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AI Watch

Artificial Intelligence in Medicine and Healthcare: applications, availability and societal impact

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Contents

Preface

This research is framed in the context of the HUMAINT project (Human Behaviour and Machine Intelligence, web portal at https://ec.europa.eu/jrc/communities/en/community/humaint) of the Centre for Advanced Studies, Joint Research Center of the European Commission and linked to AI Watch, the European Commission knowledge service to monitor the development, uptake and impact of Artificial Intelligence (AI) for Europe, launched in December 2018.

AI has become an area of strategic importance and a key driver of economic development. As part of its Digital Single Market Strategy, the Commission put forward in April 2018 a European strategy on AI in its Communication 'Artificial Intelligence for Europe' COM(2018)237 [1]. The aims of the European AI strategy announced in the communication are:

- To boost the EU's technological and industrial capacity and AI uptake across the economy, both by the private and public sectors.
- To prepare for socio-economic changes brought about by AI.
- To ensure an appropriate ethical and legal framework.

Subsequently, in December 2018, the European Commission and the Member States published a 'Coordinated Plan on Artificial Intelligence' COM(2018)795 [2], on the development of AI in the EU. The Plan foresees the creation of EU AI Watch, the 'Commission Knowledge Service to Monitor the Development, Uptake and Impact of Artificial Intelligence for Europe'. AI Watch is developed by the Joint Research Centre (JRC) in collaboration with the Directorate-General for Communications Networks, Content and Technology (DG CONNECT).

AI Watch aims to monitor industrial, technological and research capacity, policy initiatives in the Member States, uptake and technical developments of Artificial Intelligence and its impact in the economy and public services. It provides a number of analyses necessary to monitor and facilitate the implementation of the European Strategy for AI. All results of this analysis are published on the AI Watch portal (https://ec.europa.eu/knowledge4policy/ai-watch_en). AI Watch has a European focus within the global landscape, and engages in its activities with Member States. From AI Watch in-depth analyses, we will be able to understand better European Union's areas of strength and areas where investment is needed. AI Watch will provide an independent assessment of the impacts and benefits of AI on growth, jobs, education, and society.

The Commission also established a High-Level Expert Group that published Guidelines on trustworthy AI in April 2019 [3], and in the 'White Paper On Artificial Intelligence - A European approach to excellence and trust' COM(2020)65 [4], the Commission acknowledges that as with any new technology, the use of AI brings both opportunities and risks. Citizens fear being left powerless in defending their rights and safety when facing the information asymmetries of algorithmic decision-making, and companies are concerned by legal uncertainty.

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Executive Summary

This report reviews and classifies the current and near-future applications of Artificial Intelligence (AI) in Medicine and Healthcare according to their ethical and societal impact and the availability level of the various technological implementations. It provides conceptual foundations for well-informed policy-oriented work, research, and forward-looking activities that address the opportunities and challenges created in the field of AI in Medicine and Healthcare. This report is aimed for policy developers, but it also makes contributions that are of interest for researchers studying the impact and the future of AI on Healthcare, for scientific and technological stakeholders in this field and for the general public.

This report is based on an analysis of the state of the art of research and technology, including software, personal monitoring devices, genetic tests and editing tools, personalized digital models, online platforms, augmented reality devices, and surgical and companion robotics. From this analysis, it is presented the concept of 'extended personalized medicine', and it is explored the public perception of medical AI systems, and how they show, simultaneously, extraordinary opportunities and drawbacks. In addition, this report addresses the transformation of the roles of doctors and patients in an age of ubiquitous information and identifies three main paradigms in AI-supported Medicine: 'fake-based', 'patient-generated', and 'scientifically tailored' views.

This Report presents:

- An updated overview of the many aspects related to the social impact of Artificial Intelligence and its applications in Medicine and Health. A new 'Technology Availability Level (TAL) Scale' is defined to evaluate and compare their current status.
- Recent examples of the growing social concerns and debates in the general press, social media and other web-bases sources.
- A 'Visual Overview of AI and AI-mediated technologies in Medicine and Healthcare', in which two figures show, respectively, a (newly proposed) classification according to their ethical and social impact, and the most relevant ethical and social aspects considered for such classification. Some key questions, controversies, significant, and conflicting issues are outlined for each aspect.
- A 'Structured Overview', with a sorted list of technologies and their implementations, including perspectives, conflicting views and potential pitfalls, and a corresponding, extensive list of references.
- A conclusive set of policy challenges, namely the need of informed citizens, key aspects (of AI and AI-mediated technologies in Medicine and Healthcare) to evaluate, and some recommendations towards a European leadership in this sector.
- We finally relate our study with an update on the use of AI technologies to fight the SARS-CoV-2 virus and COVID-19 pandemic disease.

The main scientific result of this Report has been published in the following reference:

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List of acronyms and abbreviations

Acronyms and abbreviations employed in this Report and related references are listed in the following Table 1. It is important to note that some of them are also used -with the same or different meaning and expression- in other contexts of science and technology, even in areas related to Medicine and Health.

Table 1. List of the main acronyms and abbreviations employed in this Report.

AI	Artificial Intelligence
AR	Augmented Reality
BCI	Brain Computer Interfaces
CAD, CADx	Computer Aided Diagnosis
CADe	Computer Aided Detection
CDSS	Clinical Decision Support System
CNN	Convolutional Neural Networks
CT	Computed Tomography
DIY	Do-It-Yourself
DL	Deep Learning
DS	Decision Support
DTC	Direct-to-Consumer (genetic) test
EC	European Commission
ED	Emergency Department
EHR	Electronic Health Record
EU	European Union
FDA	Food and Drug Administration (of the USA)
GDPR	General Data Protection Regulation (of the EU)
HCI	Human-Computer Interaction/Interface
ICT	Information and Communication Technologies
ICU	Intensive Care Unit
IGS	Image Guided Surgery

IOI	Intra-Operative Imaging (during a surgical procedure)
IO	Intra-Operative (inside the OR, during the procedure)
IoT	Internet Of Things
IT	Information and Telecommunications
IMDRF	International Medical Device Regulators Forum
JRC	Joint Research Centre (of the European Commission)
(L)AWS	(Lethal) Autonomous Weapons System
ML	Machine Learning
MR(I)	Magnetic Resonance (Imaging)
OR	Operating Room
PET	Positron Emission Tomography
R&D	Research and Development
R&D&I	Research and Development and Innovation
SaMD	Software as a Medical Device
SAR, SR	Socially Assistive Robot, Social Robot
SME	Small and Medium Enterprise
SW	Software
TAL	Technology Availability Level
TRL	Technology Readiness Level
UN	United Nations
UNESCO	United Nations Educational, Scientific and Cultural Organization
USA	United States of America
VR	Virtual Reality
WHO	World Health Organization
WIPO	World International Patent Organization
WMA	World Medical Association

Definitions

In the context of this Report, the terms listed in the following Table 2 are to be understood as declared in this section. Their definitions are quoted from the indicated references and links.

Table 2. Some specific terms in this Report.

Artificial Intelligence	Big Data	Declaration of Geneva	Deep Learning
Digital Health	eHealth	Global Health Ethics	Health
In-silico	In-vitro	In-vivo	International Medical Device Regulators Forum
Machine Learning	Medicine	Software as a Medical Device	Social Impact (of a technology)
Sustainable Goals	The Global South	The Goal of Health	The West
Universal Health Coverage			

Artificial Intelligence: Modern dictionary definitions focus on Artificial Intelligence (AI) being a sub-field of computer science and how machines can imitate human intelligence (being human-like rather than becoming human) [6]. In a broad sense, it may be understood as the study of how to produce machines that have (some of the) qualities of the human mind, such as the ability to understand language, recognize pictures, solve problems, take decisions and learn [7]. Other authors consider AI 'broadly defined as the science and engineering of making intelligent machines, especially intelligent computer programs' [8].

However, definitions of artificial intelligence begin to shift based upon the goals trying to be achieved with the AI system [6]. Generally, there may be considered three types of AI: systems aimed at genuinely simulating human reasoning (and behavior) tends to be called 'strong AI', systems that can produce results similar to humans (but may use very different methods) are 'weak AI' and 'in-between' systems are those informed or inspired by human reasoning. This tends to be where most of the more powerful work is happening today (in industry). The 'in-between' systems use human reasoning as a guide, but they are not driven by the goal to perfectly model or reproduce it [9].

Most current applications of AI in Medicine and Health may be considered of the 'in-between' type, as 'only inspired' by the human reasoning, but many others are certainly evolving to become 'strong AI' systems.

UNESCO states that 'Artificial intelligence can be a great opportunity to accelerate the achievement of sustainable development goals. But any technological revolution leads to new imbalances that we must anticipate'.

From: https://en.unesco.org/artificial-intelligence

Big Data: Digital data that, through its volume or complexity, surpasses human analytical abilities and traditional data processing methods.

From: https://en.unesco.org/courier/2018-3/lexicon-artificial-intelligence and https://en.wikipedia.org/wiki/Big_data

Declaration of Geneva[1]**:** It is one of the World Medical Association's (WMA) oldest policies. As stated by the WMA, 'it was adopted by the Second General Assembly in Geneva in 1947. It builds on the principles of the Hippocratic Oath. It also remains one of the most consistent documents of the WMA. With only very few and careful revisions over many decades, it safeguards the ethical principles of the medical profession, relatively uninfluenced by zeitgeist and modernism'.

From: https://www.wma.net/what-we-do/medical-ethics/declaration-of-geneva/

The WMA furthers states that 'the Oath should not be read alone, but in parallel with the more specific and detailed policies of the WMA especially the International Code of Medical Ethics, which followed the Declaration of Geneva as early as 1948'.

From: https://www.wma.net/policies-post/wma-international-code-of-medical-ethics/

Deep Learning: As defined by UNESCO, it is 'a technique, at the cutting edge of machine learning, that enables a machine to independently recognize complex concepts such as elements in images. This is done by scouring millions of images […] that have not been labelled by humans. The result of a combination of learning algorithms and formal neural networks and the use of mass data, deep learning has revolutionized artificial intelligence. It has countless applications, including search engines, medical diagnosis, autonomous cars, etc'.

From: https://en.unesco.org/courier/2018-3/lexicon-artificial-intelligence

Digital Health: As recognized by the World Health Organization, digital technologies 'can offer limitless possibilities to improve health, from personal fitness to building stronger health systems for entire countries'.

From: https://www.who.int/behealthy/digital-health

eHealth: As defined by the World Health Organization, 'it is the use of information and communication technologies (ICT) for health'.

From: https://www.who.int/ehealth/en/

Global Health Ethics: The Global Health Ethics Unit from the World Health Organization 'provides a focal point for the examination of ethical issues raised by activities throughout the Organization. The unit also supports Member States in addressing ethical issues that arise in their own countries. This includes a range of global bioethics topics; from public health surveillance to developments in genomics, and from research with human beings to fair access to health services'.

From: https://www.who.int/ethics/en/

Health: As defined by the World Health Organization, 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'.

The Universal Declaration of Human Rights states, in its 25th Article, that 'Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care […]'.

From: https://www.un.org/en/universal-declaration-human-rights/index.html

The World Health Organization Constitution was the first international instrument to enshrine the enjoyment of the highest attainable standard of health as a fundamental right of every human being ('the right to health').

From: https://www.who.int/en/news-room/fact-sheets/detail/human-rights-and-health

1 Not to be confused with the Convention of Geneva (1949) which defines the international law for humanitarian treatment in war.

In-silico: Medical, biological research performed on computer or via computer simulation, that is, 'in chips', as opposed to being conducted in living organisms (*in-vivo*) or in a laboratory environment outside living organisms (*in-vitro*).

