



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Perspective

Interventional research to tackle antimicrobial resistance in Low Middle Income Countries in the era of the COVID-19 pandemic: lessons in resilience from an international consortium



Gabriel Birgand^{1,*,#}, Esmita Charani^{1,2,3,*}, Raheelah Ahmad^{1,4}, Candice Bonaconsa³, Oluchi Mbamalu³, Vrinda Nampoothiri², Surya Surendran², Tom G. Weiser⁵, Alison Holmes¹, Marc Mendelson^{3,**}, Sanjeev Singh^{2,**}, on behalf of the ASPIRES study researchers

¹ NIHR Health Protection Research Unit in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London, Hammersmith Campus, Du Cane Road, London, UK

² Department of Medicine, Amrita Institute of Medical Sciences, Amrita University, Kerala, India

³ Division of Infectious Diseases & HIV Medicine, Department of Medicine, Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa

⁴ School of Health Sciences, City, University of London, UK

⁵ Department of Surgery, Stanford University, Stanford, USA; Stanford-Surgery Policy Improvement Research and Education Center, Department of Surgery, Stanford University, Palo Alto, USA; Department of Clinical Surgery, University of Edinburgh, Edinburgh, UK

ARTICLE INFO

Article history:

Received 5 January 2022

Revised 4 February 2022

Accepted 5 February 2022

Keywords:

Capacity building
antimicrobial resistance
resilience
COVID-19
research
LMICs

ABSTRACT

This article summarizes the consequences of the COVID-19 pandemic, on an international project to tackle antimicrobial resistance (AMR). The research leadership and process, the access to data, and stakeholders were deeply disrupted by the national and international response to the pandemic, including the interruption of healthcare delivery, lockdowns, and quarantines. The key principles to deliver the research through the pandemic were mainly the high degree of interdisciplinary engagement with integrated teams, and equitable partnership across sites with capacity building and leadership training. The level of preexisting collaboration and partnership were also keys to sustaining connections and involvements throughout the pandemic. The pandemic offered opportunities for realigning research priorities. Flexibility in funding timelines and projects inputs are required to accommodate variance introduced by external factors. The current models for research collaboration and funding need to be critically evaluated and redesigned to retain the innovation that was shown to be successful through this pandemic.

© 2022 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Introduction

The COVID-19 pandemic continues to impose significant health, economic, and social impacts. (Douglas et al., 2020) Nonpharmaceutical interventions implemented to prevent the spread of COVID-19, including intermittent lockdowns instituted in many countries, have suspended the lives of citizens, by disrupting their professional and social activities. Academic research was not

spared by these restrictions, and although the need for research and real-time evaluation was all the more important, universities and healthcare institutions closed laboratories and sites for all but essential work. (WHO, 2015; WHO; World Health Organization, n.d.) In response to the pandemic, many research activities were put on hold or redirected to investigate the evolving pandemic. (Lv et al., 2020) Global projects in the oft-labeled ‘continuous pandemic’ of antimicrobial resistance (AMR) were among those particularly affected owing to the reliance on international collaborations and data sharing. (Charani et al., 2017) AMR projects were particularly challenged by reliance on the workforce that is one of the most affected in the pandemic, namely antimicrobial stewardship and infection prevention and control resources.

The Antibiotic use across Surgical Pathways - Investigating, Redesigning and Evaluating Systems (ASPIRES) project, led by the Imperial College London started in May 2017. (Imperial College Lon-

Correspondence to: Dr Gabriel Birgand, NIHR Health Protection Research Unit in Healthcare, Associated Infection and Antimicrobial Resistance at Imperial College London, Hammersmith Campus, Du Cane Road, London W12 0NN, UK. Tel.: +44 203 313 2732.

E-mail address: g.birgand@imperial.ac.uk (G. Birgand).

* Equal first position.

