

Non-communicable diseases: research priorities to mitigate impact of health system shocks

Amitava Banerjee and colleagues argue that the long term impact of non-communicable diseases should be prioritised in planning the response to and management of future health shocks

During pandemics and other health system shocks, such as natural disasters, climate change, or humanitarian emergencies, non-communicable diseases have been neglected, despite them causing the highest burden of morbidity and mortality globally.¹ Since the early waves of the covid-19 pandemic, for example, policy, public health, and the media globally have focused on admission to critical care, hospital admission, and mortality related to covid-19.

However, excess all cause mortality, mostly due to non-communicable diseases, greatly exceeded mortality due to covid-19 in the first two years of the pandemic, with an estimated 18.2 million overall excess deaths worldwide and 5.94 million covid-19 related deaths.² In England and Wales in the first two months of the pandemic alone, one fifth (9948/47 243) of excess deaths were not associated with covid-19.³ Research played a central role in planning and implementing responses during the covid-19 pandemic, particularly in the UK, but non-communicable diseases before and during pandemics received limited attention, and this is a global phenomenon.

SARS-CoV-2 infection has had substantial direct effects (associated with

infection, typically in the acute phase), indirect effects (non-covid consequences associated with disruptions at individual and system level), and long term effects (beyond the acute phase of infection, with lasting consequences). Non-communicable diseases are implicated in all three, whether as risk factors for covid-19 related mortality, concomitant diseases affected by disruptions due to covid-19, or chronic outcomes,⁴ but are overlooked for four reasons.

Firstly, a culture of siloed thinking of non-communicable diseases versus infectious diseases spans funding, research, policy, guidelines, and care. Secondly, pandemic preparedness is concerned with gathering and acting on evidence of acute insults to individuals and populations rather than more chronic timescales of non-communicable diseases. Thirdly, resources, whether financial, human, research, policy, or care for non-communicable diseases and post-infectious consequences, have been substantially less than for infectious diseases. Fourthly, research and policy data for measurement and monitoring have emphasised mortality rather than morbidity, neglecting important effects of, and populations affected by, shocks, so that the true impact, particularly of non-communicable diseases, is poorly captured.

In this article, we use examples from the covid-19 pandemic in the UK to provide recommendations for including non-communicable diseases in research and policy for future shock preparedness that may be applicable internationally. Although non-communicable disease complications of infectious diseases such as HIV/AIDS and flu are well documented,^{5,6} the unprecedented scale and pace of the effects of covid-19 have highlighted the need for more timely research.

Culture: integrated thinking about non-communicable and communicable diseases

Better representation of non-communicable diseases in preparedness for shocks requires fundamental shifts

in involvement of patients and the public in all areas of research and at all stages from research design to dissemination. The covid-19 pandemic has led to greater use and dissemination of, and public interest in, routine health data. However, without integrated patient and public involvement, including people with lived experience of non-communicable diseases, from priority setting through funding allocation to implementation, research may not be inclusive in terms of study populations, baseline characteristics and risk factors, outcomes, and health system characteristics.^{7,8}

The NHS England Secure Data Environment funded by the charity the British Heart Foundation has been used extensively for covid-19 related research since its inception, and every research protocol is published with lay summaries and reviewed and approved by a separate patient and public panel, showing how government, research funders, researchers, and patients can enact change.^{7,8} Large scale efforts to use Office for National Statistics data have also involved patients and public, including research reports or publications.⁹ Encouraging trends include patients leading research agendas and publishing research independently,¹⁰ which should inform future research in non-communicable diseases during shocks.

