From ‘Black Box’ to Trusted Healthcare Tools
Physiology’s role in unlocking the potential of AI for health

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Foreword

Through my academic work, I have seen the promise of artificial intelligence (AI) to revolutionise healthcare by significantly improving disease detection and prevention. In recognition of this transformative opportunity, the UK Government has emphasised the need to address major health conditions that contribute to extended periods of ill health by harnessing the opportunities of AI technologies. By adopting an integrated, whole-person approach to care, the Government aims to increase healthy life expectancy and reduce the prevalence of ill-health-related labour market inactivity. These ambitions have been supported by The Physiological Society in its previous reports, Growing Older, Better and Understanding ‘Early Exiters’: The Case for a Healthy Ageing Workforce Strategy.

Today, there is a keen desire to transition the NHS from what is often more akin to a “national sickness service” to a model focused on preserving good health by leveraging innovation and technology for early disease detection. This shift will facilitate timely interventions, alleviate pressure on an overburdened NHS and enable individuals to enjoy healthier lives for longer.

However, the successful implementation of AI tools in healthcare is not without its challenges and risks. From inaccurate diagnoses to perpetuating existing health inequalities through biased data and access, it is crucial to carefully develop, adopt and monitor AI tools to prevent potential harm.

To explore current perspectives on the role of physiology in developing and using AI tools within the UK health system, The Physiological Society consulted a diverse range of stakeholders. The consultation underscored the importance of incorporating physiological measurements and insights into the development of AI tools, as well as fostering a research ecosystem that leverages physiological understanding rather than dealing with sliced areas of specialism. Integrating physiological knowledge into relevant AI models and systems can enhance the understanding and interpretation of complex health data, ultimately leading to better-informed decision-making.

This report presents a set of recommended action for the Government, the NHS, research funders and other stakeholders to utilise physiology as a ‘guardrail’ when developing AI in health, in order to maximise the benefits while minimising risks. Our recommended actions highlight the critical role that physiologists and physiology play in underpinning effective AI tools by ensuring model plausibility, assessing relevant training datasets and improving the interrelationship between biomedical understanding, machine-learning systems and clinical expertise.

I am grateful to those who participated in the evidence-gathering and developed case studies that highlight how physiological measurements and knowledge are already being used alongside AI to support clinical decision-making and transform healthcare. I look forward to working alongside colleagues from across all sectors identified in this policy report to ensure we have a health system that is enhanced, and not stymied, by the introduction and deployment of innovative AI applications.

Richard Slow
Director, Ageing Research, King’s College London
Chair of The Physiological Society’s AI & Health Steering Group

1. www.physoc.org/policy/public-health-and-ageing/healthyageing/
Our call for change

The Physiological Society is concerned that artificial intelligence (AI) healthcare tools are being developed, approved, and adopted without sufficient physiological input. Based on our consultation with over 30 leading experts in this area (see Appendix), we argue that the limited inclusion of physiological evidence in the development of AI tools can lead to reduced trust, challenges with applicability and, at worst, to the identification of spurious correlations without sufficient physiological plausibility and ultimately harm to patients.

To harness the full potential of AI in healthcare and ensure its safe and effective implementation, we believe it would be beneficial to adopt a comprehensive approach based on the establishment of a Physiology & AI Framework, the prioritisation of physiological plausibility in research funding mechanisms and the inclusion of physiological evidence in the regulatory approval process.

The following recommended actions outline a strategic roadmap for achieving these goals, aiming to achieve improved patient outcomes, higher trust in innovative AI technologies and a more efficient healthcare system.

ACTION 1. Establish a Physiology & AI Framework to set improved guardrails for AI in health

To ensure that AI tools in healthcare are not only safe, but also accepted by their intended users and beneficiaries, The Physiological Society will coordinate efforts to establish a Physiology & AI Framework, working with stakeholders across healthcare services, research and AI.

The framework will set out principles for physiologically plausible technologies, improve dialogue and knowledge transfer between stakeholders and establish training programmes. This will help establish guardrails around AI and health by identifying how to integrate physiological measurements and expertise into technology development and testing, prior to deployment in healthcare settings.

Our ambition is that the framework will form the platform and evidence base on which regulators, funding organisations and policymakers make decisions on effective implementation of trustworthy AI health tools. The framework will include three key elements:

- The development and adoption of a set of principles and success criteria that describe physiologically plausible technological applications, to help lift the lid on the ‘black box’ that is AI.
- A forum to regularly bring physiologists together with other key stakeholders, to achieve a shared understanding of physiological plausibility, opportunities and risks of AI tools in healthcare.
- A training programme for physiologists, developers and data scientists, to create a shared language and understanding to build physiologically plausible technology by design.

ACTION 2. Ensure that research funding mechanisms prioritise physiologically plausible AI tools

Research funders should review the governance of funding mechanisms that concern the use of AI in healthcare. Where relevant, physiological plausibility should be included as a key decision factor in assessing the quality of grant proposals, and research teams should include physiological expertise.

ACTION 3. Embed physiological evidence in the regulatory approval of AI tools

The Medicines and Healthcare Products Regulatory Agency (MHRA), in partnership with other relevant regulators, should make physiological evidence and insight a foundation of their regulatory approval process for AI tools as medical devices.

Similarly, the National Health Service (NHS) and the National Institute for Health and Care Excellence (NICE) should update their assessment mechanisms for digital health technologies to include coverage of physiological evidence.

Through their centralised coordination function, the AI and Digital Regulations Service should ensure all collaborating regulatory organisations include physiological expertise and evidence in the assessment of relevant AI tools for healthcare.

