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AI Watch

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

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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:

Gómez-González Emilio, Gómez Emilia, Márquez-Rivas Javier, Guerrero-Claro Manuel, Fernández-Lizaranzu Isabel, Relimpio-López María Isabel, Dorado Manuel E., Mayorga-Buiza María José, Izquierdo-Ayuso Guillermo, Capitán-Morales Luis. Artificial intelligence in medicine and healthcare: a review and classification of current and near-future applications and their ethical and social impact. arXiv 2020. http://arxiv.org/abs/2001.09778 [5].

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.

9 References

[1] Artificial Intelligence for Europe, COM(2018)237. European Commission. 2018. https://ec.europa.eu/transparency/regdoc/rep/1/2018/EN/COM-2018-237-F1-EN-MAIN-PART-1.PDF (accessed May 5, 2020).

[2] Coordinated Plan on Artificial Intelligence, COM(2018)795. European Commission. 2018. https://ec.europa.eu/knowledge4policy/node/32954_sl (accessed May 5, 2020).

[3] High-Level Expert Group on Artificial Intelligence of the European Commission. Ethics guidelines for trustworthy Artificial Intelligence. European Commission. 2018. https://ec.europa.eu/futurium/en/ai-alliance-consultation/guidelines (accessed Dec 12, 2019).

[4] White Paper on Artificial Intelligence: a European approach to excellence and trust, COM(2020)65. European Commission. 2020. https://ec.europa.eu/knowledge4policy/node/32954_sl (accessed May 5, 2020).

[5] Gómez-González E, Gomez E, Márquez-Rivas J, Guerrero-Claro M, Fernández-Lizaranzu I, Relimpio-López MI, Dorado ME, Mayorga-Buiza MJ, Izquierdo-Ayuso G, Capitán-Morales L. Artificial intelligence in medicine and healthcare: a review and classification of current and near-future applications and their ethical and social Impact. *arXiv* 2020. http://arxiv.org/abs/2001.09778.

[6] Marr B. The Key Definitions Of Artificial Intelligence (AI) That Explain Its Importance. Forbes. 2018. https://www.forbes.com/sites/bernardmarr/2018/02/14/the-key-definitions-of-artificial-intelligence-ai-that-explain-its-importance/#4dbe46174f5d (accessed July 29, 2019).

[7] Cambridge Dictionary. Cambridge University Press. 2019. https://dictionary.cambridge.org/ (accessed July 29, 2019).

[8] Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD). FDA. 2019. https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device (accessed July 25, 2019).

[9] Hammond K. What is artificial intelligence (AI), and what is the difference between general AI and narrow AI? Computer World. 2015. https://www.computerworld.com/article/2906336/what-is-artificial-intelligence.html (accessed July 29, 2019).

[10] Balžekiene A, Butkevičiene E, Telešiene A. Methodological Framework for Analyzing Social Impact of Technological Innovations. *Social Sciences* 2008; 1: 71–80.

[11] Top European Newspapers in English. TheBigProject. http://www.thebigproject.co.uk/news/european newspapers in english.html#.XU9CSsrtafA (accessed Aug 13, 2019).

[12] Rao A, Verweij G, Cameron E. Sizing the prize. PwC's Global Artificial Intelligence Study: Exploiting the AI Revolution. PwC. 2017. https://www.pwc.com/gx/en/issues/data-and-analytics/publications/artificial-intelligence-study.html (accessed Dec 4, 2019).

[13] Craglia M (Ed), Annoni A, Benczur P, Bertoldi P, Delipetrev P, De Prato G, Feijoo C, Fernandez ME, Gomez E, Iglesias M, Junklewitz H, López CM, Martens B, Nascimento S, Nativi S, Polvora A, Sanchez I, Tolan S, Tuomi I, *et al.* Artificial Intelligence: A European Perspective. Luxembourg: EUR 29425 EN, Publications Office, 2018.

[14] Bughin J, Seong J, Manyika J, Hämäläinen L, Windhagen E, Hazan E. Notes from the AI frontier: Tackling Europe's gap in digital and AI. Mckinsey Global Institute. 2019.

https://www.mckinsey.com/featured-insights/artificial-intelligence/tackling-europes-gap-in-digital-and-ai (accessed July 25, 2019).

[15] Gurry F. WIPO Technology Trends 2019: Artificial Intelligence. *World Intellectual Property Organization* 2019. https://www.wipo.int/edocs/pubdocs/en/wipo_pub_1055.pdf (accessed July 29, 2019).

[16] Healthcare expenditure statistics. Eurostats. 2019. https://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_expenditure_statistics (accessed Aug 1, 2019).

[17] Collier M, Fu R, Yin L. Artificial Intelligence: Healthcare's New Nervous System - Accenture Report. Accenture. 2017. https://www.accenture.com/_acnmedia/pdf-49/accenture-health-artificial-intelligence.pdf (accessed July 25, 2019).

[18] Phillips KA, Deverka PA, Hooker GW, Douglas MP. Genetic Test Availability And Spending: Where Are We Now? Where Are We Going? *Health Affairs* 2018; 37: 710–6.

[19] Naming the coronavirus disease (COVID-19) and the virus that causes it. World Health Organization. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it (accessed May 5, 2020).

[20] WHO announces COVID-19 outbreak a pandemic. World Health Organization. 2020. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic (accessed March 27, 2020).

[21] Ghebreyesus TA. Urgent health challenges for the next decade [WHO Declaration, 13/1/2020]. World Health Organization. 2020. https://www.who.int/news-room/photo-story/photo-story-detail/urgent-health-challenges-for-the-next-decade (accessed Jan 19, 2020).

[22] Short Overview of the Human Brain Project. Human Brain Project. 2017. https://www.humanbrainproject.eu/en/about/overview/ (accessed Jan 14, 2020).

[23] The BRAIN Initiative. NIH USA. https://braininitiative.nih.gov/about/overview (accessed Jan 14, 2020).

[24] Artificial intelligence: Commission kicks off work on marrying cutting-edge technology and ethical standards. European Commission Press Release. 2018. https://ec.europa.eu/commission/presscorner/detail/en/IP_18_1381 (accessed Dec 11, 2019).

[25] A European approach on Artificial Intelligence. European Commission. 2018. http://europa.eu/rapid/press-release_MEMO-18-3363_en.pdf (accessed March 18, 2019).

[26] The Mobile Economy. GSMA Intelligence. 2018. https://www.gsma.com/mobileeconomy/ (accessed March 18, 2019).

[27] Mobile Consumer Survey 2019. Deloitte. 2019. https://www.deloitte.co.uk/mobileuk/ (accessed March 18, 2019).

[28] Smith G. The AI Delusion. Oxford University Press, 2018.

[29] Fazal MI, Patel ME, Tye J, Gupta Y. The past, present and future role of artificial intelligence in imaging. *European Journal of Radiology* 2018; 105: 246–50.

[30] Starikov A, Al'Aref SJ, Singh G, Min JK. Artificial intelligence in clinical imaging: An introduction. *Clinical Imaging* 2018; 49: vii–ix.

[31] Buzaev IV, Plechev VV, Nikolaeva IE, Galimova RM. Artificial intelligence: Neural network

model as the multidisciplinary team member in clinical decision support to avoid medical mistakes. *Chronic Diseases and Translational Medicine* 2016; 2: 166–72.

[32] Lebedev G, Klimenko H, Kachkovskiy S, Konushin V, Ryabkov I, Gromov A. Application of artificial intelligence methods to recognize pathologies on medical images. *Procedia Computer Science* 2018; 126: 1171–7.

[33] Obermeyer Z, Emanuel EJ. Predicting the Future — Big Data, Machine Learning, and Clinical Medicine. *New England Journal of Medicine* 2016; 375: 1216–9.

[34] Maddox TM, Rumsfeld JS, Payne PRO. Questions for Artificial Intelligence in Health Care. *JAMA* 2019; 321: 31–2.

[35] Tarassenko L, Topol EJ. Monitoring Jet Engines and the Health of People. *JAMA* 2018; 320: 2309.

[36] Mathur P, Khanna AK, Cywinski JB, Maheshwari K, Naylor DF, Papay FA. 2018 Year in Review: Machine Learning in Healthcare. On behalf of Team BrainX and BrainX Community. Brainxai. 2019. https://www.brainxai.org/wp-content/uploads/2019/03/PDF-of-2018-Year-in-ReviewMachine-Learning-in-Healthcare..pdf (accessed March 19, 2019).

[37] Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine* 2019; 25: 44–56.

[38] Londhe VY, Bhasin B. Artificial intelligence and its potential in oncology. *Drug Discovery Today* 2019; 24: 228–32.

[39] Suzuki K, Chen Y, editors. Computer-Aided Prognosis. In: Artificial Intelligence in Decision Support Systems for Diagnosis in Medical Imaging. Springer International Publishing, 2018: 225–333.

[40] Suzuki K, Chen Y, editors. Computer-Aided Diagnosis. In: Artificial Intelligence in Decision Support Systems for Diagnosis in Medical Imaging. Springer International Publishing, 2018: 135–222.

[41] Yu KH, Beam AL, Kohane IS. Artificial intelligence in healthcare. *Nature Biomedical Engineering* 2018; 2: 719–31.

[42] Medicine in the digital age. *Nature Medicine* 2019; 25: 1–1.

[43] Topol EJ. A decade of digital medicine innovation. *Science Translational Medicine* 2019; 11: eaaw7610.

[44] Couzin-Frankel J. Medicine contends with how to use artificial intelligence. *Science* 2019; 364: 1119–20.

[45] Ghassemi M, Naumann T, Schulam P, Beam AL, Chen IY, Ranganath R. Practical guidance on artificial intelligence for health-care data. *The Lancet Digital Health* 2019; 1: e157–9.

[46] Artificial Intelligence in Healthcare. *Academy of Medical Royal Colleges* 2019; January.

[47] Weng SF, Vaz L, Qureshi N, Kai J. Prediction of premature all-cause mortality: A prospective general population cohort study comparing machine-learning and standard epidemiological approaches. *PLOS ONE* 2019; 14: e0214365.

[48] The top 10 causes of death. World Health Organization. 2018. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed July 25, 2019).

[49] Ding Y, Sohn JH, Kawczynski MG, Trivedi H, Harnish R, Jenkins NW, Lituiev D, Copeland TP, Aboian MS, Mari Aparici C, Behr SC, Flavell RR, Huang S-Y, Zalocusky KA, Nardo L, Seo Y, Hawkins RA, Hernandez Pampaloni M, Hadley D, *et al.* A Deep Learning Model to Predict a Diagnosis of Alzheimer Disease by Using 18 F-FDG PET of the Brain. *Radiology* 2019; 290: 456–

64.

[50] Steele AJ, Denaxas SC, Shah AD, Hemingway H, Luscombe NM. Machine learning models in electronic health records can outperform conventional survival models for predicting patient mortality in coronary artery disease. *PLOS ONE* 2018; 13: e0202344.

[51] Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, Gavin A, Visser O, Bray F. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *European Journal of Cancer* 2018; 103: 356–87.

[52] Cancer Facts & Figures. American Cancer Society. 2019. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf#page23 (accessed Sept 18, 2019).

[53] The EUROCARE-4 database on cancer survival in Europe. EuroCare. 2002. http://www.eurocare.it/Results/tabid/79/Default.aspx (accessed Sept 18, 2019).

[54] Artificial Intelligence in medicine. IBM. 2019. https://www.ibm.com/watson-health/learn/artificial-intelligence-medicine (accessed July 25, 2019).

[55] Are medical errors really the third most common cause of death in the U.S.? Science-Based Medicine. 2019. https://sciencebasedmedicine.org/are-medical-errors-really-the-third-most-common-cause-of-death-in-the-u-s-2019-edition/ (accessed July 25, 2019).

[56] Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, Aboyans V, Adetokunboh O, Afshin A, Agrawal A, Ahmadi A, Ahmed MB, Aichour AN, Aichour MTE, Aichour I, Aiyar S, Alahdab F, Al-Aly Z, Alam K, *et al.* Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet* 2017; 390: 1151–210.

[57] Sunshine JE, Meo N, Kassebaum NJ, Collison ML, Mokdad AH, Naghavi M. Association of Adverse Effects of Medical Treatment With Mortality in the United States. *JAMA* 2019; 2: e187041.

[58] Patient Safety: Data and Statistics. World Health Organization. 2019. http://www.euro.who.int/en/health-topics/Health-systems/patient-safety/data-and-statistics (accessed Aug 1, 2019).

[59] Universal Health Coverage (definition). World Health Organization. 2019. https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc) (accessed July 25, 2019).

[60] Sustainable Development Goals. Goal 3: Ensure healthy lives and promote well-being for all at all ages. United Nations. https://www.un.org/sustainabledevelopment/health/ (accessed March 18, 2019).

[61] Bloom DE, Khoury A, Subbaraman R. The promise and peril of universal health care. *Science* 2018; 361: eaat9644.

[62] Universal Declaration of Human Rights. United Nations. https://www.un.org/en/universal-declaration-human-rights/ (accessed Oct 1, 2019).

[63] Harnessing the economic benefits of Artificial Intelligence. European Commission. 2017. https://ec.europa.eu/growth/tools-databases/dem/monitor/content/harnessing-economic-benefits-artificial-intelligence (accessed July 25, 2019).

[64] Faircloth B, Heskett C, Roper S. Artificial Intelligence: Six Challenges for the European Healthcare Sector. *LEK Consulting / Executive Insights*; XX: 1–5.

[65] AI In Numbers: Global Funding, Exits, And R&D Trends In Artificial Intelligence. CB Insights. 2019. https://www.cbinsights.com/research/report/ai-in-numbers-q2-2019/ (accessed July 26, 2019).

[66] Bens CA. Policy Developments Raise New Concerns for Personalized Medicine as FDA Sharpens Focus on Field. *Personalized Medicine Coallition* 2019; 12: 4–5.

[67] Meet Your New Genetic Counselor. Forbes. 2019. https://www.forbes.com/sites/insights-intelai/2019/02/11/meet-your-new-genetic-counselor/#3f2c1b0667c2 (accessed Oct 15, 2019).

[68] Dieleman JL, Templin T, Sadat N, Reidy P, Chapin A, Foreman K, Haakenstad A, Evans T, Murray CJL, Kurowski C. National spending on health by source for 184 countries between 2013 and 2040. *The Lancet* 2016; 387: 2521–35.

[69] AI and healthcare: A giant opportunity. Forbes. 2019. https://www.forbes.com/sites/insights-intelai/2019/02/11/ai-and-healthcare-a-giant-opportunity/ (accessed July 25, 2019).

[70] Bughin J, Seong J, Manyika J, Hämäläinen L, Windhagen E, Hazan E. Tackling Europe's gap in digital and AI. Mckinsey Global Institute. 2019. https://www.mckinsey.com/featured-insights/artificial-intelligence/tackling-europes-gap-in-digital-and-ai (accessed July 25, 2019).

[71] 10 imperatives for Europe in the age of AI and automation. Mckinsey Global Institute. 2017. https://www.mckinsey.com/featured-insights/europe/ten-imperatives-for-europe-in-the-age-of-ai-and-automation (accessed July 25, 2019).

[72] Zhu Q, Long K. How will artificial intelligence impact Sino–US relations? *China International Strategy Review* 2019; 1: 139–51.

[73] O'Meara S. Will China lead the world in AI by 2030? *Nature* 2019; 572: 427–8.

[74] HARPA. The Patients Are Waiting. The Suzanne Wright Foundation. 2019. https://www.suzannewrightfoundation.org/ (accessed Sept 18, 2019).

[75] NHS to set up national artificial intelligence lab. BBC News. 2019. https://www.bbc.com/news/health-49270325 (accessed Aug 13, 2019).

[76] Can the EU become another AI superpower? The Economist. 2018. https://www.economist.com/business/2018/09/20/can-the-eu-become-another-ai-superpower (accessed Nov 6, 2019).

[77] 'Whoever leads in AI will rule the world': Putin to Russian children on Knowledge Day. Russia Today. 2017. www.rt.com/news/401731-ai-rule-world-putin/ (accessed July 25, 2019).

[78] Select Committee on Artificial Intelligence of the National Science & Technology Council. The National Artificial Research and Development Strategic Plan: 2019 Update. Executive Office of the President of the United States. 2019. https://www.nitrd.gov/pubs/National-AI-RD-Strategy-2019.pdf (accessed Sept 25, 2019).

[79] Kalantari A, Kamsin A, Shamshirband S, Gani A, Alinejad-Rokny H, Chronopoulos AT. Computational intelligence approaches for classification of medical data: State-of-the-art, future challenges and research directions. *Neurocomputing* 2018; 276: 2–22.

