Written Evidence Submitted by the British Pharmacological Society (C190075)

About us

The British Pharmacological Society (BPS) is the primary UK learned society concerned with research into drugs and the way they work. The Society has around 4,000 members working in academia, industry, regulatory agencies and the health services, and many are medically qualified. The Society covers the whole spectrum of pharmacology, including laboratory, clinical, and toxicological aspects. The science of pharmacology is essential for the development and testing of medicines, and for their adoption in clinical practice. Teaching and research in pharmacology are crucial to a thriving pharmaceutical and biotechnology industry in the UK. Members of the Society identify therapeutic areas of clinical need, develop novel treatments that target these areas and ensure these new treatments are incorporated into healthcare practice bringing benefit to patients. The Society publishes three scientific journals: the British Journal of Pharmacology, the British Journal of Clinical Pharmacology, and, in collaboration with the American Society for Pharmacology and Experimental Therapeutics, Pharmacology Research and Perspectives.

Executive summary

The Society's response focuses on issues related to clinical research and efforts to find a safe and effective treatment for COVID-19. Our main reflection is that the reliance on a pandemic response based originally on a virus acting like influenza, rather than a novel virus such as Sars-Cov-2, was the reason that developing a therapeutics strategy had to start in real time during the crisis. The UK has demonstrated that it has the expertise and the ability to coordinate a large-scale therapeutics and vaccine response, but this was held back by having to devise the relevant processes and structures from a standing start, rather than having them in place from the beginning. The UK is unlikely to be unique in this regard. Although it is important to celebrate successes, including the agility of regulators and the RECOVERY trial, it is perhaps more important to use this period to critically appraise the UK's response. With this in mind, our overall recommendation is that the UK should establish **a framework for a therapeutics strategy that is nationally coordinated, allows room for innovation, and supports connectivity and alignment across the full spectrum of drug discovery and development**.

Specifically, we recommend:

- **Alignment, coordination and global leadership**
    - The Government should convene a national, independent body to oversee and coordinate the discovery and development of therapeutics for novel health threats.
    - The UK should fully align approaches and funding for all stages of research and development, ensuring this is informed by a therapeutics strategy, by appropriate subgroups that span the R&D pathway, and is joined up with implementation and follow up in healthcare settings. As part of this, there should be a clear therapeutic hypothesis linked to demonstrable patient benefit. Choice of drugs should be transparent and based on robust exposure response data. Specifically, we advocate that one of the subgroups should focus on early phase research, and should capture expertise in drug development, clinical pharmacology and relevant diseases (e.g. respiratory, ITU, infection).
    - The Government should advocate for, and commit funding to, a coordinated, international, public-private collaboration for novel virus preclinical research (including fundamental research, screening potential drug targets at scale and diagnostics) to help identify novel treatments

for COVID-19. This will lay the infrastructure that will help the global community be more prepared for future viral pandemics.
    - The Government should commit UK leadership, expertise and funding to global structures in order to support development of a robust international therapeutics strategy. This would provide the opportunity to address global health threats, without the duplication of effort that is a feature of the current response.
    - The UK response should be reviewed with the intention of capturing and integrating innovations and improvements to processes made during this time, for the benefit of patients and to improve the UK's competitiveness.
- **Prioritising investment in the NHS**
    - The NHS People Plan 2020-21 draws on the lessons of COVID-19, highlighting the contribution of NHS people to research and the RECOVERY trial's successes. Future iterations should deepen commitments to enhancing research in the NHS.
    - A joint NHS-Life Sciences Steering Group should be set up to support and encourage connectivity and training across the NHS, academia, biopharmaceutical industry and regulators.
    - The NHS should include medicines specialists (such as clinical pharmacologists) in multi-professional teams to aid rational medicines use, to prevent inappropriate polypharmacy and to further inform research efforts (e.g. into the long-term consequences of COVID-19).
- **Coordinated communication**
    - The UK should use the opportunity of increased awareness of research to enhance interest and engagement in science within formal and informal learning settings to enhance future capacity and capability in scientific research and innovation.
    - A coordinated therapeutics strategy needs an accompanying communications strategy to help patients and publics engage with the 'big picture', particularly regarding the implications of emerging research.

