BACKGROUND NOTE ON UNLOCKING THE POTENTIAL OF ARTIFICIAL INTELLIGENCE (AI) IN CANCER RESEARCH AND CARE

According to the 2018 European Commission’s definition, Artificial Intelligence (AI) refers to systems that display intelligent behaviour by analysing their environment and taking action - with some degree of autonomy - to achieve specific goals.\(^1\) AI includes a wide range of technologies and applications in non-medical (e.g. search engines) and medical (e.g. radiology) fields. Initially detailed in the 1950s, the use of AI has skyrocketed in the past decade. In medicine, more specifically in cancer, health ‘big data’ can be analysed with help of AI to accelerate the processing of these vast amounts of data and facilitate ‘precision medicine.’\(^2\) In other words, this could facilitate the development of more personalised and precise treatments based on an individuals’ genetic makeup. AI has the potential to revolutionise cancer care with the promise of a future optimised for the highest quality diagnosis and patient care.

Cancer care can benefit greatly from AI, however several potential barriers have been identified, when it comes to interoperability, legal and ethical standards, governance, cybersecurity, and technical requirements.\(^3\) Europe’s Beating Cancer Plan aims to stimulate and improve the use of new approaches to data analytics using AI. The possibilities and application of AI can play an important role in enhancing the quality of cancer detection, treatment and overall cancer care.\(^4\) This background note aims to demystify AI technology, to explain its applications in

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\(^1\) A definition of Artificial Intelligence: main capabilities and scientific disciplines | Shaping Europe’s digital future (europa.eu)

The recently published Artificial Intelligence Act proposal defines AI system as a “software that is developed with one or more of the techniques and approaches listed in (...) [the legislation] and can, for a given set of human-defined objectives, generate outputs such as content, predictions, recommendations, or decisions influencing the environments they interact with.”

\(^2\) ‘Big data’ refers to datasets that are so large and complex - including content from different sources, in different formats, and with different degrees of authenticity and accuracy - that they cannot be stored or processed in the same way as smaller datasets. ‘Precision medicine’ refers to the customisation of healthcare for a specific subgroup of patients.

\(^3\) AIDA Working Paper on Artificial Intelligence and Health

\(^4\) N.Couspel and others, European Cancer Organisation: Strengthening Europe in the fight against cancer. Study for the ENVI Committee, by the Policy Department, 2020

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In this note:

- Introduction to Artificial Intelligence
  - How AI works
  - Uptake of AI in healthcare
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The application of AI in cancer diagnostics, surgery and treatment
  - Computer-aided detection, diagnosis and decision support
  - Applied AI in surgery and treatment
  - Personalised medicine: the right therapy for the right person at the right time

AI legal and ethical challenges
  - Trustworthiness of AI systems, ethical standards
  - Big data and data protection rules
cancer care and research, and to present its opportunities, future perspectives and limitations with a view to the upcoming BECA Committee hearing. The hearing is organised in association with AIDA, and is complementary to the hearing held by the AIDA Committee about AI and health in December 2020.

I. Introduction to artificial intelligence (AI)

I.1. How AI works

AI-systems can be embedded either in hardware (e.g. advanced robots, drones) or in software (e.g. search engines, voice assistants, face recognition systems, image analysis). AI is an umbrella term for several different technologies and methodologies for approaching big data:

- Symbolic AI (expert systems)

Symbolic AI refers to the classical programming, embedding human knowledge and behaviour rules, and represents the dominant paradigm of AI applications from its inception in the 1950s. This approach uses symbolic reasoning to represent and solve problems (i.e. using symbols for a particular solution, such as in a mathematical problem). Although symbolic AI is still used to date, it has its limitations: it requires human expertise to encode their knowledge in an understandable way and perform tasks, which can only be improved by direct human intervention. This means that symbolic AI is less effective for dynamic complex problems.

- Machine learning (data-driven AI)

Machine learning (ML) is an automated learning process of algorithms that improve their performance without the interference of human encoding. In ML, the computer receives input data as well as answers expected from the data, and the ML agent needs to produce the rules. These rules can then be applied to new data to produce original answers. Therefore, in an ML system, the algorithm usually improves by training itself on large quantities of data (i.e. ‘data-driven’ AI).

  o Artificial neural networks (ANNs): refer to computing systems that simulate the working of the brain, specifically in analysing and processing of information.
  o Deep learning: is a subset of ML and refers to ANNs with more complexities, each containing many neurons, which may deliver more nuanced, and accurate responses. It has facilitated object recognition in images and video labelling *inter alia*.

