ACCESS DENIED

EXTRACTIVE RESEARCH AND DEVELOPMENT DURING THE COVID-19 PANDEMIC

STOPAIDS. just TREATMENT

REPORT BY

STOPAIDS & JUST TREATMENT

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WITH THANKS TO WRITERS DR MANUEL MARTIN AND RHIANNON OSBORNE

About STOPAIDS

STOPAIDS is a UK-based HIV, health and rights network. We draw on our 35-year experience working on the HIV response to support UK and global movements to challenge systemic barriers and inequalities so that we can end AIDS and support people around the world to realise their right to good health and wellbeing.

About Just Treatment

Just Treatment is a patient-led campaign fighting to ensure everyone gets the healthcare they need by challenging the power of the pharmaceutical and health industries and demanding that the government acts to put patients before corporate profits.

We would like to thank Open Societies Foundation for making this research possible.

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CONTENTS

ABBREVIATIONS

ACT-A	Access to COVID-19 Tools (ACT) Accelerator
BEIS	Department for Business, Energy and Industrial Strategy
FCDO	Foreign, Commonwealth and Development Office
C-TAP	WHO COVID-19 Technology Access Pool
EID	Emerging Infectious Disease
FVMH	Future Vaccine Manufacturing Hub
HIC	High-Income Country
UKRI	UK Research and Innovation
NIHR	National Institute for Health and Care Research
R&D	Research and Development
LMICs	Low- and Middle-Income Countries
NHS	UK National Health Service
PHE	Public Health England
DHSC	Department for Health and Social Care
ODA	Official Development Assistance
MHRA	Medicines and Healthcare Products Regulatory Agency
VTF	Vaccines Taskforce
MRC	UK Medical Research Council
saRNA	Self-amplifying RNA
FOIs	Freedom of Information Act Requests
CEPI	Coalition for Epidemic Preparedness Innovations

EXECUTIVE SUMMARY

Three years on, the COVID-19 pandemic has officially caused the deaths of over 7 million people, with excess mortality statistics finding a number two to four times higher.[1] The pandemic disrupted livelihoods globally and continues to have a devastating impact on communities without widespread access to health technologies. The world's response to the pandemic has demonstrated the flaws in the existing global system for the research, development and dissemination of health technologies. As of 8 March 2023, over three years into the pandemic, and despite 13.32 billion doses having been administered globally, 79.5% of the population in high-income countries (HICs) had been vaccinated with at least one dose, while only 28.1 % had been vaccinated in low-income countries.[2]

The pandemic has been characterised by unprecedented progress in scientific research, including the rapid development of diagnostics, vaccines and therapeutics. Public funding played a critical role in the research and development, manufacturing and distribution of these COVID-19 tools. However, we argue that the governance of such tools, including their distribution, pricing and manufacturing, has too often been dominated by narrow commercial or nationalistic motives rather than the interests of global public health.

The 'Access Denied' series explores how such motives have been protected and enabled by a systemic lack of transparency within government decision making, between some pharmaceutical companies and in their relations with the governments of the UK and the EU.[3] [4] Through legal and investigative research, the series uncovers how this opacity prevented public accountability and good governance, which we argue contributed to the gross inequity we have seen in access to COVID-19 health technologies. Each report in the series sets out recommended legal and policy options to improve transparency and public oversight regarding public health matters to ensure that access to health tools, during pandemics and beyond, is never denied again.

This report details the role that UK public entities have played in supporting the development of COVID-19 tools such as diagnostics, vaccines and treatments. It highlights how the lack of equitable access safeguards across the research and development (R&D) continuum results in the perpetuation of an extractive global health system that compounds existing health inequalities. We consider a 'extractive global health system' as a model where risk and investment are socialised, profits are privatised, and health products are monopolised by a small number of firms. This raises prices in the UK and limits global access, impacting communities in Low- and Middle-Income Countries (LMICs) the most. We argue the actions of some pharmaceutical companies and high income countries throughout the pandemic reinforce and perpetuate racist and colonial dynamics that threaten everyone's health.

Support from public entities across the world was critical to the rapid development and manufacture of COVID-19 tools during the pandemic. The UK has invested huge amounts of public resources into the development and procurement of COVID-19 health technologies. The UK Research and Innovation (UKRI), National Institute for Health and Care Research (NIHR) and the then Department for Business, Energy and Industrial Strategy (BEIS) stand out as non-departmental and government bodies supporting the development of specific COVID-19 tools. Moreover, they have supported an ecosystem of knowledge and infrastructure necessary to advance the development of all COVID-19 medical tools and future EID R&D.

Despite this, this report finds that the governance of COVID-19 tools, including their distribution, pricing and manufacturing, has too often been dominated by narrow commercial or nationalistic motives rather than the interests of global public health systems.

As the case studies at Part 2 of the report highlight, some companies whose medical technologies benefited from the extensive ecosystem of UK public support engaged in significant value extraction. This was enabled by limiting supply and charging high prices for their products in the UK and abroad. HICs wielded their economic and political power to secure priority access but were forced to pay monopoly prices guaranteed by the global intellectual property system. Meanwhile developing countries were deprioritised and often unable to afford essential COVID-19 tools altogether.

Despite some limited public interest conditions placed on some UK public funds, there is an absence of a coherent strategy to ensure that the extensive support from UK public entities results in affordable access for the NHS and populations across the world. The lack of equitable access safeguards throughout the R&D continuum, which could have prevented this inequitable access, reinforces rather than dismantles the colonial roots of global health.

Conservative estimates by the authors of this report put the total spent by various government agencies to fund the development of COVID-19 diagnostics, vaccines, and therapeutics; and to scale up the UK's vaccine manufacturing capacity at almost £1.5 billion.[5] Furthermore, the medical tools highlighted in this report (Sotrovimab, Tocilizumab, the Oxford-AstraZeneca vaccine, and Surescreen's diagnostics) are estimated to have incurred costs to the NHS of at least £912 million. This amounts to a huge transfer of publicly developed knowledge and public funds from the state to the private sector with little accountability and no safeguards to protect the public good.

This dynamic has been repeated throughout the pandemic across many countries, companies and medical tools. As the Part 2 case studies highlight, this has resulted in windfall profits for some corporations, and monopoly pricing and gross inequality of access to lifesaving COVID-19 medical products.

The following six case studies of COVID-19 medical tools demonstrate the variety of ways in which UK public entities provide support along the R&D to manufacturing continuum, how accessible these medical tools are for the UK National Health Service (NHS) and across the world, and whether strategies to ensure affordable access were utilised.

The case studies highlight that the introduction of equitable access during different stages of development is possible, effective, and stimulates innovation. The case studies also highlight how the nature of R&D for EID is changing, particularly with the emergence of platform technologies. Experiences in the COVID-19 pandemic also highlight the unique, innovative role of the public sector and that access increases, not stifles innovation. This presents an opportunity to democratise R&D to create a more equitable and innovative R&D system for EID.

MONOCLONAL ANTIBODY-BASED THERAPEUTICS

Sotrovimab - Sotrovimab is based on a proprietary antibody platform and marketed jointly by Vir Biotechnology and GlaxoSmithKline. Whilst we were told by a Glaxosmithkline representative that 'Vir and GSK did not receive any government funding for the research and development of sotrovimab', prior to its regulatory approval, research involving the antibody was supported by non-UK public funders. After conditional marketing authorisation was granted by the MHRA in 2021, Sotrovimab was evaluated in four post-approval clinical studies funded by UK public entities. This included the RECOVERY trial. Such studies, while not formally part of the traditional R&D process, are essential to the value of the products they study. They also determine whether products receive a full marketing authorisation.

We have been unable to find any public records of efforts made by either manufacturer to ensure Sotrovimab was accessible across the world. Despite the WHO exploring "access plans" with the manufacturers, no doses of the therapeutic were ever sold to the Access to COVID-19 Tools Accelerator (ACT-A).

We estimate that, according to the published NHS indicative price, the NHS spent GBP 62.2 million procuring just 28 thousand vials of Sotrovimab, equating to GBP 2,209 per vial. Due to secrecy surrounding the real prices paid, an exact figure is not known.

Despite public support from both ends of the R&D value chain, Sotrovimab access was limited by high prices and limited availability.

Tocilizumab - The discovery of Tocilizumab can be traced back to research performed at the university of Osaka in the 1980s. However, critical steps to create the first humanised antibody that later became Tocilizumab were conducted at the UK Medical Research Council (MRC). Today, Tocilizumab is supplied solely by Roche pharmaceuticals and its subsidiary, Chugai Pharmaceuticals.

Tocilizumab received several marketing authorisations for other immune-related disorders. This was often underpinned by publicly supported research in the USA, before being approved for COVID-19. The publicly funded UK RECOVERY trial was critical in confirming the efficacy of Tocilizumab after market approval.

Tocilizumab's access was limited by both availability and affordability. Despite being urged by the WHO and UNITAID to facilitate technology transfer to additional producers to mitigate supply shortages, Roche pharmaceuticals did not take sufficient steps to expand the number of independent manufacturers able to produce Tocilizumab. We believe that the price of Tocilizumab globally far exceeded the likely low cost of production, thus unnecessarily limiting access.

We estimate that according to the published NHS indicative price, the NHS spent GBP 47.5 to 62.2 million procuring Tocilizumab. However, due to secrecy surrounding the real prices paid, the exact figure is not known.

RECOVERY Trial - The RECOVERY trial is a ground-breaking collaborative, adaptive, randomised controlled trial whose results have been and continue to be critical in informing policy makers and healthcare workers on the efficacy of COVID-19 therapeutics in hospital settings.

Both Sotrovimab and Tocilizumab have been included in the RECOVERY trial; however, to date, only data on Tocilizumab have been published. NIHR and UKRI grant databases list the RECOVERY trial as having received a joint grant of GBP 2.1 million. However, this grant does not cover all costs absorbed by the NHS infrastructure which provided all sites at which the clinical trial took place. Using published clinical trial cost estimates, we find that the

RECOVERY trial for the evaluation of Tocilizumab alone can be estimated at GBP 115 million.

Despite the huge value the recovery trial provided for manufacturers, there was no attempt by public entities supporting the clinical trial to introduce conditions for the accessibility or affordability of the tools it evaluated.

LATERAL FLOW DIAGNOSTICS

Surescreen Diagnostics - The origins of Surescreen's lateral flow technology are not publicly available. However, like other lateral flow tests, Surescreen Diagnostics was validated by Public Health England (PHE). The Surescreen diagnostic tests were the first UK-developed and -produced tests to be validated in a laboratory funded by PHE and supported by the NIHR Clinical Research Network Portfolio. This made the test eligible for procurement by the NHS.

The Surescreen tests have been procured by the Department for Health and Social Care (DHSC) through contracts worth at least GBP 503 million, will analysis from the Good Law Project suggesting this could translate to a price of GBP 25.15 per test. Surescreen state the price was lower but declined the opportunity to provide more information citing confidentiality agreements. The Surescreen COVID-19 antigen test is now commercially available for GBP 6 per test. This per-test premium of the early orders reflects a significant de-risking of scaled-up manufacturing.

The high price per test, even for the NHS, suggests that UK public research entities involved in key comparative studies neglected to ensure equitable access principles such as affordable pricing in their support for Surescreen's R&D. This occurred despite the fact that some of the entities involved in NHS trusts are financed by the same governmental department that had to place the orders.

Mologic Diagnostics - Mologic utilised its previous experience in developing a rapid test for Ebola, work that was jointly funded by UK aid and the Wellcome Trust, to develop its COVID-19 lateral flow test. For this purpose, Mologic received a GBP 1 million grant from the Wellcome Trust and the Department for International Development (now Foreign, Commonwealth and Development Office - FCDO) for R&D.

The FCDO also provided GBP 1.5 million through FIND to scale up the manufacturing of the test in collaboration with the Institut Pasteur Dakar, Senegal.

Mologic was able to utilise its sourcing and manufacturing plan to price the test at GBP 1.25 per test, and further volume increases are expected to bring the price down further. This compares favourably with the guaranteed ceiling price of USD 2.50 (GBP 2.01) per test that the diagnostics pillar of ACT-A was able to agree together with the Global Fund.

This case study demonstrates that commercial incentives do not need to supersede public health impact, even in the case of commercial developers, and that encouraging models such as the one pursued by Mologic could form part of a coherent access strategy for UK public funders.

VACCINES

Imperial College self-amplifying RNA (saRNA) vaccine candidate - Imperial College began the development of its saRNA vaccine platform before the pandemic with funding from several UK public entities. Its saRNA was initially targeted at influenza, chlamydia and HIV but was later adapted to COVID-19.

Imperial's saRNA platform was developed as part of the Future Vaccine Manufacturing Hub (FVMH), which was supported by the UKRI with GBP 9.9 million prior to the pandemic. During the pandemic, Imperial College London received GBP 41 million from BEIS, UKRI and NIHR for the development of its COVID-19 saRNA vaccine candidate.

Despite not reaching licensure, Imperial has worked with collaborators in LMICs, including the Uganda Virus Research Institute, to trial its saRNA vaccine platform COVID-19 vaccine.

In September 2021, Imperial licensed a modified version of the saRNA platform to AstraZeneca via a start up company, VaxEquity, in exchange for up to USD 195 million to future royalty payments. The public announcement of this deal made no mention of how access to the products would be ensured in LMICs. The lack of transparency or public interest commitments regarding the deal with AstraZeneca threaten equitable access to this publicly funded technology.

Oxford/AstraZeneca vaccine - A previous estimate of the total public and charitable financing backing the Oxford/AstraZeneca vaccine platform at 97%–99% of identifiable funding from 2000 to 2020 was of up to GBP 228 million. This report identifies an additional GBP 68 million for research into primer and boosting doses as well as support for clinical trial sites. The manufacturing scale up was also directly supported by the UK Government through grants worth GBP 74.3 million.

The UK Government secured itself a priority supply as a condition of the financial support in the development of this vaccine. Oxford and AstraZeneca collaborated with multiple independent vaccine manufacturers across the world to ramp up the supply and access of the vaccine.

Due to a clause included in the contract between Oxford and AstraZeneca, the vaccine had to be supplied on a not-for-profit basis globally until October 2021, at which point AstraZeneca was able to charge for-profit prices in HICs. In the following three months, AstraZeneca recorded sales of USD 1.8 billion.

This case study illustrates how public interest conditions on publicly funded health tools are both feasible and can have a positive impact on affordable access. However, the lack of transparency surrounding contracts relating to funding, licensing, and advance purchase of the vaccine hinders public entities from learning from this experience.

BASED ON THE FINDINGS CONTAINED IN THIS REPORT,

THE UK GOVERNMENT SHOULD IMPLEMENT

THE FOLLOWING RECOMMENDATIONS TO ENSURE AFFORDABLE ACCESS

TO FUTURE PANDEMIC HEALTH TOOLS:

SCALE UP INVESTMENT IN PUBLIC-HEALTH-DRIVEN RESEARCH AND DEVELOPMENT

Public investments in research and development are crucial. The public plays an indispensable role that cannot be replicated by private or philanthropic entities. Further investment into UK manufacturing excellence (including scoping the potential for a publicly owned pharmaceutical company) and the establishment of mission-driven wealth funds to support medical innovation are required, exercising a mandate to maximise public value. To repair the damage of the UK Government's recent Official Development Assistance (ODA) funding cuts for R&D and scale up further innovation, the UK Government should urgently return to the commitment to spend 0.7% of Gross National Income (GNI) on ODA and ring-fence the equivalent of 0.5% GNI in the ODA budget for expenditure on development assistance delivered outside the UK.

INTRODUCE EQUITABLE ACCESS CONDITIONS ACROSS THE R&D CONTINUUM

The UK Government should ensure that all support for the research, development and manufacture of pandemic medical tools comes with public interest conditions covering availability, affordability, tech transfer, open access, and transparency. The specific conditions of any particular contract can be tailored to the tool, disease, stage of R&D and type of leverage the funder has over the manufacturer.

DEVELOP AND EVOLVE EQUITABLE ACCESS STRATEGIES ACROSS UK R&D FUNDERS

To ensure that equitable access conditions are coherent and complimentary, an ecosystem approach is necessary for implementing them. UK Government departments and non-departmental public bodies should develop a common strategy and standards in relation to access conditions and apply these consistently to ensure equitable access to UK-funded innovation.

Where UK public entities are seminal in the creation of new technologies, a common access plan should be developed to maximise the global public value of the technology. Further, funders should act as learning entities by conducting regular reviews of their access strategies and conditions and alter their approach based on the resulting findings.

ENSURE TRANSPARENCY ALONG THE R&D VALUE CHAIN

In order to increase transparency along the R&D value chain, UK public entities should:

-Ensure that all public funding provided for research and development is made available in a centralised database. Wherever possible, a detailed cost breakdown of the funding provided should be made available too.

-Ensure that all producers of products registered by the MHRA publicly disclose net-prices, public, private and other contributions to their R&D, patent status, licensing agreements, and a summary of contractual access conditions to which they have agreed.

-Ensure that all clinical trials conducted in the UK are compliant with international standard clinical trial transparency norms such as the WHO joint statement on clinical trial transparency.

SUPPORT GLOBAL INITIATIVES WHICH SAFEGUARD EQUITABLE ACCESS

The UK Government should support global initiatives and frameworks which aim to increase equitable access to pandemic tools, including The WHO mRNA technology transfer hub which aims to build geographically diverse and independent R&D and improve the manufacturing capacity of mRNA vaccines in LMICs. Ideally these initiatives support equitable sharing of not only end-products but also the means and control of their production.

The UK Government should also urgently support the extension of the WTO TRIPS waiver to include COVID-19 therapeutics and diagnostics.

National and international options to support public manufacturing of essential health tools for EIDs should be explored as a sustainable alternative to market failure in inter-pandemic times and profiteering and limited access during public health emergencies.

INCORPORATE EQUITY IN INTERNATIONAL POSITIONS ON R&D

Supporting global R&D beyond LMICs by shifting resources and power has the potential to deliver large global public health benefits by enabling further innovation. This is especially the case for platform technologies. As a global leader in EID R&D, the UK could systematise its positioning at international fora to support LMIC countries in becoming future co-leaders.

INTRODUCTION

As the COVID-19 pandemic enters its third year, the official global death toll approaches 7 million.[6] Excess mortality statistics, which are better able to reflect the true death toll by including deaths not correctly diagnosed or recorded, indicate a number two to four times higher. However, statistics are unable to quantify the true economic and social hardship endured by the world in the last three years. This hardship and loss of life have fallen disproportionately on those already marginalised by race, gender, ability and class across the world. This compounded existing health inequalities in part due to the inequitable distribution of COVID-19 tools, vaccines and diagnostics. In the year following the approval of the first effective COVID-19 vaccines, the continent of Africa received just 3% of the global vaccine supply despite representing one-fifth of the world's population.[7] While these dynamics of inequality were well-publicised for COVID-19 vaccines, it has also played out in other COVID-19 tools such as diagnostics and therapeutics, **and disproportionately affected communities in low- and middle-income countries (LMICs).**

The pandemic has been characterised by unprecedented progress in scientific research—including the rapid development of diagnostics, vaccines and therapeutics. Public support was critical within this innovation. In the context of the pandemic, **public support included both financial and non-financial mechanisms. National and global taxpayer-funded institutions led, funded, or contributed to critical research and development, manufacturing or distribution of COVID-19 tools**. This large and complex web of public support included critical support from the UK Government, as this report demonstrates. Conservative estimates by the authors of this report put the total spent by various government agencies to fund the development of COVID-19 diagnostics, vaccines, and therapeutics; and to scale up the UK's vaccine manufacturing capacity at almost £1.5 billion.[8]

However, the governance of COVID-19 tools, including their distribution, pricing and manufacturing, has too often been dominated by narrow commercial or nationalistic motives rather than the interests of global public health. **The ecosystem of public support, including manufacturing, coordination and logistics from multiple contributors, that made ground-breaking COVID-19 research possible was not leveraged to ensure COVID-19 tools were turned into global public goods** (with equitable supply, pricing, and availability). **Instead, we argue the global pharmaceutical industry extracted significant financial and reputational value from the public knowledge created during the R&D process, at the expense of public health.** Furthermore, the medical tools highlighted in this report (Sotrovimab, Tocilizumab, the Oxford-AstraZeneca vaccine, and Surescreen's diagnostics) alone incurred costs to the NHS of at least £912 million. There has been a huge transfer of publicly developed knowledge and public funds from the state to the private sector with little accountability and no safeguards to protect the public good.