** Equal last position.

Table 1
Summary of pandemic issues

Pandemic related issues	Level	Potential impacts	Mitigation/Response
Interruption to healthcare delivery	On-site research teams (LMIC)	Interruption of elective surgery Disrupting in the implementation of intervention	Use the time for an intermediate analysis to improve the implementation process when the clinical activity restarts. Use the time to plan and co-design of interventions. Engage specialists by realigning the research toward COVID-19 priorities.
Research leadership and process	On-site research teams (LMIC) and UK research teams	Limited availability of IPC and AMS specialists Principal investigators and clinical researchers largely drawn to front line strategic and operational tasks	Leadership training for early career researchers. Development of a network of research management connecting junior staff to each other in different sites. Setting up regular monitoring or mentoring through different media. Encouraging junior researchers to support each other and learn from each other / to learn from and support each other Matching staff with previous field experience to manage junior researchers remotely. Spending time on research site at the initial stage of the project Staff and meetings shared across LMICs sites. Day to day dialogue and meetings between junior researchers from each site (i.e. video conferences, network servers). Keep the momentum, remaining remotely connected by regular and iterative meetings with clinicians. Organize online workshops for co-designing interventions, to discuss on the research project.
Access to data and stakeholders	All levels	Local or national lockdowns and quarantines compromising on-site visits and physical meetings Decreased on-site access to clinicians (surgeons)	Interruptions of elective surgery offered the opportunity to organize remotely reciprocal partnerships with surgeons, share learning on IPC and AMR from data collected during the pre-COVID-19 phase of the project. Build collaboration with on-site managers/workers.
Shift in research priorities globally	On-site research teams (LMIC) Global/whole project Global/whole project	Poor access to sites for local non-clinician researchers, compromising the data collection Diversion of resources from AMR prevention to COVID-19 research. Delays in funded research	Research project reorientations to reconcile the project aim with the local priorities. Flexibility in funding timelines and project outputs.

Observations and Potential Strategies to Further Mitigate the impact of COVID-19 on an international research project on AMR.

don, n.d.) This international research consortium aims to optimise infection management and antibiotic use across the surgical pathway with ambitious fieldwork in England, India, and South Africa. The initial phases of the research, include a macro-level analysis of drivers and constraints in implementing effective policy and strategy for tackling AMR, (Ahmad et al., 2019) and an in-depth examination of the local context (Bonaconsa et al., 2021; Singh et al., 2021) were successfully completed in 2018–2019. The COVID-19 pandemic began at the early stage of the critical co-design and implementation phase. In this article, we reflect on the ability to continue delivering non-COVID-19 infectious diseases research through the pandemic, and the effectiveness of a contingency plan that was implemented to meet the original research aims.

Consequences and contingencies

The healthcare and public health context

The interruption to healthcare delivery imposed by the pandemic included disruption to, or modification of, services as well as healthcare workforce capacity. (Table 1) In the ASPIRES study, we had carefully mapped quantitatively and qualitatively, patient pathways, clinical priorities, and the behaviors of stakeholders. These were all changed as primary and secondary consequences of COVID-19. With the mandate of control measures, the dynamic in the hospital ward had shifted to focus on essential activities

only. In all study sites, elective surgeries were halted and the surgical teams were deployed to support the clinical response to the pandemic, with intensive care beds prioritized for patients with COVID-19. Clinical research staff was also redeployed to clinical duties. The research priorities evolved as a result of these changes and capacity was generated for the teams to carry out COVID-19 related research.

Research leadership and processes

The principal investigators of the ASPIRES project in each participating country, being senior infectious diseases specialists, were largely drawn to frontline strategic and operational tasks to lead/support the pandemic response nationally and internationally. (Mendelson et al., 2020; Rawson et al., 2020; Zhou et al., 2020) The research teams in each of the participating countries were variably affected; some diverted to support regional level data collection or to contribute to the local clinical response. Nonclinical researchers were able to proceed with desk research working from home, which required self-organization and motivation. It was important to maintain the schedule of small and whole project meetings to keep the project progress and slippage documented. The obvious loss of opportunities for the research team to meet, train, and learn in physical proximity has been detrimental to progress against milestones but also in terms of momentum and motivation.

Access to stakeholders and data

Access to data and stakeholders was compromised. The project relied on clinicians' willingness and motivation, especially surgeons, as well as infection prevention and control (IPC) and antimicrobial stewardship (AMS) teams. The nonavailability of IPC and infectious disease specialists was 1 of the key challenges as they were fully dedicated to the COVID-19 response. The pandemic response left few opportunities for their contribution to their routine work and the project. Although interruption of the surgical program delayed the co-design and implementation of interventions, the cancellation of elective surgical procedures meant that surgeons were more available with extended possibilities to engage by way of remote meetings. Online workshops for the co-design of interventions were progressed, with uncertainty as to when interventions could be implemented.

