The Academy of Medical Sciences

Response to the Wellcome Trust consultation on oversight: emerging science and technology

November 2018

Summary

- There are many emerging innovative areas of science and technology with the potential to improve health, which will challenge existing paradigms for medical research and healthcare delivery. For example, these include advances in genomics, genome-editing, advanced therapies and data-driven technologies such as artificial intelligence.
- This creates challenges to current models of oversight for emerging science and technology, bringing new debates in areas such as regulation, ethics and privacy to the fore. However, it is important to recognise that many of the same principles of current oversight may still apply and, in some cases, simply need to evolve.
- There is a need to ensure an agile and flexible UK environment for oversight to respond to these innovations, which is able to adapt quickly as they emerge whilst protecting patient and public safety.
- Exemplars of good practice already exist where the UK has led on oversight of emerging science, such as on mitochondrial replacement in *in-vitro* fertilisation. The UK has a forward-thinking and responsive regulatory system for science and technology, and it is important that this continues to be supported as new technologies arise.
- It is essential that any mechanisms for oversight involve key stakeholders from across the life sciences including academia, industry, regulators, patients and the public, the NHS and others. Any horizon-scanning mechanisms should also involve this range of expertise to maintain an awareness of the developments that are taking place across different sectors.

Introduction

1. The Academy of Medical Sciences promotes advances in medical science and supports efforts to see these translated into healthcare benefits for society. Our elected Fellowship includes some of the UK's foremost experts in medical science, drawn from a broad range of research areas. The Academy of Medical Sciences and Wellcome share a common vision of promoting excellence in medical science and ensuring its translation into healthcare benefits for society.
2. We are pleased to have the opportunity to respond to Wellcome's inquiry into oversight of emerging technologies and science. The Academy is monitoring the rapid development and application of technologies such as genomics, genome editing, data-driven technologies such as artificial intelligence (AI) and regenerative medicine, amongst other areas, and is seeking to contribute to these discussions.[1,2,3,4]
3. While there is not a universally accepted definition of 'emerging science and technologies' for medical science and health, these can be considered as emerging innovations that have the

[1] Academy of Medical Sciences (2016). *Response to the Nuffield Council on Bioethics Genome Editing Call for Evidence.* https://acmedsci.ac.uk/file-download/38579-56bc88dc0dea4.pdf
[2] Academy of Medical Sciences (2016). *Response to the House of Commons Science and Technology Committee inquiry into regenerative medicine.* https://acmedsci.ac.uk/file-download/41544-579600d1a3795.pdf
[3] https://acmedsci.ac.uk/policy/policy-projects/use-of-patient-data-in-healthcare-and-research
[4] Academy of Medical Sciences (2017). *Response to the House of Commons Science and Technology Committee inquiry into genomics and genome-editing.* https://acmedsci.ac.uk/file-download/83063056

potential to substantially impact society in the future, with significant potential to both improve research and development processes as well as healthcare. Therefore it is critical that such innovations are supported by a robust evidence base and oversight mechanism which is sufficiently flexible and balanced to support the development and uptake of novel technologies whilst ensuring they are introduced in a safe, reliable and transparent manner.

4. Our response is based on input from our Fellowship with expertise across many different scientific disciplines and applications, as well as our recent policy work in these areas. It focuses on scientific areas such as genome editing, advanced therapies, genomics and data-driven technologies such as AI, but there are other emerging areas within medical science which will also demand considered approaches to oversight. Our response addresses three areas: opportunities and areas of emerging science and technology where oversight could be improved; what 'good' approaches to oversight look like, and mechanisms for horizon scanning for these areas in the future.

What are emerging areas of science and technology where oversight may need to be improved or considered for the future?

5. The Academy previously explored animals containing human material as an emerging scientific area for oversight, and processes have since been put in place for the scientific community to enable such oversight.[5] This area needs to be monitored and kept under review for further developments.