[80] Henriksen EL, Carlsen JF, Vejborg IM, Nielsen MB, Lauridsen CA. The efficacy of using computer-aided detection (CAD) for detection of breast cancer in mammography screening: a systematic review. *Acta Radiologica* 2019; 60: 13–8.

[81] Ranschaert ER, Morozov S, Algra PR. Artificial Intelligence in Medical Imaging: Opportunities, Applications and Risks. Springer, 2019.

[82] Doshi-Velez F, Kim B. Towards A Rigorous Science of Interpretable Machine Learning. *arXiv*

2017. http://arxiv.org/abs/1702.08608.

[83] Esteva A, Robicquet A, Ramsundar B, Kuleshov V, DePristo M, Chou K, Cui C, Corrado G, Thrun S, Dean J. A guide to deep learning in healthcare. *Nature Medicine* 2019; 25: 24–9.

[84] Ranschaert ER, Morozov S, Algra PR, editors. Artificial Intelligence in Medical Imaging. Cham: Springer International Publishing, 2019 DOI:10.1007/978-3-319-94878-2.

[85] Litjens G, Kooi T, Bejnordi BE, Setio AAA, Ciompi F, Ghafoorian M, van der Laak JAWM, van Ginneken B, Sánchez CI. A survey on deep learning in medical image analysis. *Medical Image Analysis* 2017; 42: 60–88.

[86] Alberich-Bayarri A. Image Interpretation. In: Quality and Safety in Imaging. Springer International Publishing, 2017: 135–43. DOI:10.1007/978-3-319-42578-8.

[87] Donoso-Bach L, Boland GWL, editors. Quality and Safety in Imaging. Springer International Publishing, 2017. DOI:10.1007/978-3-319-42578-8.

[88] Mitchell JR, Bilbily A, Geis R, Gallix B, Cadrin-Chênevert A, Barfett J, Reinhold C, O'Connell T, Gray B, Jaremko JL, Tam R, Cairns R, Guest W, Shabana W, Derkatch S, Babyn P, Cicero MD, Chepelev L, Koff D, *et al.* Canadian Association of Radiologists White Paper on Artificial Intelligence in Radiology. *Canadian Association of Radiologists Journal* 2018; 69: 120–35.

[89] Yasaka K, Abe O. Deep learning and artificial intelligence in radiology: Current applications and future directions. *PLOS Medicine* 2018; 15: e1002707.

[90] Gharbi M, Chen J, Barron JT, Hasinoff SW, Durand F. Deep bilateral learning for real-time image enhancement. *ACM Transactions on Graphics* 2017; 36: 1–12.

[91] Oktay O, Ferrante E, Kamnitsas K, Heinrich M, Bai W, Caballero J, Cook SA, de Marvao A, Dawes T, O'Regan DP, Kainz B, Glocker B, Rueckert D. Anatomically Constrained Neural Networks (ACNNs): Application to Cardiac Image Enhancement and Segmentation. *IEEE Transactions on Medical Imaging* 2018; 37: 384–95.

[92] Valsecchi A, Damas S, Santamaría J, Marrakchi-Kacem L. Intensity-based image registration using scatter search. *Artificial Intelligence in Medicine* 2014; 60: 151–63.

[93] Huang P, Park S, Yan R, Lee J, Chu LC, Lin CT, Hussien A, Rathmell J, Thomas B, Chen C, Hales R, Ettinger DS, Brock M, Hu P, Fishman EK, Gabrielson E, Lam S. Added Value of Computer-aided CT Image Features for Early Lung Cancer Diagnosis with Small Pulmonary Nodules: A Matched Case-Control Study. *Radiology* 2018; 286: 286–95.

[94] Boone D, Mallett S, McQuillan J, Taylor SA, Altman DG, Halligan S. Assessment of the Incremental Benefit of Computer-Aided Detection (CAD) for Interpretation of CT Colonography by Experienced and Inexperienced Readers. *PLOS ONE* 2015; 10: e0136624.

[95] Verger R. Google is working on 'self-healing' maps, thanks to artificial intelligence. Popular Science. 2019. https://www.popsci.com/google-maps-artificial-intelligence-self-healing/ (accessed July 25, 2019).

[96] Nicolini A, Ferrari P, Duffy MJ. Prognostic and predictive biomarkers in breast cancer: Past, present and future. *Seminars in Cancer Biology* 2018; 52: 56–73.

[97] Barillot C, Edan G, Commowick O. Imaging biomarkers in multiple Sclerosis: From image analysis to population imaging. *Medical Image Analysis* 2016; 33: 134–9.

[98] Marti-Bonmati L, Alberich-Bayarri A, editors. Imaging Biomarkers. Springer, 2017.

[99] Kehl KL, Elmarakeby H, Nishino M, Van Allen EM, Lepisto EM, Hassett MJ, Johnson BE, Schrag D. Assessment of Deep Natural Language Processing in Ascertaining Oncologic Outcomes From Radiology Reports. *JAMA Oncology* 2019; 5: 1421.

[100] Benaroia M, Elinson R, Zarnke K. Patient-directed intelligent and interactive computer medical history-gathering systems: A utility and feasibility study in the emergency department. *International Journal of Medical Informatics* 2007; 76: 283–8.

[101] Norgeot B, Glicksberg BS, Butte AJ. A call for deep-learning healthcare. *Nature Medicine* 2019; 25: 14–8.

[102] Rashidian S, Hajagos J, Moffitt RA, Wang F, Noel KM, Gupta RR, Tharakan MA, Saltz JH, Saltz MM. Deep Learning on Electronic Health Records to Improve Disease Coding Accuracy. *AMIA Joint Summits on Translational Science proceedings* 2019; 2019: 620–9.

[103] Lu MT, Ivanov A, Mayrhofer T, Hosny A, Aerts HJWL, Hoffmann U. Deep Learning to Assess Long-term Mortality From Chest Radiographs. *JAMA* 2019; 2: e197416.

[104] El-Gamal F, Elmogy M, Atwan A. Current trends in medical image registration and fusion. *Egyptian Informatics Journal* 2016; 17: 99–124.

[105] Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJWL. Artificial intelligence in radiology. *Nature Reviews Cancer* 2018; 18: 500–10.

[106] Vashistha R, Yadav D, Chhabra D, Shukla P. Artificial Intelligence Integration for Neurodegenerative Disorders. In: Leveraging Biomedical and Healthcare Data. Elsevier, 2019: 77–89.

[107] Shahdoosti HR, Tabatabaei Z. MRI and PET/SPECT image fusion at feature level using ant colony based segmentation. *Biomedical Signal Processing and Control* 2019; 47: 63–74.

[108] He C, Liu Q, Li H, Wang H. Multimodal medical image fusion based on IHS and PCA. *Procedia Engineering* 2010; 7: 280–5.

[109] Manchanda M, Sharma R. An improved multimodal medical image fusion algorithm based on fuzzy transform. *Journal of Visual Communication and Image Representation* 2018; 51: 76–94.

[110] Kim W-J. Knowledge-based diagnosis and prediction using big data and deep learning in precision medicine. *Investigative and Clinical Urology* 2018; 59: 69.

[111] May M. Translating big data: The proteomics challenge. Science Magazine. 2018. https://www.sciencemag.org/features/2018/06/translating-big-data-proteomics-challenge (accessed Sept 19, 2019).

[112] Snyder M, Zhou W. Big data and health. *The Lancet Digital Health* 2019; 7500: 8–10.

[113] Precision Medicine for Alzheimer Disease and Related Disorders. Biomedical Genetics. http://www.bumc.bu.edu/genetics/research/precision-medicine-in-alzheimer-disease-arc/ (accessed Oct 1, 2019).

[114] Razzaki S, Baker A, Perov Y, Middleton K, Baxter J, Mullarkey D, Sangar D, Taliercio M, Butt M, Majeed A, DoRosario A, Mahoney M, Johri S. A comparative study of artificial intelligence and human doctors for the purpose of triage and diagnosis. *arXiv* 2018. http://arxiv.org/abs/1806.10698.

[115] Wetsman N. Artificial intelligence is taking an increased role in diagnosing and treating cancer. Popular Science. 2019. https://www.popsci.com/machine-learning-tool-AI-cancer/ (accessed July 29, 2019).

[116] Benzebouchi NE, Azizi N, Ayadi K. A Computer-Aided Diagnosis System for Breast Cancer Using Deep Convolutional Neural Networks. In: Behera HS, Nayak J, Naik B, Abraham A, editors. Computational Intelligence in Data Mining. Singapore: Springer Singapore, 2019: 583–93.

[117] Robertson S, Azizpour H, Smith K, Hartman J. Digital image analysis in breast pathology—from image processing techniques to artificial intelligence. *Translational Research* 2018; 194: 19–

35.

[118] Khosravan N, Celik H, Turkbey B, Jones EC, Wood B, Bagci U. A collaborative computer aided diagnosis (C-CAD) system with eye-tracking, sparse attentional model, and deep learning. *Medical Image Analysis* 2019; 51: 101–15.

[119] Suzuki K, Chen Y, editors. Computer-Aided Detection. In: Artificial Intelligence in Decision Support Systems for Diagnosis in Medical Imaging. Springer International Publishing, 2018: 87–132.

[120] Bhatia S, Sinha Y, Goel L. Lung Cancer Detection: A Deep Learning Approach. In: Bansal JC, Das KN, Nagar A, Deep K, Ojha AK, editors. Soft Computing for Problem Solving. Singapore: Springer Singapore, 2019: 699–705.

[121] Masood A, Sheng B, Li P, Hou X, Wei X, Qin J, Feng D. Computer-Assisted Decision Support System in Pulmonary Cancer detection and stage classification on CT images. *Journal of Biomedical Informatics* 2018; 79: 117–28.

[122] Setio AAA, Traverso A, de Bel T, Berens MSN, Bogaard C van den, Cerello P, Chen H, Dou Q, Fantacci ME, Geurts B, Gugten R van der, Heng PA, Jansen B, de Kaste MMJ, Kotov V, Lin JY-H, Manders JTMC, Sóñora-Mengana A, García-Naranjo JC, *et al.* Validation, comparison, and combination of algorithms for automatic detection of pulmonary nodules in computed tomography images: The LUNA16 challenge. *Medical Image Analysis* 2017; 42: 1–13.

[123] Firmino M, Angelo G, Morais H, Dantas MR, Valentim R. Computer-aided detection (CADe) and diagnosis (CADx) system for lung cancer with likelihood of malignancy. *BioMedical Engineering OnLine* 2016; 15: 2.

[124] Ardila D, Kiraly AP, Bharadwaj S, Choi B, Reicher JJ, Peng L, Tse D, Etemadi M, Ye W, Corrado G, Naidich DP, Shetty S. End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography. *Nature Medicine* 2019; 25: 954–61.

[125] Jacobs C, van Ginneken B. Google's lung cancer AI: a promising tool that needs further validation. *Nature Reviews Clinical Oncology* 2019; 16: 532–3.

[126] Horie Y, Yoshio T, Aoyama K, Yoshimizu S, Horiuchi Y, Ishiyama A, Hirasawa T, Tsuchida T, Ozawa T, Ishihara S, Kumagai Y, Fujishiro M, Maetani I, Fujisaki J, Tada T. Diagnostic outcomes of esophageal cancer by artificial intelligence using convolutional neural networks. *Gastrointestinal Endoscopy* 2019; 89: 25–32.

[127] Krittanawong C, Zhang H, Wang Z, Aydar M, Kitai T. Artificial Intelligence in Precision Cardiovascular Medicine. *Journal of the American College of Cardiology* 2017; 69: 2657–64.

[128] Massalha S, Clarkin O, Thornhill R, Wells G, Chow BJW. Decision Support Tools, Systems, and Artificial Intelligence in Cardiac Imaging. *Canadian Journal of Cardiology* 2018; 34: 827–38.

[129] Narula S, Shameer K, Salem Omar AM, Dudley JT, Sengupta PP. Machine-Learning Algorithms to Automate Morphological and Functional Assessments in 2D Echocardiography. *Journal of the American College of Cardiology* 2016; 68: 2287–95.

[130] D'hooge J, Fraser AG. Learning About Machine Learning to Create a Self-Driving Echocardiographic Laboratory. *Circulation* 2018; 138: 1636–8.

[131] The Engineering that Will Guide Cardiologists. BBVA OpenMind. 2018. https://www.bbvaopenmind.com/en/technology/innovation/the-engineering-that-will-guide-cardiologists/ (accessed July 25, 2019).

[132] Zhou L-Q, Wang J-Y, Yu S-Y, Wu G-G, Wei Q, Deng Y-B, Wu X-L, Cui X-W, Dietrich CF. Artificial intelligence in medical imaging of the liver. *World Journal of Gastroenterology* 2019; 25: 672–82.

[133] Gallego-Durán R, Cerro-Salido P, Gomez-Gonzalez E, Pareja MJ, Ampuero J, Rico MC, Aznar R, Vilar-Gomez E, Bugianesi E, Crespo J, González-Sánchez FJ, Aparcero R, Moreno I, Soto S, Arias-Loste MT, Abad J, Ranchal I, Andrade RJ, Calleja JL, *et al.* Imaging biomarkers for steatohepatitis and fibrosis detection in non-alcoholic fatty liver disease. *Scientific Reports* 2016; 6: 31421.

[134] Lin RH. An intelligent model for liver disease diagnosis. *Artificial Intelligence in Medicine* 2009; 47: 53–62.

[135] De Fauw J, Ledsam JR, Romera-Paredes B, Nikolov S, Tomasev N, Blackwell S, Askham H, Glorot X, O'Donoghue B, Visentin D, van den Driessche G, Lakshminarayanan B, Meyer C, Mackinder F, Bouton S, Ayoub K, Chopra R, King D, Karthikesalingam A, *et al.* Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nature Medicine* 2018; 24: 1342–50.

[136] Gardner GG, Keating D, Williamson TH, Elliott AT. Automatic detection of diabetic retinopathy using an artificial neural network: a screening tool. *British Journal of Ophthalmology* 1996; 80: 940–4.

[137] Roach L. Artificial Intelligence. *Eyenet Magazine* 2017; Nov: 77–83.

[138] Ahmad O, Soares A, Mazomenos E, Brandao P, Vega R, Seward E, Stoyanov D, Chand M, Lovat L. Artificial Intelligence and computer-aided diagnosis in colonoscopy: current evidence and future directions. *The Lancet Gastroenterology & Hepatology* 2018; 4: 71–80.

[139] Bell LTO, Gandhi S. A comparison of computer-assisted detection (CAD) programs for the identification of colorectal polyps: performance and sensitivity analysis, current limitations and practical tips for radiologists. *Clinical Radiology* 2018; 73: 593.e11-593.e18.

[140] Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, Thrun S. Dermatologist-level classification of skin cancer with deep neural networks. *Nature* 2017; 542: 115–8.

[141] Massi D, Laurino M. Machine versus man in skin cancer diagnosis. *The Lancet Oncology* 2019; 20: 891–2.

[142] Kheterpal S, Shanks A, Tremper KK. Impact of a Novel Multiparameter Decision Support System on Intraoperative Processes of Care and Postoperative Outcomes. *Anesthesiology* 2018; 128: 272–82.

[143] Zhavoronkov A, Mamoshina P, Vanhaelen Q, Scheibye-Knudsen M, Moskalev A, Aliper A. Artificial intelligence for aging and longevity research: Recent advances and perspectives. *Ageing Research Reviews* 2019; 49: 49–66.

[144] Schembri F. Artificial intelligence could diagnose rare disorders using just a photo of a face. Science Magazine. 2019. https://www.sciencemag.org/news/2019/01/artificial-intelligence-could-diagnose-rare-disorders-using-just-photo-face (accessed Sept 19, 2019).

[145] Blease C, Bernstein MH, Gaab J, Kaptchuk TJ, Kossowsky J, Mandl KD, Davis RB, DesRoches CM. Computerization and the future of primary care: A survey of general practitioners in the UK. *PLOS ONE* 2018; 13: e0207418.

[146] Blease C, Kaptchuk TJ, Bernstein MH, Mandl KD, Halamka JD, DesRoches CM. Artificial Intelligence and the Future of Primary Care: Exploratory Qualitative Study of UK General Practitioners' Views. *Journal of Medical Internet Research* 2019; 21: e12802.

[147] O'Sullivan S, Heinsen H, Grinberg LT, Chimelli L, Amaro E, do Nascimento Saldiva PH, Jeanquartier F, Jean-Quartier C, da Graça Morais Martin M, Sajid MI, Holzinger A. The role of artificial intelligence and machine learning in harmonization of high-resolution post-mortem MRI (virtopsy) with respect to brain microstructure. *Brain Informatics* 2019; 6: 3.

