TONY BLAIR INSTITUTE FOR GLOBAL CHANGE

Setting the Pace: Accelerating the Race for Clinical Research and Drug Development Post-Pandemic

MARTIN CARKETT
PAUL BLAKELEY
HENRY FINGERHUT
BENEDICT MACON-COONEY

Contents

Published at https://institute.global/policy/setting-pace-accelerating-race-clinical-research-and-drug-development-post-pandemic on October 4 2022

Our Future of Britain project seeks to reinvigorate progressive politics to meet the challenges the country faces in the decades ahead. Our experts and thought leaders are setting out a bold, optimistic policy agenda across six pillars: Prosperity, Transformative Technology, Net Zero, Community, Public Services and Britain in the World.

Executive Summary

Clinical-trial regulation has been discussed as one of the key areas the UK should reform post-Brexit, to enable it to bring new treatments to patients faster. Particularly so following the pandemic, which saw greatly accelerated clinical delivery of life-saving vaccines. Indeed, one common claim is that leaving the European Union (EU) enabled the UK to move quicker on the vaccine rollout than our European counterparts. While this has been widely debunked, the spirit of this idea is right, even if its premise is wrong.

The case to bring effective, affordable and safe new treatments to patients at an accelerated pace, from both public health and economic perspectives, is inarguable. And the UK will be able to move with greater speed and agility from a regulatory standpoint post-Brexit. But this shift must be delivered strategically to avoid creating divergence for the sake of it, which could risk leaving the UK cut off from global research.

Moreover, there are more fundamental structural issues that the government must fix in order to realise this ambition. Solving workforce-capacity and data-privacy issues, developing new commercial models and delivering technological infrastructure across the health service will be equally as important as looking at regulatory reforms.

With its world-class academic institutions, flourishing life-sciences industry and universal health-care system, the UK is uniquely positioned to become the global leader in digital and data-driven clinical trials and to spearhead global efforts to eliminate preventable diseases. This should be a vital focus for Britain's future post-Brexit, and can serve as an important example of what it can still achieve and what its new role in the world can look like. But new technologies, new regulatory opportunities and a sense of urgency following the pandemic must be seized upon. The government can embrace these opportunities by taking forward the following recommendations:

1. Address the NHS workforce crisis and increase research capacity. The NHS is critical to the delivery of UK clinical research, but with more than 110,000 vacancies and rising operational pressures, we urgently need to create more capacity in the health service to support research.

2. Accelerate delivery of data infrastructure across the NHS that can connect to clinical-trial management systems. Alongside extra capacity, we must harness the power of NHS data to make clinical-trial design and delivery more efficient and effective, as we have previously called for.

3. Facilitate patient enrolment and retention by maximising patient-engagement platforms such as the NHS App. Approximately half of all commercial trials fail to recruit to target. New and existing digital platforms must be utilised to find, recruit and follow up with potential clinical-trial participants.

4. Make an assertive case for data and consent regimes to expedite collection of real-world evidence. This will help bolster post-market treatment monitoring and optimisation, but must address the significant trust gap that exists among patients.

5. Develop new commercial models to foster discovery of new treatments. Single-dose curative treatments, like cell and gene therapies and digital therapeutics, offer fresh hope to patients but create new challenges to market access. The launch of the Innovative Medicines Fund is a good start, but other innovative commercial models, like outcomes-based payments, are needed to ensure novel treatments and the benefits of clinical research are made available to patients.

6. Support innovation across drug discovery and clinical trials. The government must double-down on commitments to increase UK R&D spending and continue to invest in the infrastructure needed to deliver clinical research effectively and efficiently, without which the UK will continue to lose ground to competitors around the world.

7. Support decentralised, global clinical trials. These new models of trial delivery can help to make research more efficient, while also offering the opportunity to increase diversity in research participants. The UK must capitalise on the potential of NHS data to support this agenda and secure the UK's position at the forefront of clinical research.

8. Continuously improve regulatory frameworks without unhelpful divergence. It is right to consider where the UK can be nimbler and more efficient in clinical-research delivery post-Brexit. However, the UK must ensure it avoids unnecessary divergence that either undermines patient safety or creates an unattractive market for global clinical research delivery.

9. Set global grand challenges to systematically eliminate diseases. The UK should leverage its global expertise and capacity for clinical research to help develop new vaccines, treatments and diagnostics for major causes of global ill-health – which cause millions of deaths, cost billions to the global economy and pose an existential threat to our future health security.