From: https://en.wikipedia.org/wiki/In_silico

In-vitro: Medical, biological research performed outside living organisms, that is, 'within the glass', in a laboratory environment as opposed to being conducted in living organisms (*in-vivo*),

From: https://en.wikipedia.org/wiki/In_vitro

In-vivo: Medical, biological research performed in living organisms.

From: https://en.wikipedia.org/wiki/In_vivo

International Medical Device Regulators Forum: It is a group of medical device regulators from around the world that have voluntarily come together to harmonize the regulatory requirements for medical products that vary from country to country.

From:https://www.fda.gov/medical-devices/cdrh-international-programs/international-medical-device-regulators-forum-imdrf

Their current members represent medical device regulatory authorities in many countries. The European member is the European Commission Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs. The USA member is the Food and Drug Administration. The World Health Organization is an Official Observer.

Machine Learning: It is defined as an artificial intelligence technique that can be used to design and train software algorithms to learn from and act on data. Software developers can use machine learning to create an algorithm that is 'locked' so that its function does not change, or 'adaptive' so its behavior can change over time based on new data [8].

As stated by UNESCO, it is an automatic learning program to solve problems from examples, enabling it to compare and classify data, and even recognize complex shapes. Before the advent of **deep learning** in 2010, this type of program (i.e. machine learning) needed to be overseen by humans. For example, each image had to be explicitly designated as containing certain elements so that the machine could perform the requested recognition operation.

From: https://en.unesco.org/courier/2018-3/lexicon-artificial-intelligence

Medicine: It is the science and practice of establishing the diagnosis, prognosis, treatment, and prevention of disease. Medicine encompasses a variety of healthcare practices evolved to maintain and restore health by the prevention and treatment of illness.

From: https://en.wikipedia.org/wiki/Medicine

Software as a Medical Device: The International Medical Device Regulators Forum (IMDRF) defines it as 'software intended to be used for one or more medical purposes that performs these purposes without being part of a hardware medical device'. Use of Software as a Medical Device is continuing to increase. It can be used across a broad range of technology platforms, including medical device platforms, commercial 'off-the-shelf' platforms, and virtual networks, to name a few. Such software was previously referred to by industry, international regulators, and health care providers as 'standalone software', 'medical device software' and/or 'health software', and can sometimes be confused with other types of software.

From: https://www.fda.gov/medical-devices/digital-health/software-medical-device-samd

Social Impact (of a technology): The risks, uncertainties, ethical dilemmas and other issues (besides economical, scientific or technological impacts) that come together with technological innovations and may affect the society at any level, from individuals to structured groups and states. The social impact of a technology may influence –and even determine– its acceptance, rejection or modification [10].

Sustainable Goals: United Nations define them as the blueprint to achieve a better and more sustainable future for all. They address the global challenges we face, including those related to poverty, inequality, climate, environmental degradation, prosperity, and peace and justice. Health is the Sustainable Goal number 3. The full list of the 17 sustainable goals of the United Nations is: https://www.un.org/sustainabledevelopment/sustainable-development-goals/

The Global South: It is an emerging term (used by the World Bank) to refer to countries located in Asia, Africa, Latin America and the Caribbean and considered to have low and middle income. The Global South is one half of the global North-South divide, and does not necessarily refer to geographical south. Most people in the Global South live within the Northern Hemisphere.

From: https://en.wikipedia.org/wiki/Global_South

The Goal of Health: This is the Sustainable Goal number 3 of the United Nations. It is needed to ensure healthy lives and promote well-being for all at all ages.

From: https://www.un.org/sustainabledevelopment/health/

The West: It is an emerging term used in analogy to The Global South by the World Bank. It refers to countries located in Europe, North America and other regions considered to have high income. The West does not necessarily refer to geographical west.

Universal Health Coverage: It is one of the Sustainable Development Goals agreed by Member States of the United Nations to try to achieve by 2030.

UHC means that all individuals and communities receive the health services they need without suffering financial hardship. It includes the full spectrum of essential, quality health services, from health promotion to prevention, treatment, rehabilitation, and palliative care.

From: https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc)

1 Introduction

Artificial Intelligence (AI) is a new realm of science and technology. It already affects many human activities at all societal levels, from individuals to social groups, corporations and nations. AI is expanding rapidly, worldwide, in almost every industrial, economical and societal sector, from information technologies to commerce, manufacturing, space, remote sensing, security and defense, transport and vehicles and, since the beginning of the XXI century, it is effectively entering into Medicine and Healthcare.

Recent advances in AI systems in Medicine and Healthcare present extraordinary opportunities in many areas of deep social interest together with significant questions and drawbacks, calling for a close consideration of their implementation and how they affect –and can even change– basic definitions in the medical context.

The Objective of this Report is to provide a review of existing and near-future applications of AI in this particular sector. It also provides the first classification of such applications from the point of view of their potential benefits and pitfalls, and ethical and social impact, and presents a set of controversial issues that are not deeply discussed in the literature and should be further researched.

This Report presents:

- An updated overview of the many aspects related to the social impact of Artificial Intelligence and its applications in Medicine and Health. A new 'Technology Availability Level (TAL) Scale' is defined to evaluate and compare their current status.
- Recent examples of the growing social concerns and debates in the general press, social media and other web-bases sources. An update on the use of AI technologies to fight the SARS-CoV-2 virus and COVID-19 pandemic disease is also included.
- A 'Visual Overview', in which two figures show, respectively, the proposed classification of AI and AI-mediated technologies in Medicine and Healthcare according to their ethical and social impact (Figure 1), and the most relevant ethical and social aspects considered for such classification (Figure 2). Some key questions, controversies, significant, and conflicting issues are outlined for each aspect.
- A 'Structured Overview', with a sorted list of topics related to AI and AI-mediated applications in Medicine and Health. They include technologies and their implementations, perspectives, conflicting views and potential pitfalls, and their corresponding references, as detailed in Table 3. The total number of references included is 605.

This Report does not include:

- Thorough compilations of references for each specific technical area.
- Topics related to AI technologies that are common to other areas, such as analysis of the economic aspects and of their use for education or specialized training, productivity, efficiency, workflow or automation.

1.1 Methodology

This Report is based on systematic searches of references in standard scientific, academic, institutional, medical, corporate and technical online platforms. It also presents examples (of social impact and growing concerns and debates) from general press, social media and other web-bases sources. Most references are only from the last three years (i.e. from 2017 to 2019), to highlight only the most recent advances. However, some other works considered of relevance are also included.

Scientific references have been compiled using Mendeley Reference Manager®[2] and Vancouver Citation Style Language (CSL). Press references mainly come from media included in the *Top European Newspapers in English – TheBigProject* [11].

Full (standard) citations correspond to the numbers in square brackets.

All topics, concepts and technologies mentioned in this Report are supported by their specific references as shown in Table 3 within the 'Structured Overview' (section 5). The total number of references included is 605.

1.2 Technology Availability Level (TAL) scale

In order to analyze the different AI applications and their current status, in this Report it is proposed a novel scale named 'Technology Availability Level' (TAL) to give a qualitative description of the degree of availability of a technology. In a numerical scale in 10 steps (levels), it ranges from 0 (unknown status, not considered feasible) to 9 (available for the general public).

The TAL scale is similar in format (and related) to the standard 'Technology Readiness Level' (TRL) scale commonly used to assess R&D&I figures, but it is based on published references (in scientific and academic literature, industrial or corporate reports, and in general media citing sources considered to be reliable according to standards).

It is important to consider that 'availability' is not necessarily equivalent to 'readiness levels' due to such factors as disclosure according to industrial, proprietary and/or government strategies, and that the TAL scale does not evaluate either the fulfillment of regulatory processes.

The values defined for the TAL scale are the following:

TAL 0. Unknown status. Not considered feasible according to references.

TAL 1. Unknown status. Considered feasible according to related, indirect references.

TAL 2. General/basic idea publicly proposed.

TAL 3. Calls for public funding of research and development (R&D) open.

TAL 4. Results of academic/partial projects disclosed.

TAL 5. Early design of product disclosed.

TAL 6. Operational prototype/'first case' disclosed.

TAL 7. Products disclosed but not available.

TAL 8. Available products for restricted (e.g. professional) users.

TAL 9. Available for the public.

2 www.mendeley.com

2 The context

2.1 Artificial Intelligence defines a new and swiftly evolving scenario

The fast and powerful evolution of AI since the beginning of the XXI century results from –and is fostered by– a number of concurrent factors. The main one is the simultaneous availability of powerful and cost-effective computing (processing) tools, hardware (e.g. graphics processing units), software and applications –even in consumer-grade personal computers and mobile devices– and of large (Big) data sets, with many different types and formats of information, both in online and cloud platforms and generated in real time by user wearables and the Internet of Things (IoT).

Key roles in the generalization of AI technologies are also played by the expansion of open source coding resources, online communities of users and developers sharing resources, expertise (know-how) and experience, and the combination of computer processing with other technologies such as photonics (merging of applied optics and electronics), robotics, and human-machine interfaces.

From a geostrategic point of view, leadership in AI is openly recognized by some countries (e.g. Russia, 2017) as the key element for world supremacy in the coming decades. Some leading countries started to promote strong investment in AI since the middle (e.g. USA) and the end of the XX century (e.g. China). The European Union has reinforced its efforts and began coordination among Member States in AI relatively recently. Some European countries already have definite strategies for AI. Others are still in the process.

2.2 Economic impact

The economic impact of AI[3] is expected to be extraordinarily high in the short, medium and long terms, in all sectors, worldwide, and by 2030, estimates indicate a total global impact of 14.23 trillion euros ($15.7 trillion) [12]. The European Commission set about 2.6 billion euros for AI and robotics in the Horizon 2020 plan and 9.2 billion euros for the period 2012-2017 in related areas (including AI and high-performance computing) [13]. Although gross domestic products (GDPs) of Europe and USA are similar and slightly higher than that of China, the percentages of digital information and communications technology in 2017 was 1.66% for Europe versus 2.16% for China and 3.33% for the USA [14]. In patents related to AI systems, China, USA and Japan account for 78% of the registries (since 2014). AI patents are mainly filed by companies and of the top 20 applicants, 12 are from Japan, 3 from USA and 2 from China. Of the academic applicants, 17 out of the top 20 are from China [15]. As a global estimate, it is considered that by 2030 the economic impact of AI will increase to 26.1% of the GDP in China and 14.5% in North America. In Northern Europe, it will be 9.9% and 11.9% in Southern Europe [12].

Recent estimates value the economic impact of AI in Medicine and Health in staggering figures. Health costs are around 10% or higher for gross domestic products of many EU countries (in 2016) [16]. The growth in health AI market is about 40% and, only in the USA, AI applications in Medicine can save $150 billion in annual health costs by 2026 [17]. Only one sector, the genetic testing market, will reach $22 billion in 2024. Currently, there are about 75,000 gene tests available, many of which are direct-to-consumer tests [18].

3 The economic data from [12] to [17] are provided only as a rough, qualitative indication of the very high relevance of the sector under analysis, and of the relative position of Europe as compared to other main competitors worldwide. The study of the economic impact of AI in Medicine and Health Care is a complex task not included in this Report.

2.3 The coronavirus pandemic (COVID-19) disease

In December 2019, by the closing of references for this Report (see 1.1), news emerged about the appearance of an unknown virus in the province of Hubei, in central, mainland China. It belongs to the family of coronaviruses (CoV), particularly to those related to severe acute respiratory syndrome (SARS). On 11 February 2020 it was named as 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2) and the associated disease as 'coronavirus disease' (COVID-19) [19].