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5 AIDA hearing on AI and health; AIDA Working Paper on AI and health
6 Artificial intelligence: How does it work, why does it matter, and what can we do about it? Study by EPRS
7 Presentation Dr Mozzi Etemadi: How computers learn from humans; BECA hearing: “Why screening and early detection of cancer matter”
- **Reinforcement learning**

In reinforcement learning (RL), algorithms are used that focus on experience-driven sequential decision-making. This means that these algorithms lead to action to maximise some notion of cumulative reward. The combination of RL and ML is used in practical applications such as autonomous driving and stock markets.

![A schematic depiction of an AI-system](source: A definition of Artificial Intelligence: main capabilities and scientific disciplines / Shaping Europe’s digital future (europa.eu))

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### 1.2. AI in healthcare

Though data and analysis is not available on the specific angle of uptake of AI in cancer, the Joint Research Centre (JRC) monitors the uptake of AI in health and healthcare in general. Some of the conclusions from the JRC’s “AI watch 2020” appear to be particularly relevant:

- Within the global landscape, the EU is generally well-placed in the application of AI in the health and healthcare domains, somewhat behind China but at par with the USA. The research dimension is particularly strong in the EU, with research institutions accounting for about two thirds of all EU players in this field, compared to one third of players in China, and a relatively small proportion in the US, where developments in this field are dominated by commercial companies.

- Though the level of interest and the number of pilot projects and experimentations are growing, the level of diffusion is still relatively low, most projects are just in initial stage to “test the water”, and investment in AI applications is still just a

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fragment of the overall expenditure of digital innovation in health.

- In the short term: AI development for operational applications and streamlining tasks and processes is at a mature stage and are already deployed in several industrial sectors.

- In the medium term: the priority is to increase access to health data and ensure its interoperability, which is crucial for enabling healthcare actors to develop and use AI technologies. Though the volume of data gathered by the Member States is impressive, common data spaces will be needed for exploiting the data.

- In the long term: upskilling of healthcare practitioners at all levels is the key for the uptake of AI applications, and data science should become part of their education and training.

I.3 EU policy and regulatory framework on AI and related initiatives

Launched in 2018, the EU’s Digital Transformation of Health and Care agenda\(^9\) gave a new impetus to the eHealth sector. A Joint Action, TEHDAS\(^10\), is already in place, paving the way for the European Health Data Space. The creation of a European Data Space, including a common European Health Data Space (EHDS), is one of the priorities of the Von der Leyen Commission. It will allow better exchange and access to different types of health data (EHRs, genomics data, data from patient registries etcetera), both for primary and secondary use. For secondary data use, it will connect with the Knowledge Centre on Cancer that will be launched in 2021 as one of the Flagship initiatives of Europe’s Beating Cancer Plan, to ensure that learnings are shared efficiently. The EHDS legislative proposal is expected later in 2021 and will be built on three main pillars: (i) a strong system of data governance and rules for data exchange; (ii) data quality; and (iii) strong infrastructure and interoperability.

In order to achieve secure, interoperable, cross-border exchange and access to electronic health data in the EU, Commission Recommendation (EU) 2019/243\(^11\) sets out the framework for the development of a European Electronic Health Record (EHR) exchange format. In addition to the governing principles on access and exchange, the recommendation also includes common technical specifications. Europe’s Beating Cancer Plan underscores the importance of EHRs in the European Health Data Space (more on this in the next section), and commits the Commission to work with Member States on a common exchange format for EHRs taking into account data security, privacy and interoperability.

The EU’s AI strategy\(^12\), launched in 2018, aimed to encourage the uptake of AI by the public and private sectors; prepare for socio-economic changes brought about by AI; and ensure an appropriate ethical and legal framework. The High-Level Expert Group on Artificial Intelligence developed Guidelines for Trustworthy AI in 2019, and an Assessment List for Trustworthy AI in 2020 (more on these initiatives later, in point III.1). In parallel, the first coordinated plan on AI\(^13\), published in 2018, represents a joint commitment with Member States for policy coordination on AI, and encourages Member States to develop national

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\(^10\) Joint Action Towards the European Health Data Space, TEHDAS

\(^11\) Commission Recommendation (EU) 2019/243

\(^12\) AI Strategy, COM(2018)237

\(^13\) Coordinated Plan on Artificial Intelligence, COM (2018) 795
strategies. Bringing together the two streams, the Commission’s **White Paper on AI** was published in 2020, together with a report on the safety and liability aspects of AI, the Internet of Things and robotics\(^ {14} \).