Data-driven technologies and use of patient data

6. Data-driven technologies have the potential to transform research and healthcare through enabling the linkage and analysis of many different types of data, and potentially deriving faster, more accurate or new insights from these data.[6,7] These range from wearables and health apps, through to AI and machine learning employed in areas such as automated insulin pumps and medical scan analysis.
7. These technologies are already posing challenges to the existing oversight of traditional medical 'devices'. Firstly, they present challenges around the regulation and governance of the use of patient data, such as data control/stewardship, consent, data ownership, access, and protection of privacy and confidentiality. Secondly, these relate to the safety and effectiveness of the technology itself, with questions around reliability, safety and transparency of analytical and decision-making processes, and where liability lies for these. Therefore oversight is needed across the whole technology lifecycle from data acquisition through to deployment and evaluation of technologies. This can build on current work to address some of the specific challenges such as through the NHS Apps Library, which has started to evaluate the safety and effectiveness of different health apps to facilitate the use of high-quality products in the NHS.[8] Appropriate end-to-end oversight of data-driven technologies is needed so that the UK can make full use of them for the benefit of patient care, research and innovation, NHS services and public health.

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[5] Academy of Medical Sciences (2011). Animals containing human material. https://acmedsci.ac.uk/file-download/35228-Animalsc.pdf

[6] Government Office for Science (2017). *Technology and Innovation Futures.* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/584219/technology-innovation-futures-2017.pdf

[7] Department of Health & Social Care (2018). *Initial code of conduct for data-driven health and care technology.* www.gov.uk/government/publications/code-of-conduct-for-data-driven-health-and-care-technology/initial-code-of-conduct-for-data-driven-health-and-care-technology

[8] https://apps.beta.nhs.uk/

8. The Academy recently carried out a programme of dialogue with the public, patients and healthcare professionals on their views and expectations around use of data-driven technologies in healthcare, and will shortly publish a policy report based on the findings of this dialogue that sets out principles to guide their design, use and deployment in healthcare.[9] In particular, this emphasises the importance of continued engagement and partnership with patients and the public as part of any oversight of emerging technologies.
9. AI presents unique challenges for oversight in the context of adaptive algorithms and autonomous decision-making. It is also highly pervasive, from use in research, drug development and clinical trials, through to diagnosis, treatment decisions and patient self-management. It can be potentially used in ways that are considered 'high impact', such as the automatic administration of treatment. In addition, the algorithms evolve as they are continuously trained on more data, which means that AI examined at the initial regulatory phase will not be the same version operating at a future date.[10,11] This will demand new considerations for the ethics, regulation and evaluation of tools where decision-making processes and even the decisions themselves may change over time. There is an opportunity for the UK to lead on developing an adaptive or 'rolling' system of regulation that meets these needs.
10. Finally, a subset of data-driven technologies will operate as a 'black box' where it is not clear how they have reached a decision due to limited visibility of their analytical and decision-making processes. This creates issues for accountability and liability when using these technologies in research and healthcare when their full reasoning cannot be explained and so it may be more difficult to follow or overrule the advice given.

'Consumer health' technologies

11. 'Consumer health' technologies are becoming increasingly prevalent and will challenge current oversight and regulation for 'medical' products. These are health technologies that are available to the public, such as home genetic testing kits that can be ordered online and mobile health apps, which offer patients direct access to actionable health information and bypass an interaction with the healthcare system. For example, an individual could order a test online, which is then sent to a laboratory, and the results fed back directly to the individual with no involvement of a clinician. This circumvents the usual interaction of a patient with the healthcare system such as the NHS.
12. Consumer health products pose particular challenges around how health information can be provided in an accessible and useful manner if there is no expert healthcare professional acting as an intermediary and helping to interpret the result. In addition, there are issues around who can obtain and provide this health information, which leads to challenges around the regulation, standardisation and quality assurance of these tests and technologies for users.

