ISSUES IN MEDICINE

Research in COVID-19 times: The way forward

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The COVID-19 pandemic has had a major impact on research at universities. Universities around the world, including in South Africa, have been or are still closed as part of national lockdown strategies. Students have not been attending classes or doing hands-on experimental work, and students and academics have been working from home. Many thousands of students have had their university education interrupted, and for them, the resumption of learning programmes online, and where possible in research laboratories, is critically important. There is no question that as we emerge from lockdown we will not be entering a world that resembles a 'norm' as lived in the pre-COVID-19 era, and many changes will be required. Here we discuss the importance of research, the urgency to get things up and running again, and strategies that will need to be implemented to ensure that research activities continue. At the same time, it is necessary to ensure that students and staff are not exposed to risk in their research endeavours, which will require the development and implementation of risk management plans.

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South Africa has been in lockdown since 27 March 2020, and the government is slowly easing restrictions as part of a risk management strategy based on the number of people infected with SARS-CoV-2 balanced against the need to open up the economy. In parallel with the easing of restrictions, the country is experiencing an increase in infections with a peak expected in July/August 2020. The initial phases of the lockdown were effective in allowing healthcare services to become established to prepare for the increase in the number of cases expected. Subsequently, a delicate balancing act has ensued, in which efforts have been made to ensure the preservation of both life and livelihoods. However, as the lockdown is lifted, the numbers of infected individuals will increase.

But what about research? A university is a community of teachers and scholars, where learning at the highest level is led by the creation of new knowledge, and where scholars with different disciplinary backgrounds engage to debate and share thought. Research lies at the heart of a university. Indeed, the drive to discover, to create new knowledge and to impart it is often what motivates university researchers to choose academic careers.

Much research activity at universities has been halted by the closure of campuses, in support of lockdowns and social distancing. Many research programmes, particularly those that are dependent on access to laboratories and specialised research facilities, are being delayed, postponed or stopped, at least temporarily.[1,2] Researchers are isolated, and not able to work in the facilities that are essential for their research. Online working does, however, lend itself to analysis of existing data, typified by analysis of large datasets, so-called 'big data', for example in bioinformatics analysis of human or other genomes.[3]

Research conducted by universities often involves postgraduate students who have defined time periods in which to conduct the research components of their higher degrees, and time away from research facilities is time lost in terms of the completion of their degrees. Time is also lost in meeting research milestones, and a strategy is needed to allow for the resumption of research activities and regaining of momentum.

The recent redirection of national and international resources to address COVID-19 will mean that less funding will be available for other projects, and it will be necessary to select and prioritise research activities. Research under these circumstances will mainly be purpose-driven, and the availability of funding for so-called 'blue skies' research is likely to be limited for some time to come.[4]

Once lockdowns are (at least partially) lifted and new arrangements are made to enable research to resume, research activities will gradually begin to approach the 'norm' as occurred before the pandemic. Nowhere is the dictum that opportunity arises in situations of adversity more applicable, and this is an opportunity to ask ourselves what was working well, what was not working, and how we can create a more efficient, relevant and productive research environment.

Resuming research activity

In the short term, it is critical that researchers return to their campuses to restart or resume research programmes before they are no longer redeemable. The key activities include experimental work to generate or gather data, and the co-ordinated operational actions needed to address restarting laboratories, regaining the necessary levels of productivity, and making up for lost time. Restarting some experiments may prove to be very challenging – biological materials may no longer be viable, animal lines may be expensive to replace, instruments may malfunction, and supplies are likely to be slow to be delivered as suppliers respond to a wave of orders.[2]

Laboratory safety and efficiency will now have additional elements to be considered.[2,5] Social distancing will remain with us for some time, and this will mean establishing new ways of accessing and working in research venues, managing research time more flexibly, limiting the numbers of researchers in laboratories, and managing the use, and planning the maintenance, of common instrumentation facilities and platforms differently.

Improving on research approaches

In the medium term, we should ask ourselves what we have learned from COVID-19, and what we should do differently. Many aspects need to be considered, and three examples stand out.

First, the past few months have shown us that the previously long time periods taken to produce and publish a research article can be – and have been – significantly reduced.[6] This is not to say that we should compromise on quality and devalue excellence. We continue to strive to achieve research excellence because we believe that through excellent research, we can influence the transformations needed by our country, our continent, and the world.