The Physiological Society

As Europe’s largest society of physiologists, The Physiological Society has a worldwide membership across a wide range of disciplines and career stages. This report was written in conjunction with our members and external experts to explore the contribution that physiology can make to improving the development and rollout of AI-based technologies in healthcare.

The Physiological Society’s members are committed to improving human health and improving our dialogue with those working in decision-making roles to ensure that the most rigorous research is made available in a timely and easily understandable format so that positive changes can be made.

Physiological plausibility is defined in the field of AI and healthcare as the extent to which AI-driven models, predictions or conclusions align with known biological and physiological principles. AI algorithms or models generating results that can be convincingly linked to established medical, anatomical, or physiological knowledge are considered to have physiological plausibility. For example, an AI model predicting disease progression based on patient data would have physiological plausibility if its predictions were consistent with current medical understanding of that disease. This concept is crucial for ensuring the clinical validity and trustworthiness of AI systems in healthcare.
Introduction

The ever-increasing healthcare burden is giving rise to public health challenges

With a growing and ageing population, and an overburdened NHS, the UK healthcare system needs to adapt to ensure it is fit for the future. The Office for National Statistics\(^1\) estimates that by 2045, 4.3% of the UK’s population (3.1 million people) will be aged 85 years and over. This is almost double the figure recorded in 2020, where just 2.5% of the population were over the age of 85 (1.7 million people).

This significant demographic shift poses considerable public health challenges for the UK. In particular, older age is associated with an increase in complex and interconnected health issues. The number of people living with long-term conditions is set to increase and this will lead to increasing demand on the NHS. Chronic conditions, multi-morbidities and cognitive impairments will become more common and there will be increasing pressure on families and the care system.\(^2\)

AI tools in healthcare are developing fast but in silos

Artificial intelligence (AI) refers to the development of computer systems and algorithms that can perform tasks that would typically require human intelligence. These tasks include problem-solving, pattern recognition, learning from experience, understanding natural language and decision-making. Machine learning (ML) is a subfield of AI that involves building algorithms that can learn and improve from experience without being explicitly programmed to do so. Machine learning algorithms use statistical techniques to analyse data, identify patterns and make predictions or decisions.

There are several types of machine learning, including supervised learning, unsupervised learning and reinforcement learning.

In everyday language, AI and ML are often used synonymously. In the remainder of this report, we will only refer to AI for simplicity, but acknowledge that most applications we discuss are based on the sub-field of ML.

It’s pretty straightforward to build an AI model if you have a dataset available but the real difficulties are the practical implementation challenges.\(^3\)

Data scientist

Applications of AI in healthcare already cover a range of source data types, including structured, semi-structured and unstructured data. Several examples of using different data types are available in today’s landscape:

- Data from patient-monitoring devices collecting physiological measurements such as heart rate, blood pressure and oxygen saturation are being used to inform personalised care by KardiaMobile\(^4\).
- Participant entered data on sleep quality is being used by Sleepio\(^5\) to recommend behavioural changes.
- Combinations of different data types such as lab results, clinical notes and images can be analysed to predict risk and support treatment planning, as done by Transpera\(^6\) in the case of breast care.

Although the field is evolving rapidly, work tends to happen in silos. Because healthcare is a vast field, encompassing numerous specialties and sub-specialties, AI developers tend to focus on specific areas of expertise, leading to the creation of specialised tools that address specific medical conditions or processes. In addition, cross-disciplinary collaboration can be challenging due to differences in language, methodology and priorities, but also to growing competition. Finally, data sources can also complicate matters. Healthcare data are subject to strict privacy regulations, such as HIPAA\(^7\) in the United States and GDPR\(^8\) in Europe and are often unstructured and lacking agreements for re-use. This can limit data sharing between organisations, leading to isolated development environments.

Some of these barriers are structural and inherently difficult to address, but we believe that it is possible to achieve enhanced collaboration through the involvement of physiologists in the technology development pipeline. This will not only foster positive dialogue and cross-pollination of ideas, but most likely lead to an enhanced understanding of, and trust in, the results generated by a technology often seen as a ‘black box’.

There is a need for political commitment to validate and regulate AI tools in healthcare

In January 2023, the UK Government announced that a Major Conditions and Diseases Strategy\(^9\) will be developed, which aims to alleviate pressures on the healthcare system caused by an ageing population, increase healthy life expectancy and reduce labour market inactivity arising from ill health.

If the government wants to increase AI in healthcare, they need to engage with the disciplines that already know the subject matter. That means funding research which brings physiologists into modelling for algorithmic aspects of data processing and healthcare.\(^10\)

Academic researcher

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5. store.alivecor.co.uk/products/kardiamobile
6. www.sleepio.com
7. transperaobservetcare.com
8. www.hhs.gov/hipsaa/index.html
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10. questions-statements.parliament.uk/written-statements/detail/2023-01-24/hswe514
AI as an everyday tool: optimising intravenous fluid and vasopressor doses in patients with sepsis in intensive care

Sepsis is a life-threatening condition, when the body’s response to severe infection causes vital organs to stop working normally and is a major worldwide healthcare challenge. A key part of the treatment of sepsis is the administration of intravenous fluids and vaspressors. However, there is huge uncertainty around the individual dosing of these drugs in an individual patient. A tool to personalise these medications could improve patient survival.