In April 2021, the Commission presented a **comprehensive policy and legislative framework on AI**\(^ {15} \) and a **revised coordinated plan on AI**. Since smooth access to data is pivotal for AI, the new AI framework is closely linked to the implementation of the **European Data Strategy**, including the recent proposal for a **Data Governance Act**\(^ {16} \). The AI regulatory framework will also work together with applicable **product safety legislation** and in particular the revision of the Machinery Directive\(^ {17} \), addressing the safety risks of new technologies, including the risks emerging from human-robot collaboration, cyber risks with safety implications, and autonomous machines.

### Funds for the promotion, development and deployment of AI

Thanks to the **Digital Europe** and **Horizon Europe** programmes, 1 billion EUR per year can be invested in AI; the Commission plans to mobilise additional investments from the private sector and the Member States to reach 20 billion EUR investment per year over the course of this decade.

The **Recovery and Resilience Facility** will enable Europe to raise its ambitions and become a first mover in adopting AI. The RRF makes 672.5 billion EUR in loans and grants available to support reforms and investments by Member States for the crucial first years of the recovery; at least 20% of the available funding, amounting to up to EUR 134 billion throughout the time span of the RRF will be allocated to measures fostering the digital transition. The RRF is expected to boost Member States’ investments in AI and support leading research, innovation and testing capacities, so that the accelerated development and use of AI can contribute to economic and social recovery and improve competitiveness in the longer term.

Substantial AI innovation funding can also be obtained under the **Cohesion Policy programmes**.

### II. The application of AI in cancer research care

#### II.1. Computer-aided detection, diagnosis and decision support

At present, technology used for, for example, accurate lung cancer diagnosis (i.e. cancer type, stage of cancer and possible mutations) and treatment is through molecular biomarkers applied on biopsy material and/or blood testing. Although they are the gold standard, biopsies are specialised procedures, rather invasive, time-consuming, and can incur high costs. The use of new AI techniques, known as **deep learning technology (DELT)**, can be used for the detection

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\(^ {14} \) Report on the Safety and Liability Aspects of AI the Internet of Things and robotics, COM(2020)64

\(^ {15} \) Proposal for a regulation laying down harmonised rules on Artificial Intelligence (Artificial Intelligence Act), COM(2021)206:

Communication from the Commission: Fostering a European approach to Artificial Intelligence, COM(2021)205

\(^ {16} \) Proposal for a regulation on European data governance (Data Governance Act), COM (2020) 767

\(^ {17} \) Directive 2006/42/EC of the European Parliament and of the Council on machinery
and classification of different tumours (e.g. lung cancer).\textsuperscript{18,19} DELT has increased rapidly during the last decade because of improved availability of ‘big data’, increasing computing power and advances in learning algorithms.\textsuperscript{20,21,22,23}

Whilst currently concentrated in the research domain, significant human and financial resources have been increasingly committed to the deployment of AI. The implementation of data-driven systems is believed to improve patient care by integrating them into clinical workflows. The clinical potential of AI lies in its ability to analyse large amounts of data to generate clinical decision support. In oncology, DELT can support expert clinicians in the qualitative interpretation of cancer imaging by, \textit{inter alia}, distinguishing different types of cancer from normal tissues, identifying stages of cancer, applying volumetric tumour delineation, and evaluating response to anti-cancer treatments.\textsuperscript{24} In addition, DELT may lead to a more automated process of cancer image interpretation (e.g. in histopathology), and can assist pathologists in the detection of cancer subtypes or gene mutations, which can save time (i.e. accelerating access to appropriate therapies for patients) and costs. Furthermore, experts believe that digitalisation of the diagnostic process may lead to more equality in cancer care.

However, there are some limitations to the use of DELT in radiology (e.g. heterogeneity of datasets, lack of representative data \textit{inter alia}). Therefore, experts have underlined that deep learning applications for cancer imaging require further assessment and validation for reproducibility and generalizability in clinical practice.