Many COVID-19 publications have been made freely available online, a recognition by the global research community that open-access publishing promotes access to valuable information that in turn could lead to the more rapid development of solutions for urgent problems.[7,8]

The COVID-19 pandemic has created pressure on researchers to work more rapidly, and to conduct research and clinical trials under exceptional urgency, which could lead to the risk of compromising rigour and research integrity. The recent retraction of articles published in the top-tier medical journals *Lancet* and *New England Journal of Medicine*, of which the former had a major influence on national (UK) and international (World Health Organization) policy, highlights the pitfalls that await us and the need for 'more speed and less haste'.[6,9]

Despite the pressures imposed by the scale of the pandemic, research methodologies must be rigorous, analyses must be conducted with integrity, and clinical trials must be complete as well as feasible, whether related to drug design or vaccine development. If trials are not comprehensive, and therapies are applied based on incomplete information, the negative impact could be dangerous and far-reaching.[10] For example, clinicians may, under pressure, find themselves making choices to use new treatments based on responsibility of care before there has been time to ensure the rigour of the research underpinning the development of the therapy.

Second, researchers need to establish better ways to ensure trusted communication with the public. We need to publish to ensure that society understands our research results and their benefits – and we need to make sure that in publishing our research we do so clearly, accurately and honestly. To paraphrase a well-known quotation, we write to be understood, but perhaps more importantly, we must write in a manner which ensures that we are not misunderstood.

The danger lies not only in the academically unethical practice of publishing unreliable results, which amounts to disingenuous misrepresentation,[11] but, perhaps more seriously, in misleading the (possibly naive) reader with unfounded assertions that he or she may then act upon – with a multitude of possible consequences.[12]

Third, at the core of finding solutions to the COVID-19 pandemic is the recognition that no single discipline can resolve all the problems that have arisen. Inter- and trans-disciplinary collaboration, partnerships, and social responsibility are key to a successful outcome. The scientific and medical professions must be complemented by the economic and legal professions, and human rights must be ensured, particularly when systems are overloaded and attention to detail may be compromised.

Research priorities

In the longer term, we need to define research priorities. While many of the current research efforts globally are justifiably being re-focused on COVID-19, decisions will need to made about research in other areas.[13] COVID-19 is likely to be with us for some time to come, and the likelihood of other pandemics occurring will increase with time. However, other diseases, both communicable and non-communicable, will not diminish, and our attention must not be diverted from addressing these diseases, many of which render individuals more susceptible to poor outcomes in the context of COVID-19 (hypertension, diabetes, heart disease).

There is little doubt that at present the focus on understanding COVID-19, and the search for vaccines and treatment regimens, should be at the forefront. Since January 2020, globally, close to 10 000 publications and reports have been published on the virus and its impact, and it is admirable that such rapid progress has been made;[14] as we wrote this commentary, the first vaccine was going to human trials in the UK,[15] and the first results of mesenchymal stem cell therapy for COVID-19 were being reported.[16] In developing the vaccine, the next steps will involve the combined efforts not only of biomedical researchers, molecular biologists and virologists, but also biochemical engineers and industrial pharma production companies. The world is waiting for an effective vaccine to be produced, in sufficient quantities and in record time, to enable return to a freer way of life.

Should all our future research be directed towards solving immediate and current challenges? In saying that it should not, we should consider the importance of fundamental research. The research that is currently addressing the COVID-19 pandemic is underpinned by decades of forward-looking blue skies (fundamental) research that was thought about, designed and carried out by researchers who had creative ideas, and developed new theories and new technologies, long before they could have predicted their use, in 2020, to manage a world in crisis. We cannot afford to ignore, or under-resource, fundamental research.

Furthermore, we need to understand, and contribute to, science policy. At all levels, from individual groups to global organisations, policy drives the use of resources and steers development. In urgently seeking solutions on how to address the COVID-19 pandemic, we have seen governments looking to scientists for evidence-based recommendations and advice that has directed national and global responses and policies. It is up to us as scientists to provide sound advice.