Shift in research priorities globally

The person-power and scientific effort on AMR were diverted to COVID-19 management. At the same time, progressing AMR research had to be maintained to mitigate the longer-term public health threat of drug-resistant bacterial infections (Knight et al., 2021). The changes in antimicrobial use in some pandemic settings highlighted the need for continued AMS. (Townsend et al., 2020). The strong focus of the clinical and scientific world on COVID-19 continues alongside the response to the emergence of mutant variants of the SARS-CoV-2. There is a risk, however, that this divergence of resources may de-prioritize and potentially undo progress in other research topics, including AMR. It is not yet clear how AMR research programs can recover and accomplish their original goals.

Perspectives for resilience in research projects

The success and fate of funded research projects already underway when the restrictions were imposed will depend on the resilience of the teams, the strength of the partnerships developed, and the multidisciplinary nature of the research approach. We propose the 4 key areas mostly affected by large-scale global research (Table 1).

Integrated research teams in terms of multidisciplinary and international research

As our research project aimed to investigate the complex issue of organizational and individual behaviors in surgical care to improve infection-related outcomes, the design of the methods was highly interdisciplinary. The research methods included ethnographic qualitative, epidemiological quantitative, strategic social-political, and operations research modeling. The experience of the research team and organization of project work packages strategically enabled the integration of all these research discipline experts in a cohesive way. An overarching work package led by experienced international senior researchers was dedicated to ensuring the output of the work was not a collection from each of the disciplines but an integrated understanding of the problem and derived and tested solutions. The leadership of this overarching work package with monthly meetings organized throughout the pandemic has made it possible to avoid the "silo effect", adopting a research approach integrated across tasks and disciplines. Finally, the indisposition of some researchers for COVID-19 related issues was cross-cover by available colleagues from other disciplines.

Building on-site capacities and equitable partnerships

In international research projects spanning different healthcare economies, resources must be equitably distributed across participating sites, matching the contextual needs of each setting. Investing in knowledge exchange and training should be factored in early enough into partnerships to enable sustainability and independence in project management. This strategy minimizes the impact of unplanned restrictions in contact between the partnerships (e.g. travel restrictions during a pandemic) to the research. In our situation, a strong on-site presence (cumulated 28 weeks of on-site visits in 2018 and 32 weeks in 2019) was organized at the early stage of the project mitigating the impact of visit cancellations in 2020 and throughout the pandemic.

Firstly, funding should be proportionate to the cost of resources and the gaps identified in each setting. Project management, where possible, should be based locally to study sites. Importantly, flexibility in funding timelines and project outputs are needed to reflect the need to accommodate variances introduced by external factors. Many expenses initially planned (especially for travel) were not carried out owing to pandemic restrictions. In the current format, most funders are restricting the use of money to their initial attributions. In circumstances such as the pandemic, funders should authorize and facilitate the reallocation of funds across cost items (e.g. use of non-human resources funds for manpower requirements and vice versa). Secondly, research projects should rely on a capacity-building strategy to provide skills to the local stakeholders for better sustainability of interventions and outcomes. (Veepanattu et al., 2020) Capacity-building is defined as the "process of developing and strengthening the skills, instincts, abilities, processes, and resources that organizations and communities need to survive, adapt, and thrive in a fast-changing world." (Dako-Gyeke et al., 2020) In the SPIRES project, researchers were recruited early during the project, with an equitable distribution representing each of the disciplines to ensure that methodological skills were locally situated. Two researchers, 1 in India and 1 in South Africa started PhD studies based on emergent themes from the research. Both are co-supervised by senior investigators from across the sites (South Africa, India, and the United Kingdom). These initiatives strengthened the collaboration between the senior investigator(s) and the researchers on-site. Instituting a publications policy, all co-investigators and researchers were encouraged to contribute to the publications plan from the outset. Mid-way through the project, outputs from all international researchers, early and senior, have been published in international journals and presented at international conferences demonstrating sustained development beyond the life of the project. Finally, leadership training for early career researchers, regular mentoring, and encouraging them to learn from and support each other, succeeded in maintaining the connection and relation across researchers and teams. We developed a network of research management that connects junior staff to each other in different sites, has research leads that work with junior staff, and also liaise closely with principal investigators. Staff and meetings were shared across the 2 low middle income countries (LMICs) sites. Having contextual insight by matching staff with previous field experience to manage junior researchers remotely was perceived as a positive factor for resilience.

Building sustainable relations and connections

The relationship between the principal investigator(s), their collaborators, and the co-investigators on-site and their profiles are critical to stability in the project during erratic interruptions such as that posed by COVID-19. The challenge faced during the pandemic may be overcome by the motivation and the preexisting

degree of collaboration and partnership. There must be a degree of willingness to be flexible, adaptable, and have a measure of goodwill to work through the difficulties facing the research team members in each setting.