We believe that the value extraction by the pharmaceutical industry relies on racism and coloniality. We consider a 'extractive global health system' as a model where risk and investment are socialised, profits are privatised, and health products are monopolised by a small number of firms. High income country governments wielded their economic power to gain priority access to COVID-19 tools. They also used their geopolitical power to protect the interests of pharmaceutical companies and ensure access to essential medicines for their populations alone. This left LMIC populations without equitable access to medical tools.[9] Shared vaccines equitably with the world, it is

estimated that at least 1.3 million lives could have been saved in the first year of the vaccine rollout alone.[10]

It can be argued that this approach is not only racist but harmful to the health of populations across the world. The lack of global equitable access to COVID-19 tools poses a threat to public health by contributing to continued transmissions and risking the emergence of new variants. In addition, as will be highlighted in the case studies of this report, the extractive nature of some pharmaceutical companies extends even to HICs. This subsequently places a large burden on the UK's NHS by forcing it to pay exorbitant prices procuring products it helped to develop.

We believe that key parts of the UK Government's response to COVID-19 followed **a nationalistic, 'biosecurity'-based strategy to ensure access to COVID-19 tools for its own population**. This approach used a limited notion of public health for citizens within a particular nation state, rather than the global public. Whilst the UK supported some efforts to achieve equitable access, such as the ACT-A, these efforts are overshadowed by opposition to other initiatives that could have tackled the root causes of inequitable access. This included the TRIPS waiver and the WHO COVID-19 Technology Access Pool (C-TAP). In fact, there was a complaint filed to the UN Committee on Elimination of Racial Discrimination that highlighted the UK, Germany, Switzerland and the US' opposition to the TRIPS Waiver[11].

In this report, we examine how the UK's role in developing COVID-19 health tools supported scientific research but largely failed to ensure access to resulting products and disrupt the extractive nature of the global pharmaceutical industry.

The report is structured in three sections. **The first section provides a historical context of R&D investments in emerging infectious disease (EID) (or pandemic preparedness) R&D. It also maps the overall support the UK has provided in the development of health tools related to COVID-19**. It also outlines the general policies or guidelines that the UK has used to promote, or that have failed to promote, equitable access around the world.

The second section takes a deeper dive into the research and development history of six COVID-19 medical tools. It describes how the UK supported their development, what the NHS has spent on procuring these tools, and how the UK's funding impacted equitable access. In this section, we also explore the impact of different R&D practices on equitable access to the selected COVID-19 health tools.

The final section of the report takes stock of the state of COVID-19 R&D in the UK. It makes recommendations for how the UK Government can integrate access, affordability and equity throughout the pandemic R&D process going forward.

GLOBAL INEQUITABLE ACCESS TO VACCINES, DIAGNOSTICS AND THERAPEUTICS

DR ELIA BADJO

Dr Elia Badjo is a doctor working in the city of Gomma in the Democratic Republic of the Congo (DRC) and director of Cosamed, a health agency working with vulnerable communities in the North Kivu province—the province with the second highest rate of infections during the COVID-19 pandemic.

Working mainly in rural areas, Dr Elia noticed the acute shortage of government-supplied tests during the pandemic. The shortages would sometimes last two months. In these moments, hospitals would end up buying tests from pharmacies, and patients would be made to pay for these tests, making the test inaccessible for a large majority of the population (tests are roughly USD 5 for rapid tests and USD 40 for PCR tests). At the very beginning of the pandemic, the WHO provided the government with some COVID-19 tests and provided training to healthcare workers on how to use the tests, but this was a short-term intervention.

There were also issues around PCR testing sites being far away from rural areas. Even when tests were available, results would often come back days later, after the person was no longer infectious. In addition, because of a lack of resources, there was no system for following up people at home after they had presented at hospitals. For example, there was no system of phone check-ins.

Dr Elia suggests that the lack of testing has also had an impact on vaccination rates. Vaccination uptake in the DRC is very low, including amongst healthcare professionals. Many people do not know if they have had COVID-19, as they were not being tested; this has led to a low uptake of the vaccine because those people do not consider themselves at risk.

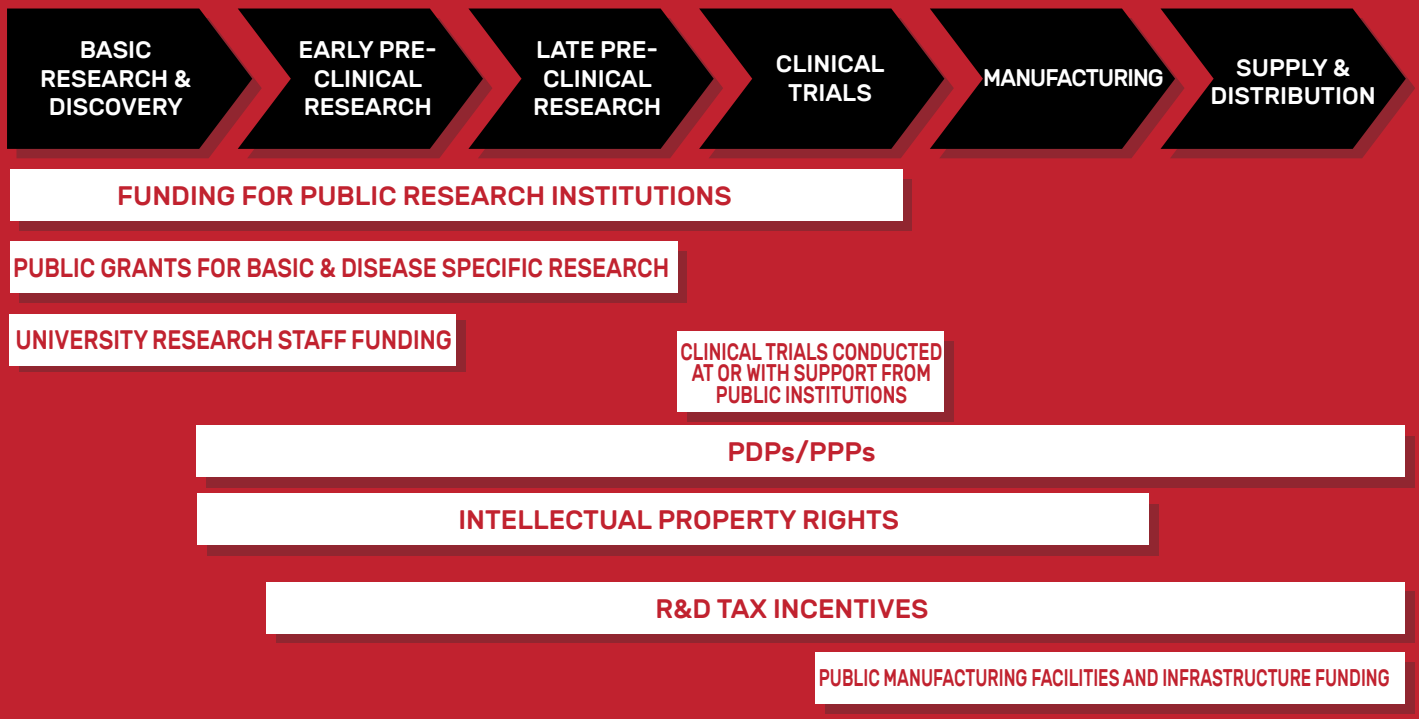
As the world transitioned from the height of the COVID-19 pandemic, massive inequities remained in access to COVID-19 tools, including access to oxygen, rapid tests and medication. In the DRC, during the pandemic, there was no access to oxygen, and today, it is still primarily available in urban areas, and in short supply in most rural areas. The DRC is yet to have access to monoclonal antibody treatments or antiviral medications for COVID-19.

Dr Badjo's testimony highlights how communities in LMICs, particularly health workers, are impacted by inequitable access not just to vaccines but also to life-saving diagnostics and therapeutics. These inequities compound each other, with lack of access to therapeutics worsening access to vaccines. It also highlights how structural issues such as health system accessibility are amplified by inequitable access to health tools.

PART 1: UK FUNDING FOR COVID-19 MEDICAL TOOLS

Public support underpinning the biomedical R&D-to-manufacturing continuum is well documented. Despite fragmented data, a diverse set of literature indicates that the public financial contribution to biomedical R&D ranges from 22% to 74%, depending on the disease area and years selected. Besides financial contributions, the public often underpins the continuum through in-kind support or incentives such as tax or intellectual property incentives. A non-exhaustive conceptualisation of the various stages and types of public support is shown in schematic form in Figure 1.

FIGURE 1: Prototypical map of public support for the development of health tools



In the following section, we highlight the depth and breadth of **vital UK public support, both financial and non-financial**, for the development and manufacture of COVID-19 tools through public funding, infrastructure, coordination and manufacturing, among others. Taken together, this ecosystem of public support enabled the development of diagnostics, vaccines and therapeutics.

We uncover the large sums of funding from public funding entities such as the UKRI and NIHR directed towards early- and late-stage research of specific COVID-19 tools and the basic science required to underpin the technologies. Additionally, we describe '**catalytic projects**' which are not specific to any single COVID-19 tool but play an essential role in coordinating and/or enabling research. These can take the form of consortiums, nationally coordinated studies and manufacturing capacity. **Catalytic investments such as the ones described are an essential component of the research ecosystem and are much less likely to be invested in by private companies**.[13]

However, the public health impact of this extensive web of UK public support is severely limited by the failure of the UK Government to put in place public interest safeguards and conditions. These could help ensure that the research outputs and end-products that result from these investments can benefit the public globally. We argue that safeguarding accessibility must be considered early on in the R&D process, especially when partnering with private sector actors, to maximise the public health benefit.

UK spend on the development of COVID tools

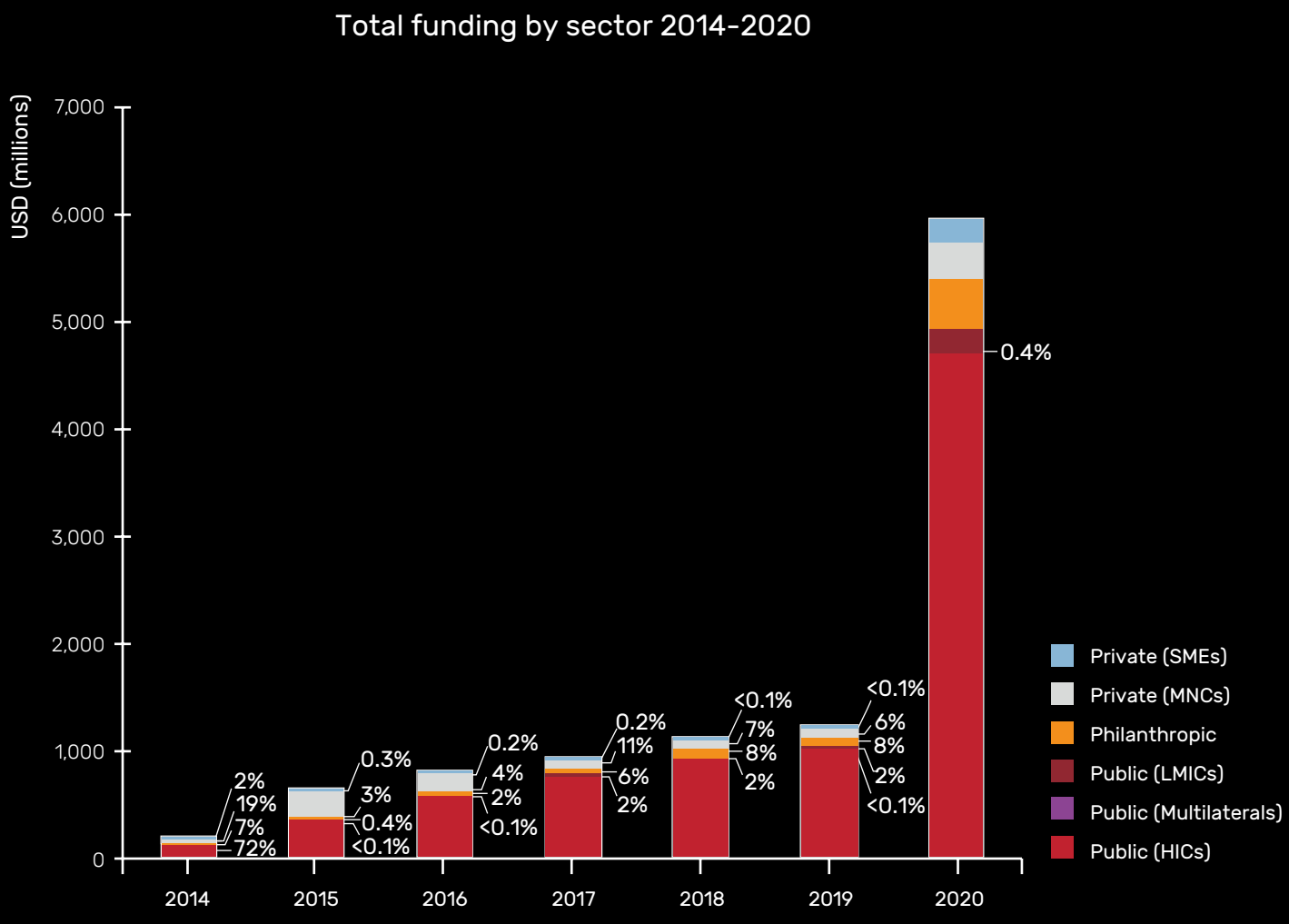
1. By the end of June 2022, the UKRI and NIHR had spent £403 million and £158 million respectively to directly fund the development of COVID-19 diagnostics, vaccines, and therapeutics.[14]
2. The UK Vaccines Taskforce funded by BEIS and the UK DHSC, funded scale up of vaccine manufacturing capacity in the UK with £200 million by the end of October 2021. In addition, the Taskforce received £429.5 million for developing UK manufacturing capacity for the period 2022-23 through to 2024-25.
3. Global funding. In terms of global funding, the two primary recipients of UK public money were CEPI and FIND.
    a. Since the Inception of CEPI in 2018, the UK Government has provided CEPI with £276 million for research and development into vaccines which was essential in supporting platform technologies (eg. Oxford vaccine platform) and vaccine candidates against COVID-19.
    b. The UK Government provided FIND with £23 million to develop diagnostics against COVID-19.

BACKGROUND TO HEALTH RESEARCH FUNDING IN THE UK

The UK has a long history of supporting global health R&D. In 2019, just prior to the pandemic, the UK spent GBP 232 million on global health R&D. UK Funding for global health R&D increased from GBP 232 million in 2019 to GBP 531 million in 2020, making it the third largest funder of global health R&D.[15] This increase was exclusively driven by a 560% (more than five-fold) rise in EID research.[16] This, however, came at a significant expense to spending in poverty-related neglected diseases and sexual and reproductive health, which decreased by 15% and 62%, respectively.

Globally, the majority of funding for EID R&D has come from public entities, who have comprised 80% of the total funding in this area since 2014 (see Figure 2).[17] Since 2017, DHSC alone has been one of the top 10 funders of Global Health R&D globally (see Figure 3).

FIGURE 2: Proportion of EID funding by funding source 2014–2020



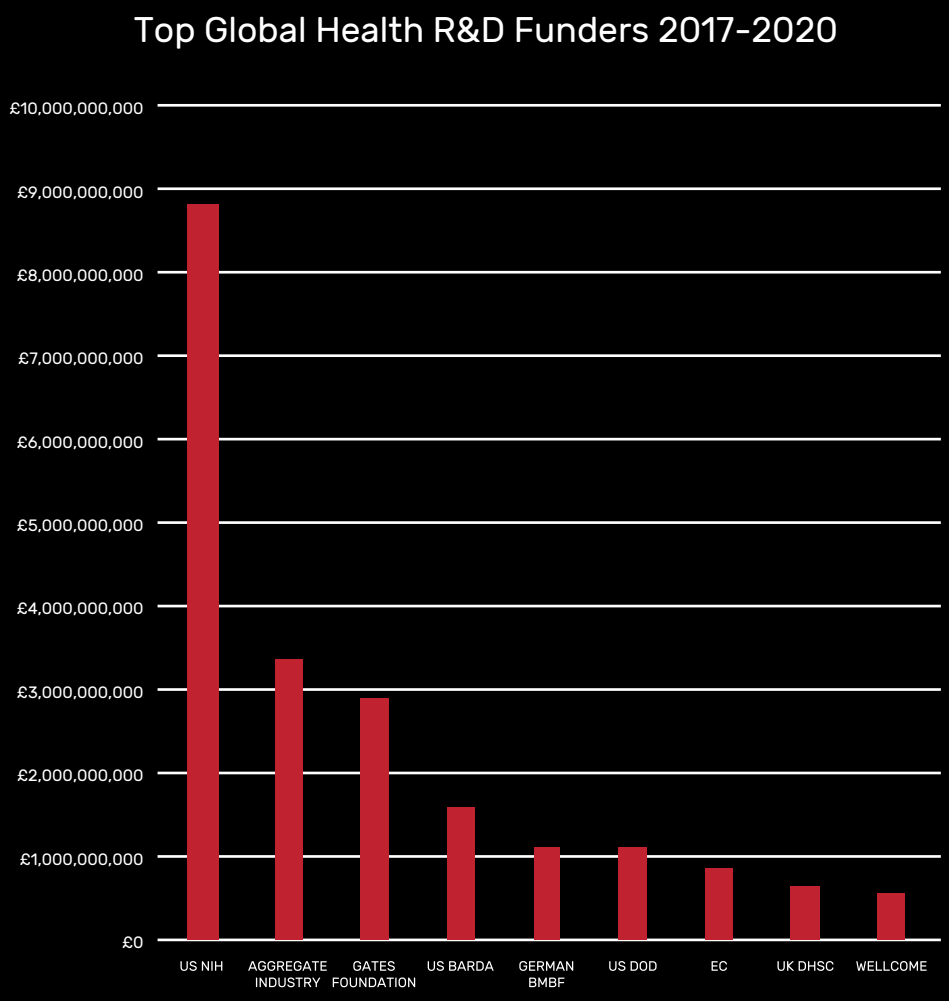
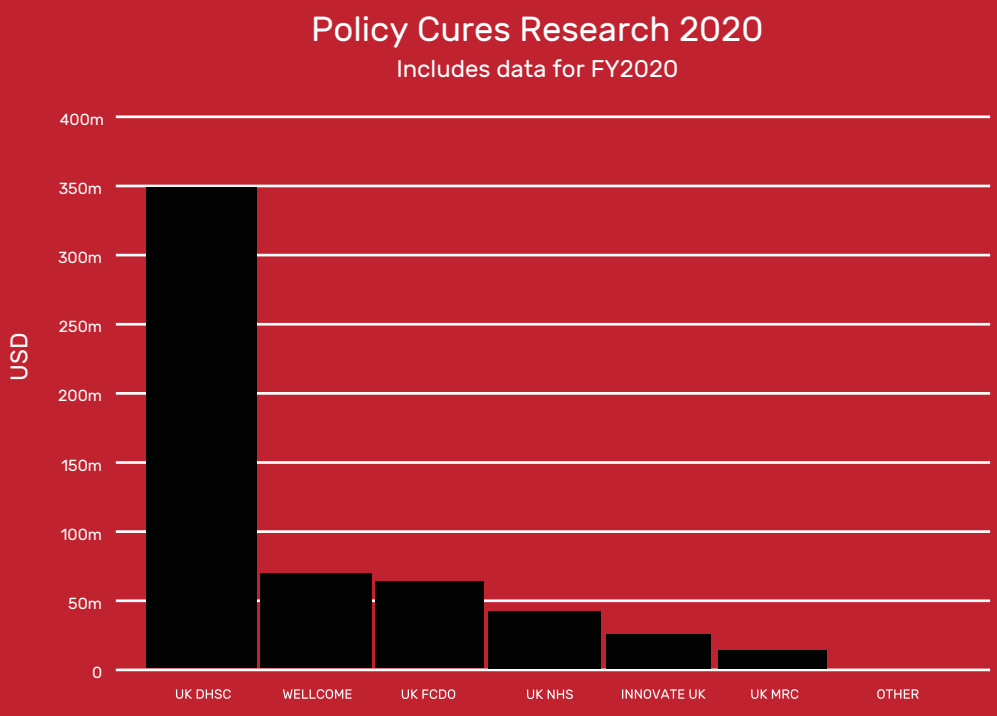


FIGURE 3: Top Global Health Funders 2017-2020

In 2020—the latest year for which this data is available—the UK's overall spending on EID amounted to GBP 476 million, with GBP 415 million coming from public sources. Of the total public EID funding, GBP 402 million was utilised for coronavirus research and development. The vast majority of the public funding was channelled through just five entities belonging to three governmental departments: DHSC; the FCDO; and the then BEIS (see Figure 4).

FIGURE 4:
Top UK EID funders in 2020



Not all public entities ensure sufficient transparency to accurately track and create a comprehensive analysis of the UK's public funding flows. This limits oversight and public accountability. However, some non-departmental public bodies, such as the National Institute for Health and Care Research (NIHR) and the UK Research and Innovation (UKRI), have made searchable databases available. These databases offer further insight into the nature and breadth of this public support.

