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Commentary

The endangered physician-scientist and COVID-19

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The COVID-19 pandemic has affected almost every stakeholder in healthcare, including the vulnerable population of clinician investigators known as physician-scientists. In this commentary, Rao et al. highlight the underappreciated challenges and opportunities, and present solutions, for physician-scientists vis-à-vis the uniquely disruptive event of the pandemic.

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has revealed weakness in our ability to seamlessly interconnect the major missions of academic health centers (AHCs): patient care, research, education, and community health. This is largely because personnel and expertise are largely siloed within each of these core missions. Further, the massive reduction in elective medical care reduced patient volumes and consequently revenue to the AHC. At no other point in modern medical history has there been such a synchronous, worldwide disruption of elective medical care. In AHCs, especially in the United States, the transfer of funds to research, education, and community health generally emanate from revenue from positive margins associated with income generated from patient care.[1] The efforts of physician-scientists typically span a majority, if not all, of these missions. The Association of American Medical Colleges defines physician-scientists as those who "conduct independent scientific investigation in the laboratory, clinic, or other setting" (https://www.aamc.org/what-we-do/mission-areas/medical-research/physician-scientist). Among those physician-scientists who conduct external/federally funded research, physician-scientists conduct research at comparable level of rigor and depth as their PhD scientist colleagues, even if they themselves do not hold a PhD degree. We recognize that pandemic-related stressors, such as lab closures, exist among PhD scientists, including those who conduct translational research. In addition, non-scientist physicians, who constitute the majority of faculty within AHCs, often care for the lion's share of patients, and thus may bear a heavier burden of patient-related stressors. While beyond the scope of this commentary, each of these allied workforces deserve separate discussions devoted to overlapping and distinct issues that have emerged during the pandemic. We detail below how the COVID-19 pandemic has affected physician-scientists in ways that are both expected and unexpected.

The efforts of physician-scientists span basic science mechanisms of disease, translating preclinical models to humans, clinical trial design, and healthcare disparities research, among many others. Physician-scientists have been integral to the development of vaccines for devastating viruses like polio that affect children,[2] rational drug design for the treatment of cancer (imatinib),[3] and now they are fundamental to the many teams that are working on new and different approaches to create COVID-19 vaccines.[4] Indeed, this pandemic, now more than ever in modern medical history, issues a clarion call to protect and support this group of medical scientists, both those working on basic mechanisms of disease and those translating their findings into clinical trials and new therapeutic approaches.

SARS-CoV-2 has many poorly understood effects on the human body. Many seemingly inscrutable features of the disease, such as silent hypoxia, thrombosis and end-organ damage, age-, gender-, and ethnic-specific differences in clinical manifestation, and social and economic determinants present challenges but also unique opportunities to advance science. As frontline doctors, physician-scientists observe these aspects of the pandemic firsthand and are therefore uniquely positioned to bridge research advances to medical innovation. As a testament to this line of reasoning, physician-scientists are present in every clinical specialty and its diverse community is comprised of those trained in health services research, epidemiology, immunology, virology, gene editing, and many other basic and translational fields. The value of the physician-scientist has long been considered their unique ability, distinct from pure clinicians and non-clinician scientists, to bridge clinical insights to the laboratory and back, which provides the so-called "bench-to-bedside" and "bedside-to-bench" bi-directional flow of translational knowledge. In the context of the pandemic, physician-scientists contribute in many ways: probing the clinical manifestations of COVID-19, understanding its transmission, and developing therapies. As laboratories had been largely shut down across AHCs and their affiliated medical schools and universities, physician-scientists

have led specially sanctioned COVID-19 research projects, by continuing their previous work or by pivoting their interests in other fields (e.g., https://research.umich.edu/covid-19/covid-19-research-index). In other cases, physician-scientists are well placed to catalyze the formation of interdisciplinary teams of PhD scientists and non-scientist physicians from a variety of disciplines, including computational biology, to capitalize on insights from their access to highly annotated, quality clinical samples. Such examples include the potential utility of using saliva (rather than nasopharyngeal sampling) to detect SARS-CoV-2, the presence of pro-thrombotic and inflammatory neutrophil extracellular traps in COVID-19,[5] as well as many fundamental and clinical aspects of COVID-19 such as ventilator management strategy and proning.[6] Many of these projects were made possible by the extensive networks that are unique to physician-scientists. Such networks often comprise other physician-scientists, non-clinician PhD scientists, and clinical colleagues with large referral-based practices that attract patients from other practices in the community to tertiary and quaternary AHCs. In sum, physician-scientists are super-connectors that are uniquely positioned to form and help guide interdisciplinary research teams.