Researchers at Imperial College London have developed a new method to automatically and continuously review and recommend the correct dose of these medications to doctors, which was created using AI techniques applied to large medical databases including large amounts of physiological data. As previous work had shown potential to improve patient survival rates, the team at Imperial College London has been developing a tool capable of processing patient data within the electronic patient record of NHS hospitals in real time, to recommend a course of action. This tool is being evaluated and refined in simulation studies.

The AI Clinician extracted implicit knowledge from an amount of patient data that exceeds many-fold the life-time experience of human clinicians and learned optimal treatment by analysing myriad (often sub-optimal) treatment decisions. However, its use is now being systematically tested to see how it performs with NHS clinicians in both simulated and real clinical scenarios. It has previously been demonstrated that the value of the AI Clinician’s selected treatment is on average reliably higher than that of human clinicians. It is currently being tested in two NHS Trusts, first in a ‘shadow mode’ when the result is not provided to the clinicians to allow comparison and understanding of actual decisions vs recommended AI decisions. In the second stage, the clinical evaluation is displayed to the treating clinicians to allow researchers to assess the clinical acceptability of the tool and also confirm the technical feasibility for future large-scale clinical trials.

Professor Anthony Gordon
Imperial College London

Dr Matthieu Komorowski
Imperial College London

Professor Aldo Faisal
Imperial College London

In the broader context of Government activity around AI (see Figure A for example developments from the last six years), the Major Conditions and Diseases Strategy aims to harness innovation and technology to tackle cancer, cardiovascular diseases, chronic respiratory disease, dementia, mental ill health and musculoskeletal disorders. There is strong cross-party commitment to the use of innovative technologies, such as AI and big data, including public pledges from the Labour Party to get into the NHS faster. Clearly, the UK’s political leadership has recognised that AI technologies present opportunities to support the NHS, but also that there are risks posed by the adoption of AI. In this context, the Government has announced they will host a summit in the autumn to consider the risks of AI and how they can be mitigated, as well as discuss a global coordinated approach with other countries.12

Rationale and methodology

The Physiological Society developed the present policy report in recognition of the limited involvement of physiologists in the development and adoption of AI tools in healthcare. Although this dynamic innovation holds significant potential to improve health outcomes, development is often happening in a fragmented way.

Our findings and recommended actions are based on desk research and engagement with over 30 experts, including academic and clinical researchers, medical professionals, data scientists and funders (see Appendix). The report was written in collaboration with GS Humphreys Consulting and Research Consulting.

A mix of focus groups, interviews and discussion with the project Steering Group helped shape a set of three recommended actions, which are covered in more detail in the following sections.

Figure A. A timeline of key developments around healthcare AI led by UK policymakers from 2017.

13. major-conditions-and-diseases-strategy-
17. questions-statements.parliament.uk/written-statements/detail/2023-01-24/hcws514
18. labour.org.uk/missions/building-an-nhs-fit-for-the-future/
20. labory.org.uk/news/uk-to-host-first-global-summit-on-artificial-intelligence
ACTION 1

Establish a Physiology & AI Framework to set improved guardrails for AI in health

To ensure that AI tools in healthcare are not only safe, but also accepted by their intended users and beneficiaries, The Physiological Society will coordinate efforts to establish a Physiology & AI Framework, working with stakeholders across healthcare services, research and AI.

Physiologists should participate in technological development to enable better AI tools in healthcare

Physiologists investigate how the body’s various systems (e.g. circulatory, respiratory, nervous and muscular systems) interact and function under different conditions. This can involve examining how these systems respond to environmental factors, stress, ageing, disease and other variables. Physiological measurements are critical to current routine assessment of human health including blood pressure, temperature, heart rate, respiratory rate, mobility and sleep monitoring, as well as many others. There are a growing number of commercially available devices that now assess these measurements and provide analysis using models developed with little or no involvement of physiologists.

Physiologists play a crucial role in building better AI tools in healthcare by contributing their expertise and knowledge of the human body’s complex systems and functions in two critical areas:

1. By providing insight into the underlying biological processes and mechanisms that drive various health conditions. This domain knowledge can help inform the development of AI algorithms and ensure that they accurately model the plausible physiological processes and reduce the risk of identifying confounding factors.

2. By helping assess, interpret and contextualise the data used to train AI models, ensuring that they contain plausible measurements and are representative against known standards for the target end users.

As a result, by engaging physiologists in technology development, there is potential to ‘lift the lid’ on the ‘black box’ of AI tools and develop human-centred technologies that have more accurate predictions and increased trust in the quality assessment. This is a critical factor that should be addressed not only by enhanced collaboration across academia, industry and health services, but also through strong government regulation and innovation frameworks.

A remarkable tale of success prediction in paediatric extubation at the Turing Institute

In an intriguing project conducted at the Turing Institute, data from Great Ormond Street Hospital (GOSH) were utilised to predict the success of extubation in children. The full details of the study can be found in their final report.

During the project, a consultant highlighted that gaps in one of the time series datasets (end tidal CO$_2$) were caused by patients coughing or making independent respiratory efforts. In clinical practice, this would prompt the removal of a part of the machine that measures end tidal CO$_2$, resulting in gaps in the trace. These gaps were subsequently quantified and became the only feature accurately predicting extubation success.

Prior to this discovery, PhDs, post-docs and professors working on the problem had employed various off-the-shelf algorithms without achieving the desired results. This fascinating case serves as a prime example of the significance of understanding physiology and its measurement.

“...It needs to be a human-centred technology, recognising that humans have limitations. Why we develop these tools is to transcend our limitations so that we can do things we couldn’t otherwise do. That surely is the point of technology.”