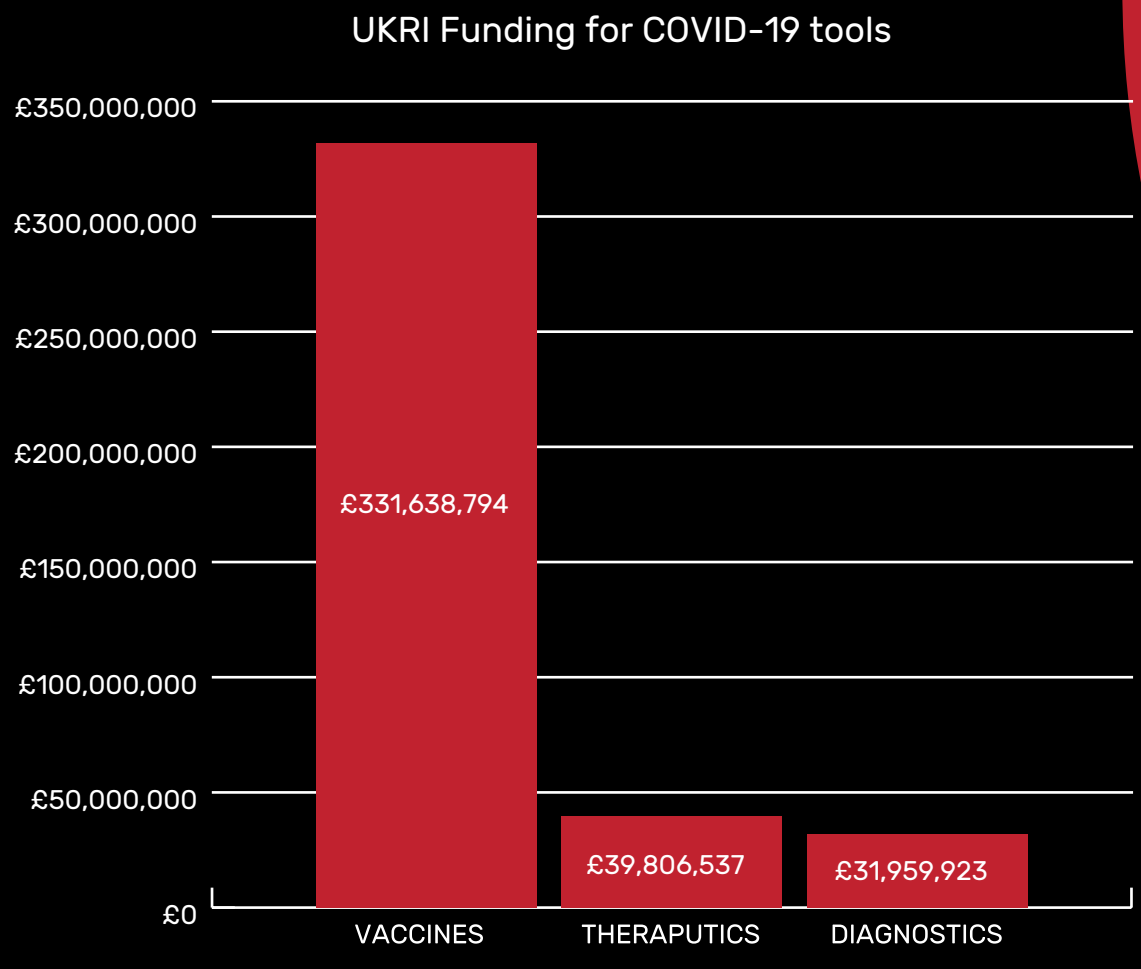
UK RESEARCH AND INNOVATION (UKRI) FUNDING FOR COVID-19 TOOLS

The UKRI was administered by the then BEIS (since February 2023, it has been sponsored by the new Department for Science, Innovation and Technology) and includes various non-departmental public bodies that have been grouped together for this report.[19]

Over the course of two years, the UKRI has invested GBP 554 million in a large number of developers and scientists working on COVID-19. Of this, GBP 403 million directly funded the development of COVID-19 diagnostics, vaccines and therapeutics (Figure 5).[20] [21] The remaining funding included some of the catalytic research projects discussed later in the report. It also included funding for epidemiology, social science, modelling, molecular research into the viral structure and variant progression and other vital pandemic research.

Many of the grants listed in the database do not report funding amounts, meaning that it is not possible to attribute exact pound sterling values to these grants. This was especially the case for grants that were 'repurposed' from other areas to COVID-19 research. This reflects the agility of public institutions during the pandemic. Therefore, the figures presented in Figure 5 are an underestimate of the true monetary value of the support provided by the UKRI.

FIGURE 5: Direct investment by UKRI into the development of COVID-19 vaccines, therapeutics and diagnostics obtained by author's analysis of publicly available databases (see Annex 1)



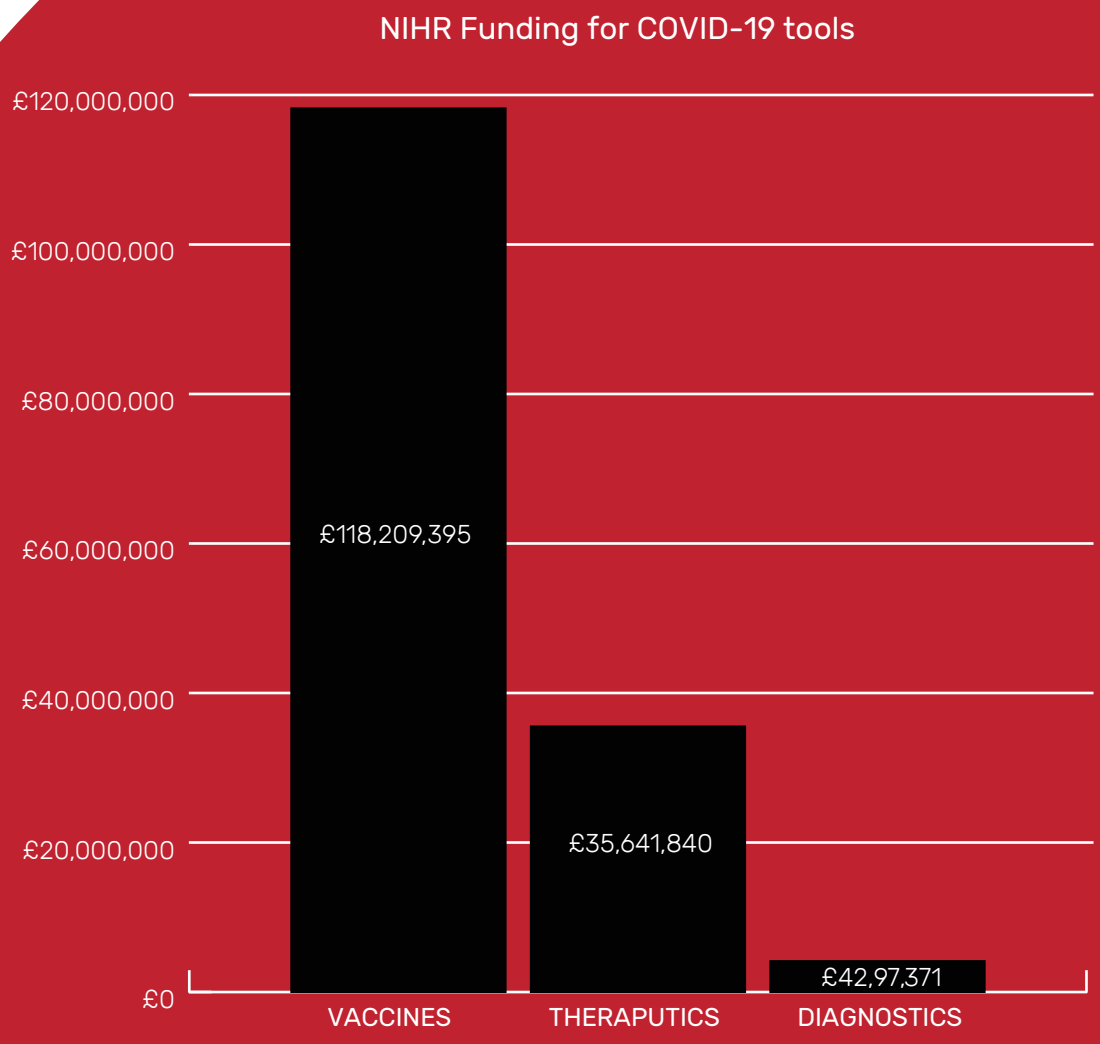
NATIONAL INSTITUTE FOR HEALTH RESEARCH (NIHR) FUNDING FOR COVID-19 TOOLS

The NIHR conducts research in and for the NHS and is funded by the UK DHSC. The NIHR funds clinical, translational, and applied health and social care research and benefits from being integrated into the NHS architecture. As such, the primary beneficiaries of NIHR funding are research groups at NHS trusts and universities.

Within one year of the beginning of the pandemic, more than one million individuals had participated in clinical trials in the UK, with the NIHR funding over half of the ongoing studies with GBP 108 million.[22] This support for clinical trials is reflected not only in the successes, but also in the null or negative results of many trials, an unavoidable and necessary part of funding innovative clinical research.

By the end of June of 2022, the NIHR had distributed an estimated total of GBP 158 million to fund the development of COVID-19 diagnostics, vaccines, and therapeutics.[23]

FIGURE 6:
Direct investment by NIHR into the development of COVID-19 vaccines, therapeutics and diagnostics obtained by author's analysis of publicly available databases (see Annex 1)



CATALYTIC PROJECTS

In addition to the broad support for pre-clinical and clinical research provided by the NIHR and UKRI for COVID-19 tools, public bodies also funded large-scale projects that did not directly develop a specific product. However, taken together, these projects create a catalytic environment consisting of scientific knowledge and industrial capacity. This catalyses both the development of diagnostics, vaccines and therapeutics. It also builds a foundation for future EID R&D.

This holistic approach to product development is a feature of public R&D support and has no private sector parallel. In fact, large pharmaceutical corporations have largely disinvested from early upstream research and focused more on the acquisition of companies with products in late-stage clinical trials.[24]. This leaves universities and small and medium enterprises, which are often the most innovative in the biomedical R&D landscape, without the support required to navigate early-stage development. [25]

Projects classified as catalytic projects were crosscutting in nature. In most cases, they made a significant contribution to the global pandemic response through knowledge generation, collaboration and the scaling-up of manufacturing capabilities.

We classify ecosystem projects under five categories:

THE VACCINES TASKFORCE (VTF)

TRIALS AND STUDIES

SUPPORT FOR GLOBAL R&D INITIATIVES

CONSORTIA

MANUFACTURING SUPPORT

The following examples and analyses are not exhaustive but are examples that demonstrate the depth and breadth of the UK's public funding of research into COVID-19 tools. In addition, these catalytic projects rely on the infrastructure and coordination of multiple public health and health system bodies.

THE VACCINES TASKFORCE AND MANUFACTURING SUPPORT

In April 2020, the UK Government established the VTF to secure access to vaccines for the UK, make provisions for the international distribution of vaccines, and support the UK's industrial strategy by establishing a long-term vaccine strategy to prepare the UK for future pandemics.[26] The VTF channelled the majority of the vaccine-related R&D and manufacturing investments made by the UK Government throughout the pandemic.

By the end of October 2021, the VTF had spent a total of GBP 3.3 billion, including GBP 2.9 billion on purchasing COVID-19 vaccines and GBP 0.2 billion on efforts to increase domestic manufacturing capacity.[27] This investment in manufacturing capacity was partly necessary because, as a result of divestment from in-house manufacturing capabilities over the decades, large pharmaceutical companies had become reliant on overseas manufacturing capabilities. This meant they were susceptible to supply chain shocks such as those caused by the pandemic.[28] As part of the BEIS Spending Review settlement, the VTF received GBP 429.5 million for developing UK manufacturing capacity for the period 2022–23 through to 2024–25.[29]

By December 2020, BEIS had committed to spend GBP 302 million on manufacturing, including:[32]

GBP 127 million to purchase, convert and run a Cell and Gene Therapy Catapult Manufacturing Innovation Centre to start vaccine production in June 2021.

GBP 93 million to accelerate the completion and expand the role of the Vaccine Manufacturing Innovation Centre (VMIC), where two vaccines against COVID-19 could be mass produced. An FOI response from 2022 reveals that this amount had increased to GBP 140.6m to accommodate an expansion of the capacity at the VMIC. This project was originally due to be completed in summer 2022 but was sold to the contract manufacturer Catalent in April 2022.[30] There is no public information about any potential public health safeguards included in the sale.[31]

GBP 42 million to put up to two different vaccines into vials so they can be delivered to vaccination sites from August 2020 for 18 months. This process is referred to as 'fill and finish'.

GBP 31 million to support skills development and early manufacturing of the vaccines developed by the University of Oxford and Imperial College London.

GBP 9 million used to train staff from VMIC and to purchase manufacturing equipment.

Further examples of UK manufacturing support can be found in Annex 2.

Of the GBP 2.9 billion spent by the VTF on vaccine purchases, many were made as advance purchase agreements. This was where a portion of the payment was typically made upfront, followed by payments in full upon delivery. Given that these payments were made ahead of regulatory approval of the vaccines, a process with a great deal of uncertainty involved, these payments acted as government-financed de-risking of late-stage R&D. However, these advanced purchase agreements limited the available vaccine supply to countries without the economic means to make at-risk investments. They also bypassed UK Government-supported initiatives, such as COVAX, attempting to distribute vaccines globally by need.

TRIALS AND STUDIES

GENETICS OF MORTALITY IN CRITICAL CARE (GENOMICC) STUDY PROGRAM

The GENOMICC study program comprised three study groups that utilise genetic information to understand the variations in COVID-19 disease severity. The study uncovered genetically determined biological mechanisms that help explain the variance in COVID-19 severity and represents an important contribution to possible therapeutic targets.

The study was financed by primarily public and philanthropic contributions from the DHSC, the MRC, LifeArc, UKRI, Sepsis Research (the Fiona Elizabeth Agnew Trust), the Intensive Care Society, the Wellcome Trust and the BBSRC Institute. The funding provided by the UKRI, DHSC and the NIHR alone amounted to GBP 28 million.[33]

HUMAN CHALLENGE STUDY PROGRAMME

In October 2020, under the auspices of the VTF, Imperial College sponsored the viral human challenge trial in collaboration with BEIS and hVIVO, a contract research organisation. The purpose of the human challenge programme was to build a model that would increase the speed and lower the cost of vaccine efficacy studies and quickly define correlates of protection by intentionally exposing the trial population to the virus. The first trial model yielded the important finding that lateral flow tests remain efficacious in the face of a changing variant landscape.[34] [35] The second trial set out to investigate the amount of delta variant virus necessary to cause infections in vaccinated adults but has yet to publish results.[36] BEIS funded the Human challenge study program with GBP 33.6 million.[37]

AGILE CLINICAL TRIAL PLATFORM

The AGILE clinical trial platform tests pandemic countermeasure therapeutics in early stages of drug development, bridging the gap between non-human trials and clinical trials. The platform was conceived by UK scientists from the University of Liverpool, Liverpool School of Tropical Medicine, Southampton Clinical trials unit and other UK publicly funded entities. The trial platform contributed to the assessment or development of four different COVID-19 therapeutics. This included the phase 1 study supporting the approval of Molnupiravir. This was the first antiviral therapeutic approved in the UK, alongside the antibody platform that included Sotrovimab (see Sotrovimab case study for more details).[38]

The AGILE platform is sponsored by multiple UK public entities or supported bodies including the NIHR, UKRI, Cancer Research UK, Unitaid and others. Further funding of GBP 3.2 million was provided by the NIHR and MRC in February 2021.[39]

PUBLIC HEALTH ENGLAND VACCINE TESTING FACILITY

The UK Government funded an expansion of PHE's capability to test blood samples from clinical trials in a new laboratory facility in Porton Down. This sought to accelerate vaccine efficacy testing and support the UK regulatory approval of novel vaccine candidates. Initially, GBP 19.7 million was invested in this facility in 2020.[40] In 2021, an additional GBP 29.3 million was invested in the site to boost PHE/Porton Down's vaccine efficacy testing capability, including against different virus variants.[41] [42]

GLOBAL R&D SUPPORT

The UK Government has channelled significant funding for EID R&D through support for multilateral initiatives, chief among them the Coalition for Epidemic Preparedness Innovations and Foundation for Innovative New Diagnostics (FIND).

The Coalition for Epidemic Preparedness Innovations (CEPI) invests in the development of vaccines against pandemic threats. Since its inception, the UK Government has provided the CEPI with GBP 276 million, which was essential in creating the CEPI's expansive COVID-19 vaccine portfolio (containing over 18 vaccine candidates).[43] Further, the UK Government has been a strong supporter of the CEPI's fundraising efforts, making early pledges and hosting its last replenishment conference.[44] The CEPI has also utilised the funding it received to spur the creation of what it calls "enabling science" initiatives. This seeks to strengthen the global vaccine R&D capacity and support vaccine implementation studies.

FIND is a global alliance that works to strengthen diagnostic global diagnostic surveillance capacity by funding R&D of diagnostics which address primarily communicable diseases such as tuberculosis, malaria, hepatitis, and COVID-19. The UK Government has supported key diagnostic R&D efforts through FIND in the past. It also provided FIND with GBP 23 million to further develop easily-manufactured testing devices against COVID-19.[45] This included the Mologic lateral flow test for COVID-19 (see the Mologic case study for more details).

CONSORTIUMS

COVID-19 UK GENOMICS CONSORTIUM (COG-UK)

The UK COVID-19 Genomics consortium (COG-UK) consists of 16 national sequencing hubs that have been able to sequence over 137,000 SARS-CoV-2 genomes. This has been critical in tracking the evolution of the virus and aiding the UK in adapting its response appropriately. Further, the COG-UK has developed novel sequencing methods and tools that are able to interpret the generated data and create data linkages.

The COG-UK received an initial GBP 20 million from the UKRI, PHE and the Wellcome Trust in March of 2020.[46] This funding was followed by a GBP 12.2 million grant from the DHSC in November of 2020, bringing the total to GBP 22.2 million.[47]

The consortium coordinates the efforts of 20 centres in the UK, and it coordinates with the International Severe Acute Respiratory Infection Consortium—Coronavirus Clinical Characterisation Consortium (ISARIC 4C).[48] The UK CIC is co-funded by the DHSC and the UKRI through a total of GBP6.5 million split equally between the two entities.[49]

NATIONAL IMMUNISATION SCHEDULE EVALUATION CONSORTIUM (NISEC)

The National Immunisation Schedule Evaluation Consortium (NISEC) has existed since 2017 and provides a platform to conduct studies that inform policy and decision making for the UK national immunisation programme. The NISEC is funded by the NIHR but received additional funding worth GBP 41.6 million from the UK VTF and NIHR for the COVID-19 response[50].

By conducting large studies through a network of NIHR-supported recruiting sites, the NISEC has conducted six studies in COVID-19 vaccination. This answered a range of public-health-driven questions such as how well young people respond to available vaccines, how current vaccines work in pregnancy, and the efficacy of various vaccine combinations. NISEC led studies have already yielded important results, which have been shared in eight academic publications and have resulted in at least five policy changes.[51]

PART 1 CONCLUSION

The extensive depth and breadth of UK public support for R&D towards COVID-19 tools was incredibly important for the global pandemic response. This critical public support is in counter to Boris Johnson's assertion that 'greed' and 'capitalism' were the success of the UK's COVID-19 vaccination programme.[52] For good public policymaking it is important the correct lessons are drawn from this experience. Public investment in early research and catalytic projects provided the environment necessary for developing specific diagnostics, vaccines and therapeutics. Direct investment in late-stage product development also enabled the finalisation and refinement of health tools. The depth and breadth of public support for research into COVID-19 tools goes so far that most COVID-19 medical tools likely benefited from some kind of support from this ecosystem.

Certain elements necessary to enable equitable access were included in the catalytic projects identified above (e.g., open access or open-source approaches), but our review found no evidence of UK R&D policies specifically addressing the urgent need for available and affordable COVID-19 health products in LMICs. The only COVID-19 projects supported by the UK Government that apply equitable access conditions to their funding are FIND and CEPI.[53] [54] However, neither organisation is governed by the UK Government and their approaches to ensuring access have been found wanting by outside observers.[55] [56] [57] [58] [59]

The NIHR appears to be the only public UK R&D funder that even has a template approach to ensuring public return on public investments. The NIHR Research Contract templates relevant to COVID-19 research grants include provisions that address the management of intellectual property (IP) and ensure a benefit return on revenue generated through the commercialisation of IP, where this return is characterised as "patient benefit". "Patient benefit" can mean receiving a portion of the financial revenue generated by the IP but also may include product discounts for the wider NHS or the dissemination of products by the NIHR on a non-commercial basis. In a response to an FOI, the NIHR stated that their COVID-19 contracts were "not intended to promote excessive reach through" and that it "does not seek to influence the management or use of intellectual property that is developed without support from NIHR".[60] Such statements once again reveal that equitable access, especially in LMICs, is not a priority when the NIHR funds research.