Genomics

13. Advances in genomics (and other 'omics such as proteomics, metabolomics etc) can significantly enhance our understanding of the molecular basis of disease for health benefit. This can range from fundamental research into the biology of the human body and the genetic determinants of human diseases, through to supporting the development of new therapies and personalised or preventative medicine.
14. Oversight of the collection, access and linking of genomic data, and how this information is applied in research and healthcare, is essential. Learnings can be drawn from the success of

[9] https://acmedsci.ac.uk/policy/policy-projects/use-of-patient-data-in-healthcare-and-research
[10] Academy of Medical Sciences (2017). *Response to the House of Commons Science and Technology Committee inquiry into algorithms in decision-making*. https://acmedsci.ac.uk/file-download/79291192
[11] Academy of Medical Sciences (2017). *Response to the House of Lords' Artificial Intelligence Committee call for evidence.* https://acmedsci.ac.uk/file-download/47067991

the 100,000 Genomes Project in the handling of genomic data and managing its use in individual care, as well as its successful establishment of committees with oversight of aspects such as ethics and data access.[12]

Advanced therapies

15. Advanced therapies such as gene and cell therapies provide exciting opportunities for more personalised medicine in areas of high unmet need, with the potential to be 'curative' for some diseases. The UK has a world-leading research base and industry in cell and gene therapies, and it is important that we continue to capitalise on this opportunity, particularly post-Brexit.
16. These types of therapies are continuously evolving. For example, there are already some gene therapies approved for use in the UK, with ongoing trials of gene therapies in multiple therapeutic areas and the potential for the future creation of regenerative medical centres (already established in the US) likely to follow in the UK. In addition, aspects such as delivery mechanisms for cell and gene therapies into the human body are also constantly evolving, such as next generation viral vectors or non-viral vectors such as exosomes, which will require new development pathways and regulatory processes in their own right.
17. Advanced therapies, therefore, present a series of new regulatory and ethical challenges, which are likely to be specific to the type of therapy. There are already examples of good practice for aspects of oversight in this area, such as the Health Research Authority's Gene Therapy Advisory Committee, that was set up specifically to review the use of gene therapies in clinical research.

Genome editing

18. Genome editing encompasses a variety of techniques, such as TALENs, zinc-finger nucleases and CRISPR-Cas9. The merits and limitations of using genome editing, as well as the surrounding regulatory and ethical discussions, differ depending on the intended use. For example whether it is used for research compared to as a therapeutic.[13] In addition, perspectives on ethics and regulation differ between somatic and germline genome editing techniques.
19. Genome editing using somatic cells for both research and clinical settings is already well regulated by the Human Tissue Authority (HTA), with any clinical applications licensed by the Medicines and Healthcare products Regulatory Agency (MHRA). The Human Fertilisation and Embryology Authority (HFEA) also represents a successful example of good oversight, in this case overseeing genome editing in embryos, currently for research purposes.
20. However, the use of genome editing techniques in gametes or embryos for clinical use is not yet legal and so constitutes an emerging technology and application, which will need further discussion around oversight, regulation and potential complications, such as off-target modifications. As genome editing evolves, new challenges will arise and so it is important that the UK is prepared to address these.

Approaches to oversight: what are the key elements of good oversight that should be in the UK's approach for emerging science and technology?

21. Oversight should span the entire pipeline for science and technology, from fundamental research through to clinical use and post-marketing surveillance. In particular, there are new challenges arising for post-marketing surveillance and so a demand for more innovative approaches to this which should build on learnings from previous issues for technologies such as vaginal mesh implants and Poly Implant Prothese (PIP) implants.

[12] www.genomicsengland.co.uk/the-100000-genomes-project/

[13] Academy of Medical Sciences (2016). *Response to the Nuffield Council on Bioethics Genome Editing Call for Evidence.* https://acmedsci.ac.uk/file-download/38579-56bc88dc0dea4.pdf