The Society's submission covers answers to questions 2, 3 and 6.

2. The capacity and capability of the UK research base in providing a response to the outbreak, in terms of:
The development and testing of therapeutics

2.1 The UK was able to rapidly set up a therapeutics taskforce, clinical trial platforms (e.g. RECOVERY and ACCORD-2), rapid response funding calls, and efforts by regulators and the Health Research Authority to safely expedite trials. The efficacy of dexamethasone, a treatment proven for severe COVID-19, was demonstrated through the UK RECOVERY trial. This trial also demonstrated that both Lopinavir-Ritonavir and hydroxychloroquine did not have any beneficial effects; this was just as important in terms of stopping therapies which do not work, and given the platform design[1], also reinforced the efficacy of dexamethasone. Further, the promising treatment SNG001[2] (inhaled interferon-β) was developed by Synairgen, a UK company founded by academics from the University of Southampton, who continue to play an active role. The trial was conducted as a collaboration between Synairgen, researchers at the University of Southampton, University Hospital Southampton NHS Foundation Trust, and research teams across the NIHR network with support from UK regulatory bodies. This example of academic contribution - to discovery, to the UK economy through the founding of a spinout company, and to patients through collaboration with the NHS demonstrates the uniqueness of the

UK environment. The UK life sciences and clinical research base is globally recognised, and it is evident that the UK has the necessary expertise to play a leading role in the response to a health crisis such as COVID-19. COVID-19 has clearly had a considerable impact on the UK economy, but the value of having a strong life sciences sector integrated with the NHS has been clearly demonstrated as part of the UK's response to the pandemic. This supports continued investment in UK R&D in line with previous commitments to invest 2.4% of GDP in UK R&D by 2027, with a longer-term goal of 3%.

2.2 However, the therapeutics strategy for COVID-19, drawn from the UK's 2016 pandemic preparedness exercise[3] 'Cygnus', appears to have initially relied on stockpiling oseltamivir (Tamiflu) and zanamivir (Relenza), two antiviral neuraminidase inhibitors. The redacted operation report notes that there were sufficient stocks of these drugs to provide treatment for 50% of the population. This strategy was carried forwards from the 2009 H1N1 pandemic, where an independent review[4] of this strategy stated that "the UK was well prepared to provide antiviral treatment for an influenza pandemic adequately and rapidly. Sufficient antiviral stocks had been procured and adequate plans were in place to ensure that they could be accessed and distributed effectively to the population". However, this strategy was based on a virus acting like influenza rather than a novel virus such as SARS-CoV-2 – and there is evidence that these drugs do not work, even for flu[5]. There does not seem to have been a contingency plan for a novel virus at a national level, and the groups that emerged to coordinate the search for a safe and effective treatment had to evolve from a standing start. The UK is unlikely to be unique in this regard. The UK did have access to the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC), a global federation of clinical research networks, meaning that UK clinical researchers had rapid access to resources and were able to start trials quickly.