[148] Hackshaw K V., Aykas DP, Sigurdson GT, Plans M, Madiai F, Yu L, Buffington CAT, Giusti MM, Rodriguez-Saona L. Metabolic fingerprinting for diagnosis of fibromyalgia and other rheumatologic disorders. *Journal of Biological Chemistry* 2019; 294: 2555–68.

[149] Niazi MKK, Parwani A V., Gurcan MN. Digital pathology and artificial intelligence. *The Lancet Oncology* 2019; 20: e253–61.

[150] Dietz RL, Pantanowitz L. The future of anatomic pathology: deus ex machina? *Journal of Medical Artificial Intelligence* 2019; 2: 4–4.

[151] Yuste R, Goering S, Agüera y Arcas B, Bi G, Carmena JM, Carter A, Fins JJ, Friesen P, Gallant J, Huggins JE, Illes J, Kellmeyer P, Klein E, Marblestone A, Mitchell C, Parens E, Pham M, Rubel A, Sadato N, *et al.* Four ethical priorities for neurotechnologies and AI. *Nature* 2017; 551: 159–63.

[152] Fosque BF, Sun Y, Dana H, Yang C-T, Ohyama T, Tadross MR, Patel R, Zlatic M, Kim DS, Ahrens MB, Jayaraman V, Looger LL, Schreiter ER. Labeling of active neural circuits in vivo with designed calcium integrators. *Science* 2015; 347: 755–60.

[153] Bouthour W, Mégevand P, Donoghue J, Lüscher C, Birbaumer N, Krack P. Biomarkers for closed-loop deep brain stimulation in Parkinson disease and beyond. *Nature Reviews Neurology* 2019; 15: 343–52.

[154] Guillén P. Deep Learning Applied to Deep Brain Stimulation in Parkinson's Disease. In: High Performance Computing. 2017: 269–78.

[155] Rashed EA, Sakai T, Gomez-Tames J, Hirata A. Brain AI: Deep Learning for Brain Stimulation. *IEEE Pulse* 2019; 10: 3–5.

[156] RaviPrakash H, Korostenskaja M, Castillo EM, Lee KH, Salinas CM, Baumgartner J, Spampinato C, Bagci U. Deep Learning provides exceptional accuracy to ECoG-based Functional Language Mapping for epilepsy surgery. *bioRxiv* 2018. DOI:10.1101/497644.

[157] Koh RGL, Balas M, Nachman A, Zariffa J. Selective peripheral nerve recordings from nerve cuff electrodes using convolutional neural networks. *Journal of Neural Engineering* 2019; published online Oct 3. DOI:10.1088/1741-2552/ab4ac4.

[158] Thomas J. Optogenetis – controlling neurons with light – may lead to cures for PTSD, Alzheimer's. Phys. 2018. https://phys.org/news/2018-08-optogenetics-neurons-ptsd-alzheimer.html (accessed July 25, 2019).

[159] Methods from optogenetics, machine learning should help improve treatment options for stroke patients. News Medical. 2018. https://www.news-medical.net/news/20180117/Methods-from-optogenetics-machine-learning-should-help-improve-treatment-options-for-stroke-patients.aspx (accessed July 25, 2019).

[160] Stanley J. Optogenetics: A Virtual Reality System for Controlling Living Cells. Techspot. 2017. https://www.techspot.com/article/1531-optogenetics/ (accessed July 25, 2019).

[161] Trafton A. Next-generation optogenetic molecules control single neurons. MIT News. 2017. http://news.mit.edu/2017/next-generation-optogenetic-molecules-control-single-neurons-1113 (accessed July 25, 2019).

[162] London A, Benhar I, Schwartz M. The retina as a window to the brain—from eye research to CNS disorders. *Nature Reviews Neurology* 2013; 9: 44–53.

[163] Ahmadi A, Davoudi S, Daliri MR. Computer Aided Diagnosis System for multiple sclerosis disease based on phase to amplitude coupling in covert visual attention. *Computer Methods and Programs in Biomedicine* 2019; 169: 9–18.

[164] Titano JJ, Badgeley M, Schefflein J, Pain M, Su A, Cai M, Swinburne N, Zech J, Kim J, Bederson J, Mocco J, Drayer B, Lehar J, Cho S, Costa A, Oermann EK. Automated deep-neural-network surveillance of cranial images for acute neurologic events. *Nature Medicine* 2018; 24: 1337–41.

[165] Suzuki K, Chen Y, editors. Advanced Machine Learning in Computer-Aided Systems. In: Artificial Intelligence in Decision Support Systems for Diagnosis in Medical Imaging. 2018: 1–83.

[166] Hambling D. The Long, Weird History of Strobe Weapons. Popular Mechanics. 2019. https://www.popularmechanics.com/military/weapons/a26253652/history-strobe-weapons/ (accessed Oct 4, 2019).

[167] Makarenko A V., Volovik MG. Implementation of deep learning algorithm for automatic detection of brain tumors using intraoperative IR-thermal mapping data. *arXiv* 2015. http://arxiv.org/abs/1512.07041.

[168] Fabelo H, Halicek M, Ortega S, Shahedi M, Szolna A, Piñeiro J, Sosa C, O'Shanahan A, Bisshopp S, Espino C, Márquez M, Hernández M, Carrera D, Morera J, Callico G, Sarmiento R, Fei B. Deep Learning-Based Framework for In Vivo Identification of Glioblastoma Tumor using Hyperspectral Images of Human Brain. *Sensors* 2019; 19: 920.

[169] Akers J, Chitikeshi S, Mahajan A, Lal S. Improved Accuracy of an Ultrasonic Based Neuro-Navigation System Using Neural Networks. In: Dynamic Systems and Control, Parts A and B. ASME, 2005: 921–5.

[170] Zhang C, Wang K, An Y, He K, Tong T, Tian J. Improved generative adversarial networks using the total gradient loss for the resolution enhancement of fluorescence images. *Biomedical Optics Express* 2019; 10: 4742.

[171] Alam IS, Steinberg I, Vermesh O, van den Berg NS, Rosenthal EL, van Dam GM, Ntziachristos V, Gambhir SS, Hernot S, Rogalla S. Emerging Intraoperative Imaging Modalities to Improve Surgical Precision. *Molecular Imaging and Biology* 2018; 20: 705–15.

[172] Singh A. Breakthrough in Artificial Intelligence-based Robotics Neurosurgery. PR Newswire. 2013. https://www.prnewswire.com/news-releases/breakthrough-in-artificial-intelligence-based-robotics-neurosurgery-196029281.html (accessed Feb 20, 2019).

[173] Suzuki K, Chen Y, editors. Computer-Aided Therapy and Surgery. In: Artificial Intelligence in Decision Support Systems for Diagnosis in Medical Imaging. Springer International Publishing, 2018: 335–87.

[174] Edelman BJ, Meng J, Suma D, Zurn C, Nagarajan E, Baxter BS, Cline CC, He B. Noninvasive neuroimaging enhances continuous neural tracking for robotic device control. *Science Robotics* 2019; 4: eaaw6844.

[175] Abiuso C, Kessler W. How one hospital gains productivity with high-tech AI. IBM. 2018. https://www.ibm.com/blogs/client-voices/hospital-gains-productivity-with-ai/ (accessed Sept 25, 2019).

[176] Sugimoto M. Holographic Mixed Reality and Artificial Intelligence for Special Navigation in Image Guided HPB Surgery. *HPB* 2018; 20: S273.

[177] Zhang T, McCarthy Z, Jow O, Lee D, Chen X, Goldberg K, Abbeel P. Deep Imitation Learning for Complex Manipulation Tasks from Virtual Reality Teleoperation. In: 2018 IEEE International Conference on Robotics and Automation (ICRA). IEEE, 2018: 5628–35.

[178] Ploch CC, Mansi CSSA, Jayamohan J, Kuhl E. Using 3D Printing to Create Personalized Brain Models for Neurosurgical Training and Preoperative Planning. *World Neurosurgery* 2016; 90:

668–74.

[179] Delanoy J, Aubry M, Isola P, Efros AA, Bousseau A. 3D Sketching using Multi-View Deep Volumetric Prediction. *Proceedings of the ACM on Computer Graphics and Interactive Techniques* 2018; 1: 1–22.

[180] Dumont TM. Prospective Assessment of a Symptomatic Cerebral Vasospasm Predictive Neural Network Model. *World Neurosurgery* 2016; 94: 126–30.

[181] Gomez Ruiz M. Present and future of robotic surgery. *Annals of Mediterranean Surgery* 2019; 2: 1–2.

[182] Aruni G, Amit G, Dasgupta P. New surgical robots on the horizon and the potential role of artificial intelligence. *Investigative and Clinical Urology* 2018; 59: 221.

[183] Rha KH. The Present and Future of Robotic Surgery. *Journal of the Korean Medical Association* 2008; 51: 67.

[184] Huang J, Zhang Z, Wang S. Efficacy of the Da Vinci surgical system in colorectal surgery comparing with traditional laparoscopic surgery or open surgery. *International Journal of Advanced Robotic Systems* 2016; 13: 172988141666484.

[185] Dandapani HG, Tieu K. The contemporary role of robotics in surgery: A predictive mathematical model on the short-term effectiveness of robotic and laparoscopic surgery. *Laparoscopic, Endoscopic and Robotic Surgery* 2019; 2: 1–7.

[186] Müller PF, Schlager D, Hein S, Bach C, Miernik A, Schoeb DS. Robotic stone surgery – Current state and future prospects: A systematic review. *Arab Journal of Urology* 2018; 16: 357–64.

[187] De Momi E, Ferrigno G. Robotic and artificial intelligence for keyhole neurosurgery: The ROBOCAST project, a multi-modal autonomous path planner. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine* 2010; 224: 715–27.

[188] Paging Dr. Robot: How Robotics Is Changing The Face Of Medicine. CB Insights. 2019. https://www.cbinsights.com/research/robotics-medicine-disruption/ (accessed July 26, 2019).

[189] BioXcel Therapeutics Announces BXCL501 Program Initiative for Prevention and Treatment of Acute Agitation using Wearable Digital Devices. BioXcel Therapeutics. 2019. https://www.bioxceltherapeutics.com/news-media/press-releases/detail/97/bioxcel-therapeutics-announces-bxcl501-program-initiative (accessed Oct 1, 2019).

[190] Yeung S, Downing NL, Fei-Fei L, Milstein A. Bedside Computer Vision — Moving Artificial Intelligence from Driver Assistance to Patient Safety. *New England Journal of Medicine* 2018; 378: 1271–3.

[191] Berlyand Y, Raja AS, Dorner SC, Prabhakar AM, Sonis JD, Gottumukkala R V., Succi MD, Yun BJ. How artificial intelligence could transform emergency department operations. *The American Journal of Emergency Medicine* 2018; 36: 1515–7.

[192] Chung HU, Kim BH, Lee JY, Lee J, Xie Z, Ibler EM, Lee K, Banks A, Jeong JY, Kim J, Ogle C, Grande D, Yu Y, Jang H, Assem P, Ryu D, Kwak JW, Namkoong M, Park J Bin, *et al.* Binodal, wireless epidermal electronic systems with in-sensor analytics for neonatal intensive care. *Science* 2019; 363: eaau0780.

[193] Jeong S, Zisook M, Plummer L, Breazeal C, Weinstock P, Logan DE, Goodwin MS, Graca S, O'Connell B, Goodenough H, Anderson L, Stenquist N, Fitzpatrick K. A Social Robot to Mitigate Stress, Anxiety, and Pain in Hospital Pediatric Care. In: Proceedings of the Tenth Annual ACM/IEEE International Conference on Human-Robot Interaction Extended Abstracts - HRI'15 Extended Abstracts. New York: ACM Press, 2015: 103–4.

[194] Logan DE, Breazeal C, Goodwin MS, Jeong S, O'Connell B, Smith-Freedman D, Heathers J, Weinstock P. Social Robots for Hospitalized Children. *Pediatrics* 2019; 144: e20181511.

[195] Facial Recognition Continuously Monitors ICU Patients. HospiMedica. 2019. https://www.hospimedica.com/health-it/articles/294778298/facial-recognition-continuously-monitors-icu-patients.html (accessed July 25, 2019).

[196] Lopez-Martinez D, Eschenfeldt P, Ostvar S, Ingram M, Hur C, Picard R. Deep Reinforcement Learning for Optimal Critical Care Pain Management with Morphine using Dueling Double-Deep Q Networks. *arXiv* 2019. http://arxiv.org/abs/1904.11115.

[197] Shafaf N, Malek H. Applications of Machine Learning Approaches in Emergency Medicine; a Review Article. *Archives of academic emergency medicine* 2019; 7: 34.

[198] Goto S, Kimura M, Katsumata Y, Goto S, Kamatani T, Ichihara G, Ko S, Sasaki J, Fukuda K, Sano M. Artificial intelligence to predict needs for urgent revascularization from 12-leads electrocardiography in emergency patients. *PLOS ONE* 2019; 14: e0210103.

[199] Launay CP, Rivière H, Kabeshova A, Beauchet O. Predicting prolonged length of hospital stay in older emergency department users: Use of a novel analysis method, the Artificial Neural Network. *European Journal of Internal Medicine* 2015; 26: 478–82.

[200] Artificial intelligence in health care: within touching distance. *The Lancet* 2017; 390: 2739.

[201] Celani NL, Ponce S, Quintero OL, Vargas-Bonilla F. Improving Quality of Life: Home Care for Chronically Ill and Elderly People. In: Caregiving and Home Care. InTech, 2018: 64.

[202] Blott J. Smart homes for the future of dementia care. *The Lancet Neurology* 2019; 4422: 30249.

[203] Landmesser U, MacRae CA. Digital technology to support self-management in patients with coronary disease. *The Lancet Digital Health* 2019; 1: e50–1.

[204] Litovitz T, Benson BE, Smolinske S. webPoisonControl: can poison control be automated? *The American Journal of Emergency Medicine* 2016; 34: 1614–9.

[205] Rigla M, Martínez-Sarriegui I, García-Sáez G, Pons B, Hernando ME. Gestational Diabetes Management Using Smart Mobile Telemedicine. *Journal of Diabetes Science and Technology* 2018; 12: 260–4.

[206] Manogaran G, Lopez D. Health data analytics using scalable logistic regression with stochastic gradient descent. *International Journal of Advanced Intelligence Paradigms* 2018; 10: 118.

[207] Gutruf P, Krishnamurthi V, Vázquez-Guardado A, Xie Z, Banks A, Su C-J, Xu Y, Haney CR, Waters EA, Kandela I, Krishnan SR, Ray T, Leshock JP, Huang Y, Chanda D, Rogers JA. Fully implantable optoelectronic systems for battery-free, multimodal operation in neuroscience research. *Nature Electronics* 2018; 1: 652–60.

[208] Blenner SR, Köllmer M, Rouse AJ, Daneshvar N, Williams C, Andrews LB. Privacy Policies of Android Diabetes Apps and Sharing of Health Information. *Journal of the American Medical Association* 2016; 315: 1051.

[209] Chen R, Maljkovic V, Sunga M, Song HH, Jung HJ, Tseng B, Trister A, Jankovic F, Marinsek N, Foschini L, Kourtis L, Signorini A, Pugh M, Shen J, Yaari R. Developing Measures of Cognitive Impairment in the Real World from Consumer-Grade Multimodal Sensor Streams. In: Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining - KDD '19. New York, New York, USA: ACM Press, 2019: 2145–55.

[210] Lilly, Evidation Health and Apple Study Shows Personal Digital Devices May Help in the Identification of Mild Cognitive Impairment and Mild Alzheimer's Disease Dementia.

eHealthNews. 2019. http://www.ehealthnews.eu/industry/5912-lilly-evidation-health-and-apple-study-shows-personal-digital-devices-may-help-in-the-identification-of-mild-cognitive-impairment-and-mild-alzheimer-s-disease-dementia (accessed Sept 18, 2019).

[211] Farr C. Apple and Eli Lilly are studying whether data from iPhones and Apple Watches can detect signs of dementia. CNBC. 2019. https://www.cnbc.com/2019/08/07/apple-eli-lilly-studying-if-iphones-apple-watches-can-spot-dementia.html (accessed Oct 1, 2019).

[212] Westman N. Apple Watches may soon decide when to administer medications. Popular Science. 2019. https://www.popsci.com/apple-watch-activity-tracker-dementia-treatment/ (accessed Oct 1, 2019).

[213] Developing guidelines for public health surveillance. World Health Organization. 2017. https://www.who.int/ethics/topics/surveillance/en/ (accessed July 25, 2019).

[214] Dankwa-Mullan I, Rivo M, Sepulveda M, Park Y, Snowdon J, Rhee K. Transforming Diabetes Care Through Artificial Intelligence: The Future Is Here. *Population Health Management* 2019; 22: 229–42.

[215] Fagherazzi G, Ravaud P. Digital diabetes: Perspectives for diabetes prevention, management and research. *Diabetes & Metabolism* 2019; 45: 322–9.