COVID-19 has laid bare the fragile economics of AHCs. The hospital component often operates on low-single-digit margins in a "good" year.[1] However, the COVID-19-related reduction in clinical services, especially elective procedures, has shrunk health system revenues such that many AHCs are projecting hundreds of millions of dollars in losses, even with federal assistance. The transfer of funds from universities and university-owned hospitals to affiliated medical schools typically provide support for the educational and research missions. Since hospitals have been financially impacted and university finances may be impacted by reduced student enrollment (https://www.npr.org/2020/12/17/925831720/losing-a-generation-fall-college-enrollment-plummets-for-first-year-students), the transfer of funds to medical schools that typically employ AHC faculty is severely threatened. Because AHCs, hospitals, and universities jointly recruit faculty, it is difficult to forecast how downturn in university finances affect their hospitals and medical schools. COVID-19 appears to preferentially impact low-income individuals who have multiple morbidities, such as obesity, diabetes, and immunosuppression. AHCs care for a disproportionate number of these patients, especially those who require intensive care and mechanical ventilators. Thus, AHCs predict higher COVID-19 patient occupancy, with further reductions in elective care and changes to the payor mix. In US AHCs, where major components of clinical faculty income and benefits depend on non-COVID-19-related direct patient care, the pandemic-associated reduction in clinical volumes impacted their total compensation. In Australia, Japan, India, and many European countries, physician-scientists care for patients in government-funded hospitals, where lower salaries are often supplemented by service in the private healthcare system (https://www.commonwealthfund.org/sites/default/files/documents/___media_files_publications_fund_report_2017_may_mossialos_intl_profiles_v5.pdf). How the reduction in non-COVID-19 elective care affected the income and benefits and research efforts of physician-scientists in these countries deserves future study.

COVID-19 has also brought a previously underappreciated economic argument for physician-scientists to the forefront. In contrast, federally funded physician-scientists have, to date, benefitted, to some degree, from uninterrupted flow of grant-based incomes, and rely less on clinical-based income. The National Institutes of Health (NIH, US) and National Institute for Health Research (UK) allowed continued grant-based compensation for physician-scientists that could not continue their research during the pandemic or were redeployed from their primary research role or clinical specialty, to aid in the care of patients diagnosed with COVID-19 (https://www.nihr.ac.uk/documents/qanda-on-the-impact-of-covid-19-on-research-funded-or-supported-by-nihr/24467). Several international and national biomedical funding agencies such as Horizon 2020 (EU), Wellcome (UK), Cancer Research UK, Australian Research Council, German Research Foundation (DFG), and others have offered costed extensions, no-cost extensions, scope changes, paperwork reductions, and other flexibilities to their grantees that may enable continued research funding during the height of the pandemic.[7] There are thus underappreciated economic arguments for the physician-scientist during the pandemic: because they have multiple income streams—hospital-based and research grants—they can more favorably weather financial downturns. Physician-scientists thus provide a "hedge," albeit temporary, against financial uncertainties that pure clinical physicians and non-clinician researchers cannot.

While revealing all of these potential advantages served by the physician-scientist, the COVID-19 pandemic has further exacerbated existing disparities in the current training pipelines and AHC infrastructure. Already, the transition to independence, and maintenance of an independent research program, are major leak points in the career pipeline of physician-scientists during which many leave academic medicine, and the pandemic may further hobble promising careers.[8] Broad hiring freezes have swept across universities and AHCs throughout the world, further decreasing potential opportunities and resources to bring the next generation of physician-scientists into the field.[9] Pauses in research activity, freezes in hiring staff, and reductions in spending are particularly harmful to current physician-scientists at the junior faculty level, as this vulnerable group does not yet have tenure and often rely on tenuous start-up packages or bridge funding schemes that often rely on transfer of funds from the clinical operation. The longer-term consequences of the pandemic redeployment of physician-scientist to clinical care on research productivity, funding, and burnout, which may be specialty specific (e.g., anesthesiologists and pulmonologists with high clinical burden), are not yet clear.[10] Furthermore, with the shutdowns of childcare centers and schools across the world, the burden of managing both a family and a career has fallen more heavily upon junior scientists and on women in particular. For example, a recent study across the workforce in the US discovered that women in heterosexual couples were forced to reduce their work hours 4–5 times more than men during the course of the pandemic.[11] These disparities will need to

be considered and addressed lest the current gap in female representation among professor-level roles in academic medicine worsen (https://www.aamc.org/what-we-do/mission-areas/medical-research/physician-scientist).