The depth and breadth of public support for the research, development and manufacturing of COVID-19 tools highlights that the international community did not need to rely on the private sector or IP protection to enable innovation. This strength should have been better utilised in negotiations with industry to strengthen the public sector position to guarantee equitable access conditions.

The worry that access to critical COVID-19 medical tools would be limited arose early on in the pandemic. This would have given the UK Government time to address this issue in its earliest R&D investments and advanced purchase agreements. Concerns around access to government-funded or -supported R&D have been raised for many years, including by STOPAIDS and Global Justice Now in their "Pills and Profits" report, which recommended integrating equitable access measures into the R&D system.[61]

Overall, the UK did not use its significant role in COVID-19 R&D to ensure any public interest conditions on the outcomes of this research. Across all government-funded COVID-19 general funding and catalytic projects, we can find no evidence of a coherent strategy that would ensure equitable access to government-funded or -supported COVID-19 medical tool technologies. **This is despite the fact that the UK Government**

has stated that it is "developing common principles for the management of research outputs to standardise the approach in research funding (grants and contracts) to encourage equitable access for less developed countries" in its 100-Day Mission implementation report.[62] A coherent national strategy would be necessary given the complexity of the public funding ecosystem. The recent establishment of the Department for Science, Innovation and Technology has created a key opportunity to establish this strategy. This would ideally be part of a global coordinated strategy for incorporating equitable access into the R&D continuum.

PART 2: CASE STUDIES

The following case studies were selected to represent some of the R&D and manufacturing models observed during the pandemic. The six COVID-19 tools (two each of therapeutics, diagnostics, and vaccines) were selected in order to illustrate the UK's public involvement across this spectrum.

The case studies illustrate a variety of strategies related to R&D conditionalities, manufacturing and other equitable access interventions. Some products were more accessible than others due to decisions made by the actors involved (both public and private) to prioritise public health and equity during the R&D process and beyond.

MONOCLONAL ANTIBODY (MAB)-BASED THERAPEUTICS

Monoclonal antibodies (mAbs) are synthetic antibodies produced to target a specific antigen. MAbs have been in use since their development by scientists at the MRC in Cambridge in the 1980s and 1990s, as covered in the STOPAIDS and Global Justice Now's "Pills and Profits" report.[63] During COVID-19, mAbs have played an important role in reducing the mortality of hospitalised patients and reducing the proportion of patients whose conditions deteriorate.

SOTROVIMAB

Sotrovimab is a proprietary mAb developed utilising an antibody platform based on a parental antibody S309 isolated from a SARS patient in 2003.[64] It is marketed jointly by VIr Biotechnology and GlaxoSmithKline.

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

Early research and preclinical development

Whilst we were told by a Glaxosmithkline representative that 'Vir and GSK did not receive any government funding for the research and development of sotrovimab'[65], early research involving SARS patient antibody isolates – one of which eventually became Sotrovimab – was supported by non-UK public funders such as the NIAID and the US NIH as well as the EU (pre-Brexit) according to funding statements in papers identified.[66] [67] [68]

Early in vitro trials assessing the efficacy of Sotrovimab against COVID-19 were supported primarily by US public funding bodies including NIH, National Institute of General Medical Sciences, NAID and philanthropic entities.[69] [70] [71] [72]

Clinical R&D

In December 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom approved Sotrovimab.[73] The pivotal clinical trial leading to the conditional market authorisation was the COMET-ICE study, which was funded by Vir Biotechnology and Glaxosmithkline.[74] [75] However, due to the paucity of evidence supporting Sotrovimab's efficacy, a full marketing authorisation was not granted. Further clinical trials of Sotrovimab were necessary to determine its efficacy.

Among many publicly supported clinical studies into the efficacy of Sotrovimab following conditional market approval, the following clinical studies were supported by UK public entities:

- PANORAMIC study: a UK-wide clinical study investigating the effect of prescribing oral antivirals to those who are a household contact of a COVID-19-positive individual. The study is sponsored by the University of Oxford and funded by the National Institute for Health Research. The NIHR database cites funding of GBP18.7 million.

- PROTECT-V: trialling Sotrovimab and Niclosamide as prophylactic drugs administered over a six-month period in vulnerable renal and immunosuppressed patients. This study was stopped, but according to the NIHR database, the study received a GBP1.7 million grant.

- The RECOVERY trial (see separate section on this trial)

- AGILE Trial: testing the efficacy of both compounds VIR-7831 (Sotrovimab) and VIR-7832 (a sister compound of Sotrovimab) and funded by a coalition of UK public entities (see AGILE Clinical trial platform section for further detail)

GLOBAL ACCESS

In its annual report ending December 2021, Vir Biotechnology reports to have received binding agreements for the sale of approximately 1.7 million doses of sotrovimab worldwide.[76] The United States price per course is reported to be USD 2,100. [77]

Whilst Glaxosmithkline told us 'the characteristics of sotrovimab meant that it was challenging to ensure clear routes to patients in lower income countries..', to date, there is no public record of any licensing or technology transfer arrangements to enable expanded manufacturing, affordability and/or access to Sotrovimab. In addition, no doses were sold to the ACT-A. This is despite the fact there were positive recommendations from the WHO for the use of Sotrovimab, and access plans were explored for recommended treatments with manufacturers.[78]

The patients to benefit from Sotrovimab were therefore significantly limited to residents of the UK, the US and the EU.

COST TO THE NHS

The NHS Business Services Authority makes NHS England's primary and secondary care medicines data publicly available. From when Sotrovimab was made first available in December 2021 to April 2022, the NHS utilised 28,156 vials at an NHS indicative price of GBP 2,209 per vial, equating to a total spend of GBP 62.2 million. However, NHS indicative prices as listed in the British National Formulary do not accurately reflect the real price paid at procurement (information on actual prices is considered to be commercially sensitive and is therefore closely guarded). Therefore, aforementioned spending figures are likely to be an overestimate, though it is unclear to what extent. In 2021, the NHS indicative prices overestimated real prices by 48% on average.[79] In 2021, GlaxoSmithKline alone made GBP 1.4 billion in COVID-related global sales in 2021, largely for Sotrovimab.[80]

SIGNIFICANCE OF CASE STUDY

Although Sotrovimab initially seems to exhibit the traditional "R&D Story" in which public entities fund early pre-clinical research and then the private sector takes over at later stages of research, this reading neglects the crucial post-approval research necessary to support a product's clinical application. In the context of a shifting epidemiology of COVID-19 variants, a continual re-evaluation of the efficacy of different mAbs, including Sotrovimab, was critical in the pandemic.

Sotrovimab's post-approval research was supported heavily by UK public entities without conditions of affordable access. This unnecessarily impacted both the NHS budget and the ability of LMICs to purchase the drug.

Finally, Sotrovimab received support from multiple different countries throughout its development, including the US and the UK. This highlights the need for and potential of a global strategy for R&D funding and conditions that prioritise equitable access.

TOCILIZUMAB

Tocilizumab is an mAb that inhibits the pro-inflammatory cytokine IL-6, a cytokine discovered in the 1980s by scientists at Osaka University.[81] mAb development was initiated by Chugai pharmaceuticals and first appears in the literature in 1993.[82] In 2014, Chugai pharmaceuticals was acquired by Roche pharmaceuticals.[83]

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

Early-stage development of the humanised mAb against IL-6 was contingent on intellectual property and know-how held by the UK MRC.[84] Due to the complexity of humanisation of intellectual property, Chugai required help from the MRC collaborative centre, and between 1990 and 1991, paid the MRC an undisclosed sum for the IP and staff time under a collaboration agreement.[85]

Prior to the COVID-19 pandemic, Tocilizumab has been approved for the treatment of a large number of autoimmune conditions. This ranged from Rheumatoid Arthritis to Giant Cell Arteritis and CAR-T therapy-induced cytokine storms. In particular, the studies supporting the indication for CAR-T therapy-induced cytokine storms suggested to researchers and clinicians that tocilizumab may be an appropriate treatment for COVID-19. This was due to similar underlying mechanisms at play. These studies involved multiple public entities in the US.[86] [87] [88] [89] [90]

When Tocilizumab gained market approval from the MHRA, the UK also provided regulatory exclusivity. This meant that the MHRA would not approve a biogeneric/biosimilar for 6 months after its approval. During this period, Roche was able to gain a substantial revenue premium without market competition.[91]

Following market approval, the key study that confirmed Tocilizumab's efficacy in COVID-19 was the RECOVERY trial (see section on RECOVERY).

GLOBAL ACCESS

In August 2021, the WHO issued a joint statement with Unitaid which expressed concern for the global shortages of Tocilizumab due to Roche's monopoly position in supplying the treatment.[92] The WHO and Unitaid urged Roche to "facilitate technology transfer and knowledge and data sharing" in order to increase the production base for Tocilizumab.[93] In July 2021, Roche and Chugai responded by declaring that they would not assert any patents for Tocilizumab "during this pandemic" in LMICs.[94] However, an analysis by Doctors Without Borders/Medecins Sans Frontieres called their declaration "insufficient" because it did not include the sharing of regulatory dossiers necessary to bring biosimilars to market and was not transparent in the way it would support technology transfer.[95]

In many countries, the price of Tocilizumab ranges from "US$410 in Australia, $646 in India to $3,625 in the USA per dose of 600mg for COVID-19."[96] A South African expert panel did not recommend the use of Tocilizumab because it was "not affordable at the current offered price".[97] Such prices stand in stark contrast to the likely cost of producing tocilizumab of just under USD 100 per gram, according to Doctors Without Borders/Medecins Sans Frontieres.[98] Roche recorded sales of CHF 3.5 billion (approximately GBP 3.1 billion) for tocilizumab in 2021, with sales increasing by 27% that year.[99]

COST TO THE NHS

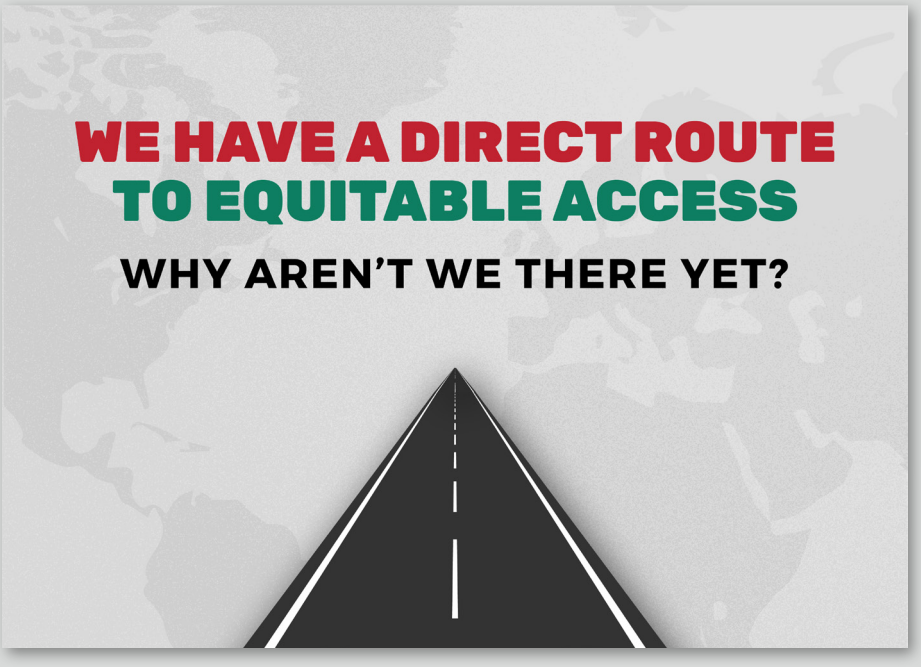
The NHS Business Services Authority makes NHS England's primary and secondary care medicines data publicly available. However, the data cannot be disaggregated by use. In order to estimate the number of doses of Tocilizumab utilised for COVID-19, the pre-COVID use was compared to the use during COVID-19. According to this comparison and utilising the BNF indicative price data, we estimate that the NHS incurred a total expenditure for Tocilizumab for the treatment of COVID-19 of GBP 47.5 million to GBP 62.2 million.

SIGNIFICANCE OF CASE STUDY

The case study of Tocilizumab tells a unique story because significant portions of its R&D occurred at times when the future indications for which it would be approved were not yet known. Although no public access conditions were included in any of the UK public funding identified, this reality raises the importance of negotiating conditions for future applications of a medical tool.

The case of Tocilizumab also demonstrates why promises to not enforce patents are not sufficient to improve the accessibility of therapeutics. This is because they benefit from other forms of market exclusivities or are costly to re-engineer.

The artificially high price created by Roche's monopoly, coupled with the refusal to transfer technology to other manufacturers, meant that this life-saving therapeutic was mostly only available to HICs, excluding communities in LMICs. Furthermore HICs health systems including the NHS, experienced supply shortages of the drug as a result of this monopoly control - as illustrated in the case study below.



IMPACT OF TOCILIZUMAB SHORTAGES ON NHS ARTHRITIS PATIENT

Kate's testimony highlights the impact of the unnecessary shortages created by Roche's monopoly on Tocilizumab.

Kate was working in the NHS as a healthcare assistant in Durham, England, during the COVID-19 pandemic. She was sheltering and working from home as the medication she was on put her at a higher risk from COVID-19.

Kate lives with rheumatoid arthritis, and had been taking Tocilizumab to support her condition for many years. Early on in the pandemic, Tocilizumab was identified as being beneficial for people with severe COVID-19.

In September 2021, Kate's medication regime was altered, and she was told that this was as a result of the demand for Tocilizumab. There were shortages and they were prioritising COVID-19 patients.

The infused version of Tocilizumab was being used for COVID-19 but not the version that is administered through injections. Kate considered switching to injection Tocilizumab, but the demand for this version of Tocilizumab was also very high as everyone was being switched to injections, so she was not able to use this version of the medication either.

At first, this was fine, but as the drug was leaving Kate's system, her inflammation levels increased, her joints flared, and she experienced high levels of pain. This made it difficult for her to move and work, and generally get about day to day.

At first, Kate was told that she would be put on a reduced dose, but in the end, she did not have any Tocilizumab between November 2020 and January 2021. Kate was on a collection of medication for her arthritis which she continued to take, but she was not given any alternatives for Tocilizumab during this time.

In February 2022, Kate experienced a flare-up and was put back on Tocilizumab at a reduced dose. Her condition settled on a reduced dose; however, she continued to experience back and neck pain, which she had not experienced before when she had been on the full dose.

Kate has been on the reduced dose for nearly a year as Tocilizumab continues to be needed for seriously ill COVID-19 patients.

Reflecting on her situation, Kate said "I was in extra pain but lives needed to be saved, however, a year down the line I thought they would have got their act together".

"Whilst manufacturers are under strain to produce what they need to produce, you want everybody to have access to something that's going to benefit them, with Covid it's going to potentially save their lives, with arthritis if they're in pain and inflammation they should be able to get it as well. Long term inflammation can have a long term impact as well".

THE RECOVERY TRIAL

The RECOVERY trial is a ground-breaking collaborative, adaptive, randomised controlled trial whose results have and continue to be critical in informing policy makers and healthcare workers on the efficacy of COVID-19 therapeutics in hospital settings. The RECOVERY trial confirmed the efficacy of dexamethasone in a context where smaller trials gave an unclear picture leading to an estimated one million lives saved.[100]

Between April 2020 and January of 2021, the RECOVERY trial recruited 4116 patients for the assessment of Tocilizumab, with a 1:1 ratio of patients receiving tocilizumab versus placebo.[101] The findings were published in the Lancet in May 2021, confirming the efficacy of Tocilizumab and supporting the continuation of the conditional marketing authorisation.[102]

The RECOVERY trial received a joint grant of GBP 2.1 million. [103] However, this figure is likely to underestimate the total public contribution to the RECOVERY trial because a significant portion of the costs are associated with running clinical trials and site-related costs. Because the RECOVERY trial was run primarily in hospitals administered by the NHS, the NHS is likely to have absorbed a significant portion of the costs.

The true public contribution to Tocilizumab's evidence base through the RECOVERY trial is approximately GBP 115 million. This is based on academic per-patient and per-indication clinical trial cost estimates (see the methodology appendix for details).

In December of 2021, the RECOVERY trial platform began recruiting patients for a Sotrovimab treatment arm. Neither the number of patients treated nor the results have been published at the time of writing.

The significance of the RECOVERY trial demonstrates the importance of comparative, agile coordinated trials conducted by the public sector during a health emergency. The private sector offers no parallel to this. The coordination, health systems infrastructure, research expertise, funding, and public participation are all examples of how public support for R&D for EID extends beyond the R&D pipeline. Despite this, the RECOVERY trial did not attempt to impact the accessibility or affordability of the tools it evaluated.

RECOVERY TRIAL PARTICIPANT

KIMBERLEY FEATHERSTONE

Kimberley's case study highlights not just the importance of coordination, financing and providing the infrastructure for trials such as RECOVERY, but the personal and emotional engagement of the public in these trials, and their desire to see the benefits of these trials shared globally.

Kimberley Featherstone was working as a Teaching Assistant at a school in her home town of Huddersfield when the pandemic began. Mother of two teenage children and five cats, when schools shut, she stayed home like everyone else. Initially, the school kept Teaching Assistants on standby in case support was needed for more vulnerable children who were still coming into school. She was not required in the end and stayed home until the summer term. She remembers at the time feeling like she wished she had a job that allowed her to contribute in some way during those challenging times. "I felt guilty about not being able to do anything useful at first".

During the summer term, there were a lot more children coming into school as it became evident that the pandemic was going on for longer. Kimberley started going into school one day a week and enjoyed having a routine again. The school where she worked is in a high-rise building; each year group had a floor, and teachers mainly had to stay in their bubble. However, Teaching Assistants weren't assigned bubbles. Kimberley would move between five different bubbles each day, moving between five different groups of thirty children. Windows were kept open, but no masks were worn. The guidance was to wear masks in the corridor, and it was hard to keep children spaced 2 metres apart.

"I knew it was inevitable I would get Covid. I wasn't going to supermarkets or doing anything other than going to work. I wanted to go into work, I was more worried about others like my sister with bad health and my parents, I wasn't so worried about getting it as I wasn't in any of the high risk categories."

During the October 2020 half term, Kimberley caught COVID, and a lot of people around her were worried. Although she felt awful and had no energy, she was mainly just bored. Three days into having COVID, she began having shortness of breath on exertion, but would be fine after sitting down for a bit. However, a few days later, on Halloween night, as she was putting her plate in the sink and sat back down, she found herself an hour later still panting. She rang 111 and went to A&E. She was given steroids and an inhaler and went home.

She felt better at first, but by the following Wednesday, she felt worse again, and by Friday, she felt as if she was trying to breathe through a straw and could barely speak. Kimberley asked her partner to ring 111, crawled into A&E with her name and date of birth written on paper as she couldn't talk and was given some oxygen. After completing the 40-step test and not passing it, she was told she had to stay in. She had developed pneumonia and was put on antibiotics and steroids. "I felt lucky to be experiencing covid seven months in, with more treatment options, can't imagine what it was like for people in the first wave".

"Two days after being in hospital a doctor approached me about the trial, I eagerly agreed to be a guinea pig. I was particularly intrigued by the monoclonal antibodies, which I later found out I was given. There were four groups you could be put on: convalescent plasma, monoclonal antibodies, antiviral medication, or remaining on standard treatment. I got attached to an IV drip and asked to report any side effects. There was a dedicated RECOVERY trial team that was amazing and always at hand. I can't say for sure that it was that particular treatment, but a few days later I felt considerably better again. Overall I was in hospital for six days. Whilst I was on the ward I was never worried for my life but it was hard to see people in the ward eating their breakfast, and by evening they were in intensive care. It felt surreal the whole time, I was like, oh I'm one of those people the council are reporting on when they report on the number of hospitalised patients."

In the summer of 2021, someone from Oxford University contacted Kimberley to say there was going to be a big announcement in the news—it turned out that the monoclonal antibodies she had been put on had turned out to be found to be very effective, and they wanted a quote for the press coverage.

Kimberley now volunteers as a patient advocate supporting the Calderdale and Huddersfield NHS Foundation Trust, where she was treated, to assist with the recruitment of people for research of all kinds. "I felt very really happy to be involved in the research and to be able to contribute. However the whole point of doing all that research and finding things that work, is to improve people's lives, health, and even save lives. There's no point finding something that works and then people not being able to access it. It comes down to putting a price tag on people lives, I know nothing comes free in the world, however this information should be shared".

COVID-19 LATERAL FLOW DIAGNOSTICS

Lateral flow diagnostics were the diagnostic technology that was able to deliver the quickest results. They have therefore played an important role in the suppression of COVID-19 cases in the pandemic. By allowing relatively simple self-testing, this technology has contributed to the suppression of transmission around the world and informed rational quarantine rules.