Introduction

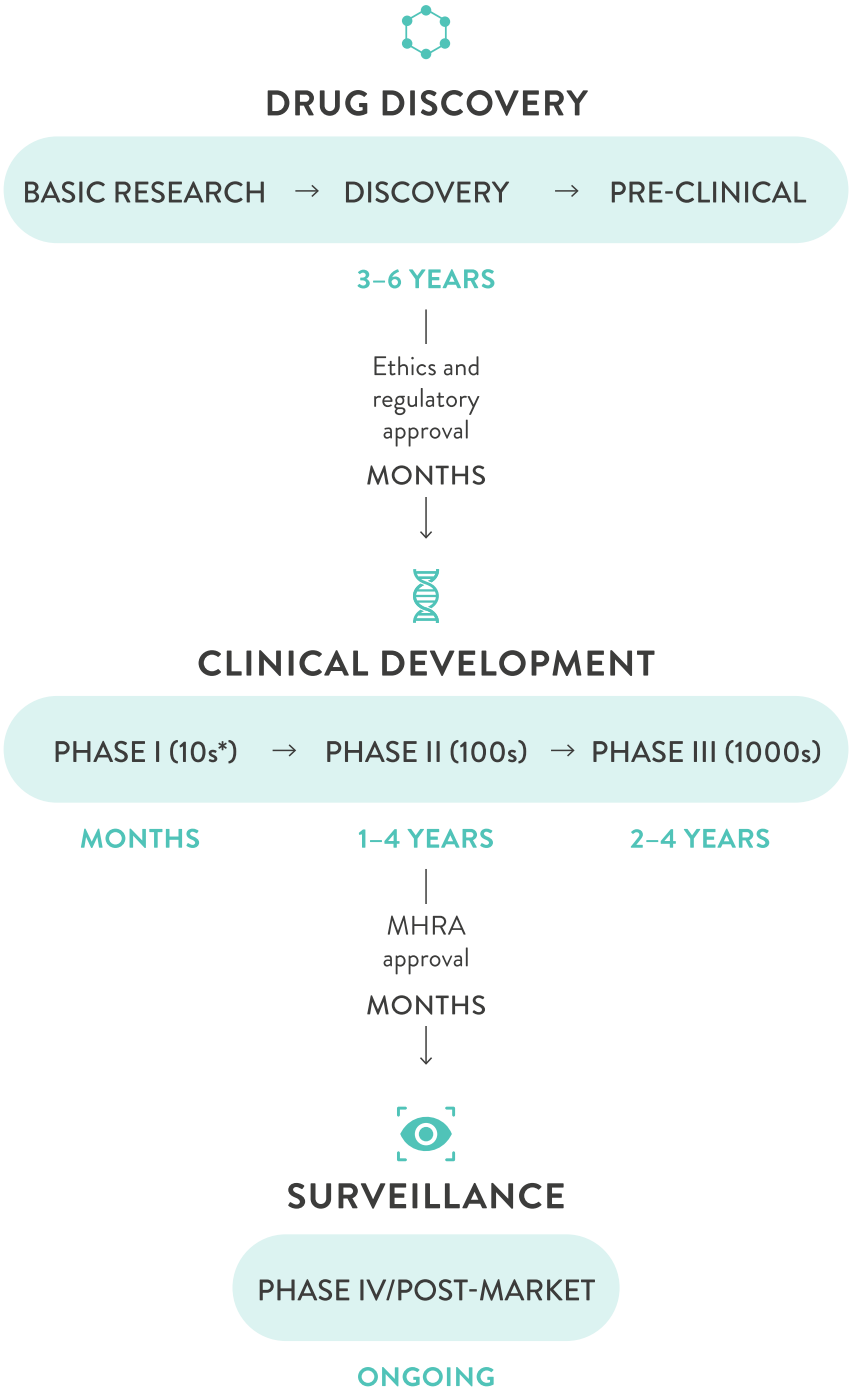
Drug development and clinical research are essential parts of modern health care, fundamental to bringing novel treatments, technologies and techniques to clinical settings to improve people's lives. With its world-class academic institutions, highly developed life-sciences industry and universal public health service underpinned by cradle-to-grave data, the UK is uniquely positioned to drive radical improvements in clinical research that can help accelerate the delivery of new treatments and diagnostics to reduce the burden of disease at home and abroad. However, currently, it takes almost twice as long to initiate a clinical trial in the UK compared to the US, and the UK clinical research is recovering slower than European counter parts after Covid-19.

Over the course of the pandemic, greatly accelerated processes saw the rapid development of vaccines and discovery of drugs that could be used in the fight against Covid-19. This was an exceptional set of circumstances that demanded resources be reprioritised and procedures fast-tracked to meet urgent needs. But it raises the question of what lessons can be learned from the pandemic to accelerate drug development and clinical research more broadly. There are a wide variety of other common and life-threatening diseases – diabetes, heart and respiratory diseases, tuberculosis, arthritis, cancer, depression and dementia – for which better treatments are also urgently needed. Dementia alone, for example, was responsible for 11.5 per cent of all deaths in the UK in 2020 (second only to Covid-19 at 12.1 per cent) and was responsible for a total societal burden of $1.3 trillion to the global economy in 2019. This is projected to increase to almost $3 trillion by 2030.

Accelerating action by increasing speed and scale is therefore critical. However, there are still significant logistical, market and strategic challenges that make bringing new drugs and treatments to patients less efficient and more costly than necessary. It has been estimated that it costs up to almost $5 billion to develop a single new drug and typically takes ten to 12 years to bring it to patients. Clinical-trial stages of drug development are usually the longest and most expensive steps (Figure 1) of bringing new medicines to patients. Failure rate is also high, with reportedly 93 per cent of all candidate drugs failing clinical trials worldwide.