Transmission of the virus from human to human was acknowledged in January 2020 and, without any vaccine or treatment, it quickly spread worldwide. On March 11th the COVID-19 outbreak was declared as a pandemic by the WHO [20]. By the end of March 2020, the epicenter of cases moved from China to Europe, strongly affecting the European Union and expanding into other geographical areas. Potential economic and societal impact is expected to be extraordinarily high. Fighting the disease is an on-going, international priority in which AI-related technologies play an essential role.

3 The social impact of Artificial Intelligence in Medicine and Healthcare

The advent of AI into Medicine and Health may be considered as an on-going, (partially) unnoticed revolution. It combines the potential of disruptive advances with extraordinary benefits in Medicine and Healthcare with many unknowns and very questionable, and clearly negative, issues. In addition, AI it has already opened the door to completely new paradigms in Medicine and Health.

In this section 3, only some significant aspects of AI and AI-mediated technologies in Medicine and Healthcare are specifically mentioned. A summarized 'Visual Overview' is shown in Figure 1 and Figure 2 in section 4, and a thorough, sorted list of every topic and their corresponding references are detailed in the 'Structured Overview' in section 5 (Table 3). The total number of references included is 605.

3.1 The main driver: the evolution of technology

As detailed in Table 3, AI and AI-mediated technologies in Medicine and Healthcare have experienced an extraordinary evolution, from computer programs to support the analysis of medical images to its integration in almost every clinical and organizational area.

Radiology was at the forefront of this transformation, together with different branches of surgery using augmented reality devices and surgical robots. They were quickly followed by other image-related specialties (e.g. pathology and laboratory, dermatology, ophthalmology) and, more recently, by virtually all areas of Medicine and Healthcare, from general practitioners to rare diseases to emergency departments, epidemiology, and disease management.

Systems for 'computer-aided diagnosis' have expanded to include online assistants (e.g. app, chatbots), both for very specific medical areas (e.g. oncology, predicting the response to treatments) and for the general public, intraoperative imaging devices have evolved into full 'image guided surgery', even with non-invasive modalities and combined with surgical robotics, while 'clinical robots' now include 'social companions' for hospitalized person, particularly children and the elderly.

In addition, wearables and IoT devices allow for real-time monitoring of physiological information, even at home, and, integrated with medical and social-media data, can trigger clinically related automated interventions (from suicide prevention calls to police to medication delivery).

From a technological perspective, some areas of particular relevance as related to AI applications in Medicine and Healthcare are photonics, robotics, and computers and data science.

Concerned –even healthy– citizens can now order direct-to-consumer genetic tests among many thousands in the market. New tools for big data modeling, analysis, and visualization are also expanding, and provide substantial, transforming improvements in clinical pathways, from the generation of 'digital twins' of individual patients to self-management of treatments. There are even online, crowd shared platforms for such high-end applications as radiotherapy. Many management aspects related to health economy (e.g. increased efficiency, quality control, fraud reduction) and policy also benefit from the new AI mediated tools. They even offer new hopes of improvements in health for environments with reduced resources and in developing regions.

However, as detailed in what follows, technical challenges and ethical concerns remain, and new important questions arise.

3.2 Potential benefits and pitfalls

For European citizens, many applications and devices based on advanced AI technologies are already integrated in daily life (e.g. social networks, online commerce and other services), with some questioning on issues related to privacy and data protection. Topics subject to discussion usually origin in some available or ‘nearly coming’ technologies (e.g. autonomous vehicles), with an open debate on some ethical and social issues (human-in-the-loop, responsibility, effects on professionals and employment). However, in general (that is, not only in Europe) the social effects and the impact of AI systems on human beings are barely studied before the technology is available and begins to spread. Questions usually arise after the systems are deployed.

A significant example of AI-related applications which have recently started an international public debate about the deep social and ethical aspects of the technology is that of (lethal) autonomous weapons systems (LAWS), popularly named as ‘(autonomous) killer robots’ (detailed in 3.5).

With reference to the classification proposed in Figure 1, some of the applications of AI in Medicine and Healthcare show clear beneficial aspects for humans, such as personalized medicine and disruptive improvements in diagnosis, drug design, tailored treatment, evaluation and monitoring of diseases (precision medicine), prosthetics and companion robots to care for the disabled and the elderly, and the development of systems for prevention, early detection and outbreak assessment of pandemics and events of public health.

Other applications of AI in Medicine and Healthcare may be considered questionable. Among them, their potential use for ‘social engineering’ and profiling, fully autonomous robotic physicians and surgeons, self-experimentation medicine, reading of brain signals and external control of neural processes, brain implants, human-animal embryos and the quest for artificial life and synthetic life forms.

And some other applications of AI in Medicine and Healthcare may be considered as clearly negative, such as scamming and malicious use of health data, bioterrorism and evil biohacking (manipulation of the human genome and introduction of malicious changes in the genetic heritage).

3.3 Levels of availability of technologies

Based on published references, many of the aforementioned AI and AI-mediated technologies in Medicine and Healthcare are already starting to become available, at very different stages and degrees of implementation. Certainly, some of them are at their very beginning (and some may even not be operational at all) but, in general, they are no longer science fiction, but really on-going technologies.

As described in the Methodology section, the availability of systems and devices is described using a (newly proposed in this Report) scale called TAL (‘Technology Availability Level’). The TAL gives a qualitative description of the degree of availability of a technology, in a numerical scale of 10 steps (levels), from 0 (unknown status, not considered feasible) to 9 (available for the general public). The TAL scale is similar in format (and related) to the standard ‘Technology Readiness Levels’ (TRL) but, as mentioned, it is based on published references (in scientific and academic literature, industrial or corporate reports, and in general media citing sources considered to be reliable according to standards). As mentioned, it is important to consider that ‘availability’ is not necessarily equivalent to ‘readiness levels’ due to such factors as disclosure according to industrial, proprietary and/or government strategies, and that the TAL scale does not evaluate either the fulfillment of regulatory processes.

3.4 A proposal of classification of technologies according to their social impact

In this Report, it is presented a graded classification of AI and AI-mediated technologies according to their ethical and social impact according to their beneficial vs detrimental character as recognized in the reviewed literature (Table 3). The aspects employed to construct this classification are detailed in 3.5 and summarized in Figure 2.

According to literature, there are no previous classification of AI systems and applications in Medicine and Healthcare taking into account their potential benefits and pitfalls from ethical and societal points of view. For each of the many applications of AI in Medicine and Healthcare, it is reported the technology, the specific implementations behind and their level of availability according to published references.

Nevertheless, the proposed classification of AI and AI-mediated applications in Medicine and Healthcare shown in Figure 1 is not intended to define an 'absolute' scale of 'goodness' or 'badness', as many technologies (e.g. gene editing, neuroprostheses) are not necessarily 'positive' or 'negative', and others may certainly be difficult to categorize. The ethical and social features employed to construct this classification (Figure 2) are also a subject open to discussion.

3.5 Ethical and social aspects to consider for classification

The ethical and social aspects to be considered for the analysis of Artificial Intelligence and AI-mediated applications in Medicine and Healthcare in this Report are summarized in Figure 2. They can be considered as divided into three partially overlapping sets (Groups G1, G2 and G3).

The First Group (G1) includes **topics currently under analysis, as raised by other areas of prior development of AI applications** (e.g. social networks, online commerce, automation in factories, autonomous vehicles), such as:

- Data privacy, integrity and anonymity, legal responsibility and accountability, and other general aspects of the relationship of humans with (at least partially autonomous) machines [see also Second Group G2].
- The effects on medical professionals and on their relationships to both patients and employers, quality control and monitoring of workers. These effects include the need for professional updates, training and qualification, and the effects on employment (lost jobs, new jobs, deep changes in some medical specialties, the risk that some of them may even disappear).
- Security and reliability [see also Second Group G2].
- Metrics of performance, improved health outcomes and clinical pathways, reduction of medical errors, personalized medicine and psychosocial outcomes. It is important to note that current AI systems are good –even outperforming humans– at 'narrow', specific tasks (e.g. locating certain elements or patterns in images) while (still) failing in global, overview analysis.
- The existence of a 'human-in-the-loop' with or without the ability to override the system, and the questions that arise if there is no time/possibility for human intervention in a critical –even life or death– situation.

The Second Group (G2) includes **topics –some of which may also be under analysis in other areas– of particular relevance for Medicine and Healthcare**, such as:

- Explainability and interpretability of the systems. These concepts refer to being able to explain the 'reasoning process' of AI systems to a human operator. It is currently required by legislation but the evolution of AI technology leads to systems too complex to be understood by a human. Since they may give better results than humans (at least, in certain tasks), should we accept the results given by AI systems without being able to understand how they ('the machines') came to them?
- Trust and reliability. If 'a machine' performs better than a human, what to do when they give conflicting opinions?

— Data quality. The generation of suitable databases and repositories of medical data and information for learning and development of AI systems.

— Data security. The social impact of malicious data alterations can be particularly severe since certain health issues (e.g. toxic consumption history, genetic disposition to diseases) may be manipulated to blackmail or discredit individuals and groups, for instance in processes related to employment and profiling.

Moreover, AI applications in Medicine and Healthcare define a business environment in which economic figures roar to the order of millions, making them a desirable target for illicit, adversarial attacks. As in any other computer services, there are risks of hacking and data theft but, in addition, those of malicious manipulation of the algorithms and data used to train the systems.

Alterations in how a system learns may produce changes in diagnosis and prescriptions, affecting billing and insurances, and even 'small' changes on images and data sets can alter such important outcomes as the benignancy or malignancy of lesions. Inserting or removing only a 'critical' element in an image (e.g. a malignant nodule, a crack in a bone) requires only a few pixels and it is much easier to make than already existing 'fake' photographs and videos. Such manipulations can be used in many malicious applications, from fraud to insurances to massive sabotage of diagnostic processes.

— Additionally, increased security risks appear when 'physical devices' are involved, such as companion robots assisting persons with disabilities or the elderly, or surgical robotic systems.

— Bias and fairness: Do AI systems have biases or are they fair with different (e.g. ethnic, gender, age) groups in diagnosis, prognosis and treatments? Do they receive proper, balanced data for training? Are results valid?

— The social impact of 'erroneous data for learning' can be very high. System may not give any warning but processing results may be incorrect.

— Empathy, including shared decisions and ('the machines') helping humans to make difficult decisions.

— Citizen (taxpayer) opinion and involvement in a 'patient-centric' model. Questions include the common-good in public-funded research, informed consent, citizen science, the 'reduced asymmetry' in information between the patient and the doctor, and citizen-generated (genetic, ...) tests without a doctor prescribing them and analyzing their results.

— Test, benchmarking. There is a clear need for updated testing and evaluation procedures. This is a key issue in which relevant changes are required.

— Regulation, and the legal aspects related to liability and malfunction. There are no (updated, international) regulatory standard for most types of AI applications. Who is legally accountable if the system fails? The 'original' human designer? The programmer? The person who provided the training cases for the AI system to learn? The physician/human operator who used the system? The AI system itself?

— Affordability and socio-economic impact. Global figures and market of AI in Medicine and Healthcare forecast very relevant, positive impact for the coming years. However, the economic analysis must include the social points related to health systems, the industries and the patients, as such technologies also risk evolving into a significant factor of inequality.

— Information for the public and professionals about the real efficacy of AI-mediated treatments and clinical tools, especially against severe diseases of deep social interest –such as cancer– as compared to the many 'announcements' of 'spectacular (initial) results' which, are not later proven to be particularly useful in routine clinical use.

- The availability of trustworthy, open-access information –warranted by public services– is essential to reduce the risks of 'fake-based' medicine and to protect citizens from 'digital health scammers',
- and, of course, as related to the issue of human-in-the-loop, the question of whether (or not) harnessing AI systems under human control on life and death decisions. Should we allow 'a machine' to take such decisions (on us, on a relative)?