Latex fixation tests first described in a 1956 study funded by US public funders are credited with forming the technical basis for modern lateral flow tests.[104] The first commercial applications were further developed in the 1980s. Today, lateral flow tests are commonly used in a variety of settings, and there are over 500 patents on the technology.[105]

SURESCREEN DIAGNOSTICS

Surescreen Diagnostics is a UK-based company established in 1996.[106] The origins of its lateral flow test are not publicly reported, but it likely has its roots in the first tests approved in the 1980s.

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

Prior to the COVID-19 pandemic, Surescreen received GBP 68,430 in funding from the University of Derby as part of its "invest to grow" scheme in 2015.[107] This public support came as part of a "Knowledge Transfer Partnership", which saw the university share its research expertise and student and graduate support for Surescreen's analytical work. This collaboration was then extended for the pandemic through the further provision of human capital to assemble and distribute kits.[108]

In the process of validating diagnostic tests, PHE tested a range of different diagnostic tests. The Surescreen diagnostic tests were the first UK-developed and -produced tests to be validated in a laboratory funded by PHE and supported by the NIHR Clinical Research Network Portfolio. This made the test eligible for procurement by the NHS.

Additionally, our research identified comparative studies[109] [110] that supported the continuous evaluation of Surescreen's test performance and received funding support from:

- King's Together Rapid COVID-19
- MRC
- Wellcome Trust
- Huo Family Foundation
- National Institute for Health Research (NIHR)
- St Thomas' NHS Foundation Trust and King's College Hospital NHS Foundation Trust

GLOBAL ACCESS

The Surescreen tests are utilised in a range of countries, but pricing data are not readily available.

COST TO THE NHS

The Surescreen tests have been procured by the DHSC through two separate orders. The first order contract was for 2 million tests and the second for 20 million tests.[111] [112] The monetary value of the first contract is not known. However, the second contract has been revealed to be worth GBP 503 million, according to confidential emails seen by the Goodlaw Project, which suggest this could translate to a price of GBP 25.15 per test.[113] Surescreen state the price was lower but declined the opportunity to provide more information citing confidentiality agreements. The Surescreen COVID-19 antigen test is now commercially available for GBP 6 per test.[114] It is reported that Surescreen's profits rose from GBP 900,000 to GBP 67.2m between 2020 and May 31 2021.[115]

SIGNIFICANCE OF CASE STUDY

The high price per test, even for the UK NHS, suggests that UK public research entities involved in key comparative studies neglected to ensure equitable access principles such as affordable pricing in their support for Surescreen's R&D. This is despite how some of the entities involved are NHS trusts that are financed by the same governmental department that had to place the orders.

This case study highlights the lack of transparency regarding diagnostics, as compared to therapeutics and vaccines, when it comes to availability, pricing and technology transfer. Despite their vital importance in the mitigation of COVID-19, the accessibility of these tools received significantly less attention and scrutiny than other tools.

MOLOGIC

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

The Mologic lateral flow test was developed based on a platform created by Paul Davis (Mologic's chief scientific officer) while he was at Unilever and was first applied in the Clearblue pregnancy test.[116]

Mologic signalled its intention to develop a lateral flow test for COVID-19 with a target price of GBP 1 per test early on in the pandemic.[117] It sought to leverage previous experience with developing a rapid test for Ebola, work which was jointly funded by UK aid and the Wellcome Trust.[118] They received a GBP 1 million grant from the Wellcome Trust and the Department for International Development (now FCDO) for R&D.[119]

GLOBAL ACCESS

The FCDO provided GBP 1.5 million through FIND to scale up the manufacturing of the test in collaboration with Global Access Diagnostics (formerly a subsidiary of Mologic and social enterprise) and Diatropix (a non-profit manufacturing initiative formed in collaboration with the Institute Pasteur Dakar, Senegal).[120] Production was launched at scale in July 2020 when the first shipment of 100,000 tests was sent to Senegal.[121] Mologic was able to utilise its sourcing and manufacturing plan to price the test at GBP 1.25 per test, and further volume increases are expected to bring the price down further.[122] By comparison, the diagnostics pillar of ACT-A was only able to guarantee a ceiling price of USD 2.50 (GBP 2.01) per test by mid-2022 through a high-volume agreement involving the Global Fund.[123]

In 2021, the Bill and Melinda Gates Foundation in collaboration with the Soros Economic Development Fund invested a reported USD 41 million to buy out Mologic's investors and turn the company into a social enterprise. This enterprise has no shareholders, reinvests 100% of its profits back into its operations and continues its close relationship with LMIC manufacturers. This looks to ensure equitable access to diagnostics for LMICs to address "the fundamental inequities" in global public health.[124] [125]

COST TO THE NHS

For production in the UK, Mologic licensed its COVID-19 lateral flow technology to Omega diagnostics, a for-profit manufacturer based in the UK. Omega had a manufacturing facility in Alva, Scotland. Omega received a manufacturing contract, which included the Mologic test, worth up to GBP 374 million. This de-risked manufacturing investments made by Omega.[126] The manufacturing site in Alva was also reported to include government-funded equipment.[127] However, due to the UK leaving the manufacturing contract unfulfilled, Omega reports having only received GBP 2.5 million of the manufacturing contract by February 2021.[128] In 2022, Omega sold its Alva facility for GBP 1 million.[129]

SIGNIFICANCE OF CASE STUDY

This case study demonstrates the unique positive impact a private developer can have on equitable access. It also demonstrates that commercial incentives do not need to supersede public health impact. It is remarkable that this was possible despite no publicly available evidence of pro-access governance from public institutions that supported the development of the technology. The sale of the manufacturing site with government-funded equipment also represents a missed opportunity to expand the provision of low-cost tests for LMICs.

The collaboration emerging from the partnership between IDP Dakar and Mologic not only impacted global access to Mologic's lateral flow test but has also spurred further innovation through a new project to develop custom assays against emerging infectious diseases such as ebola, marbug and yellow fever.[130]

VACCINES

The vaccines covered in the case studies below represent outliers in the wider COVID-19 vaccines landscape. This is due to the fact that, by comparison, significant efforts have been made by public and private entities to make them available and affordable to populations across the world. These case studies offer a counterfactual to the grossly inequitable supply of mRNA vaccines. They highlight what could have been possible if mRNA manufacturers had prioritised, or been forced to prioritise, equitable access and technology transfer. Nonetheless, both case studies have shortcomings in relation to equitable access discussed below.

IMPERIAL COLLEGE SARNA VACCINE CANDIDATE

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

Self-amplifying RNA (saRNA) vaccines are based on a similar concept to the mRNA vaccines, which have proven to be highly effective in creating COVID-19 vaccines. Imperial College began the development of its saRNA vaccine platform before the pandemic with funding from the DHSC and the Engineering and Physical Sciences Research Council. The platform has undergone testing for Influenza, chlamydia and HIV.[131] [132] [133]

Imperial's saRNA platform was developed as part of the Future Vaccine Manufacturing Hub (FVMH). The FVMH was supported by the UKRI with GBP 9.9 million prior to the pandemic.[134] During the pandemic, Imperial College London received GBP 41 million from BEIS, UKRI and NIHR for the development of its COVID-19 saRNA vaccine candidate.[135] [136] [137]

GLOBAL ACCESS

In anticipation of manufacturing scale-up and access challenges, Imperial College created VaxEquity Global Health. This entity was tasked with ensuring access by geographically distributing vaccine production through a non-exclusive licensing strategy. Despite not reaching licensure, Imperial has worked with collaborators in LMICs, including the Uganda Virus Research Institute, to trial its saRNA vaccine platform COVID-19 vaccine.

However, in September 2021, AstraZeneca invested in VaxEquity and secured the right to advance research programmes based on the saRNA platform into its own pipeline. This could make VaxEquity eligible to receive a total of up to USD 195 million in payments in addition to "mid-single digits" in royalty payments.[138] [139] The public announcement of this deal made no mention of how access to the products would be ensured in LMICs. The lack of transparency or public interest commitments regarding the deal with AstraZeneca threaten equitable access to this publicly funded technology.

COST TO THE NHS

The vaccine candidate failed in phase I/II clinical trials due to low rates of seroconversion.[140]

SIGNIFICANCE OF CASE STUDY

This case study demonstrates that public funding does not always result in successes and that the risk of publicly financed failures should be factored into discussions about financing of R&D, as is the case for the private counterpart.[141] [142]

Despite the pro-access branding of VaxEquity, the lack of transparency or public commitments regarding the deal with AstraZeneca threaten equitable access to this technology.

Despite this deal with AstraZeneca, however, VaxEquity could represent an alternative approach to governing access to a technology platform as opposed to the product-by-product approach chosen by Oxford. It could also represent a novel method for public entities to avoid relinquishing control of a tool, and its accessibility, to the pharmaceutical industry.

OXFORD/ASTRAZENECA VACCINE

PUBLIC SUPPORT FOR R&D AND MANUFACTURING

A published review of the funding history of the Oxford/AstraZeneca vaccine and its platform technology by Universities Allied for Essential Medicines estimates that public and charitable financing accounted for 97%–99% of identifiable funding from 2000 to 2020.[143] The review used two methodologies to reconstruct the funding of the vaccine over the 20-year development process of the ChadOx background vector. The review identified a total of GBP 104,226,076 in funding through the first methodology, which utilised Freedom of Information Act Requests (FOIs) to institutions involved in the vaccine's development. The second methodology utilised funding figures reconstructed through a literature search and resulted in a total of GBP 228,466,771.[144]

In addition to the funding identified in the review, additional searches were conducted for the purposes of this report. A search of the UKRI and NIHR databases identified three grants not included in the review. The grants cover a personal grant and two grants to evaluate the efficacy of a primer and a boost for the vaccine worth a total of GBP 34.2 million. Further, additional FOIs to Oxford University and the vaccine's clinical trial sites revealed an additional GBP 33.6 million in funding, of which GBP 13.3 million came from the DHSC, MRC, CEPI and Oxford Biomedical Research Centre.

The UK Government also provided GBP 65.5 million for the manufacture of the Oxford/AstraZeneca vaccine in May 2020.[145] In addition, the UK Government invested GBP 8.8 million to set up a manufacturing facility at Oxford Biomedica, a contract manufacturer, to manufacture the Oxford vaccine at scale.[146]

In total, the UK Government estimates it spent more than GBP 88 million in the R&D and manufacture of the Oxford–AstraZeneca vaccine candidate specifically (not including investments into the platform as a whole), a figure consistent with the research above.[147]

An important, mostly non-financial contribution to the research into the efficacy of the Oxford–AstraZeneca vaccine was the trials conducted by South Africa and Brazil. These were crucial in better understanding the vaccine's impact in real world settings, including the impact of variants on the vaccines efficacy.[148]

GLOBAL ACCESS

Globally, the Oxford–AstraZeneca vaccine was among the most affordable and accessible vaccines, with over 2.5 billion doses supplied across the world in 180 countries; 247 million of these were supplied through COVAX in 2021.

Before Oxford signed an exclusive licence with AstraZeneca to manufacture, market and sell their vaccine candidate, Oxford conducted a technology transfer to the Serum Institute of India (SII). This was able to scale-up production and deliver vaccines to LMICs early in 2021[149]. Although export bans and supply chain constraints limited the volume of vaccines they were able to deliver in 2021, the SII was one of the earliest suppliers of COVID-19 vaccines to COVAX.[150] Oxford–AstraZeneca continued to conduct multiple technology transfers to geographically distribute manufacturing capacity and maximise supply. One such manufacturer, Bio-Manguinhos, was able to independently produce 166 million doses from 2021 to 2022.[151]

Due to a clause included in the contract between Oxford and AstraZeneca, the vaccine had to be supplied on a not-for-profit basis globally at least until June of 2021.[152] AstraZeneca declared the end of the not-for-profit period in October 2021, at which point AstraZeneca was able to charge for profit prices in HICs, whereas the obligation to provide the vaccine to LMICs would continue in perpetuity. Since the expiry of the not-for-profit commitment to December 2021, AstraZeneca has recorded sales of USD 1.8 billion (coming from a blend of profit and non-profit sales).[153]

Despite the extensive public attention and apparent pro-access management of the platform technology and the vaccine candidate, a thorough analysis of the accessibility of the vaccine is hampered by the lack of transparency of contracts relating to funding, licensing, and advance purchase of the vaccine. This is explored within another report part of the 'Access Denied' series into the "role of trade secrets in preventing global equitable access to COVID-19 tools".[154]

COST TO THE NHS

After approval by the MHRA in December 2020, the NHS was the first health system in the world to roll out the vaccine.[155] This priority supply has been reported to be due to a condition in the UK Government's early support provided to Oxford, prior to the collaboration with AstraZeneca.[156]

The UK signed an advance purchase agreement for 100 million doses in August of 2020.[157] According to the redacted contract, the vaccine was to be supplied at the cost of production (i.e., at no profit) to the UK. The UK is reported to have paid USD 3 per dose of the vaccine, placing the value of the contract at USD 300 million.[158] While details of the contract are redacted, one can infer from other similar contracts that a portion of the total contract value was made as a downpayment, derisking manufacturing investments made by AstraZeneca.

SIGNIFICANCE OF CASE STUDY

The complex development and manufacturing story of the Oxford vaccine demonstrates the importance of long-term public funding from an international community of public entities in the success of R&D. The technology and candidate were carried by public actors from the early support for basic research through clinical development and globally distributed manufacturers

The inclusion of priority supply to the UK in the advanced purchase agreement, despite reinforcing inequities in vaccine supply, demonstrates that including conditions even at a late stage of the R&D-to-manufacturing continuum is possible. Nonetheless, the nationalistic element of this condition, in combination with the lack of transparency of these agreements, unnecessarily hindered the global coordination of vaccine supply and public-health-based prioritisation of doses.

In addition, the decision of Oxford to impose access conditions at the point of licensing to AstraZeneca, and the significant impact this had, highlights the power and potential of public entities to impact the downstream affordability and availability of a product. The conditions imposed by Oxford highlight that access conditions in the R&D continuum are not only possible but effective. It also highlights that access conditions did not hinder innovation but actively promoted it. However, the exact conditions utilised by the university remain confidential. This hinders potential learning for other public entities.

Maintaining control over technology transfer with Oxford and AstraZeneca, as opposed to the alternative through the C-TAP, may have limited the rapid scale-up of the vaccine manufacturing base.

Finally, the platform underlying this vaccine was and continues to be developed for applications beyond COVID-19, such as malaria. This highlights the potential of platform-based tools to tackle emerging and established infectious diseases. It also underscores the need to democratise access to these platforms to maximise this potential.

PART 2 CONCLUSION

These case studies highlight many important lessons in pandemic R&D. **Firstly, each case study received significant public support in its development from multiple contributors and countries. This was at different stages of the R&D lifecycle, including post-approval.** This mirrors other analysis of the crucial role of public support in the development of COVID-19 tools. For example, a study requested by the EU's COVI committee found that governments supported investments either for COVID-19 vaccine R&D, manufacturing, or both, by nearly EUR 9 billion.[159] In addition, whilst HICs such as the UK mostly contributed to these case studies, other countries made significant non-financial contributions to R&D. This includes participation in clinical trials and detection of new variants as seen in the trials of the Oxford–AstraZeneca vaccine.

Secondly, we argue that the case studies highlight the danger of allowing COVID-19 technologies to be governed solely by the pharmaceutical industry and in their commercial interests. The tools for which public entities failed to incorporate conditions on access were expensive and suffered from limited availability due to a lack of a global manufacturing base. This limited their public health impact. The negative effects where there was a failure to ensure widespread access to resulting products, including premature death, fell mostly on communities in LMICs. Had governments listened to the science and shared vaccines equitably with the world, it is estimated that at least 1.3 million lives could have been saved in the first year of the vaccine rollout alone.[160]

However, the case studies also offer outlier examples of attempts to incorporate public interest (including equitable access and into the R&D itself) to varying degrees of success. The case studies show that the introduction of equitable access during different stages of development is possible. We argue that the public impact of the tools which incorporated R&D conditionalities and equitable access were higher due to their increased affordability and availability. This owed to their diversity of manufacturers and strategies to lower prices. **Not only did this not hinder innovation, but multiple cases spurred further innovation and collaboration.**

In addition, the case studies highlight the rapidly shifting nature of EID response, with agile and adaptable platform-based technologies becoming more important. This shifts preparedness R&D focus from individual products to platforms capable of delivering several products adapted to a changing environment, for example, novel viral variants or adapted therapeutic targets. As such, **efforts to improve equitable access must also adapt and focus not only on the accessibility of end-products but the technologies necessary to develop and produce them.**

This presents an opportunity to move equitable access from a product-by-product approach to an approach that democratises the application of an entire platform with unforeseeable future benefits. **Equitable access to these platforms would enable them to be developed and adapted by regional hubs to their specific contexts.** However, most of these tools, including many beyond the scope of this report, remain controlled by pharmaceutical companies in HICs. For the majority of COVID-19 tools, even if manufacturing is allowed in LMICs, control over the technology, its distribution, price, and **crucially, the ability to conduct follow-on innovation, remains monopolised.**

PART 3: CONCLUSION & RECOMMENDATIONS

PUBLIC INVESTMENT IS FUELLING AN EXTRACTIVE R&D SYSTEM

All the technologies covered in this report received substantial public support across the R&D continuum. Conservative estimates by the authors of this report put the total spent by various government agencies to fund the development of COVID-19 diagnostics, vaccines, and therapeutics; and to scale up the UK's vaccine manufacturing capacity at almost £1.5 billion.[161] The findings show that the web of public support stretches from early basic science, through all phases of medical research and development, and even to manufacturing and post-regulatory approval clinical trials. Further, the R&D support identified often included a multitude of public entities across the globe. This highlights the globalised nature of the contemporary R&D landscape.

Early basic research is predominantly funded and conducted by public entities. It plays a critical role in creating a body of knowledge. This creates the necessary preconditions for health tool research and development. Public investments in early basic research have a high risk of failure and overall amount to a significant public expenditure. Given relatively little contribution from the private sector at this stage, the value provided by the public at this stage of the research and development continuum is indispensable. However, in the UK, responsible public entities rarely utilise this to ensure equitable access to resulting technologies. This effectively socialises risk and privatises returns.

A significant challenge that public entities face in this respect is that outputs of basic research are often not foreseeable. Supporters of early research and development also lack the legal or regulatory frameworks or instruments with which they can reliably ensure downstream access. This is well illustrated by the involvement of the MRC in humanising an antibody which would eventually become Tocilizumab, given that it was at a stage when the eventual applications of Tocilizumab were unknown and, in the case of COVID-19, did not yet exist. Despite these challenges, non-exclusive open access approaches utilising a public goods approach remain underutilised as means to lay the groundwork for downstream accessibility.

In the later stages of research and development—covering pre-clinical, clinical, and post-approval research—public support is focused on specific projects, and individual financial contributions tend to be large. Due to their size and impact, this late-stage support provides ample space for the negotiation of access commitments to a given technology. However, such negotiations are more likely to be successful if prior support for early-stage R&D already introduced equitable access commitments.[162] In the absence of earlier commitments, introducing new access commitments at a late stage is challenging given the raised expectations on financial returns by private developers, but can still be effective. The example of the University of Oxford's strong commitment to access provides a positive example here. The late-stage nature of the technology allowed the University of Oxford to negotiate the non-profit commitment. It also ensured that multiple manufacturers in LMICs had access to the necessary know-how and materials to produce their vaccine independently.

Some late-stage contributions extend beyond what is traditionally considered the R&D value chain—which ends at the regulatory approval of a health tool. Such contributions are particularly difficult to leverage in favour of access commitments due to the limited leverage that supporters of this type of R&D have over developers. The RECOVERY trial mostly tested therapeutics which were already approved for other indications, and its initial focus was to repurpose medicines such as tocilizumab. This meant that trial funders (NIHR & UKRI) had little sway over the originator companies should they attempt to introduce conditions for access. **This further highlights the need for an overarching approach to emerging infectious disease tools. This should reflect the public importance and public support for these tools, as not all public contributions can be captured by conditions across the R&D continuum.**

The extensive web of public support creates an environment conducive to private sector engagement. This is highlighted by the fact that the UK is among the top three nations with SMEs engaged in countermeasure R&D.[163] However, the **overall R&D supported by the UK supports an extractive system where risk and investment are socialised, profits are privatised, and health products are monopolised by a small number of firms. This limits global access and raises prices in the UK**. Some pharmaceutical corporations have used coercive power to maintain and entrench this system, threatening investment in the UK economy and medicine supplies to the NHS if the government does not enact policies which enable this business model.[164] [165]

This value extraction compounds the high costs of new health tools. This places pressure on an under-resourced NHS. Overall, the negative consequences of this value extraction fall disproportionately on people of colour in LMICs, who are most affected by high prices and limited availability. Where individual public funders have introduced access conditions which could curtail this value extraction, these have been applied inconsistently and not publicly disclosed in their entirety.