Furthermore, AI brings a surge in big data and costs: big data management and interpretation is resource-intense, it requires large servers and skilled bio-informaticians; AI systems have specialised computational requirements for fast processing of data; and intended users need

\begin{footnotesize}
\begin{enumerate}
\item International evaluation of an AI system for breast cancer screening | Nature
\item End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography | Nature Medicine
\item Deep learning technology for improving cancer care in society: New directions in cancer imaging driven by artificial intelligence - ScienceDirect
\item Canadian Association of Radiologists White Paper on Artificial Intelligence in Radiology | Elsevier Enhanced Reader
\item Reviewing the relationship between machines and radiology: the application of artificial intelligence (nih.gov)
\item A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: a systematic review and meta-analysis - PubMed (nih.gov)
\item Volumetric tumour delineation is the process in which the tumour is targeted as accurately as possible for radiation therapy applications.
\end{enumerate}
\end{footnotesize}
proper training before implementing AI-based systems for routine clinical practice. Using patient data for training AI and enabling machine learning, and the protection of patients’ safety and privacy remain crucial.

Under Europe’s Beating Cancer Plan, the European Cancer Imaging Initiative will be set up in 2021 to develop an EU ‘atlas’ of cancer-related imaging, making anonymised images accessible to a wide range of stakeholders across the ecosystem of hospitals, researchers and innovators. It will provide a common EU data space, complemented by a new reference facility for Testing and Experimentation that will be launched to link the data to digital technologies such as High Performance Computing and AI. Supported by dedicated Digital Innovation Hubs, which will also provide assistance on regulatory aspects of AI, the Imaging Initiative will improve personalised medicine and innovative solutions by delivering greater accuracy and reliability in diagnostic imaging and follow-up of treatments.

II.2. The AI revolution in cancer surgery and treatment

Surgical decision-making is traditionally performed using hypothetical-deductive reasoning, individual judgement, and heuristics. These methods, however, are highly subject to variability (e.g. clinical knowledge of the surgeon and ability to interpret test results) and bias, and can introduce errors leading to preventable harm. The integration of AI techniques in surgical decision-making may address these impairments and will likely accelerate the capabilities of AI in augmenting surgical care. This will eventually improve patient care and overall quality of care.

25 Translating cancer genomics into precision medicine with artificial intelligence: applications, challenges and future perspectives | SpringerLink
26 Artificial Intelligence in Surgery: Promises and Perils (nih.gov)
27 Artificial Intelligence and Surgical Decision-Making (nih.gov)
28 Hypothetical-deductive reasoning refers to the diagnostic process in which patients are assessed to develop a list of possible diagnoses to consider; heuristics refers to any approach to problem solving, which is sufficient for a short-term goal, but possibly not optimal, or perfect (e.g. “trial and error”).
Therefore, many experts believe that AI is able to transform cancer care (e.g. surgical care and personalised medicine) significantly. The theoretical potential of AI lies in the application in several aspects of cancer care and treatment, such as:

- computer-aided diagnosis;
- cancer staging;
- clinical decision-making (e.g. treatment algorithms);
- informed consent process;
- treatment monitoring;
- surgery risk prediction;
- image-guided surgery;
- prediction of adverse events and postoperative complications;
- recovery monitoring and postoperative management;
- technical skills augmentation; and
- database management.

Although several studies have shown that clinician-machine interaction can augment human performance and clinical decision-making, there are limitations to be addressed. For example, AI cannot provide an automated clinical interpretation of its analyses nor can it determine causality in data necessary for clinical implementation. In addition, big data does not provide the appropriate clinical context with which to interpret the data.

Integration of multimodal data with AI can augment surgical decision-making across all phases of care both at the individual patient and at the population level


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29 Deep Learning for Identifying Metastatic Breast Cancer (arxiv.org)
30 High-Risk Breast Lesions: A Machine Learning Model to Predict Pathologic Upgrade and Reduce Unnecessary Surgical Excision - PubMed (nih.gov)
31 Artificial intelligence performance in detecting tumor metastasis from medical radiology imaging: A systematic review and meta-analysis - PubMed (nih.gov)
II.3.  Personalised medicine: the right therapy for the right person at the right time

Given the lack of a legal definition, personalized medicine is best defined by the Horizon 2020 Advisory Group: it is “a medical model using characterisation of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, (...) to determine the predisposition to disease and (...) to deliver timely and targeted prevention”.