[216] Contreras I, Vehi J. Artificial Intelligence for Diabetes Management and Decision Support: Literature Review. *Journal of Medical Internet Research* 2018; 20: e10775.

[217] Loh BCS, Then PHH. Deep learning for cardiac computer-aided diagnosis: benefits, issues & solutions. *mHealth* 2017; 3: 45–45.

[218] Personalized Medicine in Brief. *PMC* 2019; 12. DOI:10.1001/archinte.1981.00340120019004.

[219] Delisio ER. Targeting cancer and careers: Precision Medicine. Science Magazine. 2019. https://www.sciencemag.org/features/2019/03/targeting-cancer-and-careers-precision-medicine (accessed Sept 19, 2019).

[220] Juengst ET, McGowan ML. Why Does the Shift from 'Personalized Medicine' to 'Precision Health' and 'Wellness Genomics' Matter? *AMA Journal of Ethics* 2018; 20: E881-890.

[221] Anthony A. Will genome sequencing bring precision medicine for all? The Guardian. 2019. http://www.theguardian.com/science/2019/sep/28/genome-sequencing-precision-medicine-bespoke-healthcare-nhs (accessed Oct 15, 2019).

[222] Turki T, Wang JTL. Clinical intelligence: New machine learning techniques for predicting clinical drug response. *Computers in Biology and Medicine* 2019; 107: 302–22.

[223] Bottaci L, Drew PJ, Hartley JE, Hadfield MB, Farouk R, Lee PW, Macintyre IM, Duthie GS, Monson JR. Artificial neural networks applied to outcome prediction for colorectal cancer patients in separate institutions. *The Lancet* 1997; 350: 469–72.

[224] Song M, Yang Y, He J, Yang Z, Yu S, Xie Q, Xia X, Dang Y, Zhang Q, Wu X, Cui Y, Hou B, Yu R, Xu R, Jiang T. Prognostication of chronic disorders of consciousness using brain functional networks and clinical characteristics. *eLife* 2018; 7. DOI:10.7554/eLife.36173.

[225] Reis R, Peixoto H, Machado J, Abelha A. Machine Learning in Nutritional Follow-up Research. *Open Computer Science* 2017; 7: 41–5.

[226] Personalized Medicine at FDA. *PMC* 2018. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_A_Progress_and_Outlook_Report.pdf.

[227] Pitini E, D'Andrea E, De Vito C, Rosso A, Unim B, Marzuillo C, Federici A, Di Maria E, Villari P. A proposal of a new evaluation framework towards implementation of genetic tests. *PLOS ONE*

2019; 14: e0219755.

[228] What is direct-to-consumer genetic testing? U.S. National Library of Medicine. 2018. https://ghr.nlm.nih.gov/primer/dtcgenetictesting/directtoconsumer (accessed Nov 5, 2019).

[229] What kinds of direct-to-consumer genetic tests are available? U.S. National Library of Medicine. 2018. https://ghr.nlm.nih.gov/primer/dtcgenetictesting/dtctesttypes (accessed Nov 5, 2019).

[230] Bruynseels K, Santoni de Sio F, van den Hoven J. Digital Twins in Health Care: Ethical Implications of an Emerging Engineering Paradigm. *Frontiers in Genetics* 2018; 9. DOI:10.3389/fgene.2018.00031.

[231] Virtual Patients and In Silico Clinical Studies Improve Blue Light Treatment for Psoriasis. eHealthNews. 2019. http://www.ehealthnews.eu/research/5910-virtual-patients-and-in-silico-clinical-studies-improve-blue-light-treatment-for-psoriasis (accessed Aug 12, 2019).

[232] Tanaka H. Big Data and Artificial Intelligence in Medicine and Drug Discovery. http://ngbrc.com/img/file94.pdf (accessed May 24, 2019).

[233] Popova M, Isayev O, Tropsha A. Deep reinforcement learning for de novo drug design. *Science Advances* 2018; 4: eaap7885.

[234] Press Release: Tufts CSDD Impact Report May/June 2019, Vol. 21 No.3, Available Now. Tufts Center for the Study of Drug Development. 2019. https://csdd.tufts.edu/csddnews/2019/5/7/j47q7jizd9zbvlgqpfnnmup77ir5do (accessed Aug 18, 2019).

[235] Dzau VJ, Balatbat CA. Health and societal implications of medical and technological advances. *Science Translational Medicine* 2018; 10: eaau4778.

[236] Public Perspectives on Personalized Medicine A Survey of U.S. Public Opinion. *Personalized Medicine Coallition* 2018. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/Public_Perspectives_on_PM1.pdf.

[237] Vellido A. Societal Issues Concerning the Application of Artificial Intelligence in Medicine. *Kidney Diseases* 2019; 5: 11–7.

[238] Shishehgar M, Kerr D, Blake J. A systematic review of research into how robotic technology can help older people. *Smart Health* 2018; 7–8: 1–18.

[239] Sarabia M, Young N, Canavan K, Edginton T, Demiris Y, Vizcaychipi MP. Assistive Robotic Technology to Combat Social Isolation in Acute Hospital Settings. *International Journal of Social Robotics* 2018; 10: 607–20.

[240] Yang G-Z, Dario P, Kragic D. Social robotics—Trust, learning, and social interaction. *Science Robotics* 2018; 3: eaau8839.

[241] Smart home tests first elder care robot. Science Daily. 2019. https://www.sciencedaily.com/releases/2019/01/190114130913.htm (accessed Sept 30, 2019).

[242] Ozaeta L, Graña M, Dimitrova M. Child oriented storytelling with NAO robot in hospital environment: preliminary application results. *Bulgarian Academy of Sciences* 2018. DOI:10.5281/zenodo.1169370.

[243] Crossman MK, Kazdin AE, Kitt ER. The influence of a socially assistive robot on mood, anxiety, and arousal in children. *Professional Psychology: Research and Practice* 2018; 49: 48–56.

[244] Jeong S, Breazeal C, Logan D, Weinstock P. Huggable: Impact of embodiment on promoting verbal and physical engagement for young pediatric inpatients. In: 2017 26th IEEE

International Symposium on Robot and Human Interactive Communication (RO-MAN). IEEE, 2017: 121–6.

[245] Fadhil A. Beyond Patient Monitoring: Conversational Agents Role in Telemedicine & Healthcare Support For Home-Living Elderly Individuals. *arXiv* 2018. http://arxiv.org/abs/1803.06000.

[246] Fiumara G, Celesti A, Galletta A, Carnevale L, Villari M. Applying Artificial Intelligence in Healthcare Social Networks to Identity Critical Issues in Patients' Posts. In: Proceedings of the 11th International Joint Conference on Biomedical Engineering Systems and Technologies. SCITEPRESS - Science and Technology Publications, 2018: 680–7.

[247] Coppersmith G, Leary R, Crutchley P, Fine A. Natural Language Processing of Social Media as Screening for Suicide Risk. *Biomedical Informatics Insights* 2018; 10: 117822261879286.

[248] Greene A, Greene CC, Greene C. Artificial intelligence, chatbots, and the future of medicine. *The Lancet Oncology* 2019; 20: 481–2.

[249] Bose R, Saxon LA. The Democratization of Diagnosis: Bringing the Power of Medical Diagnosis to the Masses. *EClinicalMedicine* 2019; 8: 6–7.

[250] Heaven D. Your next doctor's appointment might be with an AI. MIT Technology Review. 2018. https://www.technologyreview.com/s/612267/your-next-doctors-appointment-might-be-with-an-ai/ (accessed Aug 13, 2019).

[251] Prange A, Niemann M, Latendorf A, Steinert A, Sonntag D. Multimodal Speech-based Dialogue for the Mini-Mental State Examination. In: Extended Abstracts of the 2019 CHI Conference on Human Factors in Computing Systems. New York: ACM Press, 2019: CS13:1-CS13:8.

[252] Digital health: the good, the bad, and the abandoned. *The Lancet Psychiatry* 2019; 6: 273.

[253] Next generation public health: towards precision and fairness. *The Lancet Public Health* 2019; 4: e209.

[254] Panch T, Pearson-Stuttard J, Greaves F, Atun R. Artificial intelligence: opportunities and risks for public health. *The Lancet Digital Health* 2019; 1: e13–4.

[255] Zhang P, Chen B, Ma L, Li Z, Song Z, Duan W, Qiu X. The Large Scale Machine Learning in an Artificial Society: Prediction of the Ebola Outbreak in Beijing. *Computational Intelligence and Neuroscience* 2015; 2015: 1–12.

[256] Maxmen A. Can tracking people through phone-call data improve lives? Nature. 2019. https://www.nature.com/articles/d41586-019-01679-5 (accessed Jan 14, 2020).

[257] Bello-Orgaz G, Hernandez-Castro J, Camacho D. A Survey of Social Web Mining Applications for Disease Outbreak Detection. In: Intelligent distributed computing VIII. Springer, 2015: 345–56.

[258] Chen M, Hao Y, Hwang K, Wang L, Wang L. Disease Prediction by Machine Learning Over Big Data From Healthcare Communities. *IEEE Access* 2017; 5: 8869–79.

[259] VoPham T, Hart JE, Laden F, Chiang Y-Y. Emerging trends in geospatial artificial intelligence (geoAI): potential applications for environmental epidemiology. *Environmental Health* 2018; 17: 40.

[260] Chenar SS, Deng Z. Development of artificial intelligence approach to forecasting oyster norovirus outbreaks along Gulf of Mexico coast. *Environment International* 2018; 111: 212–23.

[261] De Castañeda RR, Durso AM, Ray N, Fernández JL, Williams DJ, Alcoba G, Chappuis F, Salathé M, Bolon I. Snakebite and snake identification: empowering neglected communities and

health-care providers with AI. *The Lancet Digital Health* 2019; 1: e202–3.

[262] COVID-19 Open Research Dataset Challenge (CORD-19). Kaggle. 2020. https://www.kaggle.com/allen-institute-for-ai/CORD-19-research-challenge/kernels (accessed March 27, 2020).

[263] Godfried I. Machine Learning methods to aid in Coronavirus Response. Towards Data Science. 2020. https://towardsdatascience.com/machine-learning-methods-to-aid-in-coronavirus-response-70df8bfc7861?gi=4317d16ee087 (accessed March 27, 2020).

[264] Barragán D, Manero J. How Big Data and Artificial Intelligence Can Help Against COVID-19. IE Business School. 2020. https://www.ie.edu/business-school/news-and-events/whats-going-on/big-data-artificial-intelligence-can-help-covid-19/ (accessed March 27, 2020).

[265] Akerman E. Autonomous Robots Are Helping Kill Coronavirus in Hospitals. IEEE Spectrum. 2020. https://spectrum.ieee.org/automaton/robotics/medical-robots/autonomous-robots-are-helping-kill-coronavirus-in-hospitals (accessed March 27, 2020).

[266] Wakefield J. Coronavirus: How can AI help fight the pandemic? BBC News. 2020. https://www.bbc.com/news/technology-51851292 (accessed March 27, 2020).

[267] Chen S, Yang J, Yang W, Wang C, Bärnighausen T. COVID-19 control in China during mass population movements at New Year. *The Lancet* 2020; 395: 764–6.

[268] Mozur P, Zhong R, Krolik A. In Coronavirus Fight, China Gives Citizens a Color Code, With Red Flags. The New York Times. 2020. https://www.nytimes.com/2020/03/01/business/china-coronavirus-surveillance.html (accessed March 27, 2020).

[269] Fowler GA. Smartphone data reveal which Americans are social distancing (and not). The Washington Post. 2020. https://www.washingtonpost.com/technology/2020/03/24/social-distancing-maps-cellphone-location/ (accessed March 27, 2020).

[270] Goh B. China rolls out fresh data collection campaign to combat coronavirus. Reuters. 2020. https://www.reuters.com/article/us-china-health-data-collection/china-rolls-out-fresh-data-collection-campaign-to-combat-coronavirus-idUSKCN20K0LW (accessed March 27, 2020).

[271] Gambhir SS, Ge TJ, Vermesh O, Spitler R. Toward achieving precision health. *Science Translational Medicine* 2018; 10: eaao3612.

[272] Shahid N, Rappon T, Berta W. Applications of artificial neural networks in health care organizational decision-making: A scoping review. *PLOS ONE* 2019; 14: e0212356.

[273] Kwon J, Kim K-H, Jeon K-H, Lee SE, Lee H-Y, Cho H-J, Choi JO, Jeon E-S, Kim M-S, Kim J-J, Hwang K-K, Chae SC, Baek SH, Kang S-M, Choi D-J, Yoo B-S, Kim KH, Park H-Y, Cho M-C, *et al.* Artificial intelligence algorithm for predicting mortality of patients with acute heart failure. *PLOS ONE* 2019; 14: e0219302.

[274] Lyu J, Zhang J. BP neural network prediction model for suicide attempt among Chinese rural residents. *Journal of Affective Disorders* 2019; 246: 465–73.

[275] McKernan LC, Clayton EW, Walsh CG. Protecting Life While Preserving Liberty: Ethical Recommendations for Suicide Prevention With Artificial Intelligence. *Frontiers in Psychiatry* 2018; 9: 1–5.

[276] White House considers new project seeking links between mental health and violent behavior. The Washington Post. 2019. https://www.washingtonpost.com/politics/2019/08/22/white-house-considers-new-project-seeking-links-between-mental-health-violent-behavior/ (accessed Sept 12, 2019).

[277] No Body's Business But Mine: How Menstruation Apps Are Sharing Your Data. Privacy

International. 2019. http://www.privacyinternational.org/es/node/3196 (accessed Oct 11, 2019).

[278] How AI Can Battle A Beast—Medical Insurance Fraud. Forbes. 2019. https://www.forbes.com/sites/insights-intelai/2019/02/11/how-ai-can-battle-a-beastmedical-insurance-fraud (accessed Oct 18, 2019).

[279] Aetna: Artificial Intelligence Goes After Health Care Fraudsters. Harvard Business School. 2018. https://digital.hbs.edu/platform-rctom/submission/aetna-artificial-intelligence-goes-after-health-care-fraudsters/ (accessed Oct 18, 2019).

[280] Raj J. The Role of AI and Machine Learning in Data Quality. Intellectyx. 2019. https://www.intellectyx.com/blog/role-of-ai-machine-learning-in-data-quality/ (accessed Nov 5, 2019).

[281] Chandler C, Foltz PW, Elvevåg B. Using Machine Learning in Psychiatry: The Need to Establish a Framework That Nurtures Trustworthiness. *Schizophrenia Bulletin* 2019; published online Nov 1. DOI:10.1093/schbul/sbz105.

[282] Wetsman N. Artificial intelligence could improve psychiatric care. Popular Science. 2019. https://www.popsci.com/story/health/artificial-intelligence-medicine-psychiatry/ (accessed Nov 18, 2019).

[283] Thase ME. Is Computer-Assisted Cognitive Therapy a Viable Solution for Cognitive Therapy's Dissemination Problems? A Brief Review and Some New Data. Anxiety and depression association of America. 2018. https://adaa.org/learn-from-us/from-the-experts/blog-posts/professional/computer-assisted-cognitive-therapy-viable (accessed July 25, 2019).

[284] Cuijpers P, Marks IM, van Straten A, Cavanagh K, Gega L, Andersson G. Computer-Aided Psychotherapy for Anxiety Disorders: A Meta-Analytic Review. *Cognitive Behaviour Therapy* 2009; 38: 66–82.

[285] Content moderators at YouTube, Facebook and Twitter see the worst of the web — and suffer silently. The Washington Post. 2019. https://www.washingtonpost.com/technology/2019/07/25/social-media-companies-are-outsourcing-their-dirty-work-philippines-generation-workers-is-paying-price/?utm_term=.4dbd54ad9472 (accessed July 26, 2019).

[286] Marshall L. A computer system that knows how you feel. Medical Xpress. 2019. https://medicalxpress.com/news/2019-07-a-computer-system-that-knows.html (accessed July 29, 2019).

[287] Silva GA. A New Frontier: The Convergence of Nanotechnology, Brain Machine Interfaces, and Artificial Intelligence. *Frontiers in Neuroscience* 2018; 12: 1–8.

[288] Murphy MD, Guggenmos DJ, Bundy DT, Nudo RJ. Current Challenges Facing the Translation of Brain Computer Interfaces from Preclinical Trials to Use in Human Patients. *Frontiers in Cellular Neuroscience* 2016; 9: 1–14.

[289] Won SM, Song E, Zhao J, Li J, Rivnay J, Rogers JA. Recent Advances in Materials, Devices, and Systems for Neural Interfaces. *Advanced Materials* 2018; 30: 1800534.