2.3 On 29 April 2020, the Government announced a new fast-track clinical trials initiative overseen by a new Therapeutics Taskforce: the Accelerating COVID-19 Research & Development platform (ACCORD-2)[6]. This was a collaboration between DHSC and UKRI, supported by NIHR, aiming to accelerate promising candidate drugs through clinical trials. The ACCORD steering group are responsible for reviewing phase 2 data and making recommendations to the Therapeutics Taskforce about which should progress to the phase 3 RECOVERY trial. The RECOVERY trial has won plaudits[7] for its design (the ability to add or subtract drugs from the trial as more data becomes available) and the pace of enrollment – however, it is important to note that ACCORD-2 missed the peak due to the time it took to approve its set up. Had approval been sooner, more drugs may have been able to be tested through RECOVERY. Further, there was still a gap in phase 1 research over the peak, and thus a limited focus on innovative therapies to broaden the pipeline. This phase 1 gap was later filled by the AGILE platform, but there was an unfortunate delay in getting such a platform set up. Despite the successes of RECOVERY, there is an argument that it 'cornered the market' in that the majority of patients were recruited to the trial, leaving very few patients for early phase trials, which ideally should have developed the future pipeline for RECOVERY. It is therefore important that early phase trials, which are smaller and quicker, are set up in parallel and if they provide some indication of efficacy, they can be pulled through into larger phase 3 trials. We need platforms for phase 1, 2 and 3 trials running concurrently so that there is a seamless pathway to test existing re-purposed drugs and new promising candidates.

2.4 There was no clear strategy to ensure that preclinical discovery work was commissioned and incorporated into the therapeutic approach. It is appropriate to

focus on repurposed candidates in the short-term because more is known about their safety profile and thus, they are likely to take less time to get to patients. However, preclinical data is important even for repurposing existing drugs – relying on *in vitro* data without evidence of pre-clinical *in vivo* effects can lead to wasted efforts and resource, as has undoubtedly happened with hydroxychloroquine, which has sucked a large proportion of trial patients and resources internationally - and which was linked to serious adverse cardiac events worldwide. A repurposing strategy will also likely only result in partial successes: a novel virus is likely to need a novel treatment. There are likely to be further 'waves' of the COVID-19 pandemic, and there is also significant risk of other viral pandemics in the future. Therefore, a rounded and long-term approach needs to focus on investing in the research and infrastructure needed to identify novel drugs – which includes preclinical drug discovery and fundamental science. Novel chemical entities that are targeted specifically against the Sars-Cov-2 virus are ultimately likely to have the most success[8], even though their development will take longer. In fact, the ACCORD platform was designed to be from 'bench to bedside' but no funding was committed to a preclinical platform during the first 'wave' so this potential was not realised.

2.5 Coordinated screening of such targets is needed to support identification of novel candidate drugs and minimise duplication. The UK has impressive drug-target screening capability in both academic and industrial settings, which could significantly contribute to an international effort.

2.6 There are currently no models of disease in animals that capture all the features of COVID-19, and those that exist are only available in a very small number of centres. Animal models must be valid, and they must be used and reported consistently. The Society has supported calls for the research and drug discovery community to work together to agree guidelines for the use of animals to model COVID-19[9] - and it is clear that investment in models of severe disease is needed.

2.7 There must also be improvements in diagnostic efforts. Having the best information about the virus itself, how it spreads, whether it mutates, why some individuals are asymptomatic and others are more seriously affected is vital in order to determine the most appropriate therapeutic response, which will inevitably not be "one-size-fits-all". Studies into pharmacology and therapeutics will fail if the information on which assays and models are constructed are based on false premises. Further, unlike China, USA and the EU, the UK has a limited diagnostic autopsy service. This type of research helped identify mechanisms of pneumonia associated with COVID-19, clearly identifying the vascular endothelium as the target of the responses to the virus[10]. This helped inform the therapeutic approach, but it is striking that this work had no UK contribution.

2.8 It is also important to recognise that clinical experience and research are interdependent. For example, an anticoagulant arm was added to the REMAP-CAP trial to answer urgent questions about the association between COVID-19 and thrombosis. Further, the assessment of the risks of dying from COVID-19 have involved the use of the GP electronic patient record systems with associated research data bases. Researchers working with NHS England provided estimates on the risk factors using 17 million UK patients in the OPEN Safely study and a diagnostic tool for GPs[11]. A major gap is that there is no 'in hospital' (where most patients die) equivalent to enable us to understand the clinical natural history of in-patients and to capture long-term complications, which are currently not well

understood. It is important to expand the hospital electronic patient record system with some urgency. Therapeutic approaches have the best chance of success when they are effectively connected with the clinic.