The sequencing of the human genome and research developments in the genetic and molecular basis of diseases contributed to a much better molecular understanding of diseases and of the impact of environmental factors, down to the level of the individual. Tools developed for detection, diagnosis and treatment of diseases include ‘-omics’ technologies, such as genomics, glycomics, lipidomics, metabolomics, pharmacogenomics, epigenomics, proteomics, transcriptomics and metagenomics; and biomarkers and biobanking.

Research over the past decades proved that there is heterogeneity not only between different tumour types and organs, but also within any tumour; and that tumours on the same site, though deriving from the same organ, can differ in many aspects. Thanks to improvements in tumour biology, cancers now can be classified based on critical molecular targets; this enables creating targeted therapies, i.e. medicines that act specifically against molecular targets in cancer cells. With personalised cancer therapy, cancer patients receive the optimum treatment according to their personal medical history, their physiological status (including their genetics), and the molecular characteristics of their tumours. (For example, a subgroup of breast cancer patients is identified with HER2 gene amplification, which is the primary mechanism of HER2 over-expression in tumours. HER2 is a so-called oncogene, a gene that has the potential to cause cancer; amplification and over-expression of an oncogene can lead to uncontrolled cell growth, resulting in tumour growth. These patients can benefit from certain therapies that are effective specifically for their genetic profile.)

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32 The Human Genome Project was an international, collaborative research program whose goal was the complete mapping and understanding of all the genes (i.e. “genom”) of human beings. The project was completed in 2003. The 1+ Million Genomes (1+MG) EU initiative is a cooperation mechanism, launched in 2018, involving by now 24 countries. Participating countries coordinate to link genomic databases, with the aim of having at least one million sequenced genomes accessible in the EU by 2022. Sharing more genomic data will improve understanding and prevention of disease, allowing for more personalised treatments and targeted drug prescription, in particular for rare diseases, cancer and brain related diseases.

33 Personalised medicine - Current status; Briefing for the ENVI Committee

34 ESMO Patients Guide Series - Personalised medicines
In oncology, AI platforms, ranging from machine learning to neural networks, can accelerate cancer drug discovery, harness biomarkers to accurately match patients to clinical trials, and personalise cancer therapy using only a patient’s own data:

- Testing all possible drug combinations at multiple doses for each drug is virtually impossible. However, AI can reduce the number of experiments needed to resolve drug and dose parameters, and thus optimise the development of combination therapy. AI can play a vital role in designing drug combinations without relying on predicted synergy between different drug targets and pathways. This could increase the pool of drugs considered for treatment, and identify unexpected combinations that outperform standards of care.

- Concerning clinical trials, including biomarkers in study recruitment has improved patient outcomes compared with traditional stratification information such as pathology or responses to prior treatments. Combining patient biomarker data and electronic health records for AI analysis may further affect trial outcomes. Although many types of data may be useful for stratification, AI would ultimately need both population-scale and individualised data to ensure that patients given therapies, including those designed by AI, have a high likelihood of responding.

- AI would also play a pivotal role in how cancer therapy is administered. Maximum tolerated dosing eliminates drug-sensitive tumour cells. However, drug-resistant cells can eventually cause treatment failure. Game theory is being explored to address this challenge, with dose-reduction algorithms competing against the tumour to prevent drug-resistant cells (which have high energy costs) from outnumbering drug-sensitive cells. This adaptive therapy may prolong treatment efficacy by maintaining threshold drug-sensitive cell populations in a tumour to combat drug-resistant cell proliferation.

35 D. Ho: Artificial intelligence in cancer therapy - Artificial intelligence can optimize cancer drug discovery, development, and administration; Science, 2020
In the EU, several research initiatives support the development of personalised medicines:

- The **International Consortium for Personalised Medicine** (ICPerMed)\(^{36}\) was launched in 2016, bringing together over 30 European and international members representing research funders and policy-making organisations, and the Commission as observer. ICPerMed supports the personalised medicine science base via a common action plan with central research and research-supporting activities; and provides evidence to demonstrate the benefit of personalised medicine to citizens and healthcare systems.

- **ERA-LEARN\(^{37}\)** is a support platform for the research & innovation partnership community, funded as a support action by Horizon 2020, with a four-year lifespan (2018-2022). On behalf of the Commission, ERA-LEARN operates a unique database of partnership initiatives, their calls and funded projects and provides studies and analyses on thematic clustering, internationalisation, alignment, etc. **ERA-PerMed** serves as a funding vehicle of topics identified in the Strategic Research and Innovation Agenda in Personalised Medicine and the Action Plan of ICPerMed. ERA PerMed coordinates research & innovation efforts of the participating partners.