To this point, it should be considered that there is an ongoing (although partially silent) social debate –even at a 2019 Meeting in the United Nations– about the development of other types of machines with the ability to make decisions with regards to human life, the already mentioned lethal autonomous weapons systems (LAWS). Their objectives are clearly the opposite of medical devices, and the popular name of 'killer robots' prevent them from being included in medical literature, but the fundamental idea to discuss is the same: will 'a machine' take the ultimate decision to keep or end a human life?

The Third Group (G3) includes **certain aspects barely -or not included at all- in analysis of AI applications in Medicine and Healthcare**, such as:

- Humanization of care, allowing for more time with the patient that improves clinical outcomes and relieves high stress levels (burnout, suicide rates) of physicians. However, AI systems still lack the (much needed) ability of a physical (contact) examination of the patient.
- Social engineering, profiling based on merged medical, health and social data. This issue questions the use of such merged information for the preventive detection of events of clinical significance (e.g. suicide) and for commercial uses (e.g. tailored marketing, insurance, health care coverage or employment). A significant topic is the potential genetic screening of (the whole, groups of) population (detailed below).
- The availability of (unsupervised, unreliable) multiple data, genetic tests for anyone, with the risk of 'patient-generated' medicine (see 3.10).
- Limits to data use? Post-mortem data inheritance? Should there be any limit to the use of very personal information (e.g. from Extended Personalized Medicine)? What happens when a person dies? Should personal data (e.g. genetic data) remain available for use by AI systems? Should there be a post-mortem limit? Can personal (medical, biological) data be inherited? By a relative or by a public institution? For commercial use? What happens if data are of high scientific value (e.g. belonging to a person with a rare disease)? Or with the potential of being directly used to treat a disease?
- The expanding availability of crowd-sourcing of algorithms and processing power. The free sharing of expertise, know-how, and experience define a debate of 'solidarity' vs risks of malicious use.
- Reading and decoding brain signals. The hope for the severely impaired may be turned into 'mind reading' technologies challenging privacy at its basics.
- Interactions with neural processes, which can be applied to help in neurological, mental diseases and, potentially, to interfere with free will.
- Gene editing as an enabler for self-experimentation in humans, with the risk of unexpected results and the potential for change of the genetic heritage.
- Gene editing 'to design' humans and human-animal embryos. With the (already documented) risk of unexpected results in newborns and the unknowns derived from the creation of new types of human-animal beings ('chimera').
- The two sides of technology. With the (relatively) easy weaponization of many of the mentioned AI and AI-mediated technologies and the corresponding high risk of bioterrorism.

- Whole-brain computerized emulation and 'head transplant', challenging the quest for immortality and the very definition of life.
- The search for artificial life forms (explicitly declared for military purposes), questioning the definitions of life (natural, artificial) and death.
- The balance of benefits versus risks and pitfalls and the very fundamental question of whether there should be (or not) limits to research and development?

Many AI systems and AI-mediated applications show an intrinsic 'mix' of positive, negative, and controversial aspects depending on their specific implementations, and that, according to published information, their readiness levels vary from commercially available to very early, conceptual designs.

The scientific and ethical criteria for the analysis of AI applications in Medicine and Healthcare also need a thorough review and updating. Current approach to test medical products and drugs is based on randomized, controlled trials on large sets of cases in which statistically significant changes are evaluated. However, the new paradigm of Personalized Medicine tailors diagnosis and treatments of very specific features -on a genetic level- of each individual. Innovative procedures should be developed to allow for valid evaluation processes within affordable limits of time and costs, and many questions arise:

- How can those treatments be rigorously tested? Which are the time and cost required to find 'enough cases' to 'generate scientific evidence'?
- How should AI systems be benchmarked? Should they be compared to a (possibly error-prone) human doctor or 'against' another 'machine'?
- Should there always be the possibility of a human-in-the-loop with the ability to override the AI system? Even if the human makes more errors than machines (in certain tasks)?

Bottom-line of this set of considerations is that regulations and legislation clearly lag the technology, and that both technical and ethical debates should take place. Common ethical guidelines for the evaluation of technologies mostly date from the pre-digital era. Nowadays, which should be the figures of merit to consider? How should they be updated? Which are the roles of the public and the policy makers?

3.6 Urgent needs identified by the World Health Organization

The social impact of AI systems in Medicine and Health is particularly broad and important. It encompasses consequences at all levels, from individual citizens (patients, professionals, caregivers) to groups, industry and to the whole society.

However, although some social aspects of the impact of AI systems in Medicine and Health are being studied, many technologies and applications are simply advancing (almost) without any further consideration about their social and ethical aspects.

Notably, many of the issues presented in this Report coincide with six of the thirteen urgent priorities recently defined by the World Health Organization (at the beginning of 2020) for the coming decade [21]. These coinciding priorities explicitly include: 'Harnessing new technologies', 'Earning public trust', 'Protecting people from dangerous products', 'Making health care fairer', 'Expanding access to medicines', and 'Preparing for epidemics'.

Within the specific priority of 'Harnessing new technologies', the WHO defines the challenge as 'New technologies are revolutionizing our ability to prevent, diagnose and treat many diseases. Genome editing, synthetic biology and digital health technologies such as artificial intelligence can solve many problems, but also raise new questions and challenges for monitoring and regulation. Without a deeper understanding of their ethical and social implications, these new technologies, which include the capacity to create new organisms, could harm the people they are intended to help'.

3.7 Changes for professionals

In general, there are many publications and studies about the technical features of AI systems in Medicine and Health, their (increasing) performance figures and metrics, and comparisons to human users and operators. The incorporation of AI-based technologies into the medical practice will produce substantial changes in (all) areas of Medicine and Healthcare, from the medical, scientific and technical grounds to workflow, clinical pathways and management, and to the relationship with the patients and the health systems and providers.

Certain medical specialties, particularly those related to image and data analysis and interpretation (e.g. Radiology, Pathology, Dermatology, and the different branches of Surgery, Forensics, Epidemiology, Public Health and others), will experience profound transformations (some of which have already started) due to the adoption of new tools with expanding capabilities and increasing autonomy. There are (professional) voices in the debate arguing that some specialties will even disappear and jobs will be lost. Other jobs (e.g. related to genetic counseling, medical data scientists and engineers) will arise.

Initial (technical) results in certain areas of application (diagnosis, surgical robotics, precision medicine) are not as spectacular as predicted, some of them even really disappointing and contradictory to the previous public announcements. Nevertheless, technology is advancing, technical challenges are being addressed, and systems improved.

3.8 Empowerment and the new role of patients

Very significant changes are happening in the role of the individuals in relation to their Healthcare and, particularly, in the relationship between the patient and the doctor in Medicine. These changes can be seen as an evolution to new paradigms of 'individual involvement' in health care and of 'patient empowerment' in medicine, and this evolution is fostered by AI and AI-mediated technologies through three main aspects:

- The availability of online information, evolving from disperse, unstructured descriptions of symptoms and medicaments to interactive platforms offering healthcare advice to diagnosis and even schemes for disease treatment, and of personal biometric and physiological data from sensors and IoT devices.
- The easy connections to a multitude of individuals or groups of persons with similar interests, diseases or treatments, all across the globe, in any language.
- The increasing access to the individual's genetic data without the need of a physician ordering such analysis. Only a drop of saliva and prices on the order of a hundred euros are required to have your own genome (at least partially) analyzed and searched for alterations which are potentially related to diseases.

The evolution of individual behavior in relation to Medicine and Health Care presents a novel array of many advantages, pitfalls and un-addressed concerns. The overall access to many types of data has an important effect in the relationship between the patient and the doctor, namely the reduction of the 'asymmetry in information' between them and the evolution towards a 'patient-centric' model. This new situation started with the generalized availability of information on online platforms of the internet and it has evolved with AI technologies for data mining and advanced –easier- user interaction. Suddenly, patients could ask 'the Google Doctor' about anything, from symptoms to the side effects of treatments to advices for healthy lifestyle and then visit the real physician's office with a list of 'informed' questions, requests and even complaints. Anyone can even have a (digital) 'personal medical coach'. In the following years, it has become evident that there is no 'a priory' guarantee of the quality –even of the certainty– of the information found on internet searches. Very valuable resources can be mixed with completely erroneous –even maliciously misleading– material and a certain level of knowledge is required to find and understand the information of real interest for any case. In addition, to evaluate the clinical situation of a patient and potential treatment options there is also a clear need of the 'integrated analysis', of the 'global vision' provided by a qualified, trained, real doctor. The evolution of technology has expanded AI systems, starting from 'basic' –but very effective– symptom checkers to increasingly autonomous 'digital doctors'.

3.9 'Extended Personalized Medicine'

The original goal of Personalized Medicine is to exploit very specific biological (genetic) features of individuals for tailored diagnosis and treatment. Decoding the genome of each patient represents a very significant change from the existing model of averaged analysis of populations to an extremely individualized approach, for treating disease –in a new paradigm defined as 'Precision Medicine'– but also to promote wellness and healthy, personalized lifestyles.

However, although not explicitly formulated in the literature, the underlying principle of Personalized Medicine can be further expanded. It can include other properties whose particular values or structures –even their spatial distribution and time evolution in the human body– may be significantly different for any single individual, in different clinical situations, at every moment of life and, possibly in strong relationship to each other.

The additional features that form the new concept of 'Extended Personalized Medicine' may come from:

- 'Known sources' from the 'basic sciences' of physics (e.g. bioelectromagnetic fields and signals, biomechanical magnitudes and properties, hydrodynamic parameters of the circulation of any fluid in the body, …), chemistry (concentrations of ions, molecules, …), and biology (metabolites, …).
- 'Not yet known' origins. This concept refers to the potential characterization of brain processing schemes, connections and functions whose details still remain veiled for science.
- Demographic data, extracted from conventional databases.
- Social data, including those about societal structures (family, groups providing psychological, emotional support) and cultural and religious beliefs which may influence health-related issues, such as restrictions on types of food or sexual activity, provided by the user or mined from social networks.
- 'Lifestyle parameters' (sleep hours, stress, physical activity, food ingestion, …) easily accessible through apps, wearables and the Internet of Things.
- Values of environmental and physical geography conditions (weather, contamination, …) transmitted by multiple platforms.
- Sensors evaluating mood through face and gesture recognition, changes in cardiac rhythms, perspiration and breathing patterns when receiving certain visual or auditory stimuli. They may be biometrics readers in smartphones, domotic environments, and wearables.
- Data about psychological and emotional status, extracted indirectly from the individual activity on social networks.

The accumulation of personal, intimate information of 'Extended Personalized Medicine' presents very high risks regarding ownership, security and privacy. From a technical point of view, the combination of so many sources of information, even 'only' using those that are already available –namely genetic data (genomics, metabolomics, proteomics, …), results coming from 'standard tests' (e.g. imaging scans, analytics), clinical scores, and medical knowledge in publications and references– requires the use of advanced AI-mediated tools, both for merging, processing and analyzing multiple data layers –extracting useful information– and to operate the devices of augmented and virtual reality for the (very much needed) interactive navigation, visualization and interpretation of the relevant information.