Emerging technologies and the evolving policy landscape offer hope of driving down costs and increasing efficiency of the drug-development process in the UK. Capitalising on the potential of health data to support faster feasibility assessments, site selection and participant recruitment and more effective follow-up is at the heart of this clinical-research revolution and will help to bring novel, effective and safe treatments to patients faster than ever before.

Figure 1 – UK medicine-development timeline



*Number of participants in each phase.

Source: TBI

Current Challenges in Drug Development and Clinical Trials

Drug development and clinical research is rightly, tightly regulated to ensure patient safety is maximised. However, the overall system is also surprisingly inefficient and there are a variety of challenges that could be reduced or overcome, without compromising on safety, to increase the pace of clinical outputs and decrease commercial risk. These hurdles broadly fall into three categories.

Logistics

- **Pre-clinical drug discovery**: drug-discovery phases to identify and trial candidate drugs in *in vitro* and animal models can be time consuming (typically three to six years) and costly and have a relatively low success rate. Only around 32 per cent of such studies identify drugs that ultimately make it to market.
- **Patient recruitment and retention**: slow identification and enrolment of appropriate patients is estimated to delay up to 80 per cent of clinical trials in the US, while 35 per cent of trials fail altogether due to lack of patient enrolment and approximately 30 per cent of patients drop out of clinical trials, incurring significant replacement costs. In the UK, around 50 per cent of commercial trials never hit their target recruitment. Meanwhile, "professional patients" who participate in multiple clinical trials simultaneously or consecutively can invalidate their participation or results, leading to reduced efficiency. Recruitment to non-Covid-19 clinical trials was significantly reduced during the pandemic. Countries are still recovering, but the UK continues to recover more slowly than most.
- **Participant diversity**: of the 292,537 participants in clinical trials globally in 2020, 76 per cent were white, 11 per cent were Asian and only 7 per cent were black, leaving many populations greatly underrepresented and clinicians less able to understand how treatment regimes can be optimised for different groups. Women have also been historically underrepresented in clinical trials, hindering progress in understanding sex-related differences in health and disease and how women may respond differently to medication, particularly during pregnancy and breastfeeding.
- **Centralisation**: clinical trials (and follow-up lab studies and procedures) are often only available at local academic medical centres and frequently require face-to-face visits, incurring burdens on both patients and researchers, including expenses for patients that aren't always eligible for reimbursement, further constraining patient recruitment to local pools. This effect has been accelerated by Covid-19, which has seen a decrease in patient willingness to attend clinical settings.
- **Admin burdens and data challenges**: researchers running clinical trials often have to manage time-consuming administrative tasks, as well as managing data across multiple systems and sites, which can lead to incompatibilities, inconsistencies, redundancies or gaps in patient data. In the UK many researchers also have to continue with their NHS work, with trial work falling outside the remit of their usual hours.
- **Regulations**: regulations, while an important enabler of high-quality, safe trials, can place overly

burdensome constraints on both those conducting clinical trials and those participating, and processes could be more streamlined. It can take five months to get Medicines & Healthcare products Regulatory Agency (MHRA) approval for drugs in the UK, while US Food & Drug Administration (FDA) approval can take more than a year.

- **Clinical capacity**: clinical trials in the UK are mainly facilitated by frontline NHS staff, as part of their day job and without specific time dedicated to these endeavours. Chronic staff shortages and limited access to clinical facilities are reducing the NHS's capacity to deliver clinical trials at pace, which are currently seen as a competing priority to the urgent care crisis and the record 7 million people awaiting elective care.

Markets

- **Competition**: the pharmaceutical and clinical-research organisation industries have become much more diverse in recent years but are still largely dominated by a relatively small number of large incumbents, leaving them potentially less competitive and innovative than other industries.
- **Data sharing**: anonymised patient-level data from clinical research (including negative data and patient background data) often has huge value beyond the original study. While organisations such as ClinicalStudyDataRequest.com (CSDR) offer platforms to share clinical-research data (where legally consented to), consent, participation in, accessibility and promotion of such platforms need to be improved for benefits to be realised.
- **Risk sharing**: while competition can have positive impacts, there are instances when pooling resources and sharing risk across private and public organisations can be conducive to progress on particularly high-risk or complex challenges for which progress is otherwise limited. The Davos Alzheimer's Collaborative is a good example of where this can be successful.
- **Commercial**: some diseases are less commercially viable to tackle as target markets are less lucrative (such as diseases predominantly affecting low-income countries, or rare diseases that only affect a limited population), inhibiting progress on developing drugs for potentially treatable or curable conditions. While the pipelines of drugs in these areas are improving, they remain relatively less developed. Meanwhile, treatments that could be curative, such as novel gene or cell therapies, require new commercial models reflecting their specificities, which are expensive at the moment of administration but bring the promise of a long durable effect.

Strategy

- **Prioritisation**: there is currently limited prioritisation of clinical-research resources to efficiently and effectively address gaps in medical evidence and alignment with clinical practice. Instead, priorities are often influenced by other incentives, such as commercial drivers.
- **Globalisation**: although there is an increasing trend towards clinical studies that are global in nature, such as the PRoVENT 2+ study, SQUEEZE study, Protas and IQVA studies, there is still relatively

limited clinical research spanning different regulatory jurisdictions. Globalising the approach could help reduce costs and open wider pools of patients.