[290] Chaudhary U, Birbaumer N, Ramos-Murguialday A. Brain–computer interfaces for communication and rehabilitation. *Nature Reviews Neurology* 2016; 12: 513–25.

[291] Focus On Neural Interfaces Research. National Institute of Neurological Disorders and Stroke. 2019. https://www.ninds.nih.gov/Current-Research/Focus-Tools-Topics/Bioengineering/Neural-Interfaces (accessed July 25, 2019).

[292] Akbari H, Khalighinejad B, Herrero JL, Mehta AD, Mesgarani N. Towards reconstructing

intelligible speech from the human auditory cortex. *Scientific Reports* 2019; 9: 874.

[293] Bloch E, Luo Y, da Cruz L. Advances in retinal prosthesis systems. *Therapeutic Advances in Ophthalmology* 2019; 11: 251584141881750.

[294] Song E, Chiang C-H, Li R, Jin X, Zhao J, Hill M, Xia Y, Li L, Huang Y, Won SM, Yu KJ, Sheng X, Fang H, Alam MA, Huang Y, Viventi J, Chang J-K, Rogers JA. Flexible electronic/optoelectronic microsystems with scalable designs for chronic biointegration. *Proceedings of the National Academy of Sciences* 2019; 116: 15398–406.

[295] Perper R. Elon Musk's company Neuralink plans to connect people's brains to the internet by next year using a procedure he claims will be as safe and easy as LASIK eye surgery. Business Insider. 2019. https://www.businessinsider.com/elon-musk-neuralink-implants-link-brains-to-internet-next-year-2019-7 (accessed Jan 14, 2020).

[296] Lopatto E. Elon Musk unveils Neuralink's plans for brain-reading 'threads' and a robot to insert them. The Verge. 2019. https://www.theverge.com/2019/7/16/20697123/elon-musk-neuralink-brain-reading-thread-robot (accessed Jan 14, 2020).

[297] Service RF. New artificial nerves could transform prosthetics. Science Magazine. 2018. https://www.sciencemag.org/news/2018/05/new-artificial-nerves-could-transform-prosthetics (accessed July 25, 2019).

[298] Neural Prosthetics. International Neuromodulation Society. https://www.neuromodulation.com/neural-prosthetics (accessed July 25, 2019).

[299] Towers-Clarck C. Cyborgs Are Here And You'd Better Get Used To It. Forbes. 2018. https://www.forbes.com/sites/charlestowersclark/2018/10/01/cyborgs-are-here-and-youd-better-get-used-to-it/#7600a7b6746a (accessed Oct 15, 2019).

[300] Solon O. Elon Musk says humans must become cyborgs to stay relevant. Is he right? The Guardian. 2017. https://www.theguardian.com/technology/2017/feb/15/elon-musk-cyborgs-robots-artificial-intelligence-is-he-right (accessed Oct 15, 2019).

[301] Proietti T, Crocher V, Roby-Brami A, Jarrasse N. Upper-Limb Robotic Exoskeletons for Neurorehabilitation: A Review on Control Strategies. *IEEE Reviews in Biomedical Engineering* 2016; 9: 4–14.

[302] Maddox S. The Bio-Engineered Future. Reeve Foundation. 2016. https://www.christopherreeve.org/blog/research-news/the-bio-engineered-future (accessed July 29, 2019).

[303] Benabid AL, Costecalde T, Eliseyev A, Charvet G, Verney A, Karakas S, Foerster M, Lambert A, Morinière B, Abroug N, Schaeffer M-C, Moly A, Sauter-Starace F, Ratel D, Moro C, Torres-Martinez N, Langar L, Oddoux M, Polosan M, *et al.* An exoskeleton controlled by an epidural wireless brain–machine interface in a tetraplegic patient: a proof-of-concept demonstration. *The Lancet Neurology* 2019; 18: 1112–22.

[304] Wahl B, Cossy-Gantner A, Germann S, Schwalbe NR. Artificial intelligence (AI) and global health: how can AI contribute to health in resource-poor settings? *BMJ Global Health* 2018; 3: e000798.

[305] Artificial intelligence in global health: a brave new world. *The Lancet* 2019; 393: 1478.

[306] Arora P. The Next Billion Users: Digital Life Beyond the West. Harvard University Press, 2019 http://www.hup.harvard.edu/catalog.php?isbn=9780674983786.

[307] Blumenstock J. Don't forget people in the use of big data for development. *Nature* 2018; 561: 170–2.

[308] Cyranoski D. Japan approves first human-animal embryo experiments. Nature. 2019. https://www.nature.com/articles/d41586-019-02275-3 (accessed July 29, 2019).

[309] Ross P. Towards Xenogeneic Generation of Human Organs. In: AAAS Annual Meeting. Austin, 2018. https://aaas.confex.com/aaas/2018/meetingapp.cgi/Paper/20877.

[310] Salk Institute. New findings highlight promise of chimeric organisms for science and medicine. Phys. 2017. https://phys.org/news/2017-01-highlight-chimeric-science-medicine.html (accessed July 29, 2019).

[311] Wu J, Platero-Luengo A, Sakurai M, Sugawara A, Gil MA, Yamauchi T, Suzuki K, Bogliotti YS, Cuello C, Morales Valencia M, Okumura D, Luo J, Vilariño M, Parrilla I, Soto DA, Martinez CA, Hishida T, Sánchez-Bautista S, Martinez-Martinez ML, *et al.* Interspecies Chimerism with Mammalian Pluripotent Stem Cells. *Cell* 2017; 168: 473-486.e15.

[312] Masaki H, Nakauchi H. Interspecies chimeras for human stem cell research. *The Company of Biologists* 2017; 144: 2544–7.

[313] Yetisen AK. Biohacking. *Trends in Biotechnology* 2018; 36: 744–7.

[314] Corea F. Life 3.0 and Biohacking: Rewriting Human Life in the Digital Age. Forbes. 2019. https://www.forbes.com/sites/cognitiveworld/2019/05/14/life-3-0-and-biohacking-rewriting-human-life-in-the-digital-age/#2a63fd056c95 (accessed July 25, 2019).

[315] Ramirez VB. Biohacking Will Let You Connect Your Body to Anything You Want. SingularityHub. 2016. https://singularityhub.com/2016/09/01/biohacking-will-let-you-connect-your-body-to-anything-you-want/ (accessed July 25, 2019).

[316] Robitzski D. This Harvard prof is listing genes that could make you superhuman. Futurism. 2019. https://futurism.com/the-byte/harvard-list-genes-superhuman (accessed Nov 5, 2019).

[317] Human Enhancement: The Scientific and Ethical Dimensions of Striving for Perfection. Pew Research Center. 2016. https://www.pewresearch.org/science/2016/07/26/human-enhancement-the-scientific-and-ethical-dimensions-of-striving-for-perfection/ (accessed Nov 5, 2019).

[318] Naughton J. Why Silicon Valley wants to thwart the grim reaper. The Guardian. 2017. https://www.theguardian.com/commentisfree/2017/apr/09/silicon-valley-wants-to-cheat-grim-reaper-google (accessed July 25, 2019).

[319] Boden MA. Artificial Intelligence. A Very Short Introduction. Oxford University Press, 2018.

[320] Knapp A. Elon Musk Sees His Neuralink Merging Your Brain With A.I. Forbes. 2019. https://www.forbes.com/sites/alexknapp/2019/07/17/elon-musk-sees-his-neuralink-merging-your-brain-with-ai/#75deb3244b07 (accessed Jan 14, 2020).

[321] Researchers take major step forward in Artificial Intelligence. Nuffield Department of Surgical Sciences. 2017. https://www.nds.ox.ac.uk/news/researchers-take-major-step-forward-in-artificial-intelligence (accessed July 25, 2019).

[322] Chang P. Brain Transplant, Artificial Intelligence and Immortality. OmniTought. 2016. https://omnithought.org/brain-transplant-artificial-intelligence-immortality/4046 (accessed Nov 5, 2019).

[323] Lamba N, Holsgrove D, Broekman ML. The history of head transplantation: a review. *Acta Neurochirurgica* 2016; 158: 2239–47.

[324] Gkasdaris G, Birbilis T. First Human Head Transplantation: Surgically Challenging, Ethically Controversial and Historically Tempting – an Experimental Endeavor or a Scientific Landmark? *Maedica* 2019; 14: 5–11.

[325] Ausman J. Is it time to perform the first human head transplant? Comment on the CSA (CephaloSomatic Ansatomisis) paper by Ren, Canavero, and colleagues. *Surgical Neurology International* 2018; 9: 28.

[326] Kriegman S, Blackiston D, Levin M, Bongard J. A scalable pipeline for designing reconfigurable organisms. In: Proceedings of the National Academy of Sciences. 2020. DOI:10.1073/pnas.1910837117.

[327] Watson System. IBM. 2019. https://www.ibm.com/watson-health (accessed July 25, 2019).

[328] Curate.AI N.1. National University of Singapore. http://www.n1labs.org/about (accessed July 25, 2019).

[329] BrainX: Transforming Healthcare Through Artificial Intelligence. Brainxai. https://www.brainxai.com/ (accessed July 26, 2019).

[330] Pathways. Dana-Farber Cancer Institute. https://www.dana-farber.org/for-patients-and-families/why-dana-farber/quality-and-patient-safety/improving-and-innovating/pathways/ (accessed July 25, 2019).

[331] Parsa A. A US$100 million investment in your health. Babylon Health. 2018. https://www.babylonhealth.com/blog/business/babylon-is-investing-us-100-million-to-build-the-next-generation-of-ai-powered-healthcare-technologies (accessed Sept 25, 2019).

[332] About Ada. Ada. https://ada.com/about/ (accessed Sept 19, 2019).

[333] O'Hear S. Ada is an AI-powered doctor app and telemedicine service. TechCrunch. 2017. https://techcrunch.com/2017/04/19/ada-health/ (accessed Sept 19, 2019).

[334] About Intermountain. Intermountain Healthcare. https://intermountainhealthcare.org/about/ (accessed Sept 19, 2019).

[335] Intermountain Healthcare Launches New 'Intermountain at Home' Service to Enable Patients to Receive Clinical Care at Home. GlobeNewswire. 2019. https://www.globenewswire.com/news-release/2019/03/11/1751331/0/en/Intermountain-Healthcare-Launches-New-Intermountain-at-Home-Service-to-Enable-Patients-to-Receive-Clinical-Care-at-Home.html (accessed Sept 19, 2019).

[336] PhenoPad Feature Overview. Phenopad. http://phenopad.ai/m (accessed Sept 19, 2019).

[337] Wang J, Yang J, Zhang H, Lu H, Ababi A, Brudno M. PhenoPad: An AI-based tool for clinical note taking utilizing speech, stylus and tablet user interfaces. Techna Institute. 2019. http://symposium.technainstitute.com/phenopad-an-ai-based-tool-for-clinical-note-taking-utilizing-speech-stylus-and-tablet-user-interfaces/ (accessed Sept 19, 2019).

[338] Stop avoidable blindness in children with pre-screening. Kanna. https://www.kanna.ai/about-us (accessed Sept 19, 2019).

[339] Ravishanker R. Teens' app to spot eye defect in kids. Deccan Herald. 2019. https://www.deccanherald.com/city/teens-app-spot-eye-defect-kids-716531.html (accessed Sept 19, 2019).

[340] This DNA Kit Does More Than Just Fill in Your Family Tree. Popular Mechanics. 2019. https://www.popularmechanics.com/promotions/a26539321/vitagene-dna/ (accessed July 25, 2019).

[341] Asad J, Jacobson AF, Estabrook A, Smith SR, Boolbol SK, Feldman SM, Osborne MP, Boachie-Adjei K, Twardzik W, Tartter PI. Does oncotype DX recurrence score affect the management of patients with early-stage breast cancer? *The American Journal of Surgery* 2008; 196: 527–9.

[342] Bertolini L, Bertolini M, Murray J, Maga E. Transgenic animal models for the production of

human immunocompounds in milk to prevent diarrhea, malnourishment and child mortality: perspectives for the Brazilian Semi-Arid region. *BMC Proceedings* 2014; 8: O30.

[343] Bailey P. Goats' milk with antimicrobial lysozyme speeds recovery from diarrhea. UC Davis. 2013. https://www.ucdavis.edu/news/goats-milk-antimicrobial-lysozyme-speeds-recovery-diarrhea/ (accessed July 26, 2019).

[344] A Consumer's Guide to Genetic Health Testing. PMC. 2019. http://www.personalizedmedicinecoalition.org/Resources/A_Consumers_Guide_to_Genetic_Health_Testing (accessed July 26, 2019).

[345] Make a difference with your DNA. Sano Genetics. 2019. https://sanogenetics.com/ (accessed Oct 15, 2019).

[346] Whole genome sequencing. Dante Labs. https://www.dantelabs.com/ (accessed July 25, 2019).

[347] 23andMe Company. 23andMe. https://mediacenter.23andme.com/ (accessed Oct 15, 2019).

[348] Regalado A. 2017 was the year consumer DNA testing blew up. MIT Technology Review. 2018. https://www.technologyreview.com/s/610233/2017-was-the-year-consumer-dna-testing-blew-up/ (accessed Oct 15, 2019).

[349] CRISPR Therapeutics and Vertex Announce Progress in Clinical Development Programs for the Investigational CRISPR/Cas9 Gene-Editing Therapy CTX001. CRISPR Therapeutics. 2019. http://ir.crisprtx.com/news-releases/news-release-details/crispr-therapeutics-and-vertex-announce-progress-clinical (accessed Jan 14, 2020).

[350] Liu A. Making CRISPR-Cas9 gene editing safer with artificial intelligence. FierceBiotech. 2018. https://www.fiercebiotech.com/research/using-machine-learning-to-predict-crispr-cas9-editing-outcomes (accessed Nov 5, 2019).

[351] Glasure E. Artificial Intelligence is the next big player in genomics. BioSpace. 2018. https://www.biospace.com/article/artificial-intelligence-is-the-next-big-player-in-genomics/ (accessed Nov 5, 2019).

[352] Innovating for minimally invasive care. Intuitive. https://www.intuitive.com/ (accessed Jan 28, 2020).

[353] We are ushering in a new era of minimally invasive surgery. TransEnterix. https://transenterix.com/ (accessed Jan 28, 2020).

[354] PRECEYES Surgical System. PRECEYES. http://www.preceyes.nl/ (accessed Jan 28, 2020).

[355] PARO Therapeutic Robot. Paro Robots. 2014. http://www.parorobots.com/ (accessed July 31, 2019).

[356] Enspectra Health. Rosenman Institute. https://rosenmaninstitute.org/portfolio-companies/2018/6/22/enspectra (accessed Sept 23, 2019).

[357] Banifatemi A. Can we use AI for global good? *Communications of the ACM* 2018; 61: 8–9.

[358] Kwok R. Five hard truths for synthetic biology. *Nature* 2010; 463: 288–90.

[359] Coiera E, Westbrook JI, Wyatt JC. Health and Clinical Mangement: The Safety and Quality of Decision Support Systems. *Yearbook of Medical Informatics* 2006; 15: 20–5.

[360] Statement on Artificial Intelligence, Robotics and 'Autonomous' Systems. European Commission. 2018. http://ec.europa.eu/research/ege/pdf/ege_ai_statement_2018.pdf (accessed July 25, 2019).

[361] The ethics of Big Data. EESC. 2017. https://www.eesc.europa.eu/en/our-work/publications-

other-work/publications/ethics-big-data (accessed July 25, 2019).

[362] AI for Good Global Summit 2018. International Telecommunication Union. 2018. https://www.itu.int/en/ITU-T/AI/2018/Pages/default.aspx (accessed July 25, 2019).

[363] Shah H. Use our personal data for the common good. *Nature* 2018; 556: 7–7.

[364] Rogers J, Malliaras G, Someya T. Biomedical devices go wild. *Science Advances* 2018; 4: 2–4.

[365] Taddeo M, Floridi L. How AI can be a force for good. *Science* 2018; 361: 751–2.

[366] European Group on Ethics in Science and New Technologies. European Commission. http://ec.europa.eu/bepa/european-group-ethics/index_en.htm (accessed July 25, 2019).

[367] Joshi I. Waiting for deep medicine. *The Lancet* 2019; 393: 1193–4.

[368] Gruber K. Is the future of medical diagnosis in computer algorithms? *The Lancet Digital Health* 2019; 1: e15–6.

[369] Prabhu SP. Ethical challenges of machine learning and deep learning algorithms. *The Lancet Oncology* 2019; 20: 621–2.

[370] Arkin R, Ulam P, Duncan B. An Ethical Governor for Constraining Lethal Action in an Autonomous System. 2009. https://smartech.gatech.edu/bitstream/handle/1853/31465/09-02.pdf (accessed Oct 1, 2019).