3.10 The risk of the division into several types of Medicine

AI-supported, even shared-decisions –with non-human systems– and patient involvement shape substantial changes in Medicine and Healthcare. However, a very dangerous division of Medicine in different subtypes may therefore take place. They are the following:

- **'Fake-based' medicine**. Based on (unfounded, unconfirmed) rumors and 'fake news', this type of 'pseudo-medicine' may present 'ancient, natural knowledge' as opposed to scientific, evidence-based medicine, considered to be under malicious control by corporations, academia, institutions and governments. Even rejecting technology, it may easily take benefit from the expanding ability of fake news in social networks and the multiplying power of online platforms and AI-mediated tools (including chatbots, interactive apps, communities of followers) for dissemination of wrongful information. This type of misinformation, such as in the case of 'anti-vaccine groups', is currently increasing, being used to discredit 'conventional' therapeutic approaches and to promote that patients abandon treatments and follow-up by physicians, with very serious potential consequences –even with the risk of death– both for the individuals affected and their surrounding environments.
- **'Patient-generated' medicine**. This type of 'pseudo-medicine' derives from the growing online availability of many (both correct and unsupervised, unreliable) sources of medical information, even on platforms and apps supposed to evaluate and interpret the results of (almost any) type of analysis, including imaging scans and genetic tests.

  Although a 'better informed patient' is a positive consequence of the availability of information, individual-ordered analysis and diagnosis lack the (fundamental) 'global vision' that the doctor can offer to the patient and the (crucial) trained skills required for proper understanding of the results of any tests and deciding subsequent steps.

  Any person, even medically illiterate, without any medical education or training, may have –through AI-mediated tools– immediate, unlimited access to a trove of information that she/he may consider correct and related to her/his disease or health issue. Resulting decisions may then –very probably– bring inadequate, even damaging, consequences, without the potential help or support from any established medical institution.
- **'Scientifically tailored' Medicine**. This type of medical science is the one that evolves from current research into extended personalized/precision medicine. For the patients, the critical decision would probably be the selection of the human doctor –perhaps the AI-system– to lead the team of 'conventional' (clinical) and 'new' (e.g. genetic counselors, medical data scientists) professional profiles required to correctly integrate the multiple, extensive sources of information to establish the diagnosis and define the corresponding treatment and monitoring strategies.

3.11 'Digital health scammers'

In addition to the beneficial sources of medical data, AI tools have allowed the emergence of new types of online platforms that target those looking for information about health issues on the web. They are relatively easy to find through automated, systematic searches of social networks using natural-language analyzers. When identified, candid patients are offered clinical advice and treatment options, even pharmacological and surgical.

Problems obviously arise when there is no guarantee about the qualification or reliability neither of the 'products' offered nor of the service provider, and it happens to be an updated, AI-mediated, digital version of –long existing– 'health scammers'. AI systems can be trained with wrongful, malicious data and have an 'appearance' of trustworthiness. This is a situation of particular relevance –and potential damage– for more vulnerable persons, such as those with severe diseases and their relatives.

Undesirable scammers taking unfair advantage of persons can be traced back to the origins of Medicine. But the extraordinary multiplying effects of the internet and AI tools can make them much more powerful and dangerous, especially for citizens without the required knowledge to make critical analysis of the information received.

In the age of expanding information, important goals of public, regulatory institutions should be to protect citizens from falling into the aforementioned types of 'pseudo-medicine' ('fake-based' and 'patient-generated') and being victims of 'digital health scammers', and to allow for the (very challenging) generalized access of the population to the 'scientifically tailored' Medicine. To achieve such objectives, the availability of fair, trustworthy, contrasted information open to public access is essential.

3.12 Affordability and inequality

Global figures and market of AI in Medicine and Healthcare forecast very relevant, positive economic impact for the coming years. However, this analysis must include the ethical and social points related to health systems, the industries and the patients.

It is important to note that the cost of decoding a human genome is substantially low –in the order of a few hundred euros– but the prices of some of AI-mediated treatments, such as certain personalized drugs, may reach 'impossible' figures, even in the order of millions of euros per case. This steep step is due to the difficulties of individually tailoring drug molecules to the specific genome of an individual. New models of health coverage, insurance, and affordability may be needed as such clinically excellent technologies pose a clear risk of evolving into a significant increasing factor of inequality for most people.

3.13 The fundamental role and risks of neuroscience

The impact of AI is especially relevant in neuroscience (neurosurgery, neurology). This area is based on the combination of AI-mediated technologies with advances in photonics (merging of applied optics and electronics) and engineering, together with other clinical disciplines (pharmacology, psychology) and related sciences (biology and genetics, biochemistry).

As detailed in Table 3, AI-mediated advances in neuroscience have paved the way for the design -and early development- of techniques and devices for some limit-defying applications. Among them, reading and decoding the complex signals of the brain and their applications (e.g. visualization of neural processes in living beings in real time) using both invasive brain (chip) implants and non-invasive, remote devices. Recently disclosed advances include a robot capable of inserting tiny (tether) electrodes inside individual nervous fibers and a monkey having being able to control a computer through a chip implanted in its brain.

Moreover, there are ambitious projects whose goals include mapping every individual signal and neural connection in the brain, and significant advances in different types of neurostimulation, e.g. using electromagnetic signals and fields, light beams (optogenetics), ultrasound beams and other forms of energy to stimulate, activate or deactivate signals in certain areas of the brain.

From a clinical point of view, the knowledge about reading and interaction with brain signals can be used to develop interfaces to the human neural system, the goal of which is the interactive control of innovative prostheses, offering great hope for many persons with severely disabling conditions.

However, this knowledge also relates to very controversial paths in which difficult questions arise: if signals inside the brain can be read using and external device, may such technology evolve to the potential ability to 'read the mind'? Also, if brain signals can be stimulated and (perhaps) de/activated (that is, controlled) may we be able to generate 'interferences'? which, in term, might lead to undesired forms of manipulation (lack of free will) and human control. And if all individual connections of neurons were correctly identified and read, would it allow for whole brain emulation (simulation)? And for 'uploading' all the brain information into a computerized system?

Although these type of applications may seem 'fantasy' –and, perhaps, some of them may never became feasible– it is important to note that there are ongoing, very strongly funded projects in closely related areas. They are oriented to the positive aspects of neuroscience, by the EU (The Human Brain Project) [22] and by the USA (The Brain Initiative) [23]. Their goals are, respectively, 'to explore brain structure and functions in humans ... and other species', and 'to deepen understanding of the inner workings of the human mind and to improve how we treat, prevent, and cure disorders of the brain'. Very recently, military projects related to research in man-machine interfaces have also been disclosed, and public calls have been open for scientists in these areas.

A particularly controversial topic related to neuroscience (neurosurgery) in relationship to AI technologies is that of 'head transplant'. It does not refer to a 'digital avatar' but to the real, physical, operative connection of the head of a (human) being to a different human body. It has been experimented in several animal models (with relative degree of success), and in 2017 it came to headlines as it was announced to have been performed on human cadavers, and to be attempted with a living human head in 2019 in China, although up to the date of this Report, there is no further public news about. The proclaimed intention is to help patients with terminal illnesses, neurodegenerative diseases and severe damage or section of the spinal cord, but such procedure obviously calls for many ethical –even philosophical– questions.

From a strictly scientific point of view, these applications present many challenges of extreme complexity, in which AI-mediated tools may play an essential role, from augmented reality devices for surgery training and simulation to exploring, identifying and connecting (every? most? certain?) individual signals pathways to and from the brain.

3.14 Gene editing, weaponization and bioterrorism

Some of the AI technologies related to Medicine and Health can be weaponized or employed in novel forms of bioterrorism and evil applications. An example of particular interest in relation to security and safety are the AI tools required to design and implement the editing of the human genome.

As in many other areas of science and technology, the same tools can be used for beneficial or malignant purposes but it is important to note the extraordinary effects –currently, mostly unknown– that some of the AI-related technologies may potentially be linked to Medicine, Biology and Chemistry.

Some of the currently available AI-related tools (see Table 3) include the possibility of introducing changes in the human genetic charge and (very possibly) the design of biological agents to target specific individuals, groups or populations. Other areas of applications of AI-related tools disclosed very recently include such issues as the design of human-animal hybrid embryos and the search for artificial life forms. Besides the unknown risks –and the very controversial ethical questions– the danger of ‘perverted’ or malicious use or design of such developments requires a thorough analysis.

4 A 'Visual Overview' of Artificial Intelligence in Medicine and Healthcare.

Figure 1. Classification of AI and AI-mediated technologies in Medicine and Healthcare according to their ethical and social impact. SW: software, AR: augmented reality, VR: virtual reality, IoT: internet of things. TAL: Technology Availability Level.

AI and AI-mediated technologies	Specific implementations.	TAL	Social Impact
Algorithms for computer-aided diagnosis.	SW for decision support in (most) clinical areas.	8, 9	Positive
Structured reports, eHealth.	SW for improved workflow, efficiency.	8, 9	
AR/VR, advanced imaging tools.	Tools for information visualization and navigation.	6, 7, 9	
	Image-guided surgery. Teleoperation.	4, 6, 9	
Digital pathology, 'virtopsy'.	SW for automated, extensive analysis.	4-9	
Personalized, precision medicine.	Tailored treatments. Prediction of response.	4-9	
	'In-silico' modeling and testing. The 'digital twin'.	4-8	
	Drug design.	4, 8	
Apps, chatbots, dashboards, online platforms.	The 'digital doctor' (assistance for professionals and for patients).	8, 9	
Companion and social robots.	For hospitalized persons, children & the elderly.	4-9	
Big Data collection and analysis.	Epidemiology, prevention and monitoring of disease outbreaks.	2-9	
	Fraud detection. Quality control, monitoring of physicians and treatments.	4-9	
IoT, wearables, mHealth.	Automated clinical/health surveillance in any environment/institution.	7, 8	
	Monitoring, automated drug delivery.	7-9	
Gene editing.	Disease treatment, prevention.	7, 8	
Merging of medical and social data. 'Social' engineering.	Prevention of episodes with clinical relevance (e.g. suicide attempts).	6, 8	Controversial
	Tailored marketing (e.g. related to female cycles).	6, 8	
Reading and decoding brain signals. Interaction with neural processes.	Treatment of diseases. Restoring damaged functions.	3-8	
	Brain-machine inferfaces.	5-8	
	Control of prostheses, exoskeletons. 'Cyborgs'.	2-7	
	Neurostimulation. Neuromodulation.	4-8	
	Neuroprostheses (for the central nervous system).	2-5	
	Mind 'reading' and 'manipulation'.	1-3	
Genetic tests. Population screening.	Disease tests. Direct-to-consumer tests.	4-9	
Personalized, precision medicine.	Individual profiling. Personalized molecules (for treatment) at 'impossible' prices.	3-8	
Gene editing.	'Engineered' humans.	2, 6	
	Gene-enhanced 'superhumans'.	2	
	Self-experimentation medicine. Biohacking.	2, 6	
Fully autonomous AI systems.	The 'digital doctor'.	2-5	
	'Robotic surgeon'.	2, 4	
Human-animal embryos.	Organs for transplants.	2, 4, 5	
	Hybrid beings ('chimera').	2, 4	
The quest for immortality.	Whole-brain emulation / 'transplant'.	1, 2	
The search for artificial life forms.	'Living machines' ('biological robots', 'biobots')	4, 6	
	Military.	2, 3	
Evil biohacking.	Targeting specific individuals or groups.	1, 2	
Weaponization.	From 'small labs' to military labs.	1, 2	
Bioterrorism.	From 'small labs'.	1, 2	Negative

Figure 2. Ethical and social aspects of AI and AI-mediated technologies in Medicine and Healthcare. They are sorted in three groups (G1, G2, and G3). Some key relevant issues, controversies, significant, and conflicting issues are outlined for each aspect.

(G1) Currently under analysis, as raised by other areas of AI applications.