Working with, and getting to know local stakeholders, will improve the sustainability of dawning collaborations. A senior researcher from Imperial College London, spent 3 consecutive months on each research site at the early stage of the international consortium to work in partnership and mentoring roles, assess the cultural norms, established hierarchies, team roles, and methods of communication around AMS and IPC and in the research institute. (Singh et al., 2021) This on-site work has led to strong collaboration with the local researchers recruited for the project, hospital leaders, and stakeholders. (Veeapanattu et al., 2020) These visits were reciprocated with 2-week long visits to the United Kingdom site from researchers in India and South Africa and a week-long visit from the India team to South Africa. The reciprocal visit from South African researchers to India was halted owing to the travel restrictions during the pandemic. This level of onsite visits not only facilitates the familiarization of researchers with all the different contexts but also created opportunities for the PhD students to gather field data relevant to their studies.

The partnership underpinning this research is sustained by being agile to working off-site and remaining remotely connected with regular and iterative meetings. These meetings were not only between senior and junior researchers but also through day-to-day dialogue and meetings between the junior researchers in each site. Staff were monitored and were mentored through different media. Resilience in partnerships and communication was built through 39 meetings with local researchers and 7 workshops with clinicians to co-design and implement the intervention organized online in 2020.

Surfing on opportunities, and realigning research priorities

Capitalizing on the movement to investigate the impact of COVID-19 on AMR and AMS is critical. The COVID-19 pandemic offered opportunities for realigning research priorities of the SPIRES project. First, the Political factors, Economic influences, Sociological trends, Technological innovations, Ecological factors, Legislative requirements, Industry analysis (PESTELI) framework employed to assess the macro-level factors of IPC and AMS at each point of the surgical pathway, was adapted for the analysis of the COVID-19 pandemic. (Ahmad et al., 2021) Moreover, a survey was developed to assess the perception of changes in IPC and AMS practices during the pandemic by stakeholders from the 2 LMICs countries. (Mbamalu et al., 2021) Second, a large amount of qualitative data has been collected on-site through ethnographic research to describe the role and context of IPC and AMS across the surgical pathway. We may assume that the pandemic largely changed preexisting organizations in the roles of stakeholders including patients, and also in terms of outcomes. We plan to reexamine the organization and the resilience of IPC and AMS after the pandemic in the SPIRES project sites in India and South Africa. The cumulated knowledge in such context will build memory for how to respond to emerging issues through contingency planning and forecasting. Finally, the COVID-19 pandemic generated research questions such as modifications of practices and the role played by the surgical ecosystem in emerging infectious diseases.

Conclusion

A worldwide event such as the COVID-19 pandemic has helped challenge the usual way of doing research. To develop resilience and sustainability in global partnerships, the current models for research collaboration and funding need to be critically evaluated

and redesigned. In these ways, being more efficient, and responsible in the use of publicly funded research, and enhancing of capacity building of local actors appear as the best solutions for the future of global health research.

Declarations

Ethics approval: Not applicable.

Competing interests

None to declare from all authors.

Availability of data and material: Not applicable

Authors' contributions: EC and GB developed the study design. The first draft of the manuscript was written by GB, EC, and RA. Subsequent versions had input from all co-authors.

Funding

This work was funded by the Economic and Social Science Research Council (ESRC) as part of the Antimicrobial Cross Council initiative [ES/P008313/1] supported by the 7 United Kingdom research councils, and the Global Challenges Research Fund, and the National Institute for Health Research, the United Kingdom Department of Health [HPRU-2012-10047] in partnership with Public Health England; The Norwegian Advisory Unit for Antibiotic Use in Hospitals, Haukeland University Hospital. The funders were not involved in the design, analysis, and writing of this study.

Acknowledgments

We would like to acknowledge the support of clinicians from Amrita, India, and Groote Schuur Hospital, South Africa, for their engagement in the project.