2.9 The NHS People Plan 2020-21[12] cites the importance of building on new multi-professional teams that were developed in response to COVID-19. This should include a pathway to support patients who are recovering from COVID-19, but also be extended to management of long-term conditions. It is important to recognise that individuals affected by COVID-19 are typically older, and that this will add to the burden of multimorbidity. Moreover, the nature of multimorbidity remains unknown, because medium to long-term consequences of infection will only begin to be clinically described with time. It is important to include medicines specialists (such as clinical pharmacologists) in such teams to help aid rational medicines use, but importantly to prevent inappropriate polypharmacy through supporting evidence-based treatments. Clinical pharmacologists also have research training, which can support connectivity between research and the clinic – including support for trial design, particularly for innovative therapies. Over 1.1 billion prescription items are dispensed in the community every year[13], and the NHS Long-Term Plan recognises the growing challenge of multimorbidity[14] for which prescription of multiple medicines (polypharmacy) is required. Although medicines have many proven benefits, 6.5% of all hospital admissions are caused by adverse drug reactions, and 237 million medication errors are made in the NHS each year[15,16]. The Society welcomes the planned investment in clinical pharmacy and is currently working with the profession to develop new ways of working between pharmacy and clinical pharmacology. Pharmacists already provide leadership in medicines optimisation[17] and a parallel investment in clinical pharmacology would help derive the maximum benefit from such a partnership for the NHS. This will enable the complementary skills of these healthcare professionals to be brought together to tackle multimorbidity and other healthcare challenges. Continued investment in multi-professional pathways, including a focus on preventing polypharmacy, would support COVID-19 recovery, but will also be of value regarding management of long-term conditions. Acknowledging and addressing these issues from the outset will enable a holistic approach to post-COVID-19 management, aim to prevent additional burden on the NHS and support research efforts.

2.10 **The Government should convene a national body to oversee and coordinate the discovery and development of therapeutics for novel health threats. This would provide the opportunity to address global health threats, without the duplication of effort that is a feature of the current response.**

2.11 **The UK should fully align approaches and funding for all stages of research and development, ensuring these are informed by a therapeutics strategy, by appropriate subgroups of expertise that span the R&D pathway, and is joined up with implementation and follow up in healthcare settings. As part of this, there should be a therapeutic hypothesis to support drug choice, and rational dose design. Specifically, we advocate that one of the subgroups should focus on early phase research, and should capture expertise in drug development, clinical pharmacology, and relevant diseases (e.g. respiratory, ITU, infection).**

2.12 **The Government should advocate for, and commit funding to, a coordinated, international, public-private collaboration for novel virus**

research (including fundamental research, screening potential drug targets at scale and diagnostics) to help identify novel treatments for COVID-19. This will lay the infrastructure that will help the global community be more prepared for future viral pandemics.

2.13 **The NHS should include medicines specialists (such as clinical pharmacologists) in multi-professional teams to aid rational medicines use, to prevent inappropriate polypharmacy and to further inform research efforts (e.g. into the long-term consequences of COVID-19).**