[371] Buch VH, Ahmed I, Maruthappu M. Artificial intelligence in medicine: current trends and future possibilities. *British Journal of General Practice* 2018; 68: 143–4.

[372] Burki T. The dangers of the digital age. *The Lancet Digital Health* 2019; 1: e61–2.

[373] Castelvecchi D. AI pioneer: 'The dangers of abuse are very real'. Nature. 2019. http://www.nature.com/articles/d41586-019-00505-2 (accessed Sept 18, 2019).

[374] Ashrafian H, Darzi A. Transforming health policy through machine learning. *PLOS Medicine* 2018; 15: e1002692.

[375] Flaxman AD, Vos T. Machine learning in population health: Opportunities and threats. *PLOS Medicine* 2018; 15: e1002702.

[376] Vayena E, Blasimme A, Cohen IG. Machine learning in medicine: Addressing ethical challenges. *PLOS Medicine* 2018; 15: e1002689.

[377] Menikoff J, Kaneshiro J, Pritchard I. The Common Rule, Updated. *New England Journal of Medicine* 2017; 376: 613–5.

[378] Loh E. Medicine and the rise of the robots: a qualitative review of recent advances of artificial intelligence in health. *BMJ Leader* 2018; 2: 59–63.

[379] McCarthy MK. Artificial Intelligence in Health: Ethical Considerations for Research and Practice. HIMSS. 2019. https://www.himss.org/artificial-intelligence-health-ethical-considerations-research-and-practice (accessed Oct 23, 2019).

[380] Ko S. Faster, more accurate diagnoses: Healthcare applications of AI research. The Conversation. 2019. https://theconversation.com/faster-more-accurate-diagnoses-healthcare-applications-of-ai-research-114000 (accessed Aug 13, 2019).

[381] Big data and artificial intelligence health ethics. World Health Organization. 2019. https://www.who.int/ethics/topics/big-data-artificial-intelligence/en/ (accessed July 25, 2019).

[382] Report of the IBC on big data and health. UNESCO. 2017. https://unesdoc.unesco.org/ark:/48223/pf0000248724 (accessed July 25, 2019).

[383] Ethical standards and procedures for research with human beings. World Health Organization. https://www.who.int/ethics/topics/research/en/ (accessed July 25, 2019).

[384] Standards and operational guidance for ethics review of health-related research with human participants. World Health Organization. 2011. https://www.who.int/ethics/publications/9789241502948/en/ (accessed July 25, 2019).

[385] International ethical guidelines for health-related research involving humans. Council for International Organizations of Medical Sciences. 2016. https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf (accessed July 25, 2019).

[386] The ethics of research related to healthcare in developing countries. Nuffield Council on Bioethics. 2014. http://nuffieldbioethics.org/wp-content/uploads/2014/07/Ethics-of-research-related-to-healthcare-in-developing-countries-I.pdf (accessed July 25, 2019).

[387] The Future Computed: Artificial Intelligence and its role in society. Microsoft. https://3er1viui9wo30pkxh1v2nh4w-wpengine.netdna-ssl.com/wp-content/uploads/2018/02/The-Future-Computed_2.8.18.pdf (accessed July 25, 2019).

[388] Ahuja AS. The impact of artificial intelligence in medicine on the future role of the physician. *PeerJ* 2019; 7: e7702.

[389] Meskó B, Hetényi G, Győrffy Z. Will artificial intelligence solve the human resource crisis in healthcare? *BMC Health Services Research* 2018; 18: 545.

[390] Pesapane F, Codari M, Sardanelli F. Artificial intelligence in medical imaging: threat or opportunity? Radiologists again at the forefront of innovation in medicine. *European Radiology Experimental* 2018; 2: 35.

[391] Kooi T, Litjens G, van Ginneken B, Gubern-Mérida A, Sánchez CI, Mann R, den Heeten A, Karssemeijer N. Large scale deep learning for computer aided detection of mammographic lesions. *Medical Image Analysis* 2017; 35: 303–12.

[392] Rajpurkar P, Hannun AY, Haghpanahi M, Bourn C, Ng AY. Cardiologist-Level Arrhythmia Detection with Convolutional Neural Networks. *arXiv* 2017. http://arxiv.org/abs/1707.01836.

[393] Vassallo L, Traverso A, Agnello M, Bracco C, Campanella D, Chiara G, Fantacci ME, Lopez Torres E, Manca A, Saletta M, Giannini V, Mazzetti S, Stasi M, Cerello P, Regge D. A cloud-based computer-aided detection system improves identification of lung nodules on computed tomography scans of patients with extra-thoracic malignancies. *European Radiology* 2019; 29: 144–52.

[394] Taylor D, Powers D. Teaching artificial intelligence to read electropherograms. *Forensic Science International: Genetics* 2016; 25: 10–8.

[395] Philpotts LE. Can Computer-aided Detection Be Detrimental to Mammographic Interpretation? *Radiology* 2009; 253: 17–22.

[396] Mayo RC, Leung J. Artificial intelligence and deep learning – Radiology’s next frontier? *Clinical Imaging* 2018; 49: 87–8.

[397] Erickson BJ, Korfiatis P, Kline TL, Akkus Z, Philbrick K, Weston AD. Deep Learning in Radiology: Does One Size Fit All? *Journal of the American College of Radiology* 2018; 15: 521–6.

[398] McBee MP, Awan OA, Colucci AT, Ghobadi CW, Kadom N, Kansagra AP, Tridandapani S, Auffermann WF. Deep Learning in Radiology. *Academic Radiology* 2018; 25: 1472–80.

[399] Buda M, Wildman-Tobriner B, Hoang JK, Thayer D, Tessler FN, Middleton WD, Mazurowski MA. Management of Thyroid Nodules Seen on US Images: Deep Learning May Match Performance of Radiologists. *Radiology* 2019; 292: 695–701.

[400] Mental Health Software reviews. Capterra. https://www.capterra.com/mental-health-software/ (accessed July 25, 2019).

[401] Hashimoto DA, Rosman G, Rus D, Meireles OR. Artificial Intelligence in Surgery. *Annals of Surgery* 2018; 268: 70–6.

[402] Maitra I, Date RS. Robotic surgery: Is the technological advance worth the bravado? *International Journal of Surgery* 2019; 62: 1–2.

[403] Trister AD. The Tipping Point for Deep Learning in Oncology. *JAMA Oncology* 2019; 5: 1429.

[404] Medeiros FA. Deep learning in glaucoma: progress, but still lots to do. *The Lancet Digital Health* 2019; 1: e151–2.

[405] Saria S, Butte A, Sheikh A. Better medicine through machine learning: What's real, and what's artificial? *PLOS Medicine* 2018; 15: e1002721.

[406] Lasalvia L, Merges R. Expanding Precision Medicine. *Journal of Precision Medicine* 2019; 5: 1–5.

[407] King DP. Personalized Medicine: Promise or Potential? In: Personalized Medicine in Brief. PMC, 2019: 12–5.

[408] Szabo L. Are We Being Misled About Precision Medicine? The New York Times. 2018. https://www.nytimes.com/2018/09/11/opinion/cancer-genetic-testing-precision-medicine.html (accessed July 25, 2019).

[409] Readers And Tweeters Slice And Dice Precision Medicine, Step Therapy. Kaiser Health News. 2018. https://khn.org/news/readers-and-tweeters-splice-and-dice-precision-medicine-step-therapy/ (accessed July 25, 2019).

[410] The Promise of Precision Medicine is Not Misleading, It's Just Beginning. GNS Helathcare Blog. 2018. https://blog.gnshealthcare.com/precision-medicine-is-not-misleading-its-just-beginning (accessed Oct 11, 2019).

[411] Regalado A. Look how far precision medicine has come. MIT Technology Review. 2018. https://www.technologyreview.com/s/612281/look-how-far-precision-medicine-has-come/ (accessed Oct 11, 2019).

[412] Rabin RC. Cancer Patients Are Getting Robotic Surgery. There's No Evidence It's Better. The New York Times. 2019. https://www.nytimes.com/2019/03/11/health/robotic-surgery-cancer.html (accessed July 25, 2019).

[413] Beil L. What's Wrong with Robotic Surgery? Men's Health. 2014. https://www.menshealth.com/health/a19539160/robot-surgery/ (accessed July 25, 2019).

[414] Kilbride MK, Domchek SM, Bradbury AR. Ethical Implications of Direct-to-Consumer Hereditary Cancer Tests. *JAMA Oncology* 2018; 4: 1327.

[415] Pritchard D. Landscape for Clinical Adoption of Personalized Medicine Still Coming into Focus, But Early Insights Underline Importance of Value Recognition. In: Personalized Medicine in Brief. 2019: 6–7.

[416] Wells CJ. Amid Criticisms of Field, Proponents for Personalized Medicine Emphasize Unchanging Biological Principles of Individual Variation. In: Personalized Medicine in Brief. PMC, 2019: 8–9.

[417] Jackson I. AI – is it Fake News for Health and Social Care? The Journal of mHealth. 2019. https://thejournalofmhealth.com/ai-is-it-fake-news-for-health-and-social-care/ (accessed Aug 23, 2019).

[418] Nichols T. The Death of Expertise: The Campaign Against Established Knowledge and Why it

Matters. Oxford University Press, 2017.

[419] Lock H. Fight the fakes: how to beat the $200bn medicine counterfeiters. The Guardian. 2019. https://www.theguardian.com/global-development/2019/jun/05/fake-medicine-makers-blockchain-artificial-intelligence (accessed Nov 5, 2019).

[420] Baxter A. Report: Understanding AI in healthcare essential to stop fake news. AI in Healthcare. 2019. https://www.aiin.healthcare/topics/business-intelligence/understanding-ai-essential-stop-fake-news (accessed Aug 23, 2019).

[421] Price WN, Cohen IG. Privacy in the age of medical big data. *Nature Medicine* 2019; 25: 37–43.

[422] Grundy Q, Chiu K, Held F, Continella A, Bero L, Holz R. Data sharing practices of medicines related apps and the mobile ecosystem: traffic, content, and network analysis. *BMJ* 2019; 364: l920.

[423] Metz C. London Lab Advances Use of A.I. in Health Care, but Raises Privacy Concerns. The New York Times. 2019. https://www.nytimes.com/2019/07/31/technology/deepmind-artificial-intelligence-health-care.html (accessed Aug 6, 2019).

[424] Copeland R. Google's 'Project Nightingale' Gathers Personal Health Data on Millions of Americans. The Wall Street Journal. 2019. https://www.wsj.com/articles/google-s-secret-project-nightingale-gathers-personal-health-data-on-millions-of-americans-11573496790 (accessed Nov 18, 2019).

[425] Shaukat T. Our partnership with Ascension. Google Cloud. 2019. https://cloud.google.com/blog/topics/inside-google-cloud/our-partnership-with-ascension (accessed Jan 19, 2020).

[426] Na L, Yang C, Lo C-C, Zhao F, Fukuoka Y, Aswani A. Feasibility of Reidentifying Individuals in Large National Physical Activity Data Sets From Which Protected Health Information Has Been Removed With Use of Machine Learning. *JAMA Network Open* 2018; 1: e186040.

[427] Parks CL, Monson KL. Automated Facial Recognition of Computed Tomography-Derived Facial Images: Patient Privacy Implications. *Journal of Digital Imaging* 2017; 30: 204–14.

[428] Evans M. Facial-Recognition Software Was Able to Identify Patients From MRI Scans. The Wall Street Journal. 2019. https://www.wsj.com/articles/facial-recognition-software-was-able-to-identify-patients-from-mri-scans-11571864543 (accessed Oct 28, 2019).

[429] Opinion of the Data Ethics Commission. Executive Summary. Data Ethics Commission, Federal Government of Germany. 2019. https://www.bmjv.de/SharedDocs/Downloads/DE/Themen/Fokusthemen/Gutachten_DEK_EN.pdf (accessed Jan 14, 2020).

[430] Alpert JS. Can You Trust a Computer to Read Your Electrocardiogram? *The American Journal of Medicine* 2012; 125: 525–6.

[431] Schläpfer J, Wellens HJ. Computer-Interpreted Electrocardiograms. *Journal of the American College of Cardiology* 2017; 70: 1183–92.

[432] Winslow R. How Artificial Intelligence Can Make Doctors More Human. OneZero. 2019. https://onezero.medium.com/how-artificial-intelligence-can-make-doctors-more-human-9424f5a8122e (accessed April 22, 2019).

[433] Goodman B, Flaxman S. European Union Regulations on Algorithmic Decision-Making and a 'Right to Explanation'. *AI Magazine* 2017; 38: 50–7.

[434] Anderson M, Anderson SL. How Should AI Be Developed, Validated, and Implemented in Patient Care? *AMA Journal of Ethics* 2019; 21: E125-130.

[435] Watson DS, Krutzinna J, Bruce IN, Griffiths CE, McInnes IB, Barnes MR, Floridi L. Clinical applications of machine learning algorithms: beyond the black box. *BMJ* 2019; 364: l886.

[436] Opening the black box of machine learning. *The Lancet Respiratory Medicine* 2018; 6: 801.

[437] Donovan F. White House Wants Transparency in Healthcare Artificial Intelligence. HIT Infrastructure. 2019. https://hitinfrastructure.com/news/white-house-wants-transparency-in-healthcare-artificial-intelligence (accessed Sept 25, 2019).

[438] McDermott MBA, Wang S, Marinsek N, Ranganath R, Ghassemi M, Foschini L. Reproducibility in Machine Learning for Health. 2019. http://arxiv.org/abs/1907.01463.

[439] Hutson M. Artificial intelligence faces reproducibility crisis. *Science* 2018; 359: 725–6.

[440] LaRosa E, Danks D. Impacts on Trust of Healthcare AI Roles for Healthcare AI. In: AAAI/ACM Conference on Artificial Intelligence, Ethics, and Society. 2018. https://www.aies-conference.com/2018/contents/papers/main/AIES_2018_paper_132.pdf.

[441] Couzin-Frankel J. Artificial intelligence could revolutionize medical care. But don't trust it to read your x-ray just yet. Science Magazine. 2019. https://www.sciencemag.org/news/2019/06/artificial-intelligence-could-revolutionize-medical-care-don-t-trust-it-read-your-x-ray (accessed Sept 19, 2019).

[442] Haupter R. AI is built on trust. Microsoft News Center. 2018. https://news.microsoft.com/apac/2018/04/17/ai-is-built-on-trust/ (accessed July 25, 2019).

[443] Buckland D. Can we convince patients to trust AI? Philips News Center. 2017. https://www.philips.com/a-w/about/news/archive/future-health-index/articles/20170608-can-we-convince-patients-trust-ai.html (accessed July 25, 2019).

[444] Khosravi B. Will you trust AI to be your new doctor? Forbes. 2016. https://www.forbes.com/sites/bijankhosravi/2016/03/24/will-you-trust-ai-to-be-your-new-doctor-a-five-year-outcome/ (accessed July 25, 2019).

[445] Building confidence and trust in artificial intelligence systems. BSA. https://ai.bsa.org/building-confidence-trust-in-artificial-intelligence-systems/ (accessed March 19, 2019).

[446] Hartford Financial activates AI programs to help achieve reductions in opioid use across the USA. The Hartford. 2019. https://www.thehartford.com/about-us/opioid-crisis (accessed Aug 13, 2019).

[447] Topol E. The patient will see you now: The Future of Medicine is in your hands. New York: Basic Books, 2016.

[448] Schwartz O. DNA databases may deter criminals, but at what cost? Popular Science. 2019. https://www.popsci.com/do-dna-databases-deter-crime/ (accessed Oct 1, 2019).

[449] Fraser H, Coiera E, Wong D. Safety of patient-facing digital symptom checkers. *The Lancet* 2018; 392: 2263–4.

[450] Finlayson SG, Bowers JD, Ito J, Zittrain JL, Beam AL, Kohane IS. Adversarial attacks on medical machine learning. *Science* 2019; 363: 1287–9.

[451] Ofri D. Empathy in the age of the electronic medical record. *The Lancet* 2019; 394: 822–3.

[452] Insel TR. How algorithms could bring empathy back to medicine. *Nature* 2019; 567: 172–3.

[453] Allegretti D. Meet the Woman Teaching Empathy to AI. Vice. 2018. https://www.vice.com/en_au/article/ywe33m/this-woman-believes-ai-can-be-taught-empathy (accessed Oct 1, 2019).

[454] Topol E. Deep Medicine. New York: Basic Books, 2019.

[455] Hart RD. Doctors are known for their poor bedside manner. Robots might be the answer. Quartz. 2018. https://qz.com/1367210/doctors-are-known-for-their-poor-bedside-manner-robots-might-be-the-answer/ (accessed Oct 1, 2019).

[456] Xu S. Machine learning-assisted prediction of surgical mortality of lung cancer patients. The Harker School. 2019. https://med.stanford.edu/content/dam/sm/frontierofaicare/documents/Presenters/Xu%2CSidra.pdf (accessed Sept 19, 2019).