References

- Ahmad R, Atun RA, Birgand G, Castro-Sánchez E, Charani E, Ferlie EB, et al. Macro level influences on strategic responses to the COVID-19 pandemic - an international survey and tool for national assessments. *J Glob Health* 2021;11:05011. doi:10.7189/jogh.11.05011.
- Ahmad R, Zhu NJ, Leather AJM, Holmes A, Ferlie E. SPIRES study co-investigators. Strengthening strategic management approaches to address antimicrobial resistance in global human health: a scoping review. *BMJ Glob Health* 2019;4. doi:10.1136/bmjgh-2019-001730.
- Bonaconsa C, Mbamalu O, Mendelson M, Boutall A, Warden C, Rayamajhi S, et al. Visual mapping of team dynamics and communication patterns on surgical ward rounds: an ethnographic study. *BMJ Qual Saf* 2021 bmjqs-2020-012372. doi:10.1136/bmjqs-2020-012372.
- Charani E, Ahmad R, Tarrant C, Birgand G, Leather A, Mendelson M, et al. Opportunities for system level improvement in antibiotic use across the surgical pathway. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis* 2017;60:29–34. doi:10.1016/j.ijid.2017.04.020.
- Dako-Gyeke P, Asampong E, Afari E, Launois P, Ackumey M, Opoku-Mensah K, et al. Capacity building for implementation research: a methodology for advancing health research and practice. *Health Res Policy Syst* 2020;18:53. doi:10.1186/s12961-020-00568-y.
- Douglas M, Katikireddi SV, Taulbut M, McKee M, McCartney G. Mitigating the wider health effects of covid-19 pandemic response. *BMJ* 2020;369:m1557. doi:10.1136/bmj.m1557.
- Imperial College London. SPIRES: Antibiotic use across Surgical Pathways - Investigating, Redesigning and Evaluating Systems n.d.
- Knight GM, Glover RE, McQuaid CF, Olaru ID, Gallandat K, Leclerc QJ, et al. Antimicrobial resistance and COVID-19: Intersections and implications. *ELife* 2021;10:e64139. doi:10.7554/eLife.64139.
- Lv M, Luo X, Estill J, Liu Y, Ren M, Wang J, et al. Coronavirus disease (COVID-19): a scoping review. *Eurosurveillance* 2020;25. doi:10.2807/1560-7917.ES.2020.25.15.2000125.
- Mbamalu O, Surendran S, Zhu N, Bonaconsa Nampouthiri V, Edathadathil S, et al. Healthcare workers experiences of infection prevention and control practices in South Africa and India during the SARS-CoV-2 pandemic. *Eur Soc Clin Microbiol Infect Dis ESCMID* 2021.

- Mendelson M, Nel J, Blumberg L, Madhi SA, Dryden M, Stevens W, et al. Long-COVID: An evolving problem with an extensive impact. *South Afr Med J Suid-Afr Tydskr Vir Geneesk* 2020;111:10–12. doi:[10.7196/SAMJ.2020.v111i11.15433](https://doi.org/10.7196/SAMJ.2020.v111i11.15433).
- Rawson TM, Moore LSP, Castro-Sanchez E, Charani E, Davies F, Satta G, et al. COVID-19 and the potential long-term impact on antimicrobial resistance. *J Antimicrob Chemother* 2020;75:1681–4. doi:[10.1093/jac/dkaa194](https://doi.org/10.1093/jac/dkaa194).
- Singh S, Mendelson M, Surendran S, Bonaconsa C, Mbamalu O, Nampoothiri V, et al. Investigating infection management and antimicrobial stewardship in surgery: a qualitative study from India and South Africa. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis* 2021. doi:[10.1016/j.cmi.2020.12.013](https://doi.org/10.1016/j.cmi.2020.12.013).
- Townsend L, Hughes G, Kerr C, Kelly M, O'Connor R, Sweeney E, et al. Bacterial pneumonia coinfection and antimicrobial therapy duration in SARS-CoV-2 (COVID-19) infection. *JAC-Antimicrob Resist* 2020;2 dlaa071. doi:[10.1093/jacamr/dlaa071](https://doi.org/10.1093/jacamr/dlaa071).
- Veepanattu P, Singh S, Mendelson M, Nampoothiri V, Edathadatil F, Surendran S, et al. Building resilient and responsive research collaborations to tackle antimicrobial resistance—Lessons learnt from India, South Africa, and UK. *Int J Infect Dis* 2020;100:278–82. doi:[10.1016/j.ijid.2020.08.057](https://doi.org/10.1016/j.ijid.2020.08.057).
- WHO. Global action plan on antimicrobial resistance. 2015.
- WHO; World Health Organization. Country progress in the implementation of the global action plan on antimicrobial resistance: who, FAO and OIE global tripartite database. n.d.
- Zhou J, Otter JA, Price JR, Cimpeanu C, Garcia DM, Kinross J, et al. Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2020. doi:[10.1093/cid/ciaa905](https://doi.org/10.1093/cid/ciaa905).