Emerging Tech Solutions

Despite these challenges, technological solutions are already emerging to make drug discovery and clinical trials more intelligent, more efficient and more effective, enabling new drugs to come to market sooner, without compromising patient safety or increasing costs.

Artificial Intelligence

Artificial intelligence (AI) offers enormous potential to accelerate drug development, as well as reform the clinical-trials process, and several private companies are already taking significant strides to utilise this potential. American tech conglomerate Alphabet Inc. recently announced the launch of a new subsidiary, Isomorphic Laboratories, with the stated aim of reimagining the entire drug-discovery process from first principles with an AI-first approach. Meanwhile, companies like BenevolentAI have already been using AI for a number of years to explore interconnected diseases with the ultimate aim of discovering new and better treatments.

There is great promise that AI can build on the success of DeepMind's AlphaFold2 – a programme capable of accurately predicting the three-dimensional structures of proteins from their amino-acid sequences – to identify new druggable targets, explore where existing drugs could be repurposed to treat different diseases, discover new therapeutic compounds and even design novel biologics in the future. This could greatly accelerate the drug-discovery phase and identify or design candidate drugs that have a better chance of succeeding in clinical trials. A recent report from Insider Intelligence estimated that AI could reduce drug-discovery costs for companies by as much as 70 per cent.

Moreover, Owkin, VeriSIM Life, AiCure and others are now using machine-learning methodologies to predict the clinical outcomes of candidate drugs before they enter human trials to more effectively select drugs that show the best potential and reduce failure rates – de-risking and accelerating the clinical-trials process.

AI is also being applied in the design of clinical-trial protocols and to source appropriate participants for trials. Trials.ai, for example, is using AI to mine vast amounts of documents that have information relevant to trial design, including client data, regulatory information and comparable studies, to design "smart protocols" for clinical trials, which can help avoid costly delays caused by poor protocol design.

Meanwhile, Deep Lens is using an AI platform to accelerate oncology clinical-trial enrolment in the US by connecting trial sponsors to community oncology practices at scale. Such technology has huge potential to be used more widely to help recruit eligible prospective trial participants at pace and tackle

one of the leading causes of clinical trials' delay and failure. Open-source platforms such as DQueST are also using AI to simplify eligibility questionnaires for trials listed on ClinicalTrials.gov (a website that enables citizens to sign up to participate in clinical trials) to make it easier for prospective participants to understand if they are suitable candidates.

Clinical-Trials Management Systems and Real-World Evidence

Major tech players are also moving into the clinical-trial business, bringing to bear their vast computing power and economies of scale. Hyperscale cloud-infrastructure and data-management platforms are being used to simplify clinical-trial data management to make trials more efficient and effective. Clinical One, the clinical-trials platform recently launched by software and cloud-computing giant Oracle, aims to do this by unifying clinical-trials data held across multiple sites on to a single, easy-to-use platform that, importantly, also links to patients' Electronic Health Records (EHRs) to harmonise data, reduce errors and admin burdens, and streamline workflows. Even more importantly, in the future, connecting such platforms to complete national-level health-data infrastructures offers the potential to massively accelerate the identification of suitable trial participants, helping to overcome another big hurdle.

Clinical One and similar systems can also continue to collect patient data even after the clinical trial has ended, enabling the longer-term impacts of treatments to be monitored by collecting **real-world data and evidence (RWD/E)**. Although this capability would require further consideration of ethics and consent, it could be immensely valuable in providing greater feedback on drugs in the market, in turn assisting refinement of treatment programmes and the development of new drugs. As an example, during the pandemic, the continued collection of real-world post-clinical-trial data for Covid-19 vaccines demonstrated that the vaccines were safe to be administered to pregnant and breastfeeding women, even though they were not explicitly included in the clinical trials.

Indeed, RWD/E is transforming the way clinical trials are conducted and there has been an explosion of companies providing these data to life-sciences companies, not just for phase IV studies but also for innovative techniques like synthetic control arms and trial-design tooling. Policy reforms on RWE, described below, are also providing a regulatory framework to help realise its potential benefits.

Disruptors

Meanwhile, smaller-scale tech start-ups are acting as disruptors to the industry, with impressive results reported. TrialSpark is using a technology-first approach that utilises automation and data across a single operational layer to simplify logistics, create more efficient processes and outsource clinical-trial appointments to local doctors' offices. Its platform can reportedly significantly decrease trials timelines and halve the timeframe in which new drugs are developed, as well as improving accessibility for

prospective trial participants. TrialSpark is already partnering with a number of pharmaceutical giants including Merck KGaA, Novartis and Sanofi.

There are now a growing number of clinical-trial management-system vendors, offering services to simplify and accelerate different parts of – or the entire – clinical-trials life cycle, including software to help build and submit clinical-trial applications, patient-recruitment tools, cloud-based data-capture and data-management platforms, systems to manage remote trial sites, and programmes for the necessary management of electronic participant binders and trial master files in order to comply with government regulations (see boxout).