Academic researcher

23. www.turing.ac.uk/sites/default/files/2020-02/the_alan_turing_institute_data_study_group_final_report_-_great_ormond_street_hospital.pdf
Physiological insight can help improve health outcomes

To date, many of the AI-driven healthcare tools developed have focused on processing images, and it is expected that the analysis of images, such as CT scans, mammogram scans and X-rays will continue to benefit significantly from AI tools in the future.

Physiological insights around body temperature, blood pressure, heart rate, respiratory rate or mobility monitoring could all be combined with AI-based analysis to support early detection, particularly in high-risk groups like those with dementia or cardiovascular disease.

There is also potential for AI tools to improve detection by separating disease from normal ageing, which is not currently well recognised. Studying large datasets from healthy individuals to identify normal ageing patterns could help distinguish where there are physiological changes associated with disease or dysfunction.

Finally, AI tools have the potential to expand access to medical care for marginalised and under-represented communities, as well as those living in geographically remote areas. The development of remote monitoring tools that frequently collect basic physiological measurements like movement and heart rate could be used to monitor those at risk of falls or other conditions.

CASE STUDY

Understanding the basis of reproductive health through machine learning

One of these TEM images is Fake!

By enabling babies to grow well in the womb, the health of both mother and the child can be improved. Research from the University of Southampton explores structure and function relationships in the placenta and endometrium. Advances in imaging techniques are helping to achieve this, but they generate complex datasets, which are time-consuming to analyse. Using machine learning, the research seeks to analyse these images more quickly and to gain additional insights from this technology.

Machine learning algorithms can effectively recognise cell types and features in placental and endometrial tissue, allowing these data to be analysed much more quickly. Researchers have also trained machine learning algorithms to make fake photorealistic electron microscope images of placental tissue. These fake images demonstrate that the trained algorithm ‘understands’ all the spatial relationships between anatomical structures within the tissue, including intracellular components. The aim is to use the knowledge within the algorithm to explore how cells change in different physiological and pathological states.

The research has demonstrated the potential of machine learning to speed up image analysis and provide new ways of extracting biologically exciting and clinically relevant data. In doing so, machine learning can help enhance the health of mothers and babies during pregnancy and across the life course.

Professor Rohan Lewis
University of Southampton

CASE STUDY

Can ambulatory blood pressure measures inform shared treatment decisions in hypertension for older adults who are at risk of falls?

Two out of three people over 65 take treatment to lower blood pressure to prevent heart attacks and strokes. Blood pressure treatment also increases the chance of having a fall if blood pressure is lowered too much. As people get older, their blood pressure tends to rise and fall more dramatically. All this makes it hard to know how to accurately prescribe blood pressure treatment in later life.

The research proposes collecting ambulatory blood pressure by equipping patients with wearable monitors that take readings two to three times an hour over the course of a day. This more reflective measurement of a patient’s blood pressure will be combined with machine learning to look at the patterns of 24-hour blood pressure, allowing for a novel pattern recognition to predict a patient’s risk of heart attack and stroke, as well as possibly falls, to allow for proactive intervention where appropriate.

If you have a model that interprets a sick physiological signal or does something more efficiently in terms of predicting an individual person’s risk, that’s only part of the problem. You then also need to incorporate what you’re going to do about it, how is the patient going to be involved? Does it lead to an improvement in outcomes and then iterations, so the models are re-evaluated on a cyclical basis?"

Clinical researcher

Dr Oliver Todd
University of Leeds

In resource-poor settings, where there are fewer qualified healthcare personnel, the benefits of AI tools in healthcare become especially pronounced. For example, some countries have no pathologists at all and many settings could benefit from access to tools like handheld mobile ultrasound devices with built-in algorithmic data analysis.

Dr Oliver Todd is a clinical researcher at the University of Leeds. His work focuses on the development of AI tools to support healthcare providers, particularly in resource-poor settings.

Professor Rohan Lewis is a professor at the University of Southampton. His research focuses on the development of AI tools to support healthcare providers, particularly in resource-poor settings.
Combining physiology and AI in the context of the COVID-19 pandemic

AI can have a positive impact in identifying novel therapeutic approaches to disease management. For example, scientists used BenevolentAI’s Knowledge Graph to search through approved drugs to find treatments that could inhibit the extreme physiological response (known as the cytokine storm) that doctors had described in COVID-19 patients in February 2020, and identified baricitinib.

Through subsequent inclusion in multiple clinical trials, conclusive evidence was later collected that baricitinib was an effective treatment for COVID-19, reducing mortality by over 35%. This case highlights the crucial role that AI could play in advancing our understanding of human health and developing innovative approaches to disease management.

The Physiological Society proposes the introduction of a Physiology & AI Framework

The Physiological Society recognises the increasing importance of artificial intelligence (AI) in the healthcare sector and calls upon stakeholders from health, research and AI communities to join us in establishing a comprehensive Physiology & AI Framework. This framework will help create improved guidelines for AI in health throughout the entire development cycle, ensuring the safe and effective implementation of these innovative technologies.

The proposed Physiology & AI Framework will focus on defining key principles that should be considered during tool development while fostering open dialogue between academia, the private sector, government departments, the National Health Service (NHS) and regulators such as the Medicines and Healthcare Products Regulatory Agency (MHRA). By pursuing the creation of this framework, we aim to provide an improved foundation to help make better informed decisions regarding the implementation of AI health tools.