Shocks are likely to have differential effects, not only through “protected characteristics” such as sex, gender, ethnicity, and disability, but also by creating or accentuating inequalities related to other social determinants of health, such as homelessness and educational attainment, which may pose a threat for both communicable and non-communicable diseases.¹¹ Therefore, during shocks, research must collect, analyse, interpret, and disseminate data that include these determinants so that potential inequalities can be recognised, prevented, and tackled.¹²

Most data driven research in non-communicable disease has been disease specific and from high or high-middle

KEY MESSAGES

- Non-communicable diseases have played a central role in the effects of the covid-19 pandemic and must be embedded in long term research agendas for future shocks
- Culture, evidence, resources, and data are important levers to ensure the incorporation of non-communicable diseases in research in pandemic preparedness and planning
- Policy makers, scientists, practitioners, and patients need to be connected in a “bird’s eye view” of shocks instead of specific emphases on certain specialties and disciplines

income countries. Availability of national data for research across multiple datasets offers huge dividends,^{7 13-15} but the UK government's emergency pandemic response restricts legislation and approvals to research related to covid-19. To guarantee the availability and benefits of data in future shocks,⁷ government must revise legislation with wide stakeholder engagement, including patients and the public.

As well as social inequalities, inequalities may exist in research and data on non-communicable diseases during shocks; this research is too often descriptive, retrospective, and outdated instead of in near real time and forward looking. Access to and use of representative national data can enable actionable research. For example, during the covid-19 pandemic, evidence of increased incidence of risk factors for cardiovascular disease, including diabetes and hypertension, which may themselves be direct or indirect effects of covid-19,^{13 14} was used to target high risk groups for vaccination. Moreover, near real time research on covid-19 vaccination uptake and cardiovascular disease and its risk factors and demographic variation, including by age, sex, socioeconomic status, and geographic location,¹⁵ informed strategies to increase vaccination uptake. This research model could be applied to non-communicable diseases in shocks. Patients and the public can and should be involved throughout, from setting research questions to access to and curation and analysis of data.

Healthcare and healthcare research include many paradigms aiming to improve the effectiveness of research pipelines and ultimately care, such as translational medicine, precision medicine, personalised medicine, and data driven healthcare. However, most paradigms assume linear processes from discovery to translation instead of "improvement cycles" or more complex systems characterising quality improvement, implementation science, and learning health systems,⁴ which are cross cutting concepts and could accelerate and maximise benefits for patients during shocks, when gaps simultaneously emerge in care and research.

In various non-communicable diseases, calls for "integrated care" have echoed across specialties, communities, and levels of healthcare, particularly in relation to long covid.¹⁶ The power of "integrated research" was shown in acute covid-19 research in many ways, such as rapid genomic sequencing of SARS-CoV-2 and

swift clinical trials and implementation of covid-19 vaccination. However, these integrated efforts have tended to consider one disease at a time. With multiple long term conditions, polypharmacy, and compound pressures including the pandemic, staff shortages, and procedural backlogs, research strategies that traverse boundaries of diseases, drugs, and disciplines are needed during shocks, including new research funding calls¹⁷ and new ways of thinking from journals and clinical guidelines to conferences and clinical specialty training. For example, conferences and specialty training could incorporate more "generalist" content and journals could have specific calls for papers relating to cross specialty themes.

Evidence: incorporating chronic as well as acute perspectives of preparedness

For covid-19, strong evidence shows a long term risk of associated non-communicable diseases, including cardiovascular disease and its risk factors and longer term post-viral syndromes, but research, practice, and policy focus on the acute impact of shocks. Risk of cardiovascular disease is over the lifetime, related to multiple comorbidities, and associated with chronic disability.¹⁸ Therefore, associations of non-communicable diseases with shocks such as pandemics may occur over much longer timescales.

During the pandemic, electronic health record data from primary and secondary care at national level have been linked with disease specific registries and other datasets enabling study of longitudinal associations with different non-communicable diseases, from cardiovascular disease and chronic lung diseases to chronic kidney disease and diabetes.⁷ The movement towards continuously updated evidence, such as living reviews and guidelines,¹⁸ should be extended to longer term consequences of shocks. To understand the true impact of shocks among all non-communicable diseases, timely evidence and guideline development that traverse disease, specialty, and disciplinary silos and over the longer term are needed. This responsibility is beyond individual researchers and funders and requires central governmental coordination with public support, by emphasising the major advances and benefits for public health.