- The **Innovative Medicines Initiative Joint Undertaking** (IMI2)\(^{38}\) is a public-private partnership between the EU and the European Federation of Pharmaceutical Industries and Associations, EFPIA. It focuses on the needs of patients and society, and on

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36 International Consortium for Personalised Medicine, [ICPerMed](#)
37 [ERA-LEARN](#)
38 Innovative Medicines Initiative, [IMI2](#)
delivering tools and resources to speed up the development of urgently-needed treatments. Its strategic research agenda includes, among others, research into personalised medicines.

- As confirmed by Commissioner Gabriel in March 2021\(^\text{39}\), personalised medicine will be of great importance in projects funded under *Horizon Europe*\(^\text{40}\) in the Health Cluster and for relevant projects funded in the European Research Council\(^\text{41}\), the Marie Skłodowska-Curie actions\(^\text{42}\) and the European Innovation Council\(^\text{43}\). Many fields will be open for proposals, without specifying the diseases to be addressed. In addition, the Commission is working on setting up a **European Partnership for Personalised Medicine** (EP PerMed) in collaboration with the Member States and regions, scheduled to start in the second half of 2023. It will address priorities for research and innovation in personalised medicine and its implementation in the healthcare sector, and co-fund projects between the Member States and the Commission.

### III. **AI legal and ethical challenges**

The rise of new technologies brought on new ethical challenges, in the health sector and in general, that must be identified and mitigated.\(^\text{44,45}\) These issues relate to the whole lifecycle of AI, from creating algorithms (data collection, data entry and cleaning) to the application of AI and the dissemination of the results:

- the trustworthiness of AI systems;
- the opacity of algorithms or “black box issue” where no logical explanation can be provided of how the algorithm arrived at its given output;
- the algorithmic bias whereby the algorithm replicates existing inequities in socioeconomic status, race, ethnic background, religion, gender, disability, or sexual orientation, and amplifies inequities in health systems; poor training and design of AI systems potentially resulting in significant errors that may undermine privacy and non-discrimination;
- the secondary use of health data and the related issue of consent and the patient’s autonomy over his data,

are all valid concerns.

In health care, questions also arise about the cooperative or competitive relationship between AI and medical staff (in other words, whether there is a real risk that AI might not complement but replace the work of doctors, nurses and other healthcare staff in the future, raising questions about the nature of the future patient-doctor relationship); and the use of artificially intelligent, virtual patients in medical education

Two challenges are described in more details below, the trustworthiness of AI systems and ethical standards, and the secondary use of health data in the light of the GDPR.

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\(^\text{39}\) Answer given by Commissioner Gabriel to a question to the Commission, [E-000307/2021](https://www.europarl.europa.eu/doceo/document/E-000307-2021.pdf)

\(^\text{40}\) [Horizon Europe](https://ec.europa.eu/ Horizon Europe)

\(^\text{41}\) [European Research Council](https://erc.europa.eu/)

\(^\text{42}\) [Marie Skłodowska-Curie Actions](https://ec.europa.eu/ facebook/erc.europa.eu/ Marie Skłodowska-Curie Actions)

\(^\text{43}\) [European Innovation Council](https://ec.europa.eu/ facebook/erc.europa.eu/ European Innovation Council)

\(^\text{44}\) [Ethical Dimensions of Using Artificial Intelligence in Health Care; Journal of Ethics, American Medical Association, 2019](https://www.nature.com/articles/s41591-019-0326-x)

\(^\text{45}\) K. J. Igoe: [Algorithmic Bias in Health Care Exacerbates Social Inequities — How to Prevent It; Harvard School of Public Health](https://www.hsph.harvard.edu/healthdataandbioinformatics/algorithmic-bias/)
III.1  Trustworthiness of AI systems, ethical standards

AI is trustworthy when three criteria are respected throughout the system's entire life cycle, i.e. during the development, deployment and use of AI systems: (i) AI has to be lawful, i.e. in compliance with all applicable laws and regulations; (ii) it has to be ethical, ensuring adherence to ethical principles and values; and (iii) it has to be robust, both from a technical and social perspective since, even with good intentions, AI systems can cause unintentional harm.