In the longer term, the overarching global agenda of achieving the Sustainable Development Goals (SDGs) remains relevant and important. It may be said that had we made more progress with achieving some of the SDGs, the impact of the COVID-19 pandemic could have been lessened. For example, food security has not been assured in some parts of the world, and had this been adequately addressed, the impact of COVID-19 on the number of people suffering acute hunger might have been reduced.[17]

One further lesson relates to research co-operation. There has been an unprecedented move towards unfettered collaboration and co-operation. Conventionally, researchers work in an environment where competition is as much a feature of life as is collaboration, but the COVID-19 crisis has galvanised a comprehensive joint global effort. Teams from leading research organisations around the world are collaborating in the search for vaccines, treatments and solutions to the health, economic and social crises caused by COVID-19. From free sharing of new data on the SARS-CoV-2 genome to design of low-cost equipment and development of rapid test kits, researchers and organisations in developed and developing countries have been co-operating to collectively meet the challenges presented by the pandemic.[18] Such collaboration will have allowed some developing countries to prepare far more effectively for the pandemic than they would have done independently.[19]

As we consider the future of research in COVID-19 times and beyond, we should do so in the context of the information era. We have for some years seen this as a digitally connected and information-driven world, but in this pandemic, with sweeping lockdowns and extreme

isolation measures, the relevance of information and data sharing has been dramatically brought to the fore. The world has shown what can be achieved through virtual information sharing and interactions, and the so-called new normal will undoubtedly include the replacement of traditional localised modes of communicating and collaborating, for instance through conferences, with virtual interactions conducted with vast networks, in real time, across the world.

Acquiring and storing research data will become increasingly important, but even more so will the ethical issues surrounding access to data and particularly personal information. As artificial intelligence becomes increasingly effective, we will need to conceptualise ethical use of information in different ways. One example is the use of cellphone data for tracing contacts of individuals infected with COVID-19.[20]

Finally, we need to re-examine the ways in which we train students for research through the globally accepted system of higher degrees. Postgraduate supervision is a key part of research at universities, and postgraduate students often play major roles in research programmes. Their research training frequently requires that they are the generators of data, and that they spend considerable time – usually years – conducting projects through which they are expected to create new knowledge and individually make an original contribution. Is this realistic in the new interconnected, co-operative and fast-moving research world?

In the new regime of open science, with the need for rapid generation of results and free information sharing, we may need to revise the way in which a researcher is trained and a doctorate achieved. If we are seeking to develop high-level, transdisciplinary thinking that enables rapid progress in solving global questions, the ability to adapt to working creatively in a collaborative and interconnected way may be the most critical skill researchers need. The future leaders of research will be those who can most effectively draw together teams, and integrate thinking across boundaries, both spatial and disciplinary.

Clinician-scientists

Understanding the pathogenesis of human disease requires input from many sources, and this is particularly relevant in the context of the COVID-19 pandemic. From the perspective of the basic scientist, by working with cells and molecules, one obtains an understanding not only of the exacting nature of the science, but also of the extent of co-ordination and fidelity that is required for normal structure and function. From the perspective of the clinician, understanding the molecular and cellular basis of disease improves the quality of care. A close interaction between clinicians and scientists is desirable. Clinician-scientists, i.e. those who are active in both fields, are a rare breed. Yet in crisis situations, as exemplified by the current pandemic and those that are likely to follow, clinician-scientists are needed in order to understand disease pathogenesis and integrate knowledge from a variety of sources, to provide preventive and therapeutic solutions. COVID-19 has highlighted more than ever before the need to (re)initiate programmes that foster the growth of the clinician-scientist workforce.[21]

Conclusions

The hardship and heartache caused by COVID-19 have led to new thinking on many levels, from the individual to the global. Research pace has been altered, investment in research has moved on its axis, and researchers have changed their focus. We must expect other pandemics in the future, and if we learn from the COVID-19 experience, we will be able to take an informed and integrated approach to the research that will be needed.[22] A quote attributed to Charles Darwin (1809 - 1882) is pertinent in the current context: 'It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change.' As our world undergoes dramatic changes in which the familiar becomes almost unrecognisable, the ability to adapt will become increasingly important, and nowhere is this more important than in the context of research, on which the survival of our species will ultimately depend.

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