The only exception is the consistent prioritisation of the UK population for the supply of COVID-19 tools seen in both the diagnostic and vaccine case studies. However, this is ultimately not in the interest of effective pandemic control. Nationalist approaches to public health are dysfunctional and limit the public health impact of tools. They also ignore historic inequities which UK public institutions have an obligation to address as part of their R&D approach.

With public funders largely failing to ensure public interest conditions for public funding that would have increased products' affordability and availability, governments should have urgently agreed to implement the TRIPS Waiver along the original terms proposed by South Africa and India. There was also insufficient use of TRIPS flexibilities during the pandemic despite the fact that the compulsory licensing of patents could have been used to improve the production of COVID-19 treatments and medicines to various degrees.[166]

However, the case studies also offer outlier examples of attempts to incorporate public interest (including equitable access and into the R&D itself) to varying degrees of success. The case studies show that the introduction of equitable access during different stages of development is possible. We argue that the public impact of the tools which incorporated R&D conditionalities and equitable access were higher due to their increased affordability and availability.

PUBLIC SUPPORT FOR R&D IN A COLONIAL SYSTEM

The UK, like several other HICs, built their wealth through the process of colonisation, whereby the British Empire extracted wealth from colonised countries. For example, wealth was extracted from the free labour of mostly African peoples through slavery, and from the 'natural resources' present in colonised countries. The extraction and export of materials such as coal, oil and gas was used to drive fossil-fuel-based industrialisation in the UK.[167]

The process of colonisation relied on the creation of systems of oppression which could devalue the lives of people of colour globally. This was used to facilitate the extraction of wealth to white majority countries. White supremacy and other systems of oppression were created in order to enable the exploitation, dispossession and violence which fuelled wealth extraction. These systems of oppression can be argued to have shaped access to COVID-19 tools by deeming the lives of people in LMICs disposable.

Understanding the dynamics of public support and (lack of) equitable access within COVID-19 R&D requires a historical analysis of the roots of the medical innovation system. The fields of medical research and innovation and the origins of global health are closely tied to the process of colonisation. In the late 19th and early 20th century, R&D efforts against "Tropical diseases" had often relied on institutions and incentives deeply rooted in colonialism.[168] [169] Research and the practice of medicine was focused on keeping colonial soldiers healthy and preventing infectious diseases from colonised countries from entering the colonial core. There was little to no concern for the health of colonised peoples. Coupled with the profit-oriented nature of the pharmaceutical industry, this coloniality continues to shape R&D today. For example, "neglected tropical diseases" - which share no clinical characteristics - all affect mostly communities living in poverty in LMICs and remain under-researched as there is no monopoly profit incentive to develop treatments.[170] This is despite their significant contributions to global morbidity and mortality.

Meanwhile, colonial wealth was used to fund the development of public services in countries such as the UK.[171] This also affects academic centres of excellence such as the universities of Oxford and Imperial College covered in the case studies. Both universities have benefited significantly from historical colonial wealth and status.[172] [173]

The extraction of wealth has continued despite the formal end of colonisation. Recent research estimated that the 'Global North' has drained up to USD 152 trillion from the 'Global South' since 1960, highlighting how colonial extraction is still at the core of the global economy.[174] This is commonly termed neocolonialism. For example, the pandemic has given rise to the largest capital outflow from developing countries ever recorded, with more than USD 100 billion flowing out of the Global South just in February and March of 2020.[175] The structures that enable neocolonialism include bilateral or multilateral trade agreements and international trade rules set by the World Trade Organisation (WTO). It is also worth noting that the origins of intellectual property rights also lie in the colonial system and continue to be used as a tool to protect the interests of multinational corporations at the expense of the health and wellbeing of communities. [176]

Much of the 'public investment' which the UK is able to put into medical research and development comes from colonial or neocolonial wealth extraction. Conversely, the historic and continued exploitation of

formerly colonised countries limits the public financing available to invest in the research and development of medical technologies, the strengthening of health systems, and other important public services. For example, in 2020, Zambia was spending 32.6% of its revenue on debt payments and only 8.8% on health public services.[177] This also makes formerly colonised countries' populations and their health systems more vulnerable to the impacts of pandemics. Debt cancellation may therefore be a key consideration for pandemic preparedness financing.

Although some middle-income countries typically do underinvest in R&D in relation to their GDP, the case studies in this report also highlight that an analysis focusing only on financial contributions fails to capture many non-financial contributions to R&D.[178] In addition, the 'brain drain' effect means that institutions in HICs often draw scientific expertise from LMICs to HIC. The development of UK-supported COVID-19 tools is no exception.[179] There is also a hesitancy to invest in global systems, such as the R&D system, when HICs repeatedly use their leverage and power to control the outcomes of these systems. A truly dynamic, emergent and responsive pandemic preparedness R&D system requires a repair of trust. It also requires assurances that the collective knowledge produced by global R&D is to be shared equitably.

The combined power of trade laws, intellectual property, and monopolised know-how actively prevent many LMICs from developing R&D capacities. This is highlighted by some of the case studies. It is also highlighted by other attempts throughout the pandemic to hinder the ability of researchers in LMICs to access, control and further develop COVID-19 tools such as the resistance of some HICs to the mRNA vaccine technology transfer hub.

BEATRICE ADLER-BOLTON & ARTIE VIERKANT[180]

"the claim that 'developing countries' are incapable of producing new drugs, or drugs of good quality, is not truth but rather political repression enforced by trade regimes; it is an expression of colonialism"

RECOMMENDATIONS

The UK has specific responsibilities to create the conditions to rebalance global power and repair harm both within and beyond the medical innovation system, and it is well-positioned to do so.

The nature of the R&D system is changing and it is becoming clearer that access increases, not stifles innovation. This could be an opportunity for the UK's public funding to be used to actively shift the global pharmaceutical industry away from extractivism and colonialism and towards a more effective, just and decentralised medical innovation system. The public support for research and development outlined in this report can and should be used as leverage in collaborations with private and philanthropic entities to ensure equitable access. Experiences of the COVID-19 pandemic also highlight that the public sector can be highly innovative without the pharmaceutical industry all the way to manufacturing and this should be built upon further.

Unlike many countries whose EID research entities have historical or current ties to the military, the UK gives the majority of its defence funding for infectious disease research to civilian institutions.[181] [182] This presents an opportunity to move beyond limited nationalistic and biosecurity approaches.

An equitable innovation ecosystem relies on the understanding that an effective response to global health challenges must cast its view beyond national borders. Nation- and profit-centric models of R&D view response to EID as a zero-sum game. It justifies opposition to the open sharing of research results with the "free rider problem". Instead, collective and globally equitable innovation recognises key contributions while encouraging the diffusion of knowledge and inviting further contributions.

The recommendations below are therefore designed as tools for the UK's public institutions to contribute to create the conditions for a more just and equitable medical innovation system:

1. Scale up investment in public-health-driven research and development
2. Introduce equitable access conditions across the R&D continuum
3. Develop and evolve equitable access strategies across UK R&D funders
4. Ensure transparency along the R&D value chain
5. Support global initiatives that safeguard equitable access
6. Incorporate equity into international positions on R&D

SCALE UP INVESTMENT IN PUBLIC-HEALTH-DRIVEN RESEARCH AND DEVELOPMENT

Public investments in research and development are crucial. The public plays an indispensable role which cannot be replicated by private or philanthropic entities. The COVID-19 pandemic highlights how this could be leveraged further without needing the pharmaceutical industry. Care must be taken, however, that public investments are driven by—or at the very least address—public health objectives. Public investments in biomedical R&D which have national security or industrial development as their only objectives are bound to neglect public health objectives and disregard equity issues.

As part of a new UK industrial strategy on innovative medical development, the UK Government should ensure public money is used to create medical breakthroughs at prices affordable to the NHS and governments around the world. At the same time, they should improve the value of educational institutions and create more skilled jobs. Part of this strategy should include further investment into UK manufacturing excellence (including scoping the potential for a publicly owned pharmaceutical company) and the establishment of mission-driven wealth funds to support medical innovation, exercising a mandate to maximise public value.

To repair the damage of recent UK Government Official Development Assistance (ODA) R&D funding and scale up further innovation, the UK should urgently return to the commitment to spend 0.7% of gross national income (GNI) on ODA. The UK Government should also implement the International Development Select Committee's recommendation for the HM Treasury to ring-fence the equivalent of 0.5% GNI in the ODA budget for expenditure on development assistance delivered outside the UK.[183] This funding should support north-south, and south-south tech transfer and increased local R&D and production capacity across the global south.

The current incentive system for drug development, both for pandemic and other health tools, is failing to deliver optimal health outcomes and must be reformed. A critical step is to 'delink' the cost of R&D from the price of any resulting product. Innovation can instead be supported through grants or subsidies and rewarded by a variety of prizes, including innovation inducement prizes, market entry rewards, or open-source dividends. Because these financing options are public in nature, they can be used to reward the achievement of R&D milestones and stipulate that results be made affordable, creating an innovation system driven by agreed health priorities and dedicated to access. There are potential large savings from this delinked system, in which new medicines enter the market at non-monopoly generic prices. STOPAIDS, Just Treatment, Global Justice Now and the UCL Institute for Innovation and Public Purpose's 'People's Prescription' report propose steps that can help transition health innovation towards such a model.[184]

INTRODUCE EQUITABLE ACCESS CONDITIONS ACROSS THE R&D CONTINUUM

There is no shortage of evidence demonstrating the kinds of R&D practices which protect and promote equitable access, or suggestions of how organisations and states could incorporate these into funding agreements.[185] [186] The specific conditions of any particular contract can be tailored to the tool, disease, context and leverage of the funder. For example, a significant number of governmental and non-governmental entities have applied a range of contractual conditions relating to access in their COVID-19 agreements or have policies on equitable access which apply across their portfolio.[187] [188]

Equitable access conditions may include but should not be limited to mechanisms to ensure affordable pricing, norms around transparency, open access to data and results, pro-access intellectual property management strategies, technology transfer to independent and geographically diverse manufacturers, regulatory registration in LMIC territories, and timely equitable supply of end products.

Depending on the product and use case, several points of engagement across the R&D continuum are possible:

1. Basic research—at this stage, possible applications and end-products may not yet be identifiable. Therefore, equitable access conditions should focus on building a solid basis for later public interest R&D by ensuring the transparency and open access of research results.
2. Early pre-clinical research—when a technology emerges, questions of ownership and potential business plans become important. Patenting should be avoided unless necessary to ensure a technology will be further developed, in which case pro-access IP management strategies should be applied to ensure the end-product remains accessible and affordable.
3. Public-to-private licensing and transfer of technology—the transfer of ownership over a technology is a critical point at which robust contractual agreements on equitable access must be made, covering manufacturing, technology transfer, supply, registration, pricing, transparency and follow-on research.
4. Direct funding of clinical trials—clinical trials occur at a point in the R&D process where business plans and technologies are already mature. In the absence of pre-existing access frameworks, it may be challenging for public entities to introduce fundamental changes. However, given the high cost and value of clinical trials, introductions of some pro-access provisions are possible by public funders.
5. Advanced purchase agreements—advanced purchase agreements play an important role in de-risking private R&D investments. They also represent a mechanism by which vaccines and therapeutics have been preferentially supplied to HICs who can afford to take on substantial risk. Introducing access conditions when signing advanced purchase agreements could counterbalance the access-limiting effect of gaining preferential access to products.

DEVELOP AND EVOLVE EQUITABLE ACCESS STRATEGIES ACROSS UK R&D FUNDERS

The ubiquity and variety of public support for R&D means that a piecemeal approach to equitable access is insufficient. To ensure that equitable access conditions are coherent and complimentary, an ecosystem approach is necessary to implementing them. UK Government departments and non-departmental public bodies should develop a common strategy and standards in relation to access conditions.These should be applied consistently to ensure equitable access to UK-funded innovation. The recent establishment of the Department for Science, Innovation and Technology creates a key opportunity to create and drive forward this cross-governmental strategy. As part of this strategy, the UK Government should look to build the capacity of public institutions to more rigorously implement and enforce conditions.

The UK's commitment to "developing common principles for the management of research outputs to standardise the approach in research funding (grants and contracts) to encourage equitable access for less developed countries" in the 100-Day Mission implementation report could form a basis for such a coherent equitable access strategy.[189]

Where UK public entities are seminal in the creation of new technologies, a common access plan should be developed to maximise the global public value of the technology. Further, funders should act as learning entities by conducting regular reviews of their access strategies and conditions and alter their approach based on the resulting findings.

Part of this UK Government access strategy should be a commitment to utilise TRIPS Flexibilities, including compulsory licensing. Further to this mandate, as explored in the 'Access Denied' report into trade secrets, a new regime of compulsory licensing of trade secrets should be implemented in UK law to supplement the existing mechanism of the compulsory licensing of patents.[190] In an urgent health crisis, this would allow for more local production of generic and biosimiliar health technologies which could also be exported to meet demand in other countries.

ENSURE TRANSPARENCY ALONG THE R&D VALUE CHAIN

Transparency is an enabler of better decision making, equity, public trust and accountability. These are all fundamental in the context of a global pandemic. In order to increase transparency along the R&D value chain, UK public entities should:

Ensure that all public funding provided for research and development is made available in a centralised database. Wherever possible, a detailed cost breakdown of the funding provided should be made available too.

Ensure that all producers of products registered by the MHRA publicly disclose net-prices, public, private and other contributions to their R&D, patent status, licensing agreements, and a summary of contractual access conditions to which they have agreed.

Ensure that all clinical trials conducted in the UK are compliant with international standard clinical trial transparency norms such as the WHO joint statement on clinical trial transparency.

Publish the terms by which procured medical products, such as vaccines, may be used and transferred onward. In a global emergency, this will assist in ensuring doses are not wasted or allowed to expire, but can be donated to countries that require them.[191]

Inform the public of the liability responsibilities and indemnities that the Government has signed up to under contracts with private companies. This will help ensure public understanding and enhance confidence in mitigating the risks of procurement.[192]

SUPPORT GLOBAL INITIATIVES WHICH SAFEGUARD EQUITABLE ACCESS

The UK Government should support global initiatives and frameworks that aim to increase equitable access to pandemic tools. Ideally, these initiatives support the equitable sharing of not only end-products but also the means and control of their production.

Two initiatives supported by the WHO meet these criteria:

- The WHO COVID Technology Access Pool (WHO C-TAP), which provides developers with a platform to share their IP, knowledge and data with quality-assured manufacturers in LMICs.

- The WHO mRNA technology transfer hub, which aims to build geographically diverse and independent R&D and improve the manufacturing capacity of mRNA vaccines in LMICs.

The UK Government should also urgently support the extension of the WTO TRIPS waiver to include COVID-19 therapeutics and diagnostics.

National and international options to support public manufacturing of essential health tools for EIDs should be explored. This would be a sustainable alternative to market failure in inter-pandemic times and profiteering and limited access during public health emergencies.

INCORPORATE EQUITY IN INTERNATIONAL POSITIONS ON R&D

Supporting global R&D beyond HICs by shifting resources and power has the potential to deliver large global public health benefits by enabling further innovation. This is especially the case for platform technologies.International collaborations where collective public financing or sharing of technical know-how with partners in LMICs was leveraged, such as is the case of the Oxford vaccine, have demonstrated the power to increase the national and international impact of UK supported R&D. Globally, such an approach would reduce the risk of systemic failure and enable more effective pandemic preparedness. As a global leader in EID R&D, the UK could systematise its positioning at international fora to support LMICs to become future co-leaders.

Such an approach requires that the UK Government embrace equity as a cross cutting principle as a highly efficient way to increase synergies which sustainably increase global EID R&D efforts, ultimately to the benefit of people in the UK and the global public. **In practice, this could include the following approaches:**

- Placing equitable access to both R&D tools and end-products at the centre of the ongoing pandemic treaty negotiations.

- Supporting global initiatives which aim to share EID intellectual property and know-know.

- For free trade agreements (FTAs), including the currently negotiated UK–India FTA, refrain from including proposals that include TRIPS-plus provisions that may have an impact on the production, registration and supply of affordable, lifesaving essential medical products.

- Introduce a "first, do no harm" principle in the process of developing health-related international policy positions which challenges policy makers to analyse the potential negative impact on equitable access and LMIC involvement in R&D of all positions taken by the UK government.

- Support policy solutions which aim to distribute not just the geographic location of manufacturing of health tools but also the control over the technologies themselves.

- Support international efforts to place equitable access conditions on public R&D funding from other HICs and global R&D initiatives. This should include the inclusion of equitable access conditions on public funding as part of the WHO Pandemic Accord and the Political Declarations to be agreed from the 2023 UN High Level Meetings on Universal Health Coverage; Tuberculosis; and Pandemic Prevention, Preparedness and Response.

ANNEX 1: METHODOLOGIES

Overall research methodology:

The research contained in this report was conducted using a mixed-methods approach. This utilised literary searches, database searches, FOIs and key informant interviews.

Data from publicly available funding databases for the NIHR and UKRI included all grants up to and including June 2022. All grants were analysed and coded individually as falling either under diagnostics, vaccines, or therapeutics research and development. If a grant covered multiple tools (e.g., research to identify potential therapeutics and vaccines), a primary category was selected based on a detailed review of the individual grant to avoid double-counting. Several grants identified in both databases did not disclose a funding amount and therefore did not contribute to the total funding figures identified. In a handful of cases, the two databases listed projects with the same title. Double-counting of overlapping projects was avoided by assuming that two grants with the same title and the same total funding amounts were duplicates, whilst grants with differing funding amounts were counted as separate projects.

For several catalytic projects, funding amounts identified in the database searches were supplemented with FOI responses. Where there was conflicting information, the authors selected one source.

Methodology used to estimate the total cost of the RECOVERY Trial:

The methodology utilised to estimate the overall cost of the RECOVERY trial is based on the data from Moore et al., 2020.[193] Data from Moore et al. estimated total and per patient costs of the pivotal clinical trials supporting the approval of 101 new therapeutic agents from 2015 to 2017. We therefore utilized the averages reported in that study from 2016 (midpoint of 2015–2017), converted the currency from dollars to pounds using historical reference rates from Bank of England for 2008, and subsequently adjusted for inflation using the Bank of England inflation calculator. [194] These figures were then adjusted for the number of trial participants which contributed to the final analysis of the Tocilizumab arm of the RECOVERY trial.[195]

Methodology used to estimate NHS expenditure on Tocilizumab and Sotrovimab:

The NHS Business Services Authority (NHSBSA) makes NHS England's primary and secondary care medicines data publicly available. For the purposes of this report, Tocilizumab and Sotrovimab usage data were extracted from the secondary care dataset (from January 2020 until April 2022). There are some limitations to the completeness and reliability of these data, which are explained on the NHSBSA site. Notably, one large hospital trust in London, the UCLH NHS Foundation Trust, does not contribute data at present.

NHS indicative prices as given in the BNF are not necessarily informative of the price paid at procurement (information which may be commercially sensitive and is therefore closely guarded). As explained in the report, one can assume a 48% discount based on the average overestimate for all indicative prices in 2021; however, the range of discounts is not known, and therefore caution must be used when applying this discount to the either product.

Methodology used to calculate total UK Government R&D support

There is no single figure that can comprehensively cover the full spectrum support the UK Government provided for the COVID-19 pandemic response. However, looking at three major channels of COVID-19 public funds can give us a good picture.

1. By the end of June 2022, the UKRI and NIHR had spent £403 million and £158 million respectively to directly fund the development of COVID-19 diagnostics, vaccines, and therapeutics.[196]
2. The UK Vaccines Taskforce funded by BEIS and the UK DHSC, funded scale up of vaccine manufacturing capacity in the UK with £200 million by the end of October 2021. In addition, the Taskforce received £429.5 million for developing UK manufacturing capacity for the period 2022-23 through to 2024-25.
3. Global funding. In terms of global funding, the two primary recipients of UK public money were CEPI and FIND.
    a. Since the Inception of CEPI in 2018, the UK government has provided CEPI with £276 million for research and development into vaccines which was essential in supporting platform technologies (eg. Oxford vaccine platform) and vaccine candidates against COVID-19.
    b. The UK government provided FIND with £23 million to develop diagnostics against COVID-19.

Methodology on how much the UK Government spent on the publicly supported case study tools

Sotrovimab

From when Sotrovimab was made first available in December 2021 to April 2022, the NHS utilised 28,156 vials at an NHS indicative price of £2,209 per vial, equating to a total spend of £62.2 million.[197]

Tocilizumab

Based off NHS indicative prices (same caveat as above) and accounting for regular use by non-Covid patients we estimate the NHS incurred a total expenditure for Tocilizumab for the treatment of COVID-19 of £47.5 million to £62.2 million.

Oxford-AstraZeneca

The UK signed an advance purchase agreement for 100 million doses in August of 2020.[198] The UK is reported to have paid $3 per dose of the vaccine, placing the value of the contract at $300 million.