Promising Clinical-Trial Management System Vendors

- Florence – a US and Serbian company providing a number of clinical-trial workflow products. These include a system to manage remote trial sites, an "eBinder" tool to manage participant data, trial master-file software to facilitate regulatory oversight and an e-consent tool.
- Clario – a global company with a handful of clinical-trial management and medical data-analysis products. These include an electronic clinical-outcome assessment tool to facilitate data collection and analysis, electronic data-capture (EDC) tools and an "end-to-end" clinical-trial management system.
- Formedix – a UK company with a range of software tools to help design, build and submit clinical trials. These include a cloud-based clinical metadata repository.
- Castor – a Dutch and US company with a handful of clinical data-management tools, including an EDC tool, a tool for collecting patient-reported outcomes (ePRO), a consent tool and a platform for managing decentralised trials.
- Medrio – a US company positioning themselves as the first cloud-based EDC company, and now providing a range of clinical-trial management software (for decentralised trials, EDC, e-consent, ePRO and more).
- Advarra – a US company with a wide range of clinical-trial management-system software serving the full clinical-trial lifecycle, review stage and consulting-offers stage.
- Stitch – a UK company building a clinical-trials patient-retention platform. They are working with trial owners and operators such as Cancer Research UK to collect non-clinical patient feedback to prevent churn and improve the patient experience.

Decentralised and Virtual Clinical-Trial Platforms

Tech is also helping to facilitate the decentralisation of clinical trials through platforms that enable patients to participate in clinical trials remotely. This can greatly reduce burdens on both patients and researchers and make clinical trials more accessible to a much wider pool of prospective participants. It also reduces the risk of Covid exposure and would allow aspects of trials to continue if there was a future pandemic, rather than being forced to pause as we saw during the first wave of Covid-19.

To take one example, the RELIEVE IBS-D study has shown the power of virtual and decentralised trial-delivery protocols. After Covid-19 interrupted participant recruitment through trial sites, the study pivoted to use digital tools to recruit and monitor participants remotely. This new virtual approach opened up the study to more people across the UK and significantly bolstered recruitment, with a single site using the virtual method recruiting 67 per cent faster than all 28 sites using a traditional approach.

Huma in the UK and Medable in the US have developed similar virtual clinical-trial platforms that can remotely monitor patients and collect data, enable easier patient and researcher communication via telemedicine platforms and provide automated in-trial support. This has seen accelerated patient recruitment, improved patient engagement and retention rates, and improved adherence to protocols, greatly improving the efficiency of its trials. The global decentralised clinical-trials market is projected to almost double to $14 billion by 2026, and continue to grow at around 6 per cent annually until 2032.

Meanwhile, UK non-profit Protas, led by Sir Martin Landray, who previously led the world's largest decentralised Covid-19 clinical trials (RECOVERY), is designing and delivering large-scale, global, randomised and decentralised clinical trials of treatments for common and life-threatening diseases. It aims to fix the market failures that have led to a decline in the development of treatments.

Wearable technology is also emerging as a vital component of decentralised platforms. For example, smart watches can be used to collect continuous longitudinal data on patients' vital signs, such as heart rate, body temperature and sleeping patterns, to remotely monitor patient responses to treatment regimes. They can also provide helpful reminders to patients on when to take medication, improving adherence to protocols. In the UK, the NHS has already started to take advantage of wearables for remote-monitoring purposes, providing smartwatches to more than 120,000 patients suffering with Parkinson's disease; this approach should be expanded upon.

Policy Landscape

Policymakers in the UK, EU and US have also developed a multitude of reforms over the past 30 years to make clinical trials more efficient and informative and, more broadly, to incentivise drug discovery in the most-needed areas. Though all three jurisdictions have seen clinical-trial reforms over the past five years, the Covid-19 response required changes to normal approval processes that policymakers and health-system professionals are now reviewing for broader post-pandemic applications.

UK Clinical-Trial Regulatory Reform

The UK is investing in improving its clinical-research environment and infrastructure. The Department of Health & Social Care's policy paper "The Future of UK Clinical Research Delivery" sets out an ambitious vision for the future, with delivery being overseen by the Recovery, Resilience and Growth (RRG) programme, which has helped to secure more than £375 million of funding to deliver a sector-wide, sustained shift in how UK clinical research is designed and delivered.

Central to these reforms are the legislative changes being proposed by the MHRA. These changes include:

- Mandating transparency around what clinical trials are being conducted and what their key findings are within 12 months.
- Streamlining clinical-trial approval and Requests for Information (RFI) processes, including combining regulatory and ethics approvals.
- Relaxing restrictive provisions on the composition of Research Ethics Committees.
- Enabling informed consent to participate in cluster trials.
- Removing ineffective and burdensome safety-reporting requirements.
- Making sanctions and corrective measures more stringent.
- Updating UK terminology and promoting international harmonisation of definitions.

If successfully delivered, these proposed legislative changes and broader improvements will help the UK move towards a more streamlined and flexible clinical-research environment while protecting the interests of patients. But the UK must also look to best practice around the world to ensure it is being as far-reaching as possible in its ambitions.