To achieve this goal, the Physiology & AI Framework will encompass the following key components:

- Development and adoption of a coordinated set of principles and success criteria that outline physiologically plausible technological applications, ultimately demystifying the ‘black box’ nature of AI. This will ensure that AI-based health solutions are grounded in physiological understanding and adhere to best practices.
- Establishment of a dedicated forum for regular engagement between physiologists and key stakeholders, fostering a shared understanding of physiological plausibility, opportunities and risks associated with AI tools in healthcare. This collaborative environment will facilitate knowledge exchange, driving innovation while addressing potential concerns and challenges.
- Implementation of a comprehensive training programme designed for physiologists, developers and data scientists. This programme will create a shared language and understanding, enabling participants to collaboratively build physiologically plausible technology by design. By equipping professionals with the necessary skills and knowledge, the programme will bridge the gap between physiology and AI, ensuring that emerging health technologies are both effective and grounded in scientific rigour.

ACTION 2

Ensure that research funding mechanisms prioritise physiologically plausible AI tools

To ensure that the most useful and effective tools are developed, research funders should review the governance of funding mechanisms that concern the use of AI in healthcare and, where relevant, include physiological plausibility as a key decision factor in assessing the quality of grant proposals.

ENSURE THAT RESEARCH FUNDING MECHANISMS PRIORITISE PHYSIOLOGICALLY PLAUSIBLE AI TOOLS

The funding landscape for AI healthcare research continues to develop

To date, millions of pounds of public funds have been allocated to research and development of AI-based applications in healthcare, including through collaborative investments – an approach that has been recommended by the Academy of Medical Sciences report.28 In 2019, the NHS AI Lab29 was set up to create an environment for collaboration and co-creation, by bringing together programmes that address the barriers to developing and deploying AI systems in health and care.

The following commitments provide an overview of this fast-developing area of research, as well as the key actors that have been influencing the funding landscape:

- In 2018 multiple agencies partnered30 to invest £210 million in the development of precision medicine for improved early diagnosis and treatment of common life-changing diseases.
- UK Research and Innovation are committed to supporting ‘bringing research, innovators and problem owners together for application-driven research and innovation in health’.31 In 2019, they contributed £79 million alongside £160 million from business and charities to fund the Our Future Health Programme,32 and from 2023 will invest £250 million33 in development of AI, quantum technologies and engineering biology, £110m of which will fund AI technology missions including a theme on ‘Healthy ageing’.
- In 2019, the AI in Health and Care Awards34 committed £123 million to invest in testing and evaluation of AI technologies with the aim to address clinical and operational challenges of implementing AI tools in the NHS.
- In 2020, the Office for Life Science awarded £16 million35 to the London Medical Imaging and AI Centre for Value-Based Healthcare to provide more innovative healthcare solutions to the public.
- In 2023, nine funders jointly awarded £70 million for five years36 of support for Health Data Research UK to ‘accelerate trustworthy access to health data and improve treatments’.
- Additionally, as part of 2023’s London’s Tech Week, UKRI announced £51 million investment in the UK’s position as a pioneer in artificial intelligence (AI) technology.37

What is currently missing is more significant inclusion of basic physiological principles and the involvement of physiologists, including in the grant review process. Moreover, funders should evaluate the presence of physiological expertise within project teams in grant proposals involving AI in healthcare settings. This emphasises the significance of a comprehensive understanding of the human body, complementing specialised knowledge.

Physiological plausibility should be embedded in AI tool development

Most AI applications currently in use in healthcare extract patterns from observational data. Often, this process leads to associations with no plausible physiological causation. This is why the methods of experimental science have been developed, for example randomised clinical trials, and why it is so important to involve scientists in the development process of AI tools.

In 2019, the AI in Health and Care Awards committed £123 million to invest in testing and evaluation of AI technologies with the aim to address clinical and operational challenges of implementing AI tools in the NHS.

- In 2020, the Office for Life Science awarded £16 million to the London Medical Imaging and AI Centre for Value-Based Healthcare to provide more innovative healthcare solutions to the public.

CASE STUDY

Using AI to develop better treatments for ovarian cancer

Ovarian cancer comes back after treatment in around seven out of ten patients, often within two years. The disease recurs because tiny quantities of cancer cells are left behind after the first treatment, which then grow in number and possibly spread to other organs. Researchers at the University of Oxford are trying to understand what makes these residual cancer cells different and enables them to survive initial treatments. This knowledge will help to develop new treatments to target and destroy these cells, preventing the disease from coming back again.

In collaboration with Singula Bio, laboratory-based and AI researchers have worked together to create new DNA sequencing tools and computer programs that enable the study of these residual cancer cells. Conventional DNA sequencing methods require the availability of hundreds or thousands of cells, but new techniques were needed that could analyse samples containing only tens of cells. However, data from these experiments also tend to be more complicated and so AI algorithms were developed to interpret the data and identify the mutations linked to these residual cells.

One model identified any image with a ruler as associated with poor cancer outcomes because images of likely tumours included a ruler for sizing purposes, and these images had been used to train the model.

Academic researcher

Academic researcher

CURRENT OVARIAN CANCER TREATMENT AND OUTCOME

Ovarian Cancer Cells

Residual Cancer Cells

Before Chemotherapy

After Chemotherapy

Recurrence

DNA and AI Analysis

ImmunoTherapy

CASE STUDY

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One model identified any image with a ruler as associated with poor cancer outcomes because images of likely tumours included a ruler for sizing purposes, and these images had been used to train the model.