Surescreen diagnostics

The Surescreen tests have been procured by the DHSC through two separate orders. The first order contract was for 2 million tests and the second for 20 million tests.[199] [200] The monetary value of the first contract is not known. However, the second contract has been revealed to be worth GBP 503 million, according to confidential emails seen by the Goodlaw Project, which suggest this could translate to a price of GBP 25.15 per test.

ANNEX 2: ADDITIONAL CATALYTIC PROJECTS

INNOVATE UK CATAPULT NETWORK

The catapult medicines discovery network is a UK Government not-for-profit organisation established by Innovate UK. It taps into a wide range of public and private entities, building links between them to accelerate drug discovery efforts. One of their focus areas is infectious disease and during the pandemic they have facilitated the creation of several initiatives to tackle COVID-19:

1. UK Lighthouse labs network—the largest national laboratory network including universities, research institutes and private companies supported by the NHS and PHE.[201]
2. Medicines Discovery Catapult collaboration with LifeArc, a medical research charity, to accelerate translational drug development through the building of biomarker validation platforms, including for COVID-19.[202]

The VTF also supported the Cell & Gene Therapy Catapult (also a Innovate UK launched catapult) with a GBP 4.7m grant to start an Advanced Therapy Skills and Training Network programme to boost cell and gene therapy as well as vaccine skills in advanced manufacturing.

UK CORONAVIRUS IMMUNOLOGY CONSORTIUM

The UK Coronavirus Immunology Consortium (UK-CIC) was set up to harness immunology expertise across UK research entities and knowledge hubs. The goal of this consortium is to better understand immunity, immune evasion, and how COVID-19 damages the body's tissues.[203]

The consortium coordinates efforts of 20 centres in the UK, and it coordinates with the International Severe Acute Respiratory Infection Consortium—Coronavirus Clinical Characterisation Consortium (ISARIC 4C).[204] The UK CIC is co-funded by the DHSC and the UKRI through a total of GBP 6.5 million split equally between the two entities.[205]

VALNEVA LIVINGSTONE SITE MANUFACTURING SITE

The UK VTF recommended the UK government support Valneva's vaccine manufacturing capability in 2020. The UK government subsequently secured 60 million doses and an option to purchase another 40 million doses in addition to a "multi-million-pound up-front investment in a Livingston manufacturing site".[206] [207] In 2021, Valneva was awarded up to GBP 20 million by Scottish Enterprise, the national economic development agency of Scotland. [208]

THE NATIONAL BIOLOGICS MANUFACTURING CENTRE

As part of the Budget 2021, the government announced funding of an additional GBP 5 million on top of a previous GBP 9 million for the Centre for Process Innovation's National Biologics Manufacturing Centre, an amount that rose to GBP 26.5 million by 2022. The purpose of the centre is to expand the UK's manufacturing capacity of biologics and to create a 'variant mRNA library' to shorten the pathway to deployment of a licensed vaccine.

ANNEX 3: ACKNOWLEDGEMENTS

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ENDNOTES:

1. WHO (2023) 'WHO Coronavirus (COVID-19) Dashboard' Available at: https://covid19.who.int/?mapFilter=deaths

2. Our World in Data, 'Coronavirus (COVID-19) vaccination). Available at https://ourworldindata.org/covid-vaccinations>.

3. STOPAIDS (2023) Access Denied: report series launch, March 2023. Available at: https://stopaids.org.uk/resources/cover-page-report-launch/

4. STOPAIDS, Global Health Advocates (2023) Access Denied: What happens when Big Pharma is in the driver's seat. Available at: https://stopaids.org.uk/resources/access-denied-what-happens-when-big-pharma-is-in-the-drivers-seat

5. See methodology

6. World Health Organisation (2023), WHO Coronavirus Dashboard, Available at: https://covid19.who.int

7. WHO (2022), Global Vaccine Market Report 2022, Available at; https://www.who.int/publications/m/item/global-vaccine-market-report-2022

8. See methodology

9. The term "equitable access" is used throughout the report and broadly defined as the timely availability of affordable therapeutics, vaccines or diagnostics that are suitable for the target population.

10. According to a study published in Nature (Moore et al, 2022), an estimated 1.3 million fewer people would have died if COVID-19 vaccines were distributed equitably in 2021: https://www.nature.com/articles/s41591-022-02064-y

11. Center for economic and social rights (2022) UN: Countries blocking the TRIPS waiver guilty of racial discrimination. Available at: https://www.cesr.org/un-countries-blocking-the-trips-waiver-guilty-of-racial-discrimination/

12. Graduate Institute, Geneva, (2019), Research Synthesis: Public Funding of Pharmaceutical R&D, Available at: https://www.knowledgeportalia.org/_files/ugd/356854_73a1ff84b65642a0926ae81f045b7c5e.pdf

13. Smith, Inglesby and O'Toole, (2004), Biodefense R&D: Anticipating Future Threats, Establishing a Strategic Environment, Available at: https://doi.org/10.1089/153871303769201842

14. This data was gathered from the publicly available NIHR and UKRI funding databases and coded by the authors of the report. Not all COVID-19 related projects in both databases "directly" contributed to the development of COVID-19 vaccines, diagnostics, or therapeutics and are therefore excluded from this figure.

15. Donor Tracker (2019), United Kingdom Global Health R&D, Available at: https://web.archive.org/web/20221014180709/https://donortracker.org/united-kingdom/globalhealthrd

16. Coronavirus is considered an emerging infectious disease

17. Policy Cures Research (2022), Landscape of Emerging Infectious Disease Research and Development: From Pandemic Response to Pandemic Resilience: https://policy-cures-website-assets.s3.ap-southeast-2.amazonaws.com/wp-content/uploads/2022/06/16191104/2022-G-FINDER-EID-Report.pdf

18. In 2023, the Department for Business, Energy and Industrial Strategy was merged with the Department for International Trade to create the Department for Business and Trade

19. These include the Arts and Humanities Research Council (AHRC), Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Economic and Social Research Council (ESRC), Innovate UK, Medical Research Council (MRC), Natural Environment Research Council (NERC), Research England, Science and Technology Facilities Council (STFC).

20. UK Research and Innovation (2023), COVID-19 Research Projects and Awards Funded by UKRI, Available at: https://www.ukri.org/publications/covid-19-research-projects-and-awards-funded-by-ukri/

21. UK Research and Innovation (2023), Tackling the Impact of COVID-19, Available at: https://www.ukri.org/news-and-events/tackling-the-impact-of-covid-19/

22. National Institute for Health and Care Research (2021), UK COVID-19 research passes one million participants, Available at: https://www.nihr.ac.uk/news/uk-covid-19-research-passes-one-million-participants/27215

23. National Institute for Health and Care Research (2023), Available at: https://www.nihr.ac.uk/

24. A. Arora and A. Gambardella (1995) "The Division of Innovative Labor in Biotechnology," in Sources of Medical Technology: Universities and Industry: 188–206.

25. Mazzucato, M., & Li, H. L. (2021). A Market Shaping Approach for the Biopharmaceutical Industry: Governing Innovation Towards the Public Interest, Available at: doi:10.1017/jme.2021.8

26. UK COVID-19 vaccines delivery plan (2021) Available at: https://www.gov.uk/government/publications/uk-covid-19-vaccines-delivery-plan/uk-covid-19-vaccines-delivery-plan

27. National Audit Office (2022), The Rollout of the COVID-19 Vaccination Programme in England, Available at: https://www.nao.org.uk/wp-content/uploads/2022/02/The-rollout-of-the-COVID-19-vaccination-programme-in-England.pdf

28. Andreoni, A. and Chang, H. J. (2016). Industrial policy and the future of manufacturing. Economia e Politca Industriale, 43, pp. 491–502.

29. National Audit Office (2022), The Rollout of the COVID-19 Vaccination Programme in England, Available at: https://www.nao.org.uk/wp-content/uploads/2022/02/The-rollout-of-the-COVID-19-vaccination-programme-in-England.pdf

30. BBC News (2022), Harwell VMIC: New vaccine centre sold to company, Available at: https://www.bbc.com/news/uk-england-oxfordshire-61011189

31. UK Parliament (2022), Vaccine Manufacturing and Innovation Centre: Finance, Available at https://questions-statements.parliament.uk/written-questions/detail/2022-04-20/156444

32. Research Professional News (2020), UK spent nearly £12bn on Covid vaccines, with more needed, Available at: https://www.researchprofessionalnews.com/rr-news-uk-politics-2020-12-uk-spent-nearly-12bn-on-covid-vaccines-with-more-needed/

33. UK Government (2020) New partnership to sequence human genomes in fight against coronavirus. Available at: https://www.gov.uk/government/news/new-partnership-to-sequence-human-genomes-in-fight-against-coronavirus

34. Imperial College London (2022), COVID-19 human challenge study reveals detailed insights into infection, Available at: https://www.imperial.ac.uk/news/233514/covid-19-human-challenge-study-reveals-detailed/

35. Killingley et al (2022), Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adult, Available at: https://www.nature.com/articles/s41591-022-01780-9#Abs1

36. Imperial College London (2022), COVHIC002 Coronavirus Human Infectious Challenge Study,, Available at: https://www.imperial.ac.uk/media/imperial-college/medicine/infectious-disease/COVHIC002-Participant-Information-Sheet.pdf

37. What Do They Know (2022), Vaccine Task Force grants, Available at: https://www.whatdotheyknow.com/request/901212/response/2140068/attach/html/3/FOI2022%2022591%20Vaccines%20Task%20Force%20Grants.pdf.html

38. AGILE (2023), Available at: https://www.agiletrial.net/

39. AGILE (2021) Government funding boost for COVID-19 drug testing platform, Available at: https://www.agiletrial.net/government-funding-boost-for-covid-19-drug-testing-platform/

40. Salisbury Journal (2020), Porton Down to accelerate testing for Covid-19 vaccine, Available at: https://www.salisburyjournal.co.uk/news/18811611.porton-accelerate-testing-covid-19-vaccine/

41. UK Government (2021), New cutting-edge testing centre to fast-track COVID-19 variant vaccines, Available at: https://www.gov.uk/government/news/new-cutting-edge-testing-centre-to-fast-track-covid-19-variant-vaccines

42. What Do They Know (2022), Vaccine Task Force grants, Available at: https://www.whatdotheyknow.com/request/901212/response/2140068/attach/html/3/FOI2022%2022591%20Vaccines%20Task%20Force%20Grants.pdf.html

43. UK Government (2022), UK pledges £160 million to boost global vaccine development, Available at: https://www.gov.uk/government/news/uk-pledges-160-million-to-boost-global-vaccine-development

44. CEPI (2021), UK to host global summit with CEPI to speed up new vaccine development, Available at: https://cepi.net/news_cepi/uk-to-host-global-summit-with-cepi-to-speed-up-new-vaccine-development/

45. UK Government (2020) PM announces record funding to find a coronavirus vaccine. Available at: https://www.gov.uk/government/news/pm-announces-record-funding-to-find-a-coronavirus-vaccine

46. UK Government (2020), UK launches whole genome sequence alliance to map spread of coronavirus, Available at: https://www.gov.uk/government/news/uk-launches-whole-genome-sequence-alliance-to-map-spread-of-coronavirus

47. UK Government (2020), £12.2 million boost for genomic surveillance to help stop transmission of COVID-19, Available at: https://www.gov.uk/government/news/122-million-boost-for-genomic-surveillance-to-help-stop-transmission-of-covid-19

48. British Society for Immunology (2023), UK Coronavirus Immunology Consortium, Available at: https://www.immunology.org/partnerships/uk-coronavirus-immunology-consortium

49. What Do They Know (2022), Funding for GENOMICC study, Available at: https://www.whatdotheyknow.com/request/901406/response/2148165/attach/html/3/FOI%201419361%201419362%201419365%20002%20DS.pdf.html

50. What Do They Know (2022), Vaccine Task Force grants, https://www.whatdotheyknow.com/request/901212/response/2140068/attach/html/3/FOI2022%2022591%20Vaccines%20Task%20Force%20Grants.pdf.html

51. National Immunisation Schedule Evaluation Consortium (2023), Outputs and Policy Impact, Available at: https://nisec.ac.uk/outputs-policy-impact

52. Washington Post (2021) Boris Johnson reportedly credits 'greed' and 'capitalism' for vaccine success, sparking debate. Available at: https://www.washingtonpost.com/world/2021/03/24/johnson-vaccine-greed-capitalism/

53. FIND (2018), Global Access Policy, Available at: https://www.finddx.org/wp-content/uploads/2021/07/FIND-Global-Access-Policy_PL-02-08-07_V1.1_JUL2021.pdf

54. CEPI (2022), Equitable Access Review of CEPI's COVID-19 Vaccine Development Agreements, Available at: https://cepi.net/wp-content/uploads/2022/05/EQUITABLE-ACCESS-REVIEW-OF-CEPIS-COVID-19-VACCINE-DEVELOPMENT-AGREEMENTS_Final_April-2022.pdf

55. MSF Access Campaign (2021), Local Diagnostics to Meet Local Health Needs, Available at: https://msfaccess.org/sites/default/files/2021-07/IP_IssueBrief_Local-diagnostics-local-health-needs_ENG_13.7.2021.pdf

56. MSF Access Campaign (2019), TIME FOR $5: GENEXPERT DIAGNOSTIC TESTS, Available at: https://msfaccess.org/sites/default/files/2019-12/MSF_Access_TechnicalBrief_GeneXpert-Time-for-5_0.pdf

57. Public Citizen (2020), COVAX's Choices, Available at: https://www.citizen.org/article/covaxs-choices/

58. The People's Vaccine Alliance (nd), Embedding equitable access in vaccine R&D: Why CEPI's access policy and governance need an overhaul, Available at: Why CEPI's access policy and governance need an overhaulhttps://peoplesvaccine.org › uploads › 2022/06

59. MSF Access Campaign (2019), The Wrong Prescription for Vaccine Access, Available at: https://msfaccess.org/wrong-prescription-vaccine-access

60. What Do They Know (2022), COVID-19 research grant terms, Available at: https://www.whatdotheyknow.com/request/878484/response/2094773/attach/html/3/FOI%201411923%20final%20reply.pdf.html

61. STOPAIDS (2017), Pills and Profits, Available at: https://stopaids.org.uk/resources/pills-and-profits-how-drug-companies-make-a-killing-out-public-research/

62. 100 Days Mission (2021), First Implementation Report, Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1038969/100_Days_Mission_-_First_Implementation_Report__1_.pdf

63. STOPAIDS, Global Justice Now (2017), Pills and Profits, Available at: https://stopaids.org.uk/resources/pills-and-profits-how-drug-companies-make-a-killing-out-public-research/

64. Liu et al (2021), A combination of cross-neutralizing antibodies synergizes to prevent SARS-CoV-2 and SARS-CoV pseudovirus infection, Available at: https://www.sciencedirect.com/science/article/pii/S1931312821001815

65. Statement from GSK representative received on Tuesday 9th May 2023: Vir and GSK did not receive any government funding for the research and development of sotrovimab.

The characteristics of sotrovimab meant that it was challenging to ensure clear routes to patients in lower income countries during the pandemic. Sotrovimab is an IV therapy which needs to be given early in the course of infection. It needs a surrounding healthcare infrastructure in place including access to a clinical setting for administration, as well as access to testing and refrigeration for storage.

During the height of the pandemic, GSK and Vir prioritised our activities in places where there was an urgent need and a clear path to access for patients.

Sotrovimab continues to be used by patients outside of the US and remains an effective and well tolerated treatment option for people at high risk of progressing to severe COVID-19.

66. Traggiai (2004), An efficient method to make human monoclonal antibodies from memory B cells: potent neutralization of SARS coronavirus, Available at: https://pubmed.ncbi.nlm.nih.gov/15247913/

67. Rockx et al (2008), Structural basis for potent cross-neutralizing human monoclonal antibody protection against lethal human and zoonotic severe acute respiratory syndrome coronavirus challenge, Available at: https://pubmed.ncbi.nlm.nih.gov/18199635/

68. Rockx et al (2010), Escape from human monoclonal antibody neutralization affects in vitro and in vivo fitness of severe acute respiratory syndrome coronavirus, https://pubmed.ncbi.nlm.nih.gov/20144042/

69. Pinto et al (2020), Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody, Available at: https://pubmed.ncbi.nlm.nih.gov/32422645/

70. Wec et al (2020), Broad neutralization of SARS-related viruses by human monoclonal antibodies, Available at: https://pubmed.ncbi.nlm.nih.gov/32540900/

71. Jette et al (2021), Broad cross-reactivity across sarbecoviruses exhibited by a subset of COVID-19 donor-derived neutralizing antibodies, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8423902/

72. Tortorici (2020), Ultrapotent human antibodies protect against SARS-CoV-2 challenge via multiple mechanisms, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857395/

73. UK Government, MHRA approves Xevudy (sotrovimab), a COVID-19 treatment found to cut hospitalisation and death by 79%, Available at: https://www.gov.uk/government/news/mhra-approves-xevudy-sotrovimab-a-covid-19-treatment-found-to-cut-hospitalisation-and-death-by-79

74. Gupta et al (2021), Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab, Available at: https://pubmed.ncbi.nlm.nih.gov/34706189/

75. Gupta et al (2022), Effect of Sotrovimab on Hospitalization or Death Among High-risk Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial, Available at: https://pubmed.ncbi.nlm.nih.gov/35285853/

76. UNITED STATES SECURITIES AND EXCHANGE COMMISSION (2022), ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the fiscal year ended December 31, 2021, Available at: https://investors.vir.bio/static-files/74f51fbf-4a2f-4f21-a042-3244d6b01f8d

77. Reuters (2022), Price of COVID treatments from Pfizer, Merck, GSK align with patient benefits -report, Available at: https://www.reuters.com/business/healthcare-pharmaceuticals/price-covid-treatments-pfizer-merck-gsk-align-with-patient-benefits-report-2022-02-03/

78. World Health Organisation (2022), WHO recommends two new drugs to treat COVID-19, Available at: https://www.who.int/news/item/14-01-2022-who-recommends-two-new-drugs-to-treat-covid-19

79. National Health Service (2023), Secondary Care Medicines Data (SCMD) with indicative price, Available at: https://opendata.nhsbsa.net/dataset/secondary-care-medicines-data-indicative-price

80. RTE, GSK's Covid-related sales hit £1.4 billion, but profit boost to wane in 2022. Available at: https://www.rte.ie/news/business/2022/0209/1278708-gsk-results/

81. Yamasaki (1988), Cloning and expression of the human interleukin-6 (BSF-2/IFN beta 2) receptor, Available at: https://pubmed.ncbi.nlm.nih.gov/3136546/

82. Ding and Jones (2003), Technology evaluation: MRA, Chugai, Available at: https://pubmed.ncbi.nlm.nih.gov/12669473/

83. Reuters (2014), Shares in Japan's Chugai surge on report of Roche buyout offer, Available at: https://www.reuters.com/article/us-chugai-pharm-roche-shares-idINKBN0GI0PH20140818

84. Ohsugi (2020), The immunobiology of humanized Anti-IL6 receptor antibody: From basic research to breakthrough medicine, Available at: https://pubmed.ncbi.nlm.nih.gov/32743515/

85. UK Research and Innovation (2022), Collaboration with Chugai & IP on humanizing antibodies, Available at: https://ukri.disclosurelog.co.uk/case/ab6d670c-107f-4920-a886-0613d657fb70

86. Fitzgerald et al (2017), Cytokine Release Syndrome After Chimeric Antigen Receptor T Cell Therapy for Acute Lymphoblastic Leukemia, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452983/

87. Porter et al (2015), Chimeric antigen receptor T cells persist and induce sustained remissions in relapsed refractory chronic lymphocytic leukemia, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5909068/

88. Lee et al (2014), T cells expressing CD19 chimeric antigen receptors for acute lymphoblastic leukaemia in children and young adults: a phase 1 dose-escalation trial, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7065359/

89. Davila (2014), Efficacy and Toxicity Management of 19-28z CAR T Cell Therapy in B Cell Acute Lymphoblastic Leukemia, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4684949/

90. Maude et al (2014), Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4267531/

91. What Do They Know (2022), Label extension and market exclusivity, Available at: https://www.whatdoChimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia - PMCtheyknow.com/request/label_extension_and_market_exclu#incoming-2147510

92. Unitaid (2021) Joint Statement from Unitaid and the World Health Organization (on behalf of the Access to COVID-19 Tools Accelerator) regarding availability of tocilizumab. Available at: https://unitaid.org/news-blog/joint-statement-unitaid-who-tocilizumab/#en

93. ibid

94. Health Policy Watch (2021) Roche Suspends Patents on Tocilizumab in LMICs After WHO Recommends it as Treatment for Severe COVID-19, Available at:

https://healthpolicy-watch.news/roche-suspends-patents-on-tocilizumab-for-lmics-after-who-recommends-it-as-treatment-for-severe-covid/

95. MSF Access Campaign (2021), MSF response to Roche's statement on access to tocilizumab, Available at: https://msfaccess.org/msf-response-roches-statement-access-tocilizumab

96. Health Policy Watch (2021) Roche Suspends Patents on Tocilizumab in LMICs After WHO Recommends it as Treatment for Severe COVID-19, Available at:

https://healthpolicy-watch.news/roche-suspends-patents-on-tocilizumab-for-lmics-after-who-recommends-it-as-treatment-for-severe-covid/

97. Third World Network (2021), Intellectual Property Monopolies Perpetuate Inequitable Access to COVID-19 Therapeutics, Available at: https://www.twn.my/title2/intellectual_property/info.service/2021/ip211011.htm

98. MSF Access Campaign (2021), Tocilizumab, second drug ever recommended by WHO for COVID-19, will remain unaffordable and inaccessible for most of the world, Available at: https://msfaccess.org/tocilizumab-second-drug-ever-recommended-who-covid-19-will-remain-unaffordable-and-inaccessible?utm_source=Twitter&utm_campaign=COVID19

99. Roche (2021) Finance Report. Available at: https://assets.cwp.roche.com/f/126832/x/8df367bf68/fb21e.pdf

100. RECOVERY (2022), RECOVERY trial celebrates two-year anniversary of life-saving dexamethasone result, Available at: https://www.recoverytrial.net/news/recovery-trial-celebrates-two-year-anniversary-of-life-saving-dexamethasone-result

101. Recovery Collaborative Group (2021), Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial, Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext

102. The Lancet (2021) Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext

103. UKRI (2022) The RECOVERY trial. Available at: https://www.ukri.org/news-and-events/tackling-the-impact-of-covid-19/vaccines-and-treatments/recovery-trial-identifies-covid-19-treatments/

104. Singer and Piotz (1956), The latex fixation test, Available at: https://www.amjmed.com/article/0002-9343(56)90103-6/pdf

105. O'Farrell (2008), Evolution in Lateral Flow–Based Immunoassay Systems, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7119943/

106. Surescreen (2023), Available at: https://www.surescreen.com

107. University of Derby, Long term knowledge exchange collaboration with surescreen. Available at: https://www.derby.ac.uk/business-services/innovation-research/sure-screen/#:~:text=In%202015%2C%20SureScreen%20was%20awarded,breadth%20of%20its%20market%20offer.