EU and US Reforms

In Europe, the EU issued a new Regulation on Clinical Trials in 2014, which came into effect in January 2022. This too aims to speed up clinical trials by making it easier for trial sponsors to apply for regulatory approvals. In particular, the delivery of the Clinical Trials Information System, an electronic authorisation platform that enables clinical-trial sponsors to engage with regulators of all member states involved in the trial and the European Commission in one place, has been welcomed.

The EU has also begun the Accelerating Clinical Trials in the EU initiative to increase co-ordination across member states in order to enable larger-scale trials and more innovative trial methods. This initiative also develops guidance for the use of AI and machine learning in clinical trials, decentralised trials, and complex trial formats.

There have also been recent regulatory updates in the US. Over the past few decades, the FDA has promoted enrolment practices that would lead to clinical trials that better reflect the population most likely to use the drug if the drug is approved, primarily through broadening eligibility criteria. Meanwhile, in 2021, the FDA published guidelines on the use of post-market RWE in regulatory submissions. These provide a regulatory structure to incorporate post-market data on how drugs perform in real patients, with three principal impacts: first, allowing drugs to go to market faster; second, incorporating real-world performance into ongoing regulatory decisions; and third, identifying and facilitating approval to repurpose already-licensed drugs for new indications. In 2020, 75 per cent of FDA new drug applications included a RWE study.

Incentivising Research into Less Commercially Viable Drugs

The US federal government has also used targeted incentives to shape drug discovery towards the most-needed treatments through the Orphan Drug Act of 1983. Similar legislation also exists in the UK and the EU. This includes treatments for conditions that do not yet have a viable drug, rare diseases for which the target-market size is too small to justify the risk of research and development (R&D) failure, or tropical diseases that primarily afflict low- and middle-income countries. These incentives include both supply-side and demand-side mechanisms, including:

- Product development partnerships and patent pools to share risk and benefit across pharmaceutical companies
- Direct funding or tax incentives for R&D
- Intellectual Property rights to incentivise tech transfer from universities to pharmaceuticals
- Advance market commitments to ensure market size

- Priority review vouchers to streamline regulatory approval for a paired non-orphan drug
- Prizes and moon shots for specific conditions to ensure a reward for successful R&D, independent of the eventual market

Most recently in the UK, in this vein, commercial incentives have been used to increase new antibiotic development to manage the rising risk of antibiotic resistance. These initiatives are important in overcoming some of the commercial challenges that can inhibit drug development, but a large number of rare diseases are still poorly understood and many well-understood diseases, still attributable for millions of deaths worldwide, are in need of more-effective or cheaper treatments.

International Harmonisation of Technical Requirements for Pharmaceuticals

Finally, the clinical-trial industry is also self-regulated by the Good Clinical Practice (GCP) standards, established by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines, first issued in 1996. ICH brings together both regulators and the pharmaceutical industry to align registration requirements and technical processes to ensure clinical-trial quality, safety and efficacy.

The industry is currently undergoing a shift, with a planned revision to the ICH GCP standards last updated in 2015. New principles were set out in June 2021. These revisions include, among other things, an increased focus on data integrity and governance, as well as management of electronic records – recognising the need to increase the role of technology in the clinical-trial sector. Meanwhile, the UK, alongside Argentina and Peru, has also recently proposed ways in which global clinical research can be strengthened through improved common standards and co-ordination in a recent WHO draft resolution.

Recommendations

New and emerging technologies and an urgency instilled by the pandemic are providing valuable opportunities to overcome the major challenges of the drug-development and clinical-research industry. These must be seized upon and converted into real results. The UK government can embrace and facilitate these opportunities by taking forward the following recommendations, with the stated aims of making the UK the leading global destination for clinical trials and spearheading global efforts to eliminate preventable diseases.

1. Take action to address the NHS workforce crisis and increase capacity.

The NHS is facing its worst-ever workforce crisis, with more than 110,000 vacancies reported, including 12,000 hospital doctors. Given the critical dependence of UK clinical-trial delivery on NHS staff, it is vital this is addressed if the UK is to make progress on accelerating the pace of clinical trials. As well as filling vacancies for health care professionals, this should also include recruiting greater numbers of supporting staff, such as data scientists, who are also instrumental and, in due course, reforming the workforce model to provide greater capacity for NHS staff to support clinical research.

2. Accelerate delivery of data infrastructure across the NHS that can connect to clinical-trial management systems.

NHS data infrastructure that can connect to clinical-trial management systems can greatly improve the speed and effectiveness of clinical trials in three important ways: First, through administrative efficiencies, by enabling automatic population of patient data, negating the current need for laborious and error-prone double entry; second, by facilitating identification of suitable trial participants, therefore increasing the rate of enrolment and improving patient diversity; and third, by supporting the collection of RWE to improve post-market monitoring of drugs and treatment optimisation. Currently, only around 75 per cent of NHS trusts use Electronic Health Records and completing the digitisation of the NHS as soon as possible will be an important first step, before connecting data systems internally and externally. The right regulatory and legislative approvals must also be in place to enable data sharing of this kind.

