospital. In 1882, the magazine had made a thorough review of the Evolution of Species' Darwinism. Republicanism seemed committed to garner the Scientism that grew in Europe due to the second industrial revolution. Aurélio is 20 years old, and he already collects newspaper clippings. That is probably how he was exposed to Charles Darwin's ideas, by reading the O Positivismo. The works he eventually bought, maybe during one of his trips to France, are the most representative of the new evolutionary materialism: On the Origin of Species and The Descent of Man.

M. do Carmo Serén, Manual do Cidadão Aurélio da Paz dos Reis, CPF edition, 1998



Figure 1 - Dr. Ricardo Jorge at the Municipal Bacteriology Laboratory, 1899. Ricardo Jorge would confirm the diagnosis of plague on August 8, 1899, photographed by Photographia Guedes (courtesy of Municipal Archive of Porto)



Figure 2 - August 24 1899 - Meeting of traders and businessmen from Porto at the Palácio da Bolsa, to discuss the consequences for the economy of the sanitary siege, decreed by the government, photograph by Aurélio da Paz dos Reis (courtesy of CPF - Portuguese Centre of Photography)



Figure 3 - Shop window in Porto, protesting against the sanitary cordon, decreed by the government on the proposal of Ricardo Jorge, who is represented by a doll they call "The Inventor of the Pest", photograph by Aurélio da Paz dos Reis (courtesy of CPF)

CHRONOLOGY **OF EVENTS**

July 4 > 1899	Ricardo Jorge was informed about some sudden and unexplained deaths, which would have occurred at Rua da Fonte Taurina, in Ribeira. He visited the place after two days, and totalled four fatal cases among ten infected. They all lived "in miserable and filthy buildings" he would write.
July 9 > 1899	Ricardo Jorge would write: "a bacillus that microscopically covered the morphology of that of the plague - short, solid, bipolar interior, intermediate white space".
July 12 > 1899	For the first time, in a report sent to the Civil Governor, Ricardo Jorge identifies the disease as bubonic plague, explicitly and quite clearly.
July 28 > 1899	In a report, Ricardo Jorge reiterates his conviction that it is, in fact, bubonic plague.
August 8 > 1899	After a bacteriological examination, performed in the municipal laboratory that he had established, Ricardo Jorge confirms the previous diagnosis of plague. This diagnosis was validated by the laboratory work performed by Câmara Pestana, director of the Bacteriology Institute of Lisbon.
August 17 > 1899	The Government issued a decree establishing the first sanitary measures on the city.
August 23 > 1899	The army surrounded the city; entering and leaving is strictly restricted, for both people and goods. The "siege", as it will be remembered, will have very negative consequences, leading to great economic uncertainty, unemployment and famine.
August 24 > 1899	Meeting of traders and businesspersons from Porto at the Palácio da Bolsa, to discuss the blockade and the city's sanitary siege (photographed by Aurélio da Paz dos Reis).
October 4 > 1899	Ricardo Jorge leaves Porto, to assume his position at the Directorate-General of Health and Public Charity.
December > 1899	End of the siege.