2.14 A further lesson learned from the months following the emergence of COVID-19 is that a global health threat requires a global therapeutics strategy. Internationally, there has been a focus on individual drugs rather than a therapeutic approach, leading to multiplication of effort (for example, as of 29 July 2020, there are 213 interventional studies on hydroxychloroquine listed on clinicaltrials.gov), poorly designed and insufficiently powered individual studies. The RECOVERY trial chose not to duplicate efforts – omitting a remdesivir arm because this was being studied in the WHO SOLIDARITY trial - though supply also seems to have influenced this decision. It is critical to get the coordination right because as a pandemic progresses, there are further challenges due to falling patient numbers. Clinical trials must be closely coordinated globally, including a focus on nimble second-generation adaptive design rather than traditional large-scale studies. The UK has an excellent clinical research base and is well-placed to support global planning and coordination. The COVID-19 Therapeutics Accelerator[18], founded by the Gates Foundation, Wellcome and Mastercard is a collaborative effort to research, develop and bring effective treatments to market quickly and accessibly. Future approaches to global coordination include better coordination with less flexibility than in 'peacetime', but this must not stifle innovation. There needs to be more joined-up thinking for example, national governments working with the World Health Organization (WHO), the health subcommittee of the G20 and EU/EMA input. The latter did convene the COVID-19 EMA pandemic Task Force[19] (COVID-ETF) but it took some time to organise – these initiatives need to be rapidly assembled. It will be important to ensure UK expertise in drug discovery and development is well-connected to global research efforts. The Society has also been concerned about the quality of many rapidly published early studies, and therefore, their ability to generate clinically meaningful data to enable effective translation to clinical practice. This is not just a UK issue, but the UK is well-placed to support good study design due to scientific strengths including clinical pharmacology. To this end, the Society and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) released a joint statement[20] outlining clinical pharmacology principles intended to give research efforts the best chance of success regarding the identification of safe and effective treatments. Coordinated international promotion of such principles would likely increase their impact. UKRI and NIHR could help direct key UK scientific strengths (such as clinical pharmacology) at a global level, for example through the planning and conduct of clinical studies, systematic reviews of research, the development of international guidelines, and providing advice to international bodies. The UK must reinforce its role as a global player and use its funding and influence to support the development of a global therapeutics strategy.

2.15 **The Government should commit UK leadership, expertise and funding to global structures in order to support development of a robust international therapeutics strategy to address global health threats.**

3. The flexibility and agility of institutions, government departments and public bodies, and process to respond appropriately during the crisis including:

- **The availability and responsiveness of funding; and**
- **The optimal functioning of regulatory and ethical processes;**
- **The availability and influence of scientific advice in all government departments and public bodies – including by departmental Chief Scientific Advisers; and**
- **The extent to which decisions taken drew on that advice**

3.1 UK bodies were able to respond rapidly and flexibly in terms of funding, regulation and research: clinical trials approvals were accelerated, funding decisions were made more quickly, and data linkages were created in weeks when it can take years. Some of the new ways of working need to be taken forward in the future for new pandemics but also to 'normal' ways of working and other disease areas. There has been a commitment to removing unnecessary bureaucracy[21], which we support.

3.2 **The UK response should be reviewed with the intention of capturing and integrating innovations and improvements to process made during this time, for the benefit of patients and to improve the UK's competitiveness.**

3.3 The necessary focus on COVID-19 has meant other research, including clinical trials, have been stopped. A considered approach to safely restarting research is needed[22], as is a continued focus on delivering the Life Sciences Industrial Strategy and the NHS Long-Term Plan. In the case of the RECOVERY trial, there are almost 200 UK hospitals taking part, with an unprecedented level of interest from patients. This is a tremendous opportunity for the UK to build on public awareness of research and to integrate research into patient care. Research-active hospitals deliver better care (e.g. better CQC ratings) and have better patient outcomes (e.g. lower mortality rates), with benefits not limited to those patients who participate in research[23,24,25,26,27]. Part of this opportunity will be realised through ensuring the workforce is 'research ready' (meaning healthcare professionals must be familiar with, and have some exposure to, clinical trial designs, the disciplines and ethics of clinical research and structured data gathering) and 'research active' (meaning that they have the time, training and support to engage with research). The central role played by research in the NHS during COVID-19 has been recognised by the NHS People Plan 2020-21, but it needs to be further supported by national policy. Training must be flexible, and to improve the impact of translational research, trainees in the NHS and scientists must have the opportunity to work in different parts of the sector, such as the pharmaceutical industry. Further, progressing first into human studies (FIH) relies on the Principal Investigators qualified to run trials and expertise in clinical pharmacology – these are major UK skills gaps that needs addressing.