Before the current pandemic, the slow decades-long decline of the physician-scientist had been documented by several sources. During this time, the proportion of physicians engaged in research has declined from 4.7% of the total physician workforce to 1.5% today. Since physician-scientists account for nearly ~40% of winners of Nobel Prizes in Physiology or Medicine and some 70% of chief scientific officers of major pharmaceutical companies and NIH institute leadership, their retreat from research is expected to have a profound impact on medical sciences.[12] To address these issues and reverse these trends, stakeholders ranging from AHCs, philanthropists, and research funding bodies to pharmaceutical companies should consider proactive measures for turning these challenges into opportunities. These actions can start by increasing the pipeline of physician-scientists by national governments such as increasing the number of Medical Scientist Training Program (MSTP) slots, increasing protected "research track" positions in clinical residency programs, increasing physician-scientist transition awards (e.g., K99-R00 NIH award), lengthening the period of the first independent award (e.g., NIH R37 MERIT Award), broadening the scope of grant support to fund individuals rather than specific projects (e.g., the NIH R35 Maximizing Investigators' Research Award), revising the university tenure clock, and further incentives for AHCs, such as federal grant supplements to support the costs of shutting down and restarting research programs, as well as expanding hiring and protection of physician-scientists, particularly women and underrepresented minorities.

The non-grant "hard-money" allure of biopharmaceutical industry jobs has led to a reduction in the AHC physician-scientist workforce.[13] Through enhanced public-private/non-profit partnerships, industry could provide support and opportunities to expose and engage physician-scientist faculty and trainees to the steps of drug development rarely seen within the confines of academia, such as product development, regulatory affairs, marketing strategy, and policy development. We agree with a recent perspective that such opportunities be framed with a common set of standards and rules to prioritize education and reduce conflicts of interest.[14] Because AHCs and biopharmaceutical industries have unique and complementary expertise, translational research training courses for junior and established investigators, which are structured to bridge the academia industry innovation and funding divide, are necessary (e.g., PhD research training conducted in industry laboratories; the Bridging Academia with Industry Training Program, at the Massachusetts General Hospital). These governmental and industry actions are expected to result in immeasurable longer-term benefits to healthcare.

We believe that all types of physician-scientists, from wet-lab researchers to those engaged in translational science and clinical trials, ought to be protected because most have experienced the stultifying process of "shutting down non-essential" operations for several months followed by an ongoing but slow "re-opening" of research efforts. Such activities remain below baseline operations given the need for reduced space occupancy due to social distancing policies, but also due to departure of research staff as funding has dried up. At many research-intensive AHCs, restart of human-subjects (clinical) research has lagged behind resumption of elective patient care and laboratory-based research. Thus, when determining how future AHC, NIH, DFG, Wellcome, or other foundations or federal research organizations divvy up their limited resources to assist physician-scientists to revive their research programs, each situation ought to be considered for its unique circumstances. Such factors should include, among others, the length of time of the research pause, the degree to which essential funding has run out relative to the level of support required to maintain pre-pandemic research operation, other sources of support, whether loss of funding would irrevocably close the lab or end the research operation, and how the scope of research relates to potential solutions for the disease/pandemic at hand.

We conclude that the work of physician-scientists in conducting translational research related to health emergencies, due to their expertise and their "super-connector" networks, is fundamental to promote advances in modern medicine in the face of further COVID-19 waves, other viral pandemics, or unpredictable, widespread acute or chronic diseases. We acknowledge that the precise number and subtypes (computational scientist versus clinical trialist) of physician-scientists that are necessary to sustain and advance modern medicine is presently unknown. We surmise that physician-scientists are unique in that they have experienced stressors that overlap with both PhD-scientists and non-scientist physicians. Finally, given the continued decline of physician-scientists from the physician and NIH-funded research workforces,[15] concerted and deliberate governmental and industry efforts are necessary to recruit and maintain this group of physicians.

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