The photographic record of the 1899 bubonic plague was made possible by the advances in photography and the of the city remarkable photographers from Porto. Since the official invention in 1839, the evolution of photography was The irony that History keeps underlining: the third plague quite fast, leading to quality pictures and, above all, vivid epidemic that devastated the city of Porto came from portraits of day-to-day life. The development of lighter/ the province of Yunnan (China), appearing around 1840. simpler equipment and glass negatives (1851) enabled Hence, it would take about 60 years to travel to Porto, the easy and *ad infinitum* reproduction of copies, while with the first cases identified in 1899. At that time, the adoption of sophisticated techniques e.g., gelatine travelling took place at different speeds, even for the silver and silver bromide (1880), contributed to accelerate infectious agents. the process and obtain snapshots. Moreover, and unlike all expectations, all these innovations arrived quickly The "siege", enforced by the central Government in to Portugal, particularly to Porto. The photographers Lisbon, and against local authorities, was ruthless. kept themselves updated about what was happening For this reason, many people perceived the siege as in France, leading to the immediate dissemination and a retaliation against the actions on January 31 and testing of all the major developments. the pro-Republic movements in Porto. Many people The photographic record of the events took place protested against this decision, in an attempt to force quite naturally in this context, eventually leading to the Government to overturn it. Some historians claim photojournalism. Both Aurélio and Guedes de Oliveira that this traumatic event may have conditioned the are fine examples of this developing connection between future attitude of the Porto inhabitants towards the photography and journalism. The development of socially capital, always characterised by a critical distancing, inclined photography took place simultaneously, in order along with a constraining subservience, blaming Lisbon to expose the situation of poorer and more vulnerable for everything that happens in the region, but also the individuals. These new fields expanded the scope of what inability to assert autonomy. In fact, people interpreted would later become documentary photography. the siege as a humiliation for the city, leading, at a certain At the same time there were remarkable breakthroughs point, to an uprising against the healthcare services and in the field of Public Health. In 1882, Koch discovered the Ricardo Jorge himself. He would eventually leave the city, tuberculosis bacillus. It was the beginning of Medicine disheartened, and assume the position of Inspectorbased on science, replacing the Medicine based on General of the newly established Directorate-General old wives' remedies and empirical procedures, without for Health and Public Charity . This DG would constitute scientific evidence. The advances in microbiology were an important milestone in the history of Public Health the main cause of the aforementioned breakthroughs in Portugal, leading the reform of Public Health services in Public Health. Having identified many of the microbial in the country, by publishing the General Regulation of pathogens that caused most of the contagious Health and Public Charity Services, in 1901. diseases that plaqued Europe at that time, the scientific The siege would only end at the end of December, just community was able to understand a little better before Christmas, when the number of infectious cases the mechanisms of disease spreading, and was able was very small. However, some believe that the disease to address them more effectively. The plaque that remained active in Porto until 1915. Due to a series of tormented Porto at the outset of the 20th century would fortunate events, the final number of deaths turned out play a key role, by accelerating change - through the to be much lower than expected, given the severity of the valorisation of laboratory work and the microscope, as disease: there were "only" 132 deaths. resources to support medicine. It would also contribute to a deep reorganisation of Public Health Services. Ricardo Jorge would be a key agent in this reform: first in Porto, as head of the Municipal Public Health Services, and then in Lisbon, at the Directorate-General of Health and Public Charity, and then at the Directorate-General of Public Health, during the Republic.

How the plague was addressed - the siege



Figure 4 - Car from the Municipal Disinfection Service, of a special firefighter brigade, participating in the cleaning of unhealthy houses in Porto, to prevent the spread of the Bubonic Plague, photography by Photographia Guedes (courtesy of Municipal Archive of Porto)



Figure 5 - Health technicians prepared to perform the disinfection, photograph by Aurélio da Paz dos Reis (courtesy of CPF)

Analysis of the 1899 plague and the siege of Porto

It is now possible to state that the relatively limited character of the 1899 epidemic in Porto has pretty much nothing to do with the sanitary siege decreed by the central Government. This siege did not work that well, since it was not planned in advance and the city did not have the required conditions. The success is associated with other decisions made by the accountable physicians, mainly the campaigns to exterminate rats, and a set of social and environmental circumstances that fortunately did not favour the spreading of the disease. The dominant species of flea in Portugal was ineffective in transmitting the bacillus, and some believe that the rats have probably developed an immunity, associated with a mutation of the bacillus, the Yersinia pseudotuberculosis. The low mortality rate of the disease may also explain the opposing reply to the siege by the Porto bourgeoisie, which perceived other diseases - tuberculosis or typhoid - as more threatening than the plague itself. Even though the military siege of Porto is considered today as an unjustified and even counterproductive action, since it discredited the healthcare services, leading certain people to hide several cases of infection - as Ricardo Jorge said in his report: "at least a fifth of the cases are unknown" -, medical practices in this fight against the epidemic seem to reflect modernised knowledge and procedures. As examples, the bacteriological analysis and the field actions, namely against rats, identified as bacillus carriers. Moreover, the isolation of infected patients, the disinfection of homes, the vaccination of people who had contact with infected individuals, the use of disinfectant to wash the streets and sewers and the cremation of corpses were proven adequate and very effective measures.

Something that seems undeniable is the fact that the plague detected in Ribeira finally exposed to public eye a dirty city, without sanitation, often without drinking water, with very low housing conditions and serious health problems. It is crucial to destroy, as soon as possible, the filthy neighbourhoods where the plague looms, and the inhabitable 'ilhas', cesspools of diseases... in order to completely eradicate the evil, it would be necessary to clean up the city, completely destroying three neighbourhoods: Barredo, Fonte Taurina and Miragaia.

Ricardo Jorge, Demographia e Hygiena na cidade do Porto

In fact, the majority of victims belonged to the poorest strata, who lived without the least hygiene conditions. These circumstances favoured the development of pests, such as mice and fleas, and consequently, the spread of diseases. The physicians and the most progressive members of society began to advocate the importance of better housing conditions, while demanding fundamental sanitary conditions. The standards of hygiene and habitability no longer belonged exclusively to the private sphere, but became a duty of the State and Public Health Services.