Aspects.	Analyzed in relation to.
Data privacy, integrity.	Ownership. Authorization for data collection, sharing, mining, exchange.
Anonymity.	Surveillance anxiety.
Responsibility. Accountability.	Who is responsible in case of malfunction?
Effects on professionals and employment.	Lost & new jobs. Deep changes in some medical specialties (some may even disappear). Need of professional updating. Quality control, monitoring.
Security. Reliability.	Vulnerabilities. Data theft. Manipulation of the data used to train the systems.
Performance.	Improved health outcomes and clinical pathways. Reduction of medical errors. 'Personalized Medicine'. Psycho-social outcomes.
Human-in-the-loop?	Should a human operator override AI systems? Even if human is more 'error-prone'? What happens if there is no time to act?

(G2) Of particular relevance for AI applications in Medicine and Health Care.

Aspects.	Controversies.
Explainability.	Currently required by legislation. Some systems are (will be) too complex to be understood by a human. But they may give better results than a human.
Trust.	Does 'the machine' perform better than a human doctor? What to do if they (AI system, human doctor) give conflicting opinions? 'Digital health scammers'.
Data quality. Bias / fairness.	Do AI systems have biases/are fair with different (e.g. ethnic, gender, age) groups? Do they receive proper, balanced data for training? Are results valid?
Empathy.	Shared decisions? Help (the human) take difficult decisions?
Citizen (taxpayer) opinion and involvement.	Common-good in public-funded research, informed consent, citizen science. Reduced 'asymmetry' doctor-patient. 'Patient-centric' model.
Test, benchmarking.	How to evaluate results? Existing procedures for average groups are valid for individualized treatments? Comparison of AI systems 'against humans or machines'?
Regulation.	Lags behind technology. No international consensus.
Affordability. Economic impact.	Optimal treatments at 'impossible' prices? A factor of inequality? New models for health insurance and coverage?
Information for the public and professionals.	Pressure for new products. Real advances vs hypes and non-confirmed stories of success in areas of great interest (e.g. cancer cures). Risk of 'fake-based' medicine.
Life and death decisions.	Should we allow 'a machine' to take them (on us, on a relative)? The debate about lethal autonomous weapon systems.

(G3) Barely/not included in analysis of AI applications in Medicine and Heath Care.

Aspects.	Significant/conflicting issues.
Humanization of care.	Professionals with AI: More time with the patient, stress relief. AI systems: Currently, lack of physical exam/contact with patient.
Social engineering, profiling based on merged medical, health, social data.	Preventive detection of events (e.g. suicide) vs tailored marketing, insurance, health care, employment. Genetic screening of the population.
Availability of (unsupervised, unreliable) multiple data, genetic tests for anyone.	Risk of 'patient-generated' medicine.
Limits to data use? Post-mortem, inheritance.	Post-mortem use of individual (e.g. genetic) information?
Crowd-sourcing of algorithms, processing power.	Free sharing of expertise, know-how, experience. Solidarity vs risks of malicious use.
Reading, decoding brain signals.	Hope for severely impaired vs privacy at its basics.
Interaction with neural processes.	Help for neurological, mental diseases vs free will.
Gene editing as self-experimentation.	Risk of unexpected results. Change of genetic heritage.
Gene editing of (human, human-animal) embryos.	Risk of unexpected results in newborns. Creation of new beings ('chimera').
The two sides of technology.	'Easy' weaponization. High risk for bioterrorism.
Whole-brain emulation / 'transplant'.	The quest for immortality. Definition of life.
'Living machines' ('biological robots', 'biobots') The search for artificial life forms.	Definitions of life (natural, artificial) and death.
Benefits versus risks and pitfalls.	**Limits (or no) to research and development?**

5 A ‘Structured Overview’ of Artificial Intelligence in Medicine and Healthcare

The following Table 3 shows a structured overview of the field of AI in Medicine and Healthcare and their applications. It encompasses the state of the art by the date of this Report, including technologies and their implementations, perspectives, conflicting views and potential pitfalls, and the corresponding list of references consulted for this Report.

Table 3. Structured overview of the field of AI in Medicine and Healthcare, their implementations and technological set-ups and the corresponding list of references consulted for this Report.

Fields	Subfields		References
1. Motivation.			[3] [13] [15] [24] [25] [26] [27] [28]
1.1. The context: AI enters Medicine and Health Care.			[29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45]
	1.1.1. Expected impact. Many positive, beneficial ideas. Specific reasons.		[46]
		1.1.1.1. Obviously, the leading causes of death.	[47] [48] [49] [50] [51] [52] [53]
		1.1.1.2. Tackling very complex problems.	[54]
		1.1.1.3. Human (medical) errors.	[55] [56] [57] [58]
		1.1.1.4. Universal Health Coverage as part of the Sustainable Development Goals of the UN.	[42] [59] [60] [61] [62]
	1.1.2. Economy aspects of AI in different world regions. Particularities in Medicine and Healthcare.		[12] [16] [17] [18] [63] [64] [65] [66] [67] [68] [69] [70] [71]
	1.1.3 Geostrategy.		[72] [73] [74] [75] [76] [77] [78]
2. State of the art, current perspectives, conflicting views and potential pitfalls.			
2.1. Computer-aided diagnosis and decision support.			[79] [80] [81] [82] [83]
	2.1.1. The pioneers: Radiology and medical imaging.		[84] [85] [86] [87] [88] [89]

		2.1.1.1. Advanced image enhancement and analysis. New approaches from other areas.	[90] [91] [92] [93] [94] [95]
		2.1.1.2. Quantitative imaging: the definition of biomarkers.	[96] [97] [98]
	2.1.2. Extracting information from clinical documents. Structured and e-health reports.		[99] [100] [101] [102]
	2.1.3. Extracting useful (but hidden) information from standard images.		[103]
	2.1.4. Big Data and the power of integration of multiple modalities of information.		[104] [105] [106] [107] [108] [109] [110] [111] [112] [113]
2.2. Updates in some clinical areas.			[114]
	2.2.1. Cancer and oncology.		[99] [115]
		2.2.1.1. Breast.	[116] [117]
		2.2.1.2. Lung.	[118] [119] [120] [121] [122] [123] [124] [125]
		2.2.1.3. Other types of cancer.	[126]
	2.2.2. Cardiovascular.		[127] [128] [129] [130] [131]
	2.2.3. Liver diseases.		[132] [133] [134]
	2.2.4. Ophthalmology.		[135] [136] [137]
	2.2.5. Gastrointestinal.		[138] [139]
	2.2.6. Dermatology.		[140] [141]
	2.2.7. Anesthesiology.		[142]
	2.2.8. From primary care to aging to rare diseases.		[143] [144] [145] [146]

	2.2.9. Pathology and analytics. Towards optical biopsy and digital, virtual autopsy ('virtopsy').		[147] [148] [149] [150]
2.3. Of singular relevance: neuroscience. The powerful merging of AI with (neuro)photonics for neurosurgery and neurology.			[22] [23] [151]
	2.3.1. Seeing the whole brain (of living animals) in real-time operation.		[152]
	2.3.2. Neuromodulation and control of neural processes.		
		2.3.2.1. Cortical and deep brain stimulation.	[153] [154] [155] [156]
		2.3.2.2. Peripheral stimulation.	[157]
	2.3.3. Towards optical control of the brain.		
		2.3.3.1. Using inserted probes: optogenetics.	[158] [159] [160] [161]
		2.3.3.2. Non-invasively: using the eye as a window to the brain.	[162]
	2.3.4. Neurology.		[163] [164] [165] [166]
2.4. The AI revolution in surgery.			
	2.4.1. Early adopters in neurosurgery. Neuronavigation. Intraoperative fluorescence.		[167] [168] [169] [170]
	2.4.2. Image-guided surgery.		[171] [172] [173] [174] [175]
	2.4.3. Augmented reality and mixed reality. Teleoperation.		[176] [177]
	2.4.4. Personalized surgical planning.		[178] [179] [180]

	2.4.5. Robotic-assisted surgery. Towards fully autonomous robotic surgeons.		[181] [182] [183] [184] [185] [186] [187] [188]
2.5. Clinical management of patients.			
	2.5.1. Clinical surveillance and monitoring, and (preventive) treatment. Wearables, IoT.		[189]
		2.5.1.1. At bedside.	[190]
		2.5.1.2. At emergency room and the intensive care unit.	[191] [192] [193] [194] [195] [196] [197] [198]
		2.5.1.3. At long-term hospitalization and isolation rooms.	[199]
		2.5.1.4. At home and nursing homes.	[200] [201] [202] [203] [204]
		2.5.1.5. Of healthy/autonomous/aging persons.	[205] [206] [207] [208] [209] [210] [211] [212] [213]
		2.5.1.6. Of population groups.	[214] [215] [216] [217]
2.6. Towards extended personalized/precision medicine.			
	2.6.1. The application of human genomics.		[218] [219] [220] [221]
	2.6.2. Personalized medicine: diagnosis, prediction of the response, tailored treatments.		[222] [223] [224] [225] [226]
	2.6.3. Genetic testing.		
		2.6.3.1. Questions about generalized genetic screening of the population.	[227]
		2.6.3.2. Direct-to-consumer tests.	[228] [229]
	2.6.4. In-silico modeling and testing. The 'digital twin'.		[230] [231]

	2.6.5. Drug design.		[232] [233] [234]
	2.6.6. 'Extended Personalized Medicine'.		
		2.6.6.1. Demographic, social, cultural, religious data.	[235] [236] [237]
2.7. 'Social' management of patients (and of persons who need specific care).			
	2.7.1. Companion and social robots.		[238] [239] [240] [241]
		2.7.1.1. For children.	[242] [243] [244]
		2.7.1.2. For the elderly.	[245]
	2.7.2. Healthcare and social networks. Mobile health (mHealth), chatbots.		[246] [247] [248] [249] [250]
		2.7.2.1. Use of dialogue systems for diagnosis.	[251]
	2.7.3. The (always) abandoned?		[252]
2.8. Public health. Epidemiology.			[253] [254]
	2.8.1. Epidemiology.		[255] [256] [257] [258] [259] [260] [261]
		2.8.1.1. The example of the COVID-19 pandemic disease.	[20] [262] [263] [264] [265] [266] [267] [268] [269] [270]
	2.8.2. Health systems. Organizational improvements. Prediction of outcomes.		[171] [271] [272] [273]
	2.8.3. Merging of medical and social data to predict individual events of clinical relevance. The risks of 'social engineering'.		
		2.8.3.1. An example of debate: Liberty vs life protection in suicide prevention.	[274] [275]

		2.8.3.2. A conflicting proposal: the search for links between mental health and violence.	[276]
		2.8.3.3. Tailored marketing: following female cycles and sexual activity.	[277]
	2.8.4. AI tools to combat health-related fraud.		[278] [279]
	2.8.5. Quality control.		[280]
2.9. Mental health.			[281] [282]
	2.9.1. Computer-assisted therapies.		[283] [284]
	2.9.2. Workers exposed to disturbing contents.		[285]
2.10. Interfaces to the human neural system and neuroprosthetics.			
	2.10.1. Brain-machine interfaces.		[286] [287] [288] [289] [290] [291]
		2.10.1.1. Auditory implants and speech reconstruction.	[292]
		2.10.1.2. Retinal implants.	[293]
		2.10.1.3. Implants (chips) in the brain.	[294] [295] [296]
	2.10.2. Neuroprosthetics. ‘Cyborgs’.		[297] [298] [299] [300]
	2.10.3. Exoskeletons.		[301] [302] [303]
2.11. AI-based medicine in reduced-resources environments.			
	2.11.1. A very high potential.		[304] [305]
		2.11.1.1. A specific example: snakebites.	[261]