Academic researcher

Academic researcher
It is, therefore, important to ensure that the technology correctly interprets underlying physiological markers, to prevent the development of opaque methodologies. In this context, it is helpful to introduce the concept of physiological plausibility, meaning the extent to which AI-driven models, predictions, or conclusions align with known biological and physiological principles.

**Multiple strategies can help promote the integration of physiology in grant proposals related to AI in healthcare**

As we have showcased through several examples, the rapid growth and potential of AI in healthcare has generated significant interest among researchers, healthcare professionals and policymakers. However, to fully harness the benefits of AI-driven solutions, research funders should review the governance of funding mechanisms concerning the use of AI in healthcare settings. In particular, they should ensure that physiological plausibility is included as a key decision factor when assessing relevant grant proposals and that research teams incorporate physiological expertise. To support transformational medical research with potential practical applications, a strong collaboration between AI developers and healthcare professionals who have the necessary expertise in physiology is required.

"From my point of view, physiological measurement scientists are the bridge between the research and implementation, and they are currently blocked out of doing research and development because they don’t have the funding. UKRI don’t explicitly exclude them from funding calls, but they do nothing to support them or encourage them."

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**ACTION 3**

**Embed physiological evidence in the regulatory approval of healthcare AI tools**

By including physiological plausibility as a key decision factor in relevant funding mechanisms, research funders can encourage the development of AI tools that are grounded in an understanding of the human body as a system. Moreover, by advocating for the inclusion of physiological expertise in research teams, research funders can foster interdisciplinary collaboration, which is crucial for driving innovation in AI healthcare tools.

In practice, funders may approach the above in a wide range of ways, offering flexibility in implementation. For example, when assessing healthcare AI applications that use physiological measurements or publishing calls in this area, funders may:

- Ensure that grant review panels have a diverse mix of expertise, including individuals with strong backgrounds in physiology.
- Develop and provide clear guidelines for applicants, stating the importance of incorporating physiological expertise and principles into proposed research projects.
- Promote interdisciplinary collaboration by encouraging grant applicants to form research teams that include experts in physiology alongside technologists and other medical specialists.
- Create dedicated funding opportunities aimed at promoting the integration of physiological expertise in healthcare AI research.

To enhance the regulatory process to ensure safe and effective tools are approved and adopted the Medicines and Healthcare Products Regulatory Agency (MHRA), in partnership with other relevant regulators, should make physiological evidence and insight a foundation of their regulatory approval process for AI tools as medical devices. Similarly, the National Health Service (NHS) and the National Institute for Health and Care Excellence (NICE) should update their assessment mechanisms for digital health technologies to include physiological evidence. Through their centralised coordination function, the AI and Digital Regulations Service should ensure all collaborating regulatory organisations include physiological expertise and evidence in the assessment of relevant AI tools for healthcare.
AI tools can effectively support clinical decision-making

Many hours of highly trained healthcare staff time are currently employed in routine tasks, which computers may be better placed to perform in the future. Scanning data for patterns or anomalies are examples of where AI tools are best placed to increase efficiency.

We’re using AI-driven tools in a trial to identify ECGs which show signs of possible atrial fibrillation, so that they can be sent for manual review by a cardiologist. This is an important step because typically participants in this trial each record approx. 84 ECGs, so it wouldn’t be feasible to send them all for clinical review.

Academic researcher

The potential for AI tools to assist clinical decision-making processes is substantial. For example, in the case of head and neck cancer treatment, a radiotherapist can spend over four hours per patient reviewing CT scans to identify regions to avoid for radiotherapy near a tumour.24 Applying algorithms trained to identify and isolate such regions within scan images would likely lead to significant time savings for radiotherapists, although their trained eye would still be needed in checking automated outputs. As a matter of course, healthcare providers should make clear to patients when AI tools are used, supporting users to understand the role of physiological evidence in the development of accurate and trustworthy technology.

It has to be something that improves over and above what a human can do. To identify where the need is, it is key to involve the end user and people who think about end users all the time in the design and working out where tools are needed and that’s not being done, I don’t think.25

Clinical researcher

In practice, while AI has made significant advancements, human specialists remain indispensable. Their years of education, training and experience equip them with a deep understanding of their field, enabling them to make nuanced judgements and complex decisions that AI cannot replicate. For example, medical decisions also involve ethical dilemmas that require value-based judgements, which human specialists are better equipped to navigate. In addition, AI may struggle with rare or atypical cases and conditions that lack sufficient data for training, whereas specialists can draw upon their knowledge and experience to address these challenges.

Regulatory transformation is essential to keep the UK healthy

We believe that the NHS will need to play a key role in communicating the importance of a whole-person approach to care, which requires abundant, representative and well-governed data. For example, the 2019 Topol Review26 was commissioned by the Secretary of State for Health and Social Care to ensure the NHS is the world leader in using digital technologies to benefit patients. The Review acknowledged the need to explore emerging technologies in a global context where people live longer and with more long-term conditions. The Review rightly noted that “digital healthcare technologies, defined (...) as genomics, digital medicine, artificial intelligence and robotics, should not just be seen as increasing costs, but rather as a new means of addressing the big healthcare challenges of the 21st century”.

There are already internationally agreed upon broad principles for the design and use of AI in health that have been published by the World Health Organization in 2021.27 At the national level, the UK Government recently published an AI Regulation White Paper28 which highlights five principles for UK regulators to achieve responsible innovation using AI: safety, security and robustness; appropriate transparency and explainability; fairness; accountability and governance; and contestability and redress. However, more detail on how to achieve these principles is needed.