22. It is also important to consider the different contexts in which an innovation might be used. For example, whether it is being used in research compared with a clinical application, as these will have different considerations and ethical and regulatory frameworks. Ongoing dialogue between scientists and society about the merits (and limitations) of emerging science and technology in these two contexts will be important.
23. Oversight should be considered in an international context, and the UK must continue to operate a flexible system that accommodates innovation and leads on discussions around the regulation and translation of 'breakthrough' science. For example, in the case of novel mitochondrial replacement *in-vitro* fertilisation work, UK legislation was pioneering and key to facilitating this field of research.[14] It is important that the UK continues to demonstrate such leadership post-Brexit.
24. Oversight must be proportionate and fit-for-purpose, accompanied by regulatory and governance systems that are robust and also innovative and flexible so that they can rapidly respond and adapt to emerging new science and technologies. It is essential that guidance for emerging science and technologies is responsive and timely. For example, past delays in publishing guidance, such as the *'Guidance on the use of human materials in animals'*, which was published five years after the Academy's report on this topic, would impede the development and translation of new science.[15,16]
25. This flexible oversight can build upon the existing strengths of UK regulators in adapting to accommodate new technologies, such as through the MHRA's Early Access to Medicines Scheme aimed at accelerating access to innovative medicines in areas of high unmet need.[17] Opportunities for early dialogue about new science and technologies, such as the MHRA's scientific advice function, will be important for informing and preparing oversight mechanisms. The protection of patient safety is paramount, but unnecessarily burdensome regulation or governance processes have the potential to delay access to health interventions, and so a balanced is needed. Therefore oversight mechanisms should incentivise rapid uptake of interventions, taking into account the importance of faster patient access to safe, regulated medicines. For example, one area where a regulatory framework has caused a barrier to research is the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use's Good Clinical Practice (ICH-GCP). These guidelines, which are not fit-for-purpose for some research settings and are often inappropriately applied to trials where they are not relevant, can potentially stifle innovation and create barriers to developing new technologies.[18]
26. One mechanism by which new science and technologies can be tested in a 'safe' environment is through regulatory sandboxes. These sandboxes would allow innovative regulatory frameworks to be adapted and tested for different technologies in a small, controlled environment. In addition, they enable regulators to engage with innovative scientific approaches.
27. The UK is also well placed to address the ethical questions surrounding emerging science and technologies such as genome editing and regenerative medicine, building on its extensive

[14] House of Commons' Science & Technology Committee (2014). Mitochondrial donation. www.parliament.uk/documents/commons-committees/science-technology/Mitochondrial%20donation/MITCorrespondence.pdf
[15] Home Office (2016). *Guidance on the use of animals containing human material.* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/491496/Animals_Containing_Human_Material_Final_Guidance.pdf
[16] Academy of Medical Sciences (2011). *Animals containing human material*. https://acmedsci.ac.uk/file-download/35228-Animalsc.pdf
[17] www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams
[18] Academy of Medical Sciences, Bill & Melinda Gates Foundation and Wellcome Trust (2018). *Exploring Good Clinical Practice guidance in clinical trials – meeting summary.* https://acmedsci.ac.uk/file-download/76367131

history of overseeing debate on similar topics. For example, there was substantial discussion around the ethical aspects of establishing the UK Biobank in 2007 and the 100,000 Genomes Project in 2012.[19,20] In the future, appropriate regulation of genome editing, for example, will need to consider ethical questions – alongside ongoing discussions about safety and efficacy – around aspects such as the potential clinical application of these techniques and ethical considerations for where and how these might be applied. Appropriate expertise and professional input, as well as ongoing and open dialogue with the public, will be essential to understanding any concerns around use of emerging science and technologies and building a robust ethical framework. The existence of robust regulatory frameworks will provide further reassurance around the appropriate use of new technologies where there are ethical concerns.

28. Oversight structures must incorporate views from a range of experts and stakeholders. They should consider the needs of a wide variety of stakeholders including academia, industry, regulators, patients and the public, amongst others, to ensure that any approaches to oversight of emerging science and technologies are workable and useful for all sectors. Ongoing and meaningful engagement with patients and the public is essential to developing good oversight for emerging science and technologies, and this is highlighted in the Academy's forthcoming report on data-driven technologies. However, representation of these stakeholders should be balanced with the need to ensure an oversight mechanism can be responsive and does not become so large that it is unwieldly.
29. There are already existing examples of advisory bodies that have oversight in specific areas of research, such as the Animal Science Committee, which the Academy supported in its report on *'Animals containing human material'*, to help advise on progress and oversight of this field.[21]
30. Key stakeholders should be involved from the outset in the development of any oversight for emerging science and technologies. For example, it is essential to involve regulators at the start of any discussions around oversight of an innovation to ensure that the oversight is feasible and aligned with regulatory expectations and abilities, as well as to ensure buy-in from the regulators. The Innovative Medicines Initiative (IMI) is a good exemplar for proactive engagement of a range of experts and sectors such as industry, academia, patient organisations and others, in the oversight and delivery of a project, with regulators often embedded in this work from its inception. Embedding regulation and evaluation from the early development of new science helps to support and facilitate its development.