3. Facilitate patient enrolment and retention by maximising patient-engagement platforms such as the NHS App.

Finding eligible and diverse participants is one of the most significant causes of delay and failure for clinical trials. The government can help overcome this challenge by building national databases that can be used by clinical-trial sponsors to find eligible patients or, as suggested above, where possible, by connecting NHS data infrastructure to clinical-trials management systems to proactively flag eligible

potential participants. To complement this, the government could also help willing participants to find appropriate trials by better promoting websites and platforms like Be Part of Research, ClinicalTrials.gov and DQueST, or by delivering on commitments to create a holistic and data-enabled Find, Recruit and Follow-up service that allows researchers to digitally find patients, offer them places in trials and monitor health outcomes as part of the study. Existing platforms like the NHS App should be utilised to enable prospective participants to search for suitable trials or to proactively notify patients of trials they are eligible for, and could become the default way patients are contacted for trials. Primary care providers could also play a more proactive role in this space. This too may require enabling legislation to facilitate data sharing, as well as patient consent.

4. Make an assertive case for data and consent regimes to expedite collection of RWE.

The government must make a more assertive case for data and consent regimes that permit the collection of RWE to improve post-market treatment monitoring and optimisation. Tackling the significant trust gap that exists will be critical. Clarity and assurances on the anonymity of data, who will have access to such data and who controls access to such data must be provided and this should be made as simple as possible for the patient to remove frictions. For example, the NHS App could again be used to provide patients with an easy way to provide consent for their anonymised data to be used to collect RWE, in a similar way to how patients can currently manage their organ donation preferences on the app.

5. Develop new commercial and regulatory models to foster discovery of new treatments.

Novel regulatory, appraisal and funding models are needed as we enter a new era of medicine where single-dose, curative treatments (such as gene and cell therapies) and digital therapeutics will become increasingly available. As breakthrough innovative therapies, addressing the root cause of disease instead of simply addressing symptoms, and being potentially curative (often with a single administration), cell and gene therapies are very different from traditional medicines. The high cost at the moment of administration, the relatively small patient populations and the long-term effect of cell and gene therapies requires innovative regulatory and commercial models to reduce the risk of market failure, secure patient access and generate the real-world evidence to demonstrate efficacy and clinical cost-effectiveness. Recently, Bluebird Bio announced its exit from UK and other European markets due to its inability to agree appropriate reimbursement models, depriving European patients of novel, life-changing therapies. The flexibilities within NHS England's commercial framework must be utilised to develop mutually agreeable reimbursement models. This includes the use of outcome-based payments (which are based on the impact of treatments rather than the number of units administered) to incentivise the development of more effective treatments while providing value for money for the taxpayer. This is particularly applicable to digital therapeutics, which have seen a significant increase in development in Germany and France since the introduction of new reimbursement models. RWE can play an instrumental part in this, as has been seen with the UK's Cancer Drug Fund and Innovative Medicines

Fund, which provide patients access to novel, potentially life-saving treatments, helping to inform evaluation of a drug's clinical and cost-effectiveness. These commercial levers must be further supported through regulatory frameworks that account for and support the use of real-world evidence to inform decision-making. The data available to the NHS make it uniquely positioned to lead the way in the use of these new commercial and regulatory models. But with the cost of bringing new assets to market declining and profit margins increasing, industry must also play its part by pricing responsibly, and adopting technology that can help reduce costs of developing novel drugs can aid this.

6. Support innovation across drug discovery and clinical trials.

The drug-discovery and clinical-trials industries are rapidly evolving as new technologies such as AI, cloud infrastructure and remote platforms disrupt them. The UK government must use its tax, spending and regulatory powers to foster the continued development of novel processes and technologies that can further enable positive disruption and help accelerate the development of new treatments. The recent government announcement of the decision to extend R&D tax relief qualifications to include cloud and AI is welcome, but these efforts should also seek to include the development of new platforms, software and services, which can be equally transformative. At a more fundamental level, total R&D expenditure in the UK remains significantly below that of comparable nations and its share of global R&D invest is decreasing. This is a major risk to future economic growth, with recent analysis suggesting the UK could benefit from an additional £7.2 billion of investment per year by raising R&D investment to equivalent per-capita levels as the US. And by improving the UK's share of global commercial clinical-trial enrolment to that of the leading countries in Europe, the UK could benefit from an additional £165 million in additional revenue and £32 million of savings for the NHS each year. We therefore need further incentives to encourage businesses to invest in UK R&D, as well as further targeted investment in basic and high-risk, high-reward research towards specific health aims (such as the US's ARPA-H) that can help develop foundational knowledge for the private sector to build on.

7. Support decentralised, global clinical trials.

Technology now exists to allow remote, decentralised clinical trials, enabling greater access to a more diverse range of prospective trial participants from around the world. The UK government can facilitate globalisation of clinical trials by delivering on commitments made in the new Data Saves Lives strategy for reshaping health and social care data. This includes sharing national databases of ongoing trials and creating Trusted Research Environments which provide anonymised patient data to approved researchers from around the world, or platforms such as OpenSafely, which enables researchers to write code that is executed on an EHR in the cloud and can also assist clinical research. The government should also foster such collaborative approaches from other countries and, more importantly, act in concert with other governments to more fully harmonise standards and regulations across the globe by supporting, engaging and complying with GCP standards. Research and funding bodies can also help incentivise globalised trials through their funding levers.