	2.11.2. Reality versus utopia: about the use of internet in developing regions.		[304] [306] [307]
2.12. AI tools for stem cell research on human-animal embryos: chimera become real.			
	2.12.1. 2019 – Authorization for research in Japan.		[308]
	2.12.2. 2018 – Human-sheep embryo disclosed.		[309]
	2.12.3. 2017 – Interspecies (human-pig) cell growing.		[310] [311] [312]
2.13. Self-experimentation medicine and biohacking.			[313] [314] [315]
	2.13.1. Gene-enhanced 'superhumans'.		[316] [317]
2.14. The quest for immortality. Towards 'artificial life'?			[318] [319]
	2.14.1. Merging human intelligence with AI.		[320]
	2.14.2. Brain models. Whole brain emulation.		[321] [322]
	2.14.3. 'Head transplant'.		[323] [324] [325]
	2.14.4. 'Living machines', 'biological robots' ('biobots').		[326]
2.15. Some examples of available systems using advanced AI tools.			
	2.15.1. Online platforms for clinical advice.		[327] [328] [329] [330] [331]
		2.15.1.1. Symptom assessment platforms (for patients).	[332] [333]
		2.15.1.2. Dashboards for clinicians (in the hospital).	[334] [335]

		2.15.1.3. Apps for electronic health records.	[336] [337]
	2.15.2. Apps for diagnosis.		[338] [339]
	2.15.3. Genetic tests. Direct-to-consumer tests.		[340] [341] [342] [343] [344] [345] [346] [347] [348]
	2.15.4. Gene editing (to cure diseases).		[349] [350] [351]
	2.15.5. Surgical robots.		[352] [353] [354]
	2.15.6. Companion robots.		[355]
	2.15.7. Digital pathology.		[356]
3. Conflicting views and potential pitfalls.			
3.1 The general debate: AI for global good? What about Medicine? Ethics.			[37] [62] [235] [305] [357] [358] [359] [360] [361] [362] [363] [364] [365] [366] [367] [368] [369] [370] [371] [372] [373] [374] [375] [376] [377] [378] [379] [380] [381] [382] [383] [384] [385] [386] [387]
3.2 Does 'the machine' perform better than a human physician does? 'AI-enhanced' doctors?.			[388] [389]
	3.2.1. In diagnosis.		[390] [391] [392] [393] [394] [395] [396] [397] [398] [399] [400]
	3.2.2 In surgery.		[401] [402]
	3.2.3 There are (still) technical questions to be addressed.		[403]
3.3 Public perception of AI-based Medicine.			

	3.3.1 Debunking the hype (only in part): some (early) applications disappoint.		[404] [405]
		3.3.1.1. Questions about the results of precision medicine.	[406] [407] [408] [409] [410] [411]
		3.3.1.2. Questions about the results of robotic surgery.	[412] [413]
	3.3.2 The patient empowered. Direct-to-consumer genetic tests.		[407] [414] [415] [416]
	3.3.3 Undermining experts. The difficult issue of 'fake news.		[417] [418]
	3.3.4 The risk of 'fake-based' medicine.		[419] [420]
3.4. Some of the most known issues: data privacy, anonymity, security.			[421] [422] [423]
	3.4.1 Un/authorized use of medical data.		[424] [425]
	3.4.2 Re-identifying anonymous data.		[426] [427] [428]
	3.4.3 Data ownership. Post-mortem use?		[235] [424] [429]
3.5 Who is responsible? Accountability.			
	3.5.1. The case of double reading of electrocardiogram.		[430] [431]
	3.5.2. The 'pocket doctor'?		[432]
3.6. Explainability and the reality of 'black box' systems.			[78] [433] [434] [435] [436] [437]
	3.6.1. Reproducibility.		[438] [439]
3.7. Trust.			

	3.7.1. Of the patients in 'AI doctors'. Always a 'human-in-the loop'?		[440] [441] [442] [443] [444] [445]
	3.7.2. Of the employer in human physicians. Quality control?		
		3.7.2.1. An example: Use of AI to oversee prescriptions of opioids.	[446]
	3.7.3 The patient involved. Shared decisions.		[447]
		3.7.3.1 The risk of surveillance anxiety.	[448]
		3.7.3.2 The risk of 'patient-generated' medicine.	[418]
	3.7.4. Reliability. Vulnerabilities. Adversarial behavior. 'Digital health scammers'.		[372] [449] [450]
3.8. Empathy and the humanization of care.			[451] [452] [453] [454] [455]
	3.8.1. Helping the patient to take difficult decisions?		[456] [457]
	3.8.2. Predicting your life span?		[99] [458]
3.9 Bias. Fairness.			[368] [459] [460] [461] [462] [463] [464]
3.10. Professional transformations. The fear to unemployment.			[465]
	3.10.1. Who will lose their jobs? The pioneers at risk?		[150] [466]
	3.10.2. Adaptation. The (absolute) need of professional updating.		[467] [468] [469]
	3.10.3. New jobs (e.g. genetic counselors).		[67] [407] [470] [471] [472]

3.11. The economic cost of new therapies.			
	3.11.1. Optimal treatments at 'impossible' prices?		[473] [474] [475]
	3.11.2. The role of industry.		[476] [477]
	3.11.3. New models for health insurance and coverage?		[473]
3.12. Collaborative and crowd-sourcing algorithms for clinical applications.			[478]
	3.12.1. An example in radiation therapy.		[479]
3.13. The risks of unexpected results.			[480] [481] [482] [483] [484]
	3.13.1. A recent (2018) example: Engineering human genes with unknown effects.		[485] [486]
	3.13.2. Social profiling based on medical data. (Un)Fairness.		[144] [221] [487] [488] [489] [490] [491]
3.14. The two sides of technology: weapons, bioterrorism.			[492]
	3.14.1 Some (recently disclosed) areas of military applications.		
		3.14.1.1. Brain-machine interfaces.	[303] [493] [494] [495]
		3.14.1.2. The eyes and the optical access to the brain.	[166] [496] [497] [498] [499]
		3.14.1.3. The search for synthetic life forms.	[500] [501]
	3.14.2. *Evil* biohacking: genome editing and manipulation.		[502]

3.15. The growing debate in the press and social media about AI related to Health and Medicine.			
	3.15.1. About benefits and ethical questions that arise.		[115] [503] [504] [505] [506] [507] [508] [509] [510] [511] [512] [513] [514] [515] [516] [517] [518] [519] [520] [521] [522] [523]
	3.15.2. About sharing medical data.		[424] [524]
	3.15.3. About wearables, IoT and online health services.		[212] [525] [526] [527] [528]
	3.15.4. About merging of clinical and social data. Suicide prevention.		[424] [529] [530] [531]
	3.15.5. About overseeing of prescriptions.		[532]
	3.15.6. About optogenetics, neurophotonics and the key role of neuroscience.		[533] [534] [535]
	3.15.7. About direct, non-invasive mind reading.		[536] [537]
	3.15.8. About surgical robotics, (neuro)prosthetics and human-machine interfaces.		[300] [538] [539] [540] [541] [542]
	3.15.9. About genetic tests, privacy and the use of genetic and other personal data.		[221] [543] [544] [545]
	3.15.10. About gene edition.		[546] [547] [548] [549] [550] [551]
	3.15.11. About human-animal embryos.		[552]
	3.15.12. About head transplant.		[553] [554]
	3.15.13. About setting (or no) limits to research.		[555] [556] [557] [558]
	3.15.14. About the (relevant) environmental impact of AI.		[559]

	3.15.16. About the ‘dark side’ of AI in Medicine and Healthcare.		[560]
	3.15.16. About the use of AI in developing countries.		[305] [561] [562]
3.16. Regulatory difficulties.			
	3.16.1. What to evaluate? How to evaluate?		[8] [407] [563] [564] [565] [566] [567] [568] [569]
	3.16.2. How to regulate?		[476] [570] [571] [572] [573] [574] [575]
3.17. Some (initial) responses to questions.			[576] [577]
	3.17.1. In general, and in other areas of AI and robotics.		[8]
		3.17.1.1. The ‘Montréal Declaration for Responsible Development of Artificial Intelligence’ (2018).	[578]
		3.17.1.2. Giving voice to consumers in the USA.	[579]
		3.17.1.3. The social debate about autonomous killer robots. The Meeting in the United Nations about LAWS (2019) and the International Pledge for a Ban (2018).	[580] [581] [582] [583] [584] [585] [586] [587] [588] [589] [590] [591] [592] [593]
		3.17.1.4. About advances of AI in ‘typically human’ skills.	[594]
		3.17.1.5. About the cooperation of humans with machines.	[595]
		3.17.1.6. Robot teaching humans.	[596]
		3.17.1.7. About the social impact of AR/VR technologies.	[597]

		3.17.1.8. About (initially) bad results of AI in other areas of high social impact (police applications).	[598]
	3.17.2. In areas related to AI in Medicine and Health.		[407] [434] [599] [600] [601] [602] [603] [604] [605]
		3.17.2.1. The 2020 Declaration about 'Urgent health challenges for the next decade' by the World Health Organization.	[21]
	3.17.3. At the European level.		[1] [2] [3] [4] [13] [25] [63] [366] [565] [605]

6 Policy challenges

6.1 Informed citizens

The new areas –and the ethical and social challenges– that AI presents in Medicine and Health are mainly unbeknownst to most European citizens, although such aspects have profound consequences in society and relate to the adoption and expansion of the technologies.

As detailed in Table 3, a growing public debate in the press and social media has already started about certain issues, mainly related to the aforementioned (partially) disappointing initial results in some specific areas of AI-based diagnosis, and about trust with regards to the new systems and data privacy and security.

There is also an increasing number of voices (including highly-qualified scientists, physicians and entrepreneurs) asking for 'true information' about the real, applicable results of AI-mediated Medicine, particularly in areas of great social interest such as the cure of cancer and other diseases, 'preventive' regulations (especially of the most dangerous and controversial topics) before 'it is too late', and a clear orientation towards the development of 'human-centric' AI. Most of these concerns are explicitly included in the mentioned 'urgent priorities for the next decade' defined by the WHO at the beginning of 2020.

Advances of AI in Medicine and Health are partially driven by research, development and innovation based on public funding in the European Union. By the date of this Report there are some recent documents issued by EU institutions about technical issues related to AI, its extraordinary potential, adoption path, and economic impact, and about the social and ethical impact of AI in general and in the industrial context. Moreover, there is a growing concern regarding the interest and need of a specific analysis of the social impact of AI in Medicine and Health in the scientific, medical, clinical and technological communities, and an increasing number of related meetings.

However, at the European or international levels there are no references to coordinated overview or analysis of the social impact of AI in Medicine and Health. In addition, there are no specific regulations about (many) of the most conflicting issues mentioned in this Report.

6.2 Key aspects to evaluate

A thorough and global evaluation of the social impact of AI systems in Medicine and Health should include all topics described in the previous paragraphs –synthetized in Figure 1 and Figure 2– with particular attention to those aforementioned issues that pose extended challenges. Among them, and as detailed in the references listed in Table 3:

- The risk of dividing Medicine into the presented sub-types ('fake-based', 'patient-generated' and 'scientifically tailored').
- Some specific issues related to data privacy, security and safety.
- The ethics of decision for (fully) autonomous doctors, robotic surgeons or patient-controlling systems (e.g. in intensive care units).
- Trust (e.g. in the relationship with a robotic doctor and in the confidence in the diagnosis, prognosis and proposals for treatment).
- Empathy (e.g. in companion robots for the sick or the elderly and in automated systems 'helping' humans to make difficult decisions).
- Automated systems making decisions with a direct effect on the life and death of humans.

There also appear completely new –disruptive– aspects, not currently being addressed, which may impact the following:

- Individual free will, in relation to brain implants, neuroprosthetics and (external) manipulation and control of neural processes.
- Individual freedom, in applications such as generalized genetic screening, social engineering using (merged) medical data, self-experimentation medicine and do-it-yourself gene editing.
- Genetic heritage for the coming generations.
- Fundamentals and definitions of life, death and their frontiers, including the search for human-animal embryos, artificial life forms and immortality.