The independent High-Level Expert Group on AI, set up by the Commission, adopted ethics guidelines for trustworthy AI. In those guidelines, they identify the ethical principles and values that must be respected throughout the system's entire life cycle:

- Develop, deploy and use AI systems in a way that adheres to the ethical principles of: respect for human autonomy, prevention of harm, fairness and explicability. Acknowledge and address the potential tensions between these principles.

- Pay particular attention to situations involving more vulnerable groups such as children, persons with disabilities and others that have historically been disadvantaged or are at risk of exclusion, and to situations which are characterised by asymmetries of power or information, such as between employers and workers, or between businesses and consumers.

- Acknowledge that, while bringing substantial benefits to individuals and society, AI systems also pose certain risks and may have a negative impact, including impacts which may be difficult to anticipate, identify or measure (e.g. on democracy, the rule of law and distributive justice, or on the human mind itself.) Adopt adequate measures to mitigate these risks when appropriate, and proportionately to the magnitude of the risk.

The ethics guidelines also list the key requirements of trustworthy AI: (i) human agency and oversight, (ii) technical robustness and safety, (iii) privacy and data governance transparency, (iv) diversity, (v) non-discrimination and fairness, (vi) environmental and societal well-being, and (vii) accountability. The Assessment List for Trustworthy AI that the High-Level Group adopted a year later, translates AI principles into a checklist, and guides developers and deployers of AI in implementing those principles in practice.

In 2020 the European Parliament, in a legislative initiative report, called for the establishment of a robust legal framework on AI, integrating a strong ethical approach into the legislation. In particular, the EP emphasised that future legislation should include into its scope AI, robotics and related technologies, including software, algorithms and data used or produced by such technologies; and legislation should cover the whole lifecycle of the system, from development to deployment and use. The Parliament also emphasised the importance to adhere to the Charter of Fundamental Rights; considered that the precautionary

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46 The High-Level Expert Group on Artificial Intelligence is group of experts, appointed by the Commission to provide advice on the EU’s AI Strategy. Members include representatives from academia, civil society and industry.

47 High-Level Expert Group on Artificial Intelligence: Ethics Guidelines for Trustworthy Artificial Intelligence, 2019

48 High-Level Group on AI: Assessment List for Trustworthy AI (ALTAI), 2020

49 Framework of ethical aspects of artificial intelligence, robotics and related technologies, P9_TA(2020)0275
principle should be at the heart of any regulatory framework for AI; and called for a clear and coherent governance model. The EP cautioned about the asymmetry between those who employ AI technologies and those who interact and are subject to them, and stressed that citizens’ trust in AI can only be built on an ethics-by-default and ethics-by-design regulatory framework. The resolution includes further specific provisions about risk assessment, safety features, transparency and accountability, non-bias and non-discrimination, etc. The resolution, in line with Rule 47 of Parliament’s Rules of Procedure, includes the text of the proposed draft legislation.

In April 2021 the Commission presented a proposal for an Artificial Intelligence Act, which is a major step towards trustworthiness, while fostering the uptake of AI and boosting the EU’s competitiveness via a risk-based approach:

- The legislation sets a technology-neutral definition of AI systems. The definition is meant to be future-proof, to the extent that it can cover techniques and approaches which are not yet known or developed.

- To avoid over-regulation, the legislation focuses on the use of AI in those cases where the risks that the AI systems pose are particularly high. The risk classification of an AI system depends on its intended purpose, the severity of the possible harm and the probability of its occurrence. High-risk AI systems need to respect a set of specifically designed requirements, which include the use of high-quality datasets, the establishment of appropriate documentation to enhance traceability, the sharing of adequate information with the user, the design and implementation of appropriate human oversight measures, and the achievement of the highest standards in terms of robustness, safety, cybersecurity and accuracy. High-risk AI systems must be assessed for conformity with these requirements before being placed on the market or put into service.

- Finally, the legislation bans a limited set of uses of AI that contravene EU values or violate fundamental rights, such as AI systems that distort a person’s behaviour through subliminal techniques or by exploiting specific vulnerabilities in ways that cause or are likely to cause physical or psychological harm. It also covers general purpose social scoring of AI systems by public authorities. The legislation includes specific provisions for remote biometric identification systems (e.g. facial recognition tools to check passers-by in public spaces).

- Other uses of AI systems would be only subject to minimal transparency requirements, for example in the case of chatbots, emotion recognition systems or deep fakes. Finally, the legislation encourages the use of regulatory sandboxes, i.e. a controlled environment to test innovative technologies for a limited time, access to Digital Innovation Hubs and access to testing and experimentation facilities.