Without regulation I worry that the current tools would be biased, inaccurate, wouldn’t respect privacy, people wouldn’t have given permission for their data to be used and that might lead to them being disadvantaged in some way by the creation of these tools.

Clinical researcher

In practice, current UK regulations for medical devices are seen as not being sufficiently agile and flexible to react to the speed of technological developments in AI, hence the MHRA embarking on the Software and AI as Medical Device Change Programme.29 Through the central coordinating advice of the AI and Digital Regulations Service30 it will be critical to involve all stakeholders in the regulatory framework, including physiologists. Guidance and resources on digital healthcare technologies provided by the service should include the importance of physiological plausibility to help improve uptake of effective and trustworthy tools.

Finally, building broader transparency and trust in AI tools includes embedding physiological insight into the mechanisms used to scrutinise public policy. Several Parliamentary committees are involved in collecting evidence as part of inquiries, including recent efforts by the Science, Innovation and Technology Committee31 and the Health and Social Care Committee.32 We strongly recommend that these bodies include requests for physiological evidence as part of their efforts, to ensure that the policymakers are better equipped to make decisions with an impact on the development of regulation and the delivery of health services using AI technologies.

CASE STUDY

Quantum healthy longevity innovation mission

A mission to increase healthy life expectancy and minimise health and wellbeing inequalities was launched in November 2022, aiming to create the world’s first test bed for health underpinned by growing understanding of the exposome. The mission is focused on innovation clusters, enabled by regulatory reform, to drive discovery and research in healthy longevity.

This mission is underpinned by the co-design and co-development of a global federated exposomic AI sandbox and data platform, to create a longitudinal map on both the exposome and critical biomarkers that will enable the understanding of healthy ageing and the prevention of frailty and age-related multimorbidity. The mission is enabled by pro-innovation regulatory reforms underway in the UK, including around crowd-sourced exposome data from new channels like personal data intermediaries and open-source platforms to capture frequent digital measurements at scale using consumer technologies. This can help identify key markers of resilience non-invasively, passively, continuously and in a real-world context. Robust and comprehensive citizen engagement and involvement is central to each aspect of the programme.

Tina Woods
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39. toplot/nuki.html
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Clear requirements should be set on the features of reliable training data

There is considerable concern around biases in the data used to train AI tools, and it is broadly agreed that AI model building is not what is preventing progress. While models are shown to be effective within the setting in which the data originate, they typically do not perform well when applied in other settings. For example, many datasets are not representative of the population on which they are intended to be used. Data have often been collected on population cohorts that have gaps relating to disadvantaged or marginalised communities, which historically have lower rates of screening programme uptake.

You’re learning about a very sparse representation of human biology and behaviour through the data available to you. So, you have to overlay reasonable structure. That is a statistical conversation between the big data world and disciplines, and I’ve not seen much of physiology in that conversation.

Academic researcher

Importantly, AI models need to be updated over time as the population changes, which requires the regular input of new physiologically relevant data.

I think this is where most of the current AI tools are going to fail completely, as they haven’t validated them on a big enough cross section that is representative of people.

Academic researcher

Diverse physiological data contribute to creating better, fairer AI for clinical decision support

Skein developed an integrated platform that collects data from patient-focused mobile app, wearable devices and subcutaneous sensors to inform AI-driven decision support for diagnostics and prognostics of neurological conditions. It is currently being tested for migraine and is planned to be piloted for people with Parkinson’s.

Incorporating heterogeneous data into the AI models, enabled more accurate and reliable predictions for the complex neurological conditions to be achieved. Moreover, by validating the quality and representativeness of the data it was possible to provide better explainability of the AI algorithms, helping distinct groups of clinical decision-makers to receive trustworthy predictions and ensure compliance with AI ethics regulations adjusted to their preferences, working patterns and goals.

While the system is still at the validation stage, it has indicated the potential to significantly cut costs and reduce pressure on the healthcare system by allowing at-home monitoring and care, reduce the time and effort by clinicians and better serve the under-represented groups of patients.

This project is part-funded by the European Commission (grant agreement 101057524)

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The UK as a centre of excellence for population-scale health data

The UK is well positioned to utilise population-scale health data to identify patterns and predict health outcomes and complications. This can facilitate proactive decision-making and effectively prevent adverse medical events. Significant progress has already been made leveraging data resources such as the UK Biobank. However, with a limited dataset containing only 60,000 individuals’ information, its generalisability is restricted and there are long-standing concerns over the equity of the collected data. Addressing this gap requires deeper engagement and investment in building inclusive, national health datasets that are assessed for representativeness against standards developed by trusted professionals like physiologists.

It seems like a lost opportunity that we’ve got the NHS who are responsible for our healthcare that has all of these data and yet it’s so fragmented. It seems so difficult to gain approvals to join up the dots to be able to create nationally available datasets and there needs to be really rapid acceleration of trusted research environments.

Clinical researcher

There are efforts to significantly improve collection, integration and access to representative health data across the UK for research and development including Our Future Health Programme and activities led by Health Data Research UK.
There is a need for coordination of physiological insight across regulators

The Government’s AI regulation impact assessment\(^1\) (currently under consultation) describes the preferred policy as delegating to existing regulators. Without central guidance from Government, there is a risk of adding to the already fragmented regulatory regime. This is of particular concern in high-risk settings such as healthcare, and it is imperative that physiological insight is applied rigorously and consistently across regulators. The UK Government has also highlighted the need to create new central functions to coordinate, monitor and adapt the approach across regulators.\(^2\)

We propose that, where appropriate for AI health tools, physiological assessment should be integrated within the suggested new central functions outlined in the AI regulation impact assessment\(^3\) in order to produce joint guidance and ensure a test of physiological plausibility is applied to each relevant tool undergoing regulation. Such guidance and coordination could perhaps be carried out by the existing AI and Digital Regulation Service and informed by the principles in our proposed Physiology & AI Framework.