108. University of Derby (2023), A Long-Term Knowledge Exchange Collaboration with Surescreen, Available at: https://www.derby.ac.uk/business-services/innovation-research/sure-screen/

109. Pickering et al (2021), Comparative performance of SARS CoV-2 lateral flow antigen tests demonstrates their utility for high sensitivity detection of infectious virus in clinical specimens, Available at: https://pubmed.ncbi.nlm.nih.gov/34226893/

110. ibid

111. UK Government (2021), British manufacturer SureScreen Diagnostics to supply 20 million rapid lateral flow, Available at: https://www.gov.uk/government/news/british-manufacturer-surescreen-diagnostics-to-supply-20-million-rapid-lateral-flow

112. East Midlands Chamber (2021) Surescreen Diagnostics Provides Two Million Lateral Flow COVID-19 Tests for UK Government, Available at: https://www.emc-dnl.co.uk/news/2021/01/22/surescreen-diagnostics-provides-two-million-lateral-flow-covid-19-tests-for-the-uk-government/

113. Good Law Project (2022), Emails Reveal Another VIP Test and Trace Contract that Leads to More Questions than Answers, Available at: https://goodlawproject.org/vip-test-and-trace-surescreen/

114. Primary Care Supplies (2023), Available at: https://www.primarycaresupplies.co.uk/surescreen-covid-19-rapid-antigen-test-3/

115. The Business Desk (2022) Profits soar at Covid-19 test manufacturer as Government contracts provide healthy bottom line. Available at: https://www.thebusinessdesk.com/eastmidlands/news/2061175-profits-soar-at-covid-19-test-manufacturer-as-government-contracts-provide-healthy-bottom-line

116. Financial Times (2021), How a Love of Science Led to Health Breakthroughs, Available at: https://www.ft.com/content/c4fce933-4faa-4e74-bfda-79a1e36435d7

117. Deloitte (2023), The £1.25 COVID-19 Antibody Test, Available at: https://www2.deloitte.com/uk/en/pages/annual-report-2020/stories/the-1-25-covid-19-antibody-test.html

118. The Scientist (2020), Mologic awarded c.£1 million by UK government to develop rapid diagnostic test for COVID-19, Available at:

https://www.the-scientist.com/the-marketplace/mologic-awarded-c-1-million-by-uk-government-to-develop-rapid-diagnostic-test-for-covid-19-67238

119. Drug Discovery News (2020), Mologic Receives COVID-19 Diagnostic Money, Available at: https://www.drugdiscoverynews.com/mologic-receives-covid-19-diagnostic-money-14039

120. https://www.finddx.org/newsroom/pr-27mar20/

121. Deloitte (2023), The £1.25 COVID-19 Antibody Test, Available at: https://www2.deloitte.com/uk/en/pages/annual-report-2020/stories/the-1-25-covid-19-antibody-test.html

122. Ibid

123. Budd et al (2023), Lateral flow test engineering and lessons learned from COVID-19, Available at: https://www.nature.com/articles/s44222-022-00007-3

124. Forbes (2021), George Soros And Bill Gates' Backed Consortium To Buy U.K. Maker Of Covid Tests For $41 Million, Available at: https://www.forbes.com/sites/daviddawkins/2021/07/19/george-soros-and-bill-gates-backed-consortium-to-buy-uk-maker-of-covid-lateral-flow-tests-for-41-million/?sh=6a023b3d2687

125. Soros Economic Development Fund (2023), Available at: https://www.soroseconomicdevelopmentfund.org/investments

126. The Herald (2021), Omega shares fall on Mologic test woes, Available at: https://www.heraldscotland.com/business_hq/19374715.omega-shares-fall-mologic-test-woes/

127. Share Talk (2022), Omega Diagnostics Gp (ODX.L) Sale of Alva manufacturing business, Available at:

https://www.share-talk.com/omega-diagnostics-gp-odx-l-sale-of-alva-manufacturing-business/

128. Omega Diagnostics (2022), Sale of Alva manufacturing business, Available at: https://www.omegadx.com/Portals/0/ODX%20Alva%20site%20sale%20%2811_02_22%29.pdf

129. Insider (2022), Omega Diagnostics confirms £1 million sale of Alva manufacturing business, Available at:

https://www.insider.co.uk/news/omega-confirms-1-million-sale-26403556

130. Global Access Diagnostics (2023), Regional Manufacturing, Available at: https://www.globalaccessdx.com/regional-manufacturing-network

131. Blakney et al (2020), Big Is Beautiful: Enhanced saRNA Delivery and Immunogenicity by a Higher Molecular Weight, Bioreducible, Cationic Polymer, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7304921/

132. Blakney et al (2019), Effects of cationic adjuvant formulation particle type, fluidity and immunomodulators on delivery and immunogenicity of saRNA, Available at: https://pubmed.ncbi.nlm.nih.gov/31071377/

133. Blakney et al (2019), Inside out: optimization of lipid nanoparticle formulations for exterior complexation and in vivo delivery of saRNA, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6760535/

134. Department of Health and Social Care (2019), Projects supported by DHSC through the UK Vaccine Network, Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/827983/projects-currently-being-funded-by-ukvn.pdf

135. UK Research and Innovation (2023), Find COVID-19 research and innovation supported by UKRI, Available at: https://www.ukri.org/what-we-offer/what-we-have-funded/find-covid-19-research-and-innovation-supported-by-ukri/

136. Imperial College London (2020), Imperial COVID-19 vaccine team secures £22.5 million support, Available at: https://www.imperial.ac.uk/news/197017/imperial-covid-19-vaccine-team-secures-225/

137. Imperial College London (2020), COVID-19 vaccine secures new government investment, Available at: https://www.imperial.ac.uk/news/197573/covid-19-vaccine-secures-government-investment/

138. AstraZeneca (2021), AstraZeneca to discover and develop self-amplifying RNA therapeutics in new collaboration with VaxEquity, Available at:

https://www.astrazeneca.com/media-centre/press-releases/2021/astrazeneca-to-discover-and-develop-self-amplifying-rna-therapeutics-in-new-collaboration-with-vaxequity.html

139. Imperial College London (2021), Imperial RNA technology to be developed by VaxEquity with AstraZeneca, Available at: https://www.imperial.ac.uk/news/230554/imperial-rna-technology-developed-vaxequity-with/

140. Pollock et al (2022), Safety and immunogenicity of a self-amplifying RNA vaccine against COVID-19: COVAC1, a phase I, dose-ranging trial, Available at: https://www.sciencedirect.com/science/article/pii/S2589537021005435

141. Pharmaceutical Technology (2017), Counting the cost of failure in drug development, Available at: https://www.pharmaceutical-technology.com/features/featurecounting-the-cost-of-failure-in-drug-development-5813046/

142. The Economist (2014), The Price of Failure: A startling new cost estimate for medicines is met with skepticism, Available at: https://www.economist.com/business/2014/11/27/the-price-of-failure

143. UAEM (2021) Who funded the research behind the Oxford–AstraZeneca COVID-19 vaccine? Available at: https://gh.bmj.com/content/6/12/e007321.info

144. A limitation of the second literature search methodology was that only 21% of exact grant amounts for funder mentions in academic publications were retrievable from publicly available information.

145. University of Oxford (2020) Funding and manufacturing boost for UK vaccine programme. Available at: https://www.ox.ac.uk/news/2020-05-18-funding-and-manufacturing-boost-uk-vaccine-programme

146. Oxford Biomedica (2020), Oxford Biomedica Signs Five Year Collaboration Agreement with the Vaccines Manufacturing and Innovation Centre, Available at: https://www.oxb.com/news-media/press-release/oxford-biomedica-signs-five-year-collaboration-agreement-vaccines

147. The UK Government (2022) One year anniversary of UK deploying Oxford-AstraZeneca vaccine, Available at: https://www.gov.uk/government/news/one-year-anniversary-of-uk-deploying-oxford-astrazeneca-vaccine

148. Madhi et al (2021), Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant, Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2102214

149. Financial Times (2021), Vaccine patents battle intensifies as poor nations struggle in war on coronavirus, Available at: https://www.ft.com/content/cf12e1ba-ee25-4a0a-870d-53f5b66b0996?shareType=nongift

150. Time (2022), The World's Largest Vaccine Manufacturer Stumbled in 2021. Its CEO Bets He Can Still Help End COVID-19, Available at: https://time.com/6132402/serum-institue-of-india-covid-19-vaccine/

151. Fiocruz (2022), Researcher who developed Oxford/Astrazeneca vaccine is honored at Fiocruz, Available at: https://portal.fiocruz.br/en/news/researcher-who-developed-oxford/astrazeneca-vaccine-honored-fiocruz

152. Financial Times (2020) AstraZeneca vaccine document shows limit of no-profit pledge, Available at: https://www.ft.com/content/c474f9e1-8807-4e57-9c79-6f4af145b686

153. AstraZeneca (2021), Annual Report, Available at: https://www.astrazeneca.com/content/dam/az/Investor_Relations/annual-report-2021/pdf/AstraZeneca_AR_2021.pdf

154. STOPAIDS, Just Treatment (2023) Access Denied: The role of trade secrets in preventing global equitable access to COVID-19 tools. Available at: https://stopaids.org.uk/access-denied-report-series-launch/

155. CNBC (2021), AstraZeneca vaccine document shows limit of no-profit pledge, Available at: https://www.cnbc.com/2021/01/04/uk-rolls-out-astrazeneca-oxford-vaccine.html

156. Financial Times (2021), AstraZeneca chief says 'vaccine has a future' after setbacks, Available at: https://www.ft.com/content/02c543e0-45a6-4189-94cf-30a5c3d5499d

157. Politico (2021), How the UK gained an edge with AstraZeneca's vaccine commitments, Available at: https://www.politico.eu/article/the-key-differences-between-the-eu-and-uk-astrazeneca-contracts/

158. Dyer (2021), Covid-19: Countries are learning what others paid for vaccines, Available at: https://www.bmj.com/content/372/bmj.n281

159. European Parliament (2023) Mapping of long-term public and private investments in the development of Covid-19 vaccines. Available at: https://www.europarl.europa.eu/thinktank/en/document/IPOL_STU(2023)740072

160. People's Vaccine (2023) Never again letter. Available at: https://peoplesvaccine.org/wp-content/uploads/2023/03/PVA-Never-Again-Open-Letter-FINAL-EMBARGOED-UNTIL-MARCH-11.pdf

161. See methodology

162. CEPI (2022), Enabling Equitable Access to COVID-19 Vaccines: Summary of equitable access provisions in CEPI's COVID-19vaccine development agreements, Available at: https://cepi.net/wp-content/uploads/2020/12/Enabling-equitable-access-to-COVID19-vaccines-v8-14-February-2022.pdf

163. Graduate Institute, Geneva, (2019), Research Synthesis: Public Funding of Pharmaceutical R&D, Available at: https://www.knowledgeportalia.org/_files/ugd/356854_73a1ff84b65642a0926ae81f045b7c5e.pdf

164. Grover, Flick (2023) AstraZeneca CEO says UK business climate deters investment. Available at: https://www.reuters.com/business/healthcare-pharmaceuticals/astrazeneca-ceo-discouraging-uk-tax-policies-led-company-invest-400-mln-ireland-2023-02-09/

165. Ralph (2023) It's not viable to supply more drugs to NHS, warn bosses. Available at: https://www.thetimes.co.uk/article/its-not-viable-to-supply-more-drugs-to-nhs-warn-bosses-hmzpgfrxf

166. For an exploration of this mechanism see Olga Gurgula, 'Compulsory Licensing vs. the IP Waiver: What Is the Best Way to End the COVID-19 Pandemic?' (2021) 104 South Centre Policy Brief https://www.southcentre.int/policy-brief-104-october-2021/

167. Kramer, Boyle (2021) Mercantilism and the Colonies of Great Britain. Available at: https://www.investopedia.com/ask/answers/041615/how-did-mercantilism-affect-colonies-great-britain.asp

168. Coghe (2020), Disease Control and Public Health in Colonial Africa, Available at: https://oxfordre.com/africanhistory/display/10.1093/acrefore/9780190277734.001.0001/acrefore-9780190277734-e-620

169. Patterson et al (1974), Disease and Medicine in African History: A Bibliographical Essay, Available at: https://www.jstor.org/stable/3171766

170. Health Poverty Action (2018) Neglected tropical diseases. Available at: https://www.healthpovertyaction.org/news-events/neglected-tropical-diseases/

171. Bhambra (2022) Relations of extraction, relations of redistribution: Empire, nation, and the construction of the British welfare state. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9306532/

172. https://www.imperial.ac.uk/news/198435/imperial-review-history-legacy/

173. https://oxfordandcolonialism.web.ox.ac.uk/home

174. Hickel et al (2021), Plunder in the Post-Colonial Era: Quantifying Drain from the Global South Through Unequal Exchange, 1960–2018, Available at: https://www.tandfonline.com/doi/abs/10.1080/13563467.2021.1899153?journalCode=cnpe20&journalCode=cnpe20

175. Jubilee Debt Campaign (2020), Drop Debt, Save Lives: Global South Debt and Covid-19, Available at: https://jubileedebt.org.uk/wp-content/uploads/2020/07/Drop-Debt-Save-Lives-Briefing.pdf

176. South Centre (2022), Doha Twenty Years On - Has the Promise Been Betrayed?, Available at: https://www.southcentre.int/wp-content/uploads/2022/06/SV238_220620-3.pdf

177. Debt Justice (2020), Sixty-four Countries Spend More on Debt Payments than On Health, Available at: https://debtjustice.org.uk/press-release/sixty-four-countries-spend-more-on-debt-payments-than-health

178. OECD (2023), Gross domestic spending on R&D, Available at: https://data.oecd.org/rd/gross-domestic-spending-on-r-d.htm

179. Bekele et al (2022), Global Health Research Funding Applications: Brain Drain Under Another Name?, Available at: https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00505-2/fulltext

180. Beatrice Adler-Bolton, Artie Vierkant, (2022), Health Communism, Verso.

181. Bailey, Mark S (2013), "A Brief History of British Military Experiences with Infectious and Tropical Diseases." Available at: https://doi.org/10.1136/jramc-2013-000087.

182. Herron, Jonathan, and James Dunbar. (2018). "The British Army's Contribution to Tropical Medicine." Available at: https://doi.org/10.7861/clinmedicine.18-5-380.

183. International Development Select Committee (2023) Aid Spending in the UK. Available at: https://publications.parliament.uk/pa/cm5803/cmselect/cmintdev/898/report.html

184. STOPAIDS, Just Treatment, Global Justice Now and the UCL Institute for Innovation and Public Purpose (2018) People's Prescription. Available at: https://stopaids.org.uk/wp/wp-content/uploads/2018/10/report.pdf

185. Graduate Institute, Geneva (2019), Patent Pools, Available at: https://www.knowledgeportalia.org/patent-pools

186. Graduate Institute, Geneva (2019), Public Funding of R&D, Available at: https://www.knowledgeportalia.org/public-funding-r-d

187. GHIAA (2023), Master Alliance Provisions Guide (MAPGuide), Available at: https://ghiaa.org/mapguide-home/search-results/?qs=covid+19

188. GHIAA (2023), MAPGuide : Equitable Access Policies, Available at: https://ghiaa.org/mapguide-home/equitable-access-policies/

189. 100 Days Mission (2021), First Implementation Report, Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1038969/100_Days_Mission_-_First_Implementation_Report__1_.pdf

190. STOPAIDS, Just Treatment (2023) Access Denied: The role of trade secrets in preventing global equitable access to COVID-19 tools. Available at: https://stopaids.org.uk/access-denied-report-series-launch/

191. STOPAIDS, Just Treatment (2023) Access Denied: The role of trade secrets in preventing global equitable access to COVID-19 tools. Available at: https://stopaids.org.uk/access-denied-report-series-launch/

192. ibid

193. Moore et al (2020), Variation in the estimated costs of pivotal clinical benefit trials supporting the US approval of new therapeutic agents, 2015–2017: a cross-sectional study, Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7295430/pdf/bmjopen-2020-038863.pdf

194. Bank of England (2023), Inflation Calculator, Available at: https://www.bankofengland.co.uk/monetary-policy/inflation/inflation-calculator

195. Recovery Collaborative Group (2021), Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial, Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext

196. This data was gathered from the publicly available NIHR and UKRI funding databases and coded by the authors of the report. Not all COVID-19 related projects in both databases "directly" contributed to the development of COVID-19 vaccines, diagnostics, or therapeutics and are therefore excluded from this figure.

197. NHS indicative prices as listed in the British National Formulary do not accurately reflect the real price paid at procurement (information on actual prices is considered to be commercially sensitive and is therefore closely guarded). Therefore, aforementioned spending figures are likely to be an overestimate, though it is unclear to which extent. In 2021, the NHS indicative prices overestimated real prices by 48% on average.

198. https://www.politico.eu/article/the-key-differences-between-the-eu-and-uk-astrazeneca-contracts/

199. https://www.gov.uk/government/news/british-manufacturer-surescreen-diagnostics-to-supply-20-million-rapid-lateral-flow

200. https://www.emc-dnl.co.uk/news/2021/01/22/surescreen-diagnostics-provides-two-million-lateral-flow-covid-19-tests-for-the-uk-government/

201. Catapult Medicines Discovery (2023), The biggest diagnostic lab network in British History, Available at: https://md.catapult.org.uk/success-stories/the-biggest-diagnostic-lab-network-in-british-history/

202. Catapult Medicines Discovery (2023) Biomarker Strategy Development, Available at: https://md.catapult.org.uk/success-stories/biomarker-strategy-development/

203. UK Coronavirus Immunology Consortium (2023), Available at: https://www.uk-cic.org

204. British Society for Immunology (2023), UK Coronavirus Immunology Consortium, Available at: https://www.immunology.org/partnerships/uk-coronavirus-immunology-consortium

205. What Do They Know (2022), Funding for GENOMICC Study, Available at: https://www.whatdotheyknow.com/request/901406/response/2148165/attach/html/3/FOI%201419361%201419362%201419365%20002%20DS.pdf.html

206. UK Government (2020), UK government invests in Livingston facility to bolster vaccine manufacturing capacity, Available at: https://www.gov.uk/government/news/uk-government-invests-in-livingston-facility-to-bolster-vaccine-manufacturing-capacity

207. Department for Business, Energy and Industrial Strategy (2020), UK Vaccine Taskforce 2020 Achievements and Future Strategy: End of Year Report, Available at: UK Vaccine Taskforce 2020 Achievements and Future Strategyhttps://assets.publishing.service.gov.uk › file › vtf...

208. Biopharma reporter (2022), UK government invests in Livingston facility to bolster vaccine manufacturing capacity, Available at: https://www.biopharma-reporter.com/Article/2022/02/22/Valneva-revives-Scottish-vaccine-manufacturing-plans