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50 European Parliament’s Rules of Procedure, Rule 47
51 Proposal for a regulation laying down harmonised rules on Artificial Intelligence (Artificial Intelligence Act), COM(2021)206
III.2  Big data and data protection rules

Health data can be used for different purposes: the primary use of data is for direct patient care; and secondary data use consists of supporting the safe and efficient functioning of healthcare systems, and driving health research and innovation such as feeding AI. Data protection rules play a key role in ensuring safe data flow.

The EU’s General Data Protection Regulation (Regulation (EU) 2016/679, GDPR), applicable since 2018, is part of the EU data protection reform package. The regulation modernises and unifies rules, allowing businesses to reduce red tape and to benefit from greater consumer trust, and citizens to better control their personal data. Its relevance for cancer research and cancer registries is that the regulation recognises the principle of one-time consent for retrospective research and biobanking, and the principle of no consent for population-based registries.

Article 7 of the GDPR regulates consent, and some key recitals elaborate on the secondary use of data. With regard to one-time consent for retrospective research and biobanking, Recital 33 of the GDPR acknowledges that it is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection, i.e. the subject of future research may be unknown at the time when a patient gives his/her consent on the use of clinical data for scientific purposes. The recital also explains that patients should be allowed to give their consent (withdrawable any time) to certain areas of scientific research, or certain areas of research or parts of research projects.

The new Clinical Trials Regulation (Regulation (EU) No 536/2014, CTR, not yet applicable) specifically acknowledges the notion of one-time consent with regard to clinical trials. CTR specifies that in order to collect data from clinical trials to be used for future scientific research, it is necessary that the trial subject gives consent (withdrawable any time) to the use of his/her data outside the trial protocol. In this case, the one-time consent is given to use data retrospectively beyond the end and scope of a clinical trial. CTR is very clear on that all this should comply with the framework of the GDPR.

Concerning epidemiological research, Recital 157 of the GDPR underlines that researchers can obtain new knowledge on widespread medical conditions such as cancer by coupling information from registries. Provided that safeguards set by EU law or national law for the protection of privacy are complied with, registries should be allowed to process data even without patient consent.

A recent study, prepared for the Commission, has assessed Member States’ rules on health data in light of the GDPR. As the interpretation of the GDPR varies across Member States and national legislation linked to its implementation has created a fragmented approach, it has negatively affected cross-border cooperation for providing healthcare, healthcare system

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52 P.G.Casali: Data protection and research in the European Union: a major step forward, with a step back; Annals of Oncology, 2020
53 J. Hansen, P. Wilson, E. Verhoeven, M. Kroneman, M. Kirwan, R. Verheij, E-B. van Veen: Assessment of the EU Member States’ rules on health data in the light of GDPR
administration and research. During previous BECA hearings in November 2020 and February 2021, experts highlighted the unfortunate consequences of the GDPR on medical research, pointing to issues concerning comparability of the data needed for proper research. The GDPR left a margin of manoeuvre for Member States to further specify the application of the regulation in the area of health and Article 168 the Treaty on the Functioning of the European Union, therefore a fully harmonised approach to the rules on processing of data in the area of healthcare provision, administration or research across the EU has not been achieved. Furthermore, the interpretation of the law is complex for researchers at national level, and patients do not always find it easy to exercise the rights granted by the GDPR. The study has concluded that there is support for actions at EU level to promote health data access and sharing; such measures may include a combination of soft law, e.g. via a code of conduct, with other non-legislative and legislative actions. A code of conduct is considered desirable to explain concepts from the GDPR and to ensure a consistent approach to health data exchange at a more practical level, e.g. defining formats for data exchange. These aspects were detailed further during the BECA hearing of April 2021.

54 BECA hearing of 12 November 2020: “Supporting research on cancer - New mission on cancer within Horizon Europe”
55 Summary of the BECA hearing on “Supporting research on cancer - New mission on cancer within Horizon Europe”
56 BECA hearing of 23 February 2021: “From lab to life: transforming childhood, adolescent and rare cancer care”
57 Summary of the BECA hearing on “From lab to life: transforming childhood, adolescent and rare cancer care”
58 BECA hearing of 15 April 2021: “Cooperation is strength: sharing knowledge and data, improving cross-border care to beat cancer”
59 Summary of the BECA hearing on “Cooperation is strength: sharing knowledge and data, improving cross-border care to beat cancer”