There is an opportunity to simplify the adoption of non-medical AI tools by national health services

NHS procurement of AI-based tools is a complex and challenging undertaking and can include regulated medical devices as well as non-medical devices like commercially available applications or wearables.\(^4\) The limited evidence of real-world effectiveness for AI-based tools can make it difficult for the NHS to justify procurement decisions. While these tools may show promise in controlled research settings, there may be insufficient evidence to demonstrate their effectiveness in real-world healthcare environments. This issue is even more significant in cases where physiological insight has not been part of the development process.

Additionally, integrating AI tools into existing technological infrastructure and systems can pose significant challenges. The NHS needs to address interoperability concerns to ensure seamless integration and avoid disruptions in clinical workflows. The use of AI in healthcare also involves the processing of sensitive patient data, which raises critical issues related to data privacy and security. Health services may struggle to assess and compare different solutions, making it difficult to determine which ones are most suitable for their needs. The NHS seeks to bridge this gap by using their Digital Technology Assessment Criteria (DTAC), which serve as a framework for evaluating digital health technologies not classified as medical devices, ensuring that they meet the necessary standards in terms of clinical safety, data protection and technical assurance. The National Institute for Health and Care Excellence (NICE) have also developed an Evidence Standards Framework (ESF) for digital health technologies to support decision makers in the health and care system to evaluate tools.\(^5\)

However, with the rapid developments in AI tools, it is essential that the DTAC and the Evidence Standards Framework is updated to address the unique challenges and opportunities presented by these technologies. A key area of focus should be on the physiological evidence underpinning AI algorithms, as this is fundamental to their effectiveness and safety in delivering patient care.

### My impression is that the NHS as a whole does not have a cohesive or coherent strategy for engaging the market, and therefore procurement and deployment are very challenging.

**Clinician**

Incorporating the evaluation of physiological evidence into NHS’ DTAC and NICE’s ESF for Digital Health Technologies will prompt AI healthcare tool developers to prioritise the robustness and validity of the data on which their algorithms are based. This includes ensuring that the data used to train AI models are representative of the diverse patient populations in the UK, reducing the risk of biased or inaccurate predictions. Additionally, a need to provide physiological evidence will encourage developers to demonstrate the clinical relevance of their AI tools, showing how their algorithms can improve patient outcomes and contribute to more efficient healthcare delivery.

Clear communication of any updates to assessment mechanisms for digital health technologies is essential for fostering trust among internal and external stakeholders. This includes engaging with healthcare professionals, patients, technology developers and regulatory bodies to ensure that they understand the rationale behind the updated criteria and the implications for AI healthcare tools. By fostering an open dialogue and promoting transparency in the evaluation process, regulators can demonstrate their commitment to responsibly developed and trustworthy technology.

### CASE STUDY

**AI technology can be used to predict heart attacks from routine coronary computed tomography angiograms**

Cardiovascular disease is the number one cause of death in the UK. Heart attacks happen when inflamed atherosclerotic plaques in our heart arteries break up, blocking blood flow to the heart. Finding these inflamed plaques would allow aggressive treatment of the right patients with low-cost drugs like statins, preventing heart attacks and saving lives.

The technology led to the Oxford Spinout company Caristo Diagnostics, to develop a CE-marked medical device called CaRi-Heart®. This cloud-based medical device is now deployed in the first NHS Trusts, allowing doctors to predict heart attacks and focus their attention to the right patients. CaRi-Heart® currently changes medical management in about 40% of the patients undergoing the test, transforming patient care.

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50. Ibid.
51. Ibid.
The way forward

Artificial intelligence has the potential to revolutionise healthcare, by helping build a proactive model that preserves good health through innovation, responsible technology development and early disease detection. However, harnessing AI’s potential in healthcare requires overcoming challenges and risks, such as inaccurate diagnoses and perpetuating health inequalities. To address these concerns, we emphasised the importance of integrating physiological measurements and expertise into AI tools and fostering a research ecosystem that encourages collaboration between biomedical understanding, machine learning systems and clinical expertise. This document presents our recommended actions for maximising the benefits of AI tools in healthcare while minimising risks. By continuing to explore and invest in the use of AI in healthcare settings, the UK Government can ensure that our healthcare systems are better equipped to tackle a changing and ageing population. This will not only improve health outcomes, but also contribute to a more sustainable and efficient healthcare system.

Together, we will unlock the potential of AI to revolutionise healthcare and improve patient outcomes, increase healthy lifespan and reduce the overall burden on the NHS.

Appendix - Contributors

Steering Group members
The Physiological Society is grateful to individuals who agreed to be members of this report’s Steering Group. The views, opinions and actions discussed in this report are those of The Physiological Society and should not be attributed to any individual or organisation listed as a Steering Group member.

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As the largest network of physiologists in Europe, with academic journals of global reach, The Physiological Society continues a 145 year tradition of being at the forefront of the life sciences. We support the advancement of physiology by promoting collaboration between physiologists around the world, organising world-class conferences and publishing the latest developments in our scientific journals. Research in physiology helps us to understand how the body works in health, what goes wrong in disease, and how the body responds to the challenges of everyday life.