Long covid is a condition that started to be defined by patient communities globally from April 2020.^{4 10} Post-infectious chronic conditions have been described

with several viruses, including influenza, Epstein-Barr virus, and SARS-CoV-1.^{16 19} However, health systems were unprepared for the scale and severity of the burden of long covid,¹⁹ reflecting relative neglect of post-infectious and chronic disease in preparedness, planning, and policy for shocks. Evidence from multiple countries shows symptoms affecting multiple organ systems, creating major strains on individuals, populations, health systems, and economies. Consensus definitions and coding in research and practice should be used as early as possible,^{10 19} and research should include modelling of the potential burden of longer term consequences of shocks, whether basic science, epidemiology, data science, or economics. For long covid, much of this effort has been led by patients and the public, whether through advocacy, setting of research funding priorities, or policy setting. In future, researchers, funders, and policy makers must better incorporate research on potential and real long term effects into their ways of working.

Resources: minimising silos across research, policy, and care

When critical care beds were prioritised early in the pandemic, beds elsewhere in hospitals and health systems were "stepped down." Across diseases, specialties, and countries, non-covid care was generally reduced during the pandemic, whether prevention or treatment in hospitals and communities.^{14 20} These evidence based strategies for treatment and prevention are known to improve health and longevity; without them, population health will suffer. For example, activity in cardiovascular disease management decreased in the UK and has not yet returned to pre-pandemic levels.¹⁴

Although each specialty faces similar challenges and backlogs, from orthopaedic surgery to neurology, from gastroenterology to emergency medicine, each has had to develop its own way of collecting, analysing, and acting on data. For both procedural and non-interventional clinical disciplines, future research, including predictive models, would benefit from common frameworks for planning, monitoring, and minimising indirect effects during shocks. Similarly, non-covid research was delayed and deprioritised during the pandemic, whether by staff, funding, or infrastructure. As well as staffing and funding new chronic disease research relating to shocks, "business as usual" research in non-communicable

diseases must continue or at least return to normal as soon as possible. In medical education, postgraduate training, and continuing medical education, this will require “cross pollination” (for example, non-communicable diseases in infectious disease training). People involved in policy, research, and dissemination need to rethink the extent to which superspecialisation has come at the expense of the value of generalisation in clinical and research spheres.

Globally, the focus on funding and policy is limited for research into the chronic effects compared with the acute effects of shocks. That non-communicable diseases are the major cause of disability in low to middle income countries or poorer populations, surpassing infectious diseases, is often still not appreciated.¹ Similarly, most funders, health service providers, and policy makers have focused on the acute impact of shocks, even though their chronic impact, if properly documented and measured, is probably more significant, warranting far greater resource.

Major funders, including the National Institute of Health and Care Research and Health Data Research UK, have mobilised reactive funding and resources to enable this type of urgent, cross disciplinary, policy relevant research, such as “reducing compound pressures,”²⁰ but funders predominantly focusing on infectious disease (for example, the Gates Foundation and Wellcome Trust) may not want to change their agendas. Future strategies to provide resource for research on non-communicable disease during pandemics and future shocks should aim to capitalise on commonalities across specialties and disciplines to avoid duplication of effort and unnecessary competition for limited resources, as well as challenging beliefs that the chronic effects of shocks are less important. Research, its funding, and its outputs have to be better matched to needs and disease burden, which despite increasingly detailed, contemporary Global Burden of Disease data,¹² has not yet happened, with fragmentation at best and competing “vertical” programmes at worst. Governments, particularly in low-to-middle income settings but also in the UK, need to be able to negotiate for and prioritise cross disciplinary and cross specialty research.