[457] Lu D. AI can predict if you'll die soon – but we've no idea how it works. NewScientist. 2019. https://www.newscientist.com/article/2222907-ai-can-predict-if-youll-die-soon-but-weve-no-idea-how-it-works/ (accessed Nov 18, 2019).

[458] Weintraub K. Want to know when you're going to die? MIT Technology Review. 2018. https://www.technologyreview.com/s/612256/want-to-know-when-youre-going-to-die/ (accessed Oct 15, 2019).

[459] Yu K-H, Kohane IS. Framing the challenges of artificial intelligence in medicine. *BMJ Quality & Safety* 2019; 28: 238–41.

[460] Nelson GS. Bias in Artificial Intelligence. *North Carolina Medical Journal* 2019; 80: 220–2.

[461] Chen IY, Szolovits P, Ghassemi M. Can AI Help Reduce Disparities in General Medical and Mental Health Care? *AMA Journal of Ethics* 2019; 21: E167-179.

[462] Artiga S, Hinton E. Beyond health care: The role of social determinants in promoting health ahd health equity. Kaiser Family Foundation. 2018. https://www.kff.org/disparities-policy/issue-brief/beyond-health-care-the-role-of-social-determinants-in-promoting-health-and-health-equity/ (accessed Sept 25, 2019).

[463] Rajkomar A, Hardt M, Howell MD, Corrado G, Chin MH. Ensuring Fairness in Machine Learning to Advance Health Equity. *Annals of Internal Medicine* 2018; 169: 866.

[464] Zou J, Schiebinger L. Design AI so that it's fair. *Nature* 2018; 559: 324–6.

[465] Budd K. Will artificial intelligence replace doctors? AAMC. 2019. https://news.aamc.org/medical-education/article/will-artificial-intelligence-replace-doctors/ (accessed Sept 18, 2019).

[466] Chockley K, Emanuel E. The End of Radiology? Three Threats to the Future Practice of Radiology. *Journal of the American College of Radiology* 2016; 13: 1415–20.

[467] Jha S, Topol EJ. Adapting to Artificial Intelligence. *JAMA* 2016; 316: 2353.

[468] Faes L, Wagner SK, Fu DJ, Liu X, Korot E, Ledsam JR, Back T, Chopra R, Pontikos N, Kern C, Moraes G, Schmid MK, Sim D, Balaskas K, Bachmann LM, Denniston AK, Keane PA. Automated deep learning design for medical image classification by health-care professionals with no coding experience: a feasibility study. *The Lancet Digital Health* 2019; 1: e232–42.

[469] Casselman B, Satariano A. Amazon's Latest Experiment: Retraining Its Work Force. The New York Times. 2019. https://www.nytimes.com/2019/07/11/technology/amazon-workers-retraining-automation.html (accessed July 25, 2019).

[470] Abacan M, Alsubaie L, Barlow-Stewart K, Caanen B, Cordier C, Courtney E, Davoine E, Edwards J, Elackatt NJ, Gardiner K, Guan Y, Huang L-H, Malmgren CI, Kejriwal S, Kim HJ, Lambert D, Lantigua-Cruz PA, Lee JMH, Lodahl M, *et al.* The Global State of the Genetic Counseling Profession. *European Journal of Human Genetics* 2019; 27: 183–97.

[471] Find a genetic counselor. National Society of Genetic Counselors.

https://www.nsgc.org/page/find-a-genetic-counselor (accessed Oct 15, 2019).

[472] National Regulation of Genetic Counselling. EuroGentest. 2008. http://www.eurogentest.org/index.php?id=679 (accessed Oct 15, 2019).

[473] Wells CJ. Emerging Gene Therapies Push Insurers Toward Innovative Payment Models Suitable for Era of Personalized Medicine. In: Personalized Medicine in Brief. PMC, 2019: 10–1.

[474] Hayden EC. This girl's dramatic story shows hyper-personalized medicine is possible—and costly. MIT Technology Review. 2019. https://www.technologyreview.com/s/614522/this-girls-dramatic-story-shows-hyper-personalized-medicine-is-possibleand-costly/ (accessed Oct 15, 2019).

[475] Regalado A. Two sick children and a $1.5 million bill: One family's race for a gene therapy cure. MIT Technology Review. https://www.technologyreview.com/s/612259/two-sick-children-and-a-15-million-bill-one-familys-race-for-a-gene-therapy-cure/ (accessed Oct 15, 2019).

[476] Benkler Y. Don't let industry write the rules for AI. *Nature* 2019; 569: 161–161.

[477] Roland D. Restrictions on $2 Million Drug Highlight Challenge for Gene Therapies. The Wall Street Journal. 2019. https://www.wsj.com/articles/insurers-balk-at-drugs-2-million-price-tag-highlighting-challenge-for-gene-therapies-11564322506 (accessed July 29, 2019).

[478] Dignan L. Researchers find crowdsourcing, AI go together in battle vs. lung cancer. ZDNet. 2019. https://www.zdnet.com/article/researchers-find-crowdsourcing-ai-go-together-in-battle-vs-lung-cancer/ (accessed Sept 18, 2019).

[479] Mak RH, Endres MG, Paik JH, Sergeev RA, Aerts H, Williams CL, Lakhani KR, Guinan EC. Use of Crowd Innovation to Develop an Artificial Intelligence–Based Solution for Radiation Therapy Targeting. *JAMA Oncology* 2019; 5: 654.

[480] Cabitza F, Rasoini R, Gensini GF. Unintended Consequences of Machine Learning in Medicine. *JAMA* 2017; 318: 517.

[481] Ash JS. Some Unintended Consequences of Information Technology in Health Care: The Nature of Patient Care Information System-related Errors. *Journal of the American Medical Informatics Association* 2003; 11: 104–12.

[482] Kitawaki R, Umezu M, Iwasaki K, Kasanuki H. Analysis of Medical Device Recalls owing to Output Information from Software. *Regulatory Science of Medical Products* 2016; 6: 281–93.

[483] Zhang Y, Masci P, Jones P, Thimbleby H. Research: User Interface Software Errors in Medical Devices: Study of U.S. Recall Data. *Biomedical Instrumentation & Technology* 2019; 53: 182–94.

[484] 80000 Deaths. 2 Million Injuries. It's Time for a Reckoning on Medical Devices. The New York Times. 2019. https://www.nytimes.com/2019/05/04/opinion/sunday/medical-devices.html (accessed July 25, 2019).

[485] Weisberg SM, Badgio D, Chatterjee A. A CRISPR New World: Attitudes in the Public toward Innovations in Human Genetic Modification. *Frontiers in Public Health* 2017; 5: 1–9.

[486] Next-generation genome editing. *Nature Biotechnology* 2015; 33: 429–429.

[487] Fernández-Alemán JL, Carrión Señor I, Oliver Lozoya PA, Toval A. Security and privacy in electronic health records: A systematic literature review. *Journal of Biomedical Informatics* 2013; 46: 541–62.

[488] Veale M, Binns R. Fairer machine learning in the real world: Mitigating discrimination without collecting sensitive data. *Big Data & Society* 2017; 4: 205395171774353.

[489] Celis LE, Straszak D, Vishnoi NK. Ranking with Fairness Constraints. *arXiv* 2017; published online April 22. http://arxiv.org/abs/1704.06840.

[490] Zehlike M, Hacker P, Wiedemann E. Matching Code and Law: Achieving Algorithmic Fairness with Optimal Transport. *arXiv* 2017. http://arxiv.org/abs/1712.07924.

[491] Iacobucci G. Digital health: GPs aren't 'Luddites' but want safe, equitable care. *BMJ* 2019; 364: l1258.

[492] Clapper JR. Worldwide Threat Assessment of the US Intelligence Community. Senate Armed Services Committee. 2016. https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf (accessed Oct 23, 2019).

[493] Scudellari M. DARPA Funds Ambitious Brain-Machine Interface Program. IEEE Spectrum. 2019. https://spectrum.ieee.org/the-human-os/biomedical/bionics/darpa-funds-ambitious-neurotech-program (accessed July 25, 2019).

[494] Six Paths to the Nonsurgical Future of Brain-Machine Interfaces. Defense Advanced Research Projects Agency. 2019. https://www.darpa.mil/news-events/2019-05-20 (accessed July 25, 2019).

[495] Center for Neurotechnology. CSNE ERC. http://www.csne-erc.org/content/welcome (accessed July 29, 2019).

[496] Aldersley M. Russia 'fits warships with non-lethal weapon that induces hallucinations and vomiting'. MailOnline. 2019. https://www.dailymail.co.uk/news/article-6666179/Russia-fits-warships-non-lethal-weapon-induces-hallucinations-vomiting.html (accessed July 31, 2019).

[497] Santos EM. How to Use a Strobing Flashlight. Police Magazine. 2010. https://www.policemag.com/340344/how-to-use-a-strobing-flashlight (accessed Oct 4, 2019).

[498] Design and fabricate a light-based immobilization / deterrent device and integrate it with an UAS. Loren Data's SAM Daily. 2007. http://www.fbodaily.com/archive/2007/02-February/11-Feb-2007/FBO-01229525.htm (accessed Oct 7, 2019).

[499] LED Incapacitator. Intelligent Optical Systems. https://www.intopsys.com/technologies/featured-technologies/led-incapacitator-2/ (accessed Oct 4, 2019).

[500] Mizokami K. The Military Wants to Create Synthetic Life Forms to Track Enemies. Popular Mechanics. 2018. https://www.popularmechanics.com/military/research/a25397792/military-synthetic-life-forms-tracking/ (accessed July 25, 2019).

[501] Singh T, Gulhane A. 8 Key Military Applications for Artificial Intelligence in 2018. Market Research Blog. 2018. https://blog.marketresearch.com/8-key-military-applications-for-artificial-intelligence-in-2018 (accessed July 25, 2019).

[502] Denton DD. The Weaponizing of Biology: Bioterrorism, Biocrime and Biohacking. *Terrorism and Political Violence* 2019; 31: 645–6.

[503] Matuchansky C. Deep medicine, artificial intelligence, and the practising clinician. *The Lancet* 2019; 394: 736.

[504] Vincent J. AI systems should be accountable, explainable, and unbiased, says EU. The Verge. 2019. https://www.theverge.com/2019/4/8/18300149/eu-artificial-intelligence-ai-ethical-guidelines-recommendations (accessed Aug 13, 2019).

[505] Artificial intelligence can predict premature death, study finds. Science Daily. 2019.

https://www.sciencedaily.com/releases/2019/03/190327142032.htm (accessed July 25, 2019).

[506] Carbone C. Google AI detected lung cancer better than radiologist, study shows. Fox News. 2019. https://www.foxnews.com/tech/google-ai-better-radiologists-identifying-lung-cancer (accessed July 25, 2019).

[507] Chen BX. CES 2019: It's the Year of Virtual Assistants and 5G. The New York Times. 2019. https://www.nytimes.com/2019/01/09/technology/ces.html?rref=collection%2Ftimestopic%2FArtificial Intelligence (accessed July 25, 2019).

[508] Helping a child's brain to heal. The Washington Post. 2019. https://www.washingtonpost.com/brand-studio/wp/2019/02/14/feature/helping-a-childs-brain-to-heal/?utm_term=.385bf54083ae (accessed July 25, 2019).

[509] Bradshaw R. Teaching AI the Ethics. Hitech News Daily. 2018. http://hitechnewsdaily.com/2018/07/teaching-ai-the-ethics/ (accessed July 25, 2019).

[510] Spanish company that works for an ethic for AI. Acuilae. https://www.acuilae.com/ (accessed July 25, 2019).

[511] Nelson C, Kovarik C, Barbieri J. Forget 'man vs. machine.' When doctors compete with artificial intelligence, patients lose. The Washington Post. 2018. https://www.washingtonpost.com/news/grade-point/wp/2018/06/12/forget-man-vs-machine-when-doctors-compete-with-artificial-intelligence-patients-lose/ (accessed July 25, 2019).

[512] AI beats doctors at predicting hearth disease deaths. Science Daily. 2018. https://www.sciencedaily.com/releases/2018/09/180904140542.htm (accessed July 25, 2019).

[513] Siegel E. The future of AI in radiology: there's an app for that! Carestream. 2018. https://www.carestream.com/blog/2018/07/10/future-of-ai-in-radiology-and-what-it-means-for-radiologists/ (accessed July 25, 2019).

[514] Paddock C. Alzheimer's: Artificial intelligence predicts onset. Medical News Today. 2018. https://www.medicalnewstoday.com/articles/323608.php (accessed July 25, 2019).

[515] Weintraub A. Artificial Intelligence Is Infiltrating Medicine - But Is It Ethical? Forbes. 2018. https://www.forbes.com/sites/arleneweintraub/2018/03/16/artificial-intelligence-is-infiltrating-medicine-but-is-it-ethical/#715ad7783a24 (accessed July 25, 2019).

[516] Could artificial intelligence replace doctors? BBC News. 2018. https://www.bbc.com/news/av/technology-44795307/could-artificial-intelligence-replace-doctors (accessed Aug 13, 2019).

[517] Senthilingam M. Technology is changing the way you see a doctor, but is that good for your health? CNN. 2018. https://edition.cnn.com/2018/08/30/health/ai-artificial-intelligence-technology-health-care-intl/index.html (accessed July 25, 2019).

[518] Roffel S. Hopes and fears for AI: the experts' view. Elsevier Connect. 2018. https://www.elsevier.com/connect/hopes-and-fears-for-ai-the-experts-view (accessed Sept 18, 2019).

[519] Mandrola J. Don't Cede Control to the Machines. Medscape. 2017. https://www.medscape.com/viewarticle/878240 (accessed July 25, 2019).

[520] Future health index. Philips. 2017. http://images.philips.com/is/content/PhilipsConsumer/Campaigns/CA20162504_Philips_Newscenter/future-health-index-report-2017-care-that-delivers.pdf (accessed July 25, 2019).

[521] Five ‘must read’ articles on hit and radiology from the past week. Carestream. 2016. https://www.carestream.com/blog/2016/07/08/radiology-and-healthit-news/ (accessed July 25, 2019).

[522] Siegel E. Will Radiologists Be Replaced by Computers? Debunking the Hype of AI. Carestream. 2016. https://www.carestream.com/blog/2016/11/01/debating-radiologists-replaced-by-computers/ (accessed July 25, 2019).

[523] Rosenthal E. Can a Computer Replace Your Doctor? The New York Times. 2014. https://www.nytimes.com/2014/09/21/sunday-review/high-tech-health-care-useful-to-a-point.html (accessed July 25, 2019).

[524] Pilkington E. Google’s secret cache of medical data includes names and full details of millions – whistleblower. The Guardian. 2019. https://www.theguardian.com/technology/2019/nov/12/google-medical-data-project-nightingale-secret-transfer-us-health-information (accessed Jan 19, 2020).

[525] Pisa N. Amazon’s Alexa will be able to answer owners’ health queries as it links up with the NHS. The Sun. 2019. https://www.thesun.co.uk/news/9473561/amazon-alexa-health-queries-nhs/ (accessed July 25, 2019).

[526] Loftus P. For Many Diabetes Patients, Skin Patches and Phones Are Replacing Finger Pricks. The Wall Street Journal. 2019. https://www.wsj.com/articles/devices-for-diabetes-patients-spur-growth-at-medical-firms-11564392603 (accessed July 30, 2019).

[527] Brown D. Healthcare spending on wearables to reach $60B by 2023. AI in Healthcare. 2019. https://www.aiin.healthcare/topics/business-intelligence/healthcare-spending-wearables-reach-60b-2023 (accessed July 25, 2019).

[528] Maldarelli C. Wearable sensors designed for premature babies could make us all healthier. Popular Science. 2019. https://www.popsci.com/wearable-sensors-preemies (accessed July 25, 2019).

[529] Card C. How Facebook AI Helps Suicide Prevention. Facebook Newsroom. 2018. https://newsroom.fb.com/news/2018/09/inside-feed-suicide-prevention-and-ai/ (accessed July 25, 2019).

[530] Resnick B. How data scientists are using AI for suicide prevention. Vox. 2018. https://www.vox.com/science-and-health/2018/6/8/17441452/suicide-prevention-anthony-bourdain-crisis-text-line-data-science (accessed July 25, 2019).

[531] Marks M. Suicide prediction technology is revolutionary. It badly needs oversight. The Washington Post. 2018. https://www.washingtonpost.com/outlook/suicide-prediction-technology-is-revolutionary-it-badly-needs-oversight/2018/12/20/214d2532-fd6b-11e8-ad40-cdfd0e0dd65a_story.html?utm_term=.1f845881e70b (accessed July 25, 2019).