The implementation of detailed analysis of the ethical and social effects of AI technologies on Medicine and Health requires a truly inter- and multi-disciplinary approach, combining the views from many areas:

- Clinical medicine and surgery, the 'bio-related' disciplines (biology, pharmacology, genetics, psychology, …) and new combined areas (neurophotonics, genetic counseling).
- Computer science, information and telecommunication technologies, natural sciences (physics, mathematics, chemistry), engineering, robotics.
- Humanistic, cultural and societal disciplines (ethics, philosophy, anthropology, sociology, history).
- Defense, security and safety.
- Legal, regulatory and policymakers.

In addition, a global perspective is also needed: what happens in developed areas (the West) is inter-related to developing regions (the Global South) and to any other world regions, both through the internet and through the easy means of transporting persons, animals and merchandise.

A possible approach to tackling some of the challenges related to new risks would be to identify key technological elements required for the most sensitive applications and then regulate and monitor the distribution, availability and access to such materials. This would be somewhat similar to current procedures implemented for substances such as explosives and their precursors and radioactive elements, and it would obviously require the corresponding regulatory updates.

6.3 Towards a European leadership

Europe can –and must– lead the on-going revolution provided by AI-related technologies in Medicine and Health. The European Union has the scientific and technological skills and resources and the –also very much-needed– philosophical, ethical, social and historical background required for the successful leadership of such a revolution. Nevertheless, other global actors (e.g. USA or China) are currently investing in AI and digital technologies, particularly in Medicine and Health.

The European Commission set out an AI strategy in April 2018 addressing the socioeconomic aspects in parallel with an increase in investment in research, innovation and AI capacity across the EU. It agreed a coordinated plan with Member States to align strategies, and established a High-Level Expert Group on AI that published Ethical Guidelines for Trustworthy AI in April 2019 [3]. These guidelines are made of seven core requirements and contain an assessment list for practical use by companies.

The Commission has considered healthcare as a high-risk sector in the 'White Paper on Artificial Intelligence – A European approach to excellence and trust' COM(2020)65 [4], given the profound consequences of the adoption and expansion of such technologies and the need for an ecosystem of trust on AI.

In this context, we foresee the need to advance on the research and development of practical solutions for trustworthy AI in Medicine and Healthcare in the following aspects:

i) **Strengthen research** into the social impact of AI in Medicine and Health in the three inter-related sectors: individuals (patients, professionals), social groups and society as a whole, by means of dedicated funding.

It is important to note that this type of research (of the very specific social and ethical aspects of AI in Medicine and Health) is different from –although it clearly complements– the many R&D&I activities that are currently being developed about the scientific, technical and clinical aspects of such AI technologies, and in the social and ethical issues that are common to other areas of AI in industrial applications (such as the privacy and security of data, trust and fairness, legal responsibility and others).

ii) **Coordination and implementation of ethical and social guidelines** for R&D&I of AI in Medicine and Health **among EU members**, starting from the Ethical Guidelines, and analyzing and prioritizing

- the application of beneficial medical advances provided by AI against the leading causes of death, disease and disability and, in particular, following the urgent priorities defined by the World Health Organization at the beginning of 2020,
- the analysis and control of the most potentially dangerous topics (namely, those related to devices for mind-reading and interaction and control of brain processes as opposed to free will, merging of medical and other types of data for 'social engineering', uncontrolled human gene editing and introduction of malicious changes in genetic heritage, human-animal hybrids, bioterrorism and weaponizing technologies and others), and
- the design and implementation of 'fundamental rules' in certain areas of research and technology, before reaching the 'it is too late' limits.

iii) **Information for European citizens**, to allow for the general public to have an educated opinion about the benefits, risks and ethical and societal impact of the technological proposals based on AI in Medicine and Health which may be funded by European taxpayers.

Particular efforts should be started –as soon as possible– to protect European citizens from the very serious health risks derived from falling into 'fake-based' and 'patient-generated' types of 'pseudo-medicine' and 'digital health scammers', and to allow for the (highly challenging) generalized access of the population to the very positive results of 'scientifically tailored' Medicine.

iv) **Leveraging European talent.** Innovative actions should be taken to promote, foster and retain talent –particularly young– related to AI within the EU. European academics and entrepreneurs have outstanding levels of values and commitment in the new challenges posed by the interdisciplinary fields –and the new professional roles– that emerge in AI related to Medicine and Healthcare. Effective initiatives should be designed to promote their development inside the EU territories, discouraging the migration of highly qualified actors –scientific, technological, start-ups– to other geographical areas, and attracting others to come.

v) **Regulation and legislative actions,** to allow for the advances of science and technology in Medicine and Health within the established ethical boundaries and, if possible, in coordination with other world regions.

In view of the current state of the art and perspectives in this field, the EU should define an R&D&I coordinated effort to analyze the social impact of AI-related systems and technologies in Medicine and Health carried out in EU institutions, and to define the principles, ethical and societal guidelines and potential boundaries of research, development and implementation of AI-related technologies in Medicine and Healthcare as soon as possible.

7 An unexpected example: the coronavirus pandemic and its extraordinary social impact

In early 2020, during the review process of this Report, the world was unexpectedly shaken by the (SARS-CoV-2) coronavirus and the COVID-19 pandemic disease, and its deep, ongoing impact in all aspects of daily life, particularly in some countries of the European Union. Given the rapid capacity of the Joint Research Centre to react to this important challenge, a brief link of this study with the current health emergency has been incorporated in this Report (see also 2.3).

SARS-CoV-2 is a barely known virus, with a very efficient mechanism of contagion, and there is no available vaccine or treatment yet. This pandemic is having consequences worldwide and in all sectors, with an expected extraordinary, negative impact on economy, and, deeply, in people's daily lives. Contention measurements trying to reduce the propagation of disease include massive quarantine and time-extended population confinement in many countries. This assumes a definite slowdown of activities and nearly a complete stop in many areas. The European Union is being strongly affected, and some European countries suffer a very difficult situation.

There is an ongoing explosion of coronavirus-related literature in all scientific fields, e.g. as illustrated by the COVID-19 Open Research Dataset Challenge (CORD-19) [262]. In this initiative, a coalition of leading research groups has prepared the COVID-19 Open Research Dataset. This is a continuously growing resource, with many tens of thousands of scholarly articles, mostly available in full text, about COVID-19, SARS-CoV-2, and related coronaviruses.

AI-mediated technologies –and the extraordinary efforts of people everywhere– lay at the main core of the response to this overwhelming health crisis. Virtually, most aspects included in the contents of our Report have proven to be important factors in the fight against the COVID-19 disease spread, as outlined below, and there is a growing arsenal of AI-related literature addressing the current coronavirus pandemic. The present condition needs a critical profound study on such questions, from medical, scientific, and technological approaches to related social and ethical aspects.

Figure 1 mentions the potential of big data collection and analysis for medical diagnosis, epidemiology prevention and monitoring of disease outbreaks, as it is happening in the current situation. Computer vision techniques are being used to support the diagnosis of coronavirus on chest scans, as well as machine learning techniques facilitate the development of vaccines and treatments, the forecasting of infection and spread rates, and the exploitation of online and social media data to monitor the spread and public perception of the disease [263] [264]. Robotics, telemedicine and virtual doctors are also being exploited to replace human-human interaction in contaminated environments, e.g. to avoid infections or to disinfect hospitals [265], and AI-mediated tools help fight against misinformation and fake news or 'fake-based medicine' as presented in 3.10 and 3.11 [266].

In addition, many other social aspects mentioned in Figure 2 also being considered. They include the balance between need of data, social monitoring and control and privacy [267] [268] [269] [270].

Saving lives and fighting the disease are clear, common goals in an exceptional situation with an extended, emotional impact at all levels of society. Society demands more than ever solutions to fight the current pandemic and prevent or minimize future crises. However, fundamentals questions pointed out in this Report suddenly arise with intricate, contradictory views in the debate: 'social distancing', extensive testing and temporary confinement of population are proposed –and, in many countries, enforced– to avoid contagion and stop the propagation of the disease. But should citizen's displacement be individually tracked and controlled? Should every person (not only actual patients) be 'classified' and 'color-tagged' in a green-yellow-red scale using big data analytics? Should health data be transmitted to law-enforcement agencies? What will happen with the enormous amounts of individual data collected? How will this emergency change the design and usage of AI tools in the future and the invention of novel AI applications to fight such pandemic diseases? Should there be any limits?

The current situation illustrates the duality addressed in this Report between controversial and positive usages of AI technologies in Medicine and Healthcare, and it will for sure be the subject of many future research.

8 Conclusions

This Report provides a detailed state of the art of the current and near-future applications of Artificial Intelligence in Medicine and Healthcare. From this literature review, the Report proposes a categorization of these application in terms of their potential benefits, risks, and availability level. In addition, it also presents the emerging social debate on some related topics, and analyses the ethical and social impact of these technologies and the way they may change human behavior, transforming the roles of doctors and patients.

From this discussion, it is formulated a set of policy challenges that will need to be addressed in the next future and some recommendations towards a European leadership in this sector.

As a future work, this Report should be converted into a dynamic state of the art to reflect the changes in the proposed applications of AI in Medicine and Healthcare, availability levels, ethical and social aspects, list of references and policy initiatives.

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Appendix: Selected conferences in 2019

This section reports the conferences held in 2019 directly related to –or with specific sections about– the ethical and social aspects of AI in Medicine and Healthcare.

Event: 105th Scientific Assembly and Annual Meeting of Radiological Society of North America.

Date: December 1st-6th, 2019.

Location: Chicago, USA.

https://www.rsna.org/annual-meeting

Event: Personalized Medicine Coalition: 15th Annual Personalized Medicine Conference.

Date: November 13-14th, 2019.

Location: Boston USA.

http://www.personalizedmedicineconference.org/

Event: Artificial Intelligence Conference.

Date: October 14-17th, 2019.

Location: London, UK.

https://conferences.oreilly.com/artificial-intelligence/ai-eu

Event: Future of Health.

Date: October 2-3th, 2019.

Location: New York, NY, USA.

https://events.cbinsights.com/future-of-health/rpaffo

Event: Frontier of AI-Assisted Care (FAC) Scientific Symposium.

Date: September 18-19th, 2019.

Location: Stanford, CA, USA.

https://med.stanford.edu/frontierofaicare.html

Event: Intelligent Health.

Date: September 11-12th, 2019.

Location: Basel, Switzerland.

https://intelligenthealth.ai/

Event: Intelligence. Innovation. Imaging. The perfect vision of AI.

Date: April 5-6th, 2019.

Location: Barcelona, Spain.

https://www.maiesr.org/programme/

Event: Health Hackathon.

Date: March 30th, 2019.

Location: Valencia, Spain.

https://www.eventbrite.com/e/school-of-ai-health-hackathon-2019-valencia-spain-tickets-55932713251

Event: European Congress of Radiology.

Date: February 27th- March 3th, 2019.

Location: Vienna, Austria.

https://www.myesr.org/past-congresses/ecr-2019

Event: Next Generation Public Health: AI and Big Data

Date: February 8th, 2019

Location: London, UK.

https://www.fondationbotnar.org/panel-event-next-generation-public-health-ai-and-big-data/

Event: HUMAINT Winter school on AI: ethical, social, legal and economic impact.

Date: February 4-8th, 2019.

Location: Centre for Advanced Studies, Joint Research Centre, European Commission. Seville, Spain.

https://ec.europa.eu/jrc/communities/en/event/humaint-winter-school-ai-ethical-social-legal-and-economic-impact

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