Horizon-scanning: how should the Government ensure that it is aware of emerging areas of science and technology in good time?

31. Government has a responsibility to support the development and introduction of scientific advances as fast as possible to benefit the health and wealth of the UK, and to ensure that we continue to position ourselves as a world leader in life sciences, whilst also ensuring that these advances are safe and supported by a robust evidence base. However, the accurate identification of future potential harms can be challenging. In this context, one approach to oversight has been to guide decisions using the 'precautionary principle', that is often applied

[19] UK Biobank (2007). *UK Biobank Ethics and Governance Framework.* www.ukbiobank.ac.uk/wp-content/uploads/2011/05/EGF20082.pdf
[20] Genomics England (2017). *The 100,000 Genomes Project Protocol v4.* https://doi.org/10.6084/m9.figshare.4530893
[21] Academy of Medical Sciences (2011). *Animals containing human material*. https://acmedsci.ac.uk/file-download/35228-Animalsc.pdf

in environmental policy and by European-level decision-makers.[22] This can be described as a risk averse approach where decisions are weighted towards considerations of possible harms, even where there may be uncertainty around the extent or probability of harm. It is important that there is an awareness of these types of approaches, and that due consideration is given to potential harms, but this must not unduly impede the development of novel science and technologies. This discussion is particularly pertinent, as highlighted by the British Academy, in the context of Brexit.[23]

32. We recognise the difficulty in predicting which emerging sciences and technologies, or applications of a given innovation, will present challenges to oversight, particularly when it may be difficult to predict how innovations will be used in the future. Moreover, many of the challenges in oversight of science and technology do not emerge from new questions arising from novel science, but from longer-standing issues on scientific advice and policy – which may be highlighted by new scientific developments – such as how scientific evidence is used or existing ethical debates.
33. Independent advisory panels may be useful for horizon scanning and/or oversight. This could build upon past efforts such as such as the Emerging Science and Bioethics Advisory Committee (ESBAC). The traction of these committees for driving policy change would need to be assured, as well as their ability to respond in an agile way. Any committee should be small and adaptable enough to be poised to comment rapidly on emergent issues, while still representing expertise in ethical, regulatory, policy and legal fields and providing reliable, evidence-based advice. It will be critical that there is close alignment between any such panels and regulators. This could be modelled upon successes such as the human genetics commission (HGC) and the HFEA, which have strong links to both practice and science, as well as regulation. In addition, public engagement is key to these structures and it is important that it is embedded into their ways of working.
34. We are very supportive of the role of Government departmental Chief Scientific Advisers, together with the Government Chief Scientific Adviser, who play a highly valuable role in advising Government on new scientific developments and challenges.[24] These positions play an important role in the horizon scanning for new innovations.
35. In this way, there is also an opportunity for Government to fully utilise existing networks in the life sciences to horizon scan and remain aware of upcoming developments. For example, Academies such as ourselves bring together a large number of researchers and scientific experts who work in new and emerging areas and can provide a useful resource to monitor those areas which are fast developing and may provide challenges for future oversight.

This response was prepared by Joanna Ciafone (Policy Intern) and was informed through the Academy's previous activities. For further information, please contact Liberty Dixon (liberty.dixon:acmedsci.ac.uk; +44(0)20 3141 3222).

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[22] The British Academy (2018). *British Academy Brexit Briefing: Legal Aspects of the Precautionary Principle.* www.thebritishacademy.ac.uk/sites/default/files/british-academy-brexit-briefing-legal-aspects-precautionary-principle.pdf.
[23] *Ibid.*
[24] Campaign for Science and Engineering (2017). *Evidence: Improving the use of evidence in UK government policymaking.* www.sciencecampaign.org.uk/asset/016176D1-09BF-4CD9-BB9C27B2D7BC50B4.62F554EC-54A4-430E-8EE849F46DAB988B/

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