Data: pursuing inclusive research

Typically, trials and observational studies in shocks have focused on infectious disease metrics and outcomes, as well

as those specific to a particular shock, such as hospital admissions related to covid-19. The relevance of measuring non-communicable disease metrics and outcomes is shown by cardiovascular disease during this pandemic. Large scale epidemiological studies of national level electronic health records in high income countries have shown increased risk of cardiovascular disease, from myocardial infarction to stroke, for at least a year following covid-19.

An English study of more than 125 000 people who were admitted to hospital and 1.3 million people who were not compared the risk of first arterial and venous thromboembolic events after a diagnosis of covid-19 in the first year of the pandemic compared with no covid-19 diagnosis over one year. The increase in risk was greater than 20-fold (adjusted hazard ratio 21.7, 95% confidence interval 21.0 to 22.4) and 30-fold (33.2, 31.3 to 35.2) in the first week after covid-19 diagnosis, decreasing to a 34% (1.34, 1.21 to 1.48) and 80% (1.80, 1.50 to 2.17) increase during weeks 27-49, for first arterial and first venous thrombotic events, respectively, with higher rates among black or Asian people than among white people.

In absolute terms, this translates to an estimated 7200 and 3500 additional arterial thromboses and venous thromboembolic events, respectively, after 1.4 million covid-19 diagnoses.²¹ Multiple potential mechanisms are implicated, including endothelial dysfunction, atherosclerosis, and thrombosis, but the

epidemiology and mechanisms of new cardiovascular disease and other non-communicable diseases associated with covid-19 have been studied in separate specialties with little joining up of research disciplines from physiology to population health (“bench to bedside to big data and back”), which slows the pace of progress in terms of translation to prevention and disease management.

Different disciplines and specialties need to work and learn together across silos, both for non-communicable diseases individually and when considered along with infectious diseases to create “learning health system” models of research. To monitor and try to prevent non-communicable disease consequences of shocks, these need to be measured.

Most early covid-19 policy and pandemic preparedness focused on mortality and critical care admissions with relatively little attention paid to other forms of healthcare use, such as general practitioner or outpatient visits and emergency department attendances, pharmacy visits, patient reported outcomes, or costs of care. As a result, covid-19 research may not have used the right metrics at the right time in the right place.

A more holistic approach is needed

In research early in the pandemic, non-communicable diseases were not included as outcomes, which tends to occur in policy and research during shocks. However, even in the first wave, non-communicable diseases were clearly an

Recommendations for researchers and policy makers to mitigate impact of non-communicable diseases in future shocks

Culture

- Involve patients and the public at all stages and in all areas of research
- Prioritise timely inequalities research
- Promote integrated research and care by providing human and financial resource to have truly embedded research in clinical care

Evidence

- Facilitate timely data linkage and guideline development for long term non-communicable disease consequences of shocks
- Prioritise long term consequences in shocks with involvement of patients and public at all stages of guideline development

Resources

- Develop frameworks across disciplines and specialties in research, including indirect effects
- Prioritise cross disciplinary resources, including funding to conduct research

Data

- Include non-communicable disease metrics in learning health system models of research before, during, and after shocks
- Plan data and research to include morbidity and healthcare use during shocks

important association of covid-19.²² For shocks, morbidity and mortality, as well as other data, are crucial to document the full impact and to plan comprehensive responses, including but not limited to patient reported outcomes, healthcare use, prescription and dispensing, costs to individuals and systems, and social care. Lack of these outcome data makes monitoring and planning for the scale of non-communicable diseases associated with shocks more difficult.

Preventing and managing future shocks in the most effective manner has to involve closer working between non-communicable diseases and infectious diseases. Moreover, data, funding, and staffing are needed to understand and tackle non-communicable diseases during shocks. An inclusive agenda to reduce inequalities starts with inclusive collection, analysis, interpretation, and dissemination of data from study populations through to health systems, and this has to include non-communicable disease research. The classification of diseases as non-communicable or communicable has been a barrier in many ways to policy to mitigate against shocks. We should prioritise new avenues of research to tackle the healthcare needs of populations and systems more holistically during shocks.

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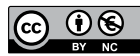
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