3.4 **The NHS People Plan 2020-21 draws on the lessons of COVID-19, highlighting the contribution of NHS people to research and the RECOVERY trial's successes. Future iterations should deepen commitments to enhancing research in the NHS.**

3.5 **A joint NHS-Life Sciences Steering Group should be set up to support and encourage connectivity and training across the NHS, academia, biopharmaceutical industry and regulators.**

3.6 Healthcare professionals need more support translating guidelines into clinical research and practice. Protocols, endpoints, and assessments must be kept as simple as possible. Often, but most notably during a pandemic, critical care and ITUs are extremely busy. There have been uncertainties about interactions of

COVID-19 with medicines being used for existing long-term conditions, and the best way to navigate guidance on clinical trials. RECOVERY worked at a national level with NHS Digital to allow collection of data via electronic patient records to help clinicians navigate national trial guidance in a way that best serves patients. The speed at which this was done was impressive and should give confidence and momentum to improving data linkages and flow across the NHS. However, there are pressures on national bodies to deliver guidance rapidly and it will be important to ensure that these are effectively resourced, aligned, and accessible.

3.7 The Society is aware of grassroots efforts by healthcare professionals to address uncertainties in the management of COVID-19. The COVID-19 Therapeutics Advice & Support Group (CTAG)[28] was established by specialists in clinical pharmacology, infectious disease, and other specialties with an interest in the therapeutics of COVID-19 working through Drugs and Therapeutics Committees and Area Prescribing Committees. The purpose was to provide frontline advice and support in the management of COVID-19 whilst national guidelines evolve, covering interim support on the appropriate use of investigational medicines for the treatment and prevention of COVID-19. Its work is a good example of grassroots flexibility – however, such energy and expertise must be captured effectively by national bodies if it is able to support the national effort. The Royal College of Physicians has provided a home for CTAG (which has also been endorsed by the Society) in recognition of this. Early trial signals need to be converted into commissioning policies. Whilst there may be collaboration across MHRA, NICE, NHSE and NIHR, what is not in place is a bottom up approach of operationalising decisions, particularly where there may be a degree of uncertainty. Clinical pharmacologists with multi-disciplinary input can help bridge this gap, for example by directing the activity of committees concerned with drugs and therapeutics.

6. The mechanisms for communication of scientific evidence internationally, within national governments and with the public:

- **Including the handling of conflicting scientific opinions**

6.1 There has been insatiable media appetite for breaking news on vaccines, clinical trials, therapeutic decision-making and other related issues. At times it has been to the extent that journalists are unable to keep up with the speed with which this abundance of research is being published.

6.2 The UK should use the opportunity of increased awareness of research to enhance interest and engagement in science within formal and informal learning settings to enhance future capacity and capability in scientific research and innovation.

6.3 The Science Media Centre (SMC)[29], an independent press office for science providing the national news media with access to a multiplicity of experts, is able to provide balanced comment on the latest breaking scientific research and has played a pivotal role in communication of scientific evidence during COVID-19. The SMC has run briefings with experts who have coordinated important trials e.g. the RECOVERY trial and they have sent third party comments to journalists about new research sometimes including that of preprint publications. Prior to the pandemic, this was not common practice as preprints were not a focus of the general media. Clearly it is important to be open and transparent about research and ensure its findings are available to all as soon as possible. However, it is also important to stress that these preprints were not peer reviewed and therefore need to be assessed critically rather than taken at face value. Consequently, as journalists have been keen to report on these non-peer reviewed studies, balanced comment from experts has

been necessary - even if to make the point that a study is inconclusive, and more research is needed. Finally, even the peer reviewed literature base will create conflicting evidence that is not always easy interpret when it comes to informing future research. Communicating emerging research must be done with an appreciation of the inherent uncertainty associated with scientific research.