[532] Scism L. Hartford Financial Takes On the Opioid Epidemic. The Wall Street Journal. 2019. https://www.wsj.com/articles/hartford-financial-takes-on-the-opioid-epidemic-11565269566 (accessed Aug 13, 2019).

[533] Controlling neurons with light -- but without wires or batteries. Science Daily. 2019. https://www.sciencedaily.com/releases/2019/01/190102151215.htm (accessed July 25, 2019).

[534] Zimmer C. Why Are These Mice Hallucinating? Scientists Are in Their Heads. The New York Times. 2019. https://www.nytimes.com/2019/07/18/science/mice-brain-hallucinations.html (accessed July 26, 2019).

[535] Fan S. Why Neuroscience Is the Key to Innovation in AI. SingularityHub. 2017.

https://singularityhub.com/2017/08/02/why-neuroscience-is-the-key-to-innovation-in-ai/#sm.00000orcwx71g2fhjr2ugy6h24p1g (accessed July 25, 2019).

[536] Facebook funds AI mind-reading experiment. BBC News. 2019. https://www.bbc.com/news/technology-49165713 (accessed Sept 18, 2019).

[537] Neuralink Launch Event. Neuralink. 2019. https://youtu.be/r-vbh3t7WVI (accessed Sept 18, 2019).

[538] Carbone C. Google donates 100,000 Home Minis to help people with paralysis. Fox News. 2019. https://www.foxnews.com/tech/google-donates-home-minis-paralysis (accessed July 29, 2019).

[539] Lu D. Bionic eye helps people who are blind read letters again. 2019. https://www.newscientist.com/article/2210632-bionic-eye-helps-people-who-are-blind-read-letters-again/ (accessed July 30, 2019).

[540] Elon Musk wants to connect brains to computers with new company. The Guardian. 2017. https://www.theguardian.com/technology/2017/mar/28/elon-musk-merge-brains-computers-neuralink (accessed July 25, 2019).

[541] Dwoskin E. Putting a computer in your brain is no longer science fiction. The Washington Post. 2016. https://www.washingtonpost.com/news/the-switch/wp/2016/08/15/putting-a-computer-in-your-brain-is-no-longer-science-fiction/?noredirect=on&utm_term=.3389da0e3f99 (accessed July 25, 2019).

[542] Bhanoo SN. A New Approach for Moving Robotic Arms with the Brain. The Washington Post. 2015. https://www.nytimes.com/2015/05/26/science/a-new-approach-for-moving-robotic-arms-with-the-brain.html (accessed July 25, 2019).

[543] Avramova N. AI technology can identify genetic diseases by looking at your face, study says. CNN. 2019. https://edition.cnn.com/2019/01/08/health/ai-technology-to-identify-genetic-disorder-from-facial-image-intl/index.html (accessed July 25, 2019).

[544] Roland D. How Drug Companies Are Using Your DNA To Make New Medicine. The Wall Street Journal. 2019. https://www.wsj.com/articles/23andme-glaxo-mine-dna-data-in-hunt-for-new-drugs-11563879881 (accessed July 25, 2019).

[545] Wall M. Are you happy to share your health data to benefit others? BBC News. 2019. https://www.bbc.com/news/business-48784205 (accessed Aug 13, 2019).

[546] Maldarelli C. Engineering HIV-resistant babies may have accidentally changed their brains. Popular Science. 2019. https://www.popsci.com/china-gene-edited-twins-more-changes (accessed July 25, 2019).

[547] Eschner K. Gene-edited animals could help humanity, but they're in 'regulatory limbo'. Popular Science. 2019. https://www.popsci.com/plant-animal-gene-editing-regulation (accessed July 25, 2019).

[548] Coffey D. Doctors altered a person's genes with CRISPR for the first time in the U.S. Here's what could be next. Popular Science. 2019. https://www.popsci.com/crispr-gene-editing-treatment-sickle-cell-anemia/ (accessed Aug 13, 2019).

[549] Bleicher A. The First Genome Surgeons: Scientists Are Preparing to Bring DNA-Editing Tools to the Clinic. University of California San Francisco. 2018. https://www.ucsf.edu/news/2018/10/412116/first-genome-surgeons-scientists-preparing-to-bring-gene-editing-tools-clinic (accessed July 25, 2019).

[550] New research could fine-tune the gene scissors CRISPR. Phys. 2018. https://phys.org/news/2018-11-fine-tune-gene-scissors-crispr.html (accessed July 25, 2019).

[551] Human Genome editing. World Health Organization. https://www.who.int/ethics/topics/human-genome-editing/en/ (accessed July 25, 2019).

[552] Grossman D. I Guess You Can Grow a Human Pancreas In a Rat Now. Popular Mechanics. 2019. https://www.popularmechanics.com/science/health/a28522349/animal-embryo-human-cells/ (accessed July 29, 2019).

[553] Knapton S. First human head transplant may be just a decade away, former NHS neurosurgeon says. The Telegraph. 2019. https://www.telegraph.co.uk/science/2019/12/21/first-human-head-transplant-may-just-decade-away-former-nhs/ (accessed Jan 14, 2020).

[554] Hjelmgaard K. Head transplant doctors Xiaoping Ren and Sergio Canavero claim spinal cord progress. USA Today. 2019. https://eu.usatoday.com/story/news/world/2019/03/27/italian-chinese-surgeons-cite-spinal-cord-repair-head-transplant-canavero-xiaoping/3287179002/ (accessed Jan 14, 2020).

[555] Eschner K. We need to police gene editing. The World Health Organization agrees. Popular Science. 2019. https://www.popsci.com/gene-editing-WHO-CRISPR-guidelines (accessed July 25, 2019).

[556] Nebehay S. WHO looks at standard in 'uncharted water' of gene editing. Reuters. 2018. https://uk.reuters.com/article/us-china-health-who/who-looks-at-standards-in-uncharted-water-of-gene-editing-idUKKBN1O227Q (accessed July 25, 2019).

[557] Kealey T. Gene editing babies is unethical: Biochemist. USA Today. 2018. https://eu.usatoday.com/story/opinion/2018/11/27/gene-editing-babies-china-aids-hiv-designer-ethics-crispr-column/2125880002/ (accessed July 25, 2019).

[558] Cobb M. Gene drives need global policing. The Guardian. 2016. https://www.theguardian.com/science/2016/feb/09/gene-drives-need-global-policing (accessed July 25, 2019).

[559] Grossman D. An AI´s carbon footprint is 5 times bigger than a car´s. Popular Mechanics. 2019. https://www.popularmechanics.com/technology/infrastructure/a27793543/artificial-intelligence-carbon-footprint/ (accessed July 25, 2019).

[560] Metz C. Warnings of a Dark Side to A.I. in Health Care. The New York Times. 2019. https://www.nytimes.com/2019/03/21/science/health-medicine-artificial-intelligence.html (accessed Oct 18, 2019).

[561] Metz C. India Fights Diabetic Blindness With Help From A.I. The New York Times. 2019. https://www.nytimes.com/2019/03/10/technology/artificial-intelligence-eye-hospital-india.html (accessed Oct 18, 2019).

[562] Artificial Intelligence in Global Health: Defining a Collective Path Forward. USAID. 2019. https://www.usaid.gov/cii/ai-in-global-health (accessed Oct 23, 2019).

[563] Pesapane F, Volonté C, Codari M, Sardanelli F. Artificial intelligence as a medical device in radiology: ethical and regulatory issues in Europe and the United States. *Insights into Imaging* 2018; 9: 745–53.

[564] Veale M, Binns R, Van Kleek M. Some HCI Priorities for GDPR-Compliant Machine Learning. *arXiv* 2018. http://arxiv.org/abs/1803.06174.

[565] European Parliament, Council of the European Union. MDR - Medical Device Regulation (EU) 2017/745. *Official Journal of the European Union* 2017; 117: 1–174.

[566] International Medical Device Regulators Forum (IMDRF). FDA. 2019. https://www.fda.gov/medical-devices/cdrh-international-programs/international-medical-

device-regulators-forum-imdrf (accessed Sept 12, 2019).

[567] Software as a Medical Device (SaMD): Clinical Evaluation. International Medical Device Regulators Forum. 2016. http://www.imdrf.org/consultations/cons-samd-ce.asp (accessed July 25, 2019).

[568] International AI ethics panel must be independent. *Nature* 2019; 572: 415–415.

[569] Parikh RB, Obermeyer Z, Navathe AS. Regulation of predictive analytics in medicine. *Science* 2019; 363: 810–2.

[570] Smallman M. Policies designed for drugs won't work for AI. *Nature* 2019; 567: 7–7.

[571] Crawford K. Regulate facial-recognition technology. *Nature* 2019; 572: 565.

[572] 'Software as a Medical Device': Possible Framework for Risk Categorization and Corresponding Considerations. International Medical Device Regulators Forum. 2014. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf (accessed Oct 15, 2019).

[573] Turner J. Robot Rules. Springer International Publishing, 2019 DOI:10.1007/978-3-319-96235-1.

[574] Wetsman N. When it comes to fitness trackers and health apps, the FDA says you figure it out. Popular Science. 2019. https://www.popsci.com/fda-regulations-fitness-trackers-apps/ (accessed Oct 15, 2019).

[575] Statement on new steps to advance digital health policies that encourage innovation and enable efficient and modern regulatory oversight. FDA. 2019. https://www.fda.gov/news-events/press-announcements/statement-new-steps-advance-digital-health-policies-encourage-innovation-and-enable-efficient-and (accessed Oct 15, 2019).

[576] WHO Guideline: recommendations on digital interventions for health system strengthening. World Health Organization. 2019. https://www.who.int/reproductivehealth/publications/digital-interventions-health-system-strengthening/en/ (accessed Oct 23, 2019).

[577] WHO releases first guideline on digital health interventions. World Health Organization. 2019. https://www.who.int/news-room/detail/17-04-2019-who-releases-first-guideline-on-digital-health-interventions (accessed Oct 23, 2019).

[578] Abrassart C, Bengio Y, Chicoisne G, de Marcellis-Warin N, Dilhac M-A, Gambs S, Gautrais V, Gibert M, Langlois L, Laviolette F, Lehoux P, Maclure J, Martel M, Pineau J, Railton P, Régis C, Tappolet C, Voarino N. Montreal Declaration for a Responsible Development of Artificial Intelligence. Université de Montréal. 2018. https://www.montrealdeclaration-responsibleai.com/the-declaration (accessed Sept 25, 2019).

[579] Scott Gottlieb MD. FDA Announces New Steps to Empower Consumers and Advance Digital Healthcare. FDA. 2018. https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/fda-announces-new-steps-empower-consumers-and-advance-digital-healthcare (accessed Sept 12, 2019).

[580] Dreifus C. Toby Walsh, A.I. Expert, Is Racing to Stop the Killer Robots. The New York Times. 2019. https://www.nytimes.com/2019/07/30/science/autonomous-weapons-artificial-intelligence.html (accessed Aug 13, 2019).

[581] Christian J. Bill Gates Compares Artificial Intelligence to Nuclear Weapons. Futurism. 2019. https://futurism.com/bill-gates-artificial-intelligence-nuclear-weapons (accessed July 25, 2019).

[582] Grossman D. Well, Boris Johnson Talking About Pink-Eyed Terminators at the UN Sure Was Weird. Popular Mechanics. 2019. https://www.popularmechanics.com/technology/a29230437/boris-johnson-united-nations-tech-speech/ (accessed Oct 1, 2019).

[583] Hambling D. Why the U.S. Is Backing Killer Robots. Popular Mechanics. 2018. https://www.popularmechanics.com/military/research/a23133118/us-ai-robots-warfare/ (accessed Oct 1, 2019).

[584] Sample I. Thousands of leading AI researchers sign pledge against killer robots. The Guardian. 2018. https://www.theguardian.com/science/2018/jul/18/thousands-of-scientists-pledge-not-to-help-build-killer-ai-robots (accessed Oct 1, 2019).

[585] Conger K. Google Plans Not to Renew Its Contract for Project Maven, a Controversial Pentagon Drone AI Imaging Program. Gizmodo. 2018. https://gizmodo.com/google-plans-not-to-renew-its-contract-for-project-mave-1826488620 (accessed Oct 1, 2019).

[586] Wakabayashi D. Google Promises Its A.I. Will Not Be Used for Weapons. The New York Times. 2018. https://www.nytimes.com/2018/06/07/technology/google-artificial-intelligence-weapons.html (accessed July 25, 2019).

[587] Fang L. Leaked emails show google expected lucrative military drone AI work to grow exponentially. The Intercept. 2018. https://theintercept.com/2018/05/31/google-leaked-emails-drone-ai-pentagon-lucrative/ (accessed July 25, 2019).

[588] Tworek H. Microsoft is right: we need a digital Geneva convention. Wired. 2017. https://www.wired.com/2017/05/microsoft-right-need-digital-geneva-convention/ (accessed July 25, 2019).

[589] Cockburn H. Tesla’s Elon Musk leads tech experts in demanding end to 'killer robots arms race’. Independent. 2017. https://www.independent.co.uk/news/science/killer-robots-arms-race-tesla-elon-musk-and-google-mustafa-suleyman-un-autonomous-weapons-a7903906.html (accessed July 25, 2019).

[590] Autonomous weapons: An open letter from AI & Robotic Researchers. 2015. https://futureoflife.org/open-letter-autonomous-weapons/ (accessed Dec 4, 2019).

[591] 2019 Group of Governmental Experts on Lethal Autonomous Weapons Systems (LAWS). United Nations. 2019. https://www.unog.ch/80256EE600585943/(httpPages)/5535B644C2AE8F28C1258433002BBF14?OpenDocument (accessed Oct 1, 2019).

[592] Lethal autonomous weapons pledge. Future of Life Institute. https://futureoflife.org/lethal-autonomous-weapons-pledge (accessed July 25, 2019).

[593] Autonomous weapons that kill must be banned, insists UN chief. UN News. 2019. https://news.un.org/en/story/2019/03/1035381 (accessed Oct 1, 2019).

[594] Metz C. Hold’ Em or Fold’ Em? This A.I. Bluffs with the Best. The New York Times. 2019. https://www.nytimes.com/2019/07/11/science/poker-robot-ai-artificial-intelligence.html (accessed July 25, 2019).

[595] Crandall JW, Oudah M, Tennom, Ishowo-Oloko F, Abdallah S, Bonnefon J-F, Cebrian M, Shariff A, Goodrich MA, Rahwan I. Cooperating with machines. *Nature Communications* 2018; 9: 233.

[596] Rauter G, Gerig N, Sigrist R, Riener R, Wolf P. When a robot teaches humans: Automated feedback selection accelerates motor learning. *Science Robotics* 2019; 4: 1–11.

[597] Moser M. The Social Impacts of AR/VR. OSA. 2019. https://www.osa-opn.org/home/newsroom/2019/september/the_social_impacts_of_ar_vr/ (accessed Oct 1,

2019).

[598] Thompson A. Facial recognition used by UK Police is alarmingly bad. Popular Mechanics. 2018. https://www.popularmechanics.com/technology/security/a20168749/facial-recognition-used-by-uk-police-is-alarmingly-bad/ (accessed July 25, 2019).

[599] FitzGerald K. Human Genome Editing. *The National Catholic Bioethics Quarterly* 2017; 17: 107–22.

[600] Wiens J, Shenoy ES. Machine Learning for Healthcare: On the Verge of a Major Shift in Healthcare Epidemiology. *Clinical Infectious Diseases* 2018; 66: 149–53.

[601] He J, Baxter SL, Xu J, Xu J, Zhou X, Zhang K. The practical implementation of artificial intelligence technologies in medicine. *Nature Medicine* 2019; 25: 30–6.

[602] The Lancet Digital Health. Walking the tightrope of artificial intelligence guidelines in clinical practice. *The Lancet Digital Health* 2019; 1: e100.

[603] Wiens J, Saria S, Sendak M, Ghassemi M, Liu VX, Doshi-Velez F, Jung K, Heller K, Kale D, Saeed M, Ossorio PN, Thadaney-Israni S, Goldenberg A. Do no harm: a roadmap for responsible machine learning for health care. *Nature Medicine* 2019; 25: 1337–40.

[604] Bentley PJ, Brundage M, Häggström O, Metzinger T. Should we fear artificial intelligence? European Parliamentary Research Office. 2018. http://www.europarl.europa.eu/RegData/etudes/IDAN/2018/614547/EPRS_IDA(2018)614547_EN.pdf (accessed Oct 18, 2019).

[605] A shared vision for the future of health in Europe. Paving the way in 2019 and beyond. Recommendations in full. EU Health Summit. 2019. https://www.youthcancereurope.org/wp-content/uploads/2018/11/GRAYLING-Future-of-health-recommendations_Annexe-BD.pdf (accessed Jan 14, 2020).

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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