After the decree of October 4 1899, which established the Directorate-General of Health and Public Charity, to where Ricardo Jorge was hired, and its regulation in 1901, there was still a crucial step to take: to cut the secular, umbilical cord that connected the public health to charity in Portugal. This would only happen in 1911, after the establishment of the Republic, with the creation of the Directorate-General for Health, by decree of the Minister of the Interior, António José de Almeida. Ricardo Jorge would then be appointed Director-General of Health. Ricardo Jorge would always remain a critical voice in advocating the health and well-being of the population, often speaking against Government excuses for the lack of resources, or the decisions to stop investing in sewerage systems, hygiene and healthcare services in the cities.

We are now in the age of a new fundamental right, of a general physical morality, according to which an urgent matter emerged, despite all other political and collective concerns: the international solidarity for hygiene.

Ricardo Jorge, in the preamble of the decree establishing the DGS reorganisation, in 1926



Figure 6 - Firefighters disinfesting a coffin, photograph by Photographia Guedes (courtesy of Municipal Archive of Porto) 1. The first epidemic dates back to the 14th century, while the second dates back to the 16th and 17th centuries

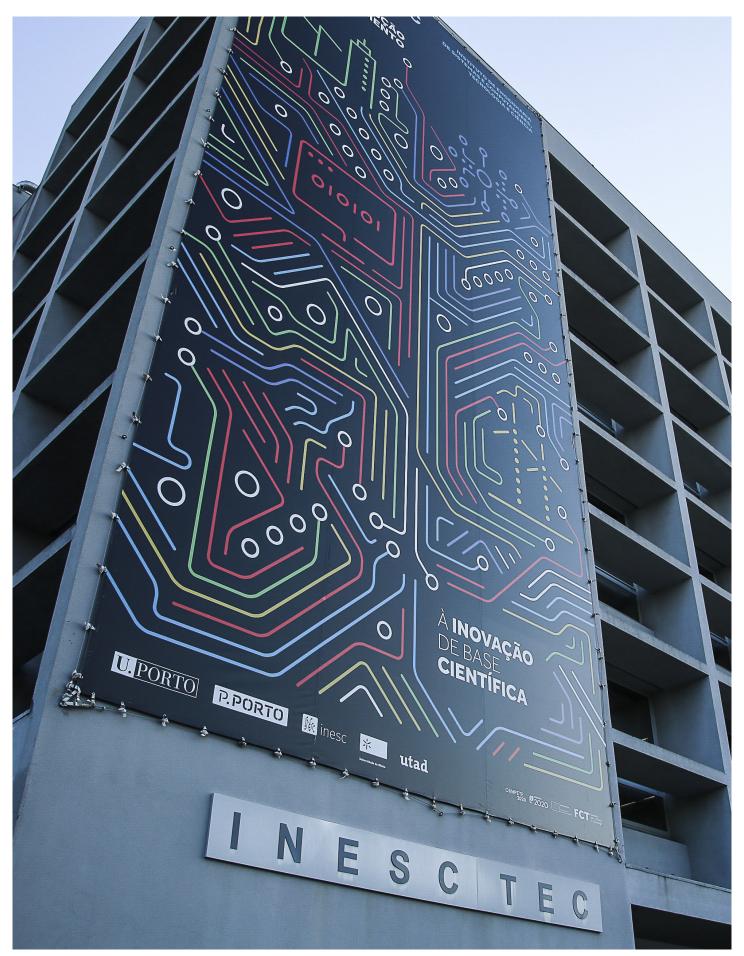
2. The author refers to Aurélio da Paz dos Reis, a prominent Porto-original and photographer, whose pictures keep us company in this article.

3. Câmara Pestana replaced Ricardo Jorge in Porto; he got infected, and died on November 15 1899, at the age of 36.

4. In order to understand how limited the bubonic plague was, one can compare it with the cholera epidemic, called cholera morbus or Asiatic cholera, which arrived in Western Europe between 1826 and 1830, and was reported extinct in 1837. It spread across Russia, Germany, England, France, Spain and Portugal, and might have caused over a million victims. The cholera invasion in Portugal took place in January 1833, in the city of Porto, with the arrival of the ship London Merchant, carrying troops destined to join the liberal army. The epidemic soon spread, with the first deaths recorded in April 1833, at the S. José hospital, in Lisbon.

5. They were sent to a hospital called Guelas de Pau, established in 1884 to isolate and treat cholera patients. In 1899, the hospital was adapted to receive patients with bubonic plague; it was then named Senhor do Bonfim hospital; finally, in 1914, it was renamed Joaquim Urbano hospital.

6. Approximately 75% of the plague cases recorded during the outbreak in 1899 correspond to inhabitants of 'medieval' Porto - Sé, S. Nicolau, Vitória and Miragaia - where the living conditions were significantly worse.



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