6.4 Furthermore, decisions about when to publish trial results (i.e. via press release as opposed to preprint with appropriate data disclosed) must be taken carefully to ensure that findings add value and not confusion. Concerns about transparency and risk should be balanced with the need to rapidly disseminate information about a potentially life-saving treatment. Confusion in communication about the outcomes of certain studies meant exposure to political influence (e.g. inclusion of chloroquine/hydroxychloroquine in trials despite questionable evidence base), and there was no centralised communication to give the 'official line' on progress in finding a treatment. It would be helpful to consider running official briefings on the progress of clinical trials for therapeutics and vaccines, running alongside other government briefings. These would outline the therapeutics strategy, update the key findings from trials and their anticipated timelines, give analysis and confidence in interpretation suitable for media and patient consumption.

6.5 A coordinated therapeutics strategy needs an accompanying communications strategy to help patients and publics engage with the 'big picture', particularly regarding the implications of emerging research.

References

[1] Normand, S. (2020) *The RECOVERY Platform*. New Eng J Med. doi: 10.1056/nejme2025674.
[2] Synairgen plc. (2020) *Synairgen announces positive results from trial of SNG001 in hospitalised COVID-19 patients*. Available at: https://www.synairgen.com/wp-content/uploads/2020/07/200720-Synairgen-announces-positive-results-from-trial-of-SNG001-in-hospitalised-COVID-19-patients.pdf (last accessed 28 July, 2020).
[3] Public Health England (2017) *Exercise Cygnus Report Tier One Command Post Exercise Pandemic Influenza 18 to 20 October 2016*. Available at: https://www.scribd.com/document/460161101/Cygnus-Redacted-Annex-01scribd-Redactedv3#download (last accessed 28 July, 2020).
[4] Hine, D. (2010) *The 2009 Influenza Pandemic: An independent review of the UK response to the 2009 influenza pandemic.* [online] UK Government. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/61252/the2009influenzapandemic-review.pdf (last accessed 28 July, 2020).
[5] Jefferson T, et al. (2014). Neuraminidase inhibitors for preventing and treating influenza in adults and children. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No.: CD008965. DOI:10.1002/14651858.CD008965.pub4.
[6] UK Government (2020) *COVID-19 treatments could be fast-tracked through new national clinical trial initiative*. Available at: https://www.gov.uk/government/news/covid-19-treatments-could-be-fast-tracked-through-new-national-clinical-trial-initiative (last accessed 28 July, 2020).
[7] Lane, H. and Fauci, A., (2020). Research in the Context of a Pandemic. *New Eng J Med*, DOI: 10.1056/NEJMe2024638.
[8] Alexander, SPH, Armstrong, JF, Davenport, AP, et al. A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development: IUPHAR Review 29. *Br J Pharmacol*. 2020; 1–25. https://doi.org/10.1111/bph.15094
[9] British Pharmacological Society (2020) *Development of valid animal models will help identify safe and effective treatments for COVID-19*. Available at: https://www.bps.ac.uk/covid-19/society-news-and-updates/development-of-valid-animal-models-will-help-ident (last accessed 28 July, 2020).
[10] Teuwen, L., Geldhof, V., Pasut, A. *et al. COVID-19: the vasculature unleashed*. Nat Rev Immunol **20,** 389–391 (2020). https://doi.org/10.1038/s41577-020-0343-0
[11] Williamson EJ, Walker AJ, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients [published online ahead of print, 2020 Jul 8]. *Nature*. 2020;10.1038/s41586-020-2521-4. doi:10.1038/s41586-020-2521-4
[12] NHS England (2020) *We are the NHS: People Plan 2020/21*. Available at: https://www.england.nhs.uk/wp-content/uploads/2020/07/We_Are_The_NHS_Action_For_All_Of_Us.pdf (last accessed 30 July, 2020).
[13] NHS Digital (2017). Prescriptions Dispensed in the Community, Statistics for England – 2006-2016 [PAS]. Available at: https://digital.nhs.uk/catalogue/PUB30014 (last accessed 9 August, 2019).
[14] Academy of Medical Sciences (2018) *Multimorbidity: a priority for global health research.* Available at:

https://acmedsci.ac.uk/policy/policy-projects/multimorbidity (last accessed 29 July, 2020).
[15] British Pharmacological Society (2016). *Clinical Pharmacology and Therapeutics: The case for savings in the NHS*. Available at: https://www.bps.ac.uk/BPSMemberPortal/media/BPSWebsite/Assets/CPT-case-for-savings-in-the-NHS.pdf (last accessed 9 August, 2019).
[16] Policy Research Unit in Economic Evaluation of Health & Care Interventions (2018). *Prevalence and Economic Burden of Medication Errors in the NHS in England*. Available at: www.eepru.org.uk/wp-content/uploads/2018/02/medication-error-report-revised-final.2-22022018.pdf (last accessed 9 August, 2019).
[17] Health Education England. *The school of medicines optimisation*. Available at: https://hee.nhs.uk/our-work/medicines-optimisation (last accessed 21 August, 2019).
[18] *COVID-19 Therapeutics Accelerator*. Available at: https://www.therapeuticsaccelerator.org/ (last accessed 28 July, 2020).
[19] European Medicines Agency (2020) *EMA establishes taskforce to take quick ad coordinated regulatory action related to COVID019 medicines*. Available at: https://www.ema.europa.eu/en/news/ema-establishes-task-force-take-quick-coordinated-regulatory-action-related-covid-19-medicines (last accessed 28 July, 2020).
[20] Baker, EH, Gnjidic, D, Kirkpatrick, CMJ, Pirmohamed, SM, Wright, DFB, Zecharia, AY. A call for the appropriate application of clinical pharmacological principles in the search for safe and efficacious COVID-19 (SARS-COV-2) treatments. *Br J Clin Pharmacol*. 2020; 1– 5. https://doi.org/10.1111/bcp.14416
[21] Department of Health and Social Care (2020) *NHS recovery to put staff wellbeing at its heart*. Available at: https://www.gov.uk/government/news/nhs-recovery-to-put-staff-wellbeing-at-its-heart (last accessed 30 July, 2020).
[22] Association of the British Pharmaceutical Industry. et al. (2020*) Life Sciences Recovery Roadmap*. Available at: https://abpi.org.uk/media/8262/life-sciences-recovery-roadmap-3rd-june-2020.pdf (last accessed 28 July, 2020).
[23] Downing A, Morris E JA, Corrigan N, *et al*. High hospital research participation and improved colorectal cancer survival outcomes: a population-based study. *Gut* 2017;66:89-96.
[24] Ozdemir BA, *et al.* (2015). *Research Activity and the Association with Mortality*. PLoS One 10, e0118253.
[25] Jonker L & Fisher SJ (2018). *The correlation between National Health Service trusts' clinical trial activity and both mortality rates and care quality commission ratings: a retrospective cross-sectional study*. Public Health 187,1-6. https://www.sciencedirect.com/science/article/pii/S0033350618300015
[26] Boaz A, *et al.* (2015). *Does the engagement of clinicians and organisations in research improve healthcare performance: a three-stage review. BMJ Open* 2015;**5:**e009415. doi: 10.1136/bmjopen-2015-009415
[27] McManus RJ, *et al.* (2008). *How representative of primary care are research active practices? Cross-sectional survey*. Family Practice 25, 56–62.
[28] *COVID-19 Therapeutics Advice and Support Group*. Available at: https://www.ctag-support.org.uk/ (last accessed 28 July, 2020).
[29] Science Media Centre. Available at: https://www.sciencemediacentre.org/ (last accessed 29 July, 2020).

(July 2020)