8. Use new flexibilities to continuously improve regulatory frameworks without unhelpful divergence.

The UK has made important interventions in response to the pandemic to reduce administrative and regulatory burdens and increase trial transparency. However, while the UK now has more regulatory freedom following its exit from the European Union (and consequently the European Medicines Agency), it must be careful that regulatory divergence doesn't create too distinct a market, as this will make it less commercially viable for global pharmaceutical companies to operate in the UK. The MHRA is globally respected and should capitalise on this respect to become a more vocal thought leader for regulatory innovation worldwide. The MHRA's decision to join the ICH is a great first step to retain and build upon the UK's regulatory leadership. The MHRA must now look to build further regulatory partnerships and lead the development of new regulations for innovative treatments and technologies. Regulators should also seek to engage clinicians, trial sponsors and trial participants to continue to make applications for regulatory approval as efficient as possible without compromising patient safety, and should look to best practice, and alignment, around the world. For example, UK regulators could seek to develop a Clinical Trials Information System similar to that used by the EU, or indeed look to collaborate with EU initiatives, such as the Accelerating Clinical Trials in the EU initiative.

9. Support global grand challenges to systematically eradicate and eliminate disease.

Many common, debilitating and life-threatening illnesses continue to plague global society for want of better or cheaper treatments. Tuberculosis, malaria and HIV alone accounted for almost 3 million deaths and cost the global economy trillions in 2020. The WHO is working on a Global Framework for multi-disease elimination, and the UK should ensure it is at the forefront of efforts to support these aims. As the pandemic showed, concerted, focused efforts can rapidly develop medical interventions to neutralise the treat of even the deadliest diseases, and governments should take on lessons from the pandemic to build the structures, coalitions, incentives and targets needed to systematically eliminate the threat of other diseases that cause widespread suffering and death. The UK should look to leverage its unique advantages and position towards these goals. This should also include looking beyond the diseases of today to prepare for the diseases of tomorrow. The White House Office of Science and Technology Policy estimates it would cost just more than $24 billion to have prototype vaccines ready for each of the 26 viral families that are known to cause human disease. Though not insubstantial, this cost would pale in comparison to the economic costs of another, potentially avoidable future pandemic. By way of comparison, the total cost to the global economy of the Covid-19 pandemic will be more than $28 trillion by 2025.

Conclusion

The global drug-discovery and clinical-research industry is ripe for revolution. Indeed, such a revolution is already underway, and the case to bring effective, affordable and safe new treatments to patients at an accelerated pace, from both public-health and economic perspectives, is inarguable.

Recent advancements in technology – from AI and cloud infrastructure to telemedicine platforms and EHRs – offer the opportunity to radically accelerate and improve candidate drug development, speed up and diversify patient enrolment, and make clinical trials drastically more efficient, providing solutions to many of the most significant challenges faced by the life-sciences industry.

The UK is uniquely positioned to be at the forefront of this effort. Its world-class academic institutions, highly developed life-science and tech industries, ability to regulate nimbly and, above all, its universal public health-care data provide the perfect conditions. By exploiting these advantages, the UK can significantly accelerate the delivery of new treatments, technologies and techniques to greatly improve health both domestically and around the world. Life sciences is also one of the UK's most reliable growth sectors and investment and reform of it is a safe bet that will not only benefit the health of the nation, but also the wealth of nation, as we continue to rebuild after the pandemic.

Covid-19 has shown us the importance of health above almost all else and left us more impatient than ever to overcome the burden of disease. As Britain seeks to establish its new role in the world and aims to become a science superpower, it must show leadership in areas that are globally significant and in which it has inherent advantages. There are few causes more worthy, or that we are better placed to lead the world on, than delivering the future of clinical research.

Acknowledgments

The authors would like to thank the following people for conversations that helped inform this paper:

- Dr Isabella Watts – Clinical and Research Fellow in Oncology at the Royal Free Hospital, London
- Dr Martin Yuille – Division of Population Health, Health Services Research and Primary Care, University of Manchester
- Michael Macdonnel – Global Head of Operations, Huma Therapeutics
- Lily Mintz – Chief of Staff at TrialSpark
- Dr Axel Heitmueller – Managing Director, Imperial College Health Partners
- Tamsin Berry – Partner, Population Health Partners

- Dr Gabriel Seidman – Director of Policy, Lawrence J. Ellison Institute for Transformative Medicine
- Dr Jennifer Harris – Director of Research Policy, the Association of British Pharmaceutical Industry
- Paolo Morgese – EU Director Market Access & Member Relations, Alliance for Regenerative Medicine
- Elisabetta Zanon – Director of EU Public Affairs & Advocacy, Alliance for Regenerative Medicine
- Dr Fiona Pereira – Associate Principle, IQVIA
- Angela McFarlane – Vice President, Strategic Planning, Northern Europe, IQVIA

FOLLOW US
facebook.com/instituteglobal
twitter.com/instituteGC
instagram.com/institutegc

GENERAL ENQUIRIES
info@institute.global

FIND OUT MORE
INSTITUTE.GLOBAL