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Antimicrobial resistance research in a post-pandemic world: Insights on antimicrobial resistance research in the COVID-19 pandemic

Jesús Rodríguez-Baño^{a,b,c,B}, Gian Maria Rossolini^{d,e}, Constance Schultsz^f,
 Evelina Tacconelli^g, Srinivas Murthy^h, Norio Ohmagariⁱ, Alison Holmes^j, Till Bachmann^k,
 Herman Goossens^l, Rafael Canton^{m,n}, Adam P. Roberts^o, Birgitta Henriques-Normark^{p,q},
 Cornelius J. Clancy^r, Benedikt Huttner^s, Patriq Fagerstedt^t, Shawon Lahiri^u,
 Charu Kaushic^{u,v}, Steven J. Hoffman^w, Margo Warren^x, Ghada Zoubiane^y,
 Sabiha Essack^{y,z}, Ramanan Laxminarayan^A, Laura Plant^{u,*}

^a Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen Macarena, Seville, Spain

^b Departamento de Medicina, Universidad de Sevilla, Seville, Spain

^c Instituto de Biomedicina de Sevilla (IBiS), Seville, Spain

^d Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy

^e Clinical Microbiology and Virology Unit, Florence Careggi University Hospital, Florence, Italy

^f Department of Global Health–AIGHD Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

^g Division of Infectious Diseases, Department of Diagnostic and Public Health, University of Verona, Verona, Italy

^h BC Children's Hospital, University of British Columbia, Vancouver, Canada

ⁱ Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan

^j Department of Medicine, Faculty of Medicine, Imperial College London, London, UK

^k The University of Edinburgh, Edinburgh Medical School, Division of Infection and Pathway Medicine, The Chancellor's Building, Edinburgh, UK

^l Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium

^m Servicio de Microbiología, Hospital Universitario Ramón y Cajal and Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain

ⁿ Red Española de Investigación en Patología Infecciosa (REIPI), Instituto de Salud Carlos III, Madrid, Spain

^o Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK

^p Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden

^q Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden

^r University of Pittsburgh, 3550 Terrace St., Scaife Hall 867, Pittsburgh, PA, USA

^s Division of Infectious Diseases, Geneva University Hospitals, Faculty of Medicine, University of Geneva, Geneva, Switzerland

^t JPIAMR Secretariat, Swedish Research Council, Stockholm, Sweden

^u Institute of Infection and Immunity, Canadian Institutes of Health Research, Canada

^v McMaster Immunology Research Center, Department Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

^w Global Strategy Lab, Dahdaleh Institute for Global Health Research, School of Global Health and Osgoode Hall Law School, York University, Toronto, Canada

^x Access to Medicine Foundation, Naritaweg 227-A, 1043 CB, Amsterdam, The Netherlands

^y International Centre for Antimicrobial Resistance Solutions (ICARS), Copenhagen, Denmark

^z Antimicrobial Research Unit, University of KwaZulu-Natal, Durban, South Africa

^A Center for Disease Dynamics, Economics & Policy, New Delhi, India

^B Red Española de Investigación en Patología Infecciosa (REIPI), Instituto de Salud Carlos III, Madrid, Spain

* Corresponding author at: JPIAMR Secretariat, Swedish Research Council, Box 1035, 101 38, Stockholm, Sweden.
 E-mail address: Laura.Plant@vr.se (L. Plant).

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ABSTRACT

Antimicrobial resistance must be recognised as a global societal priority - even in the face of the worldwide challenge of the COVID-19 pandemic. COVID-19 has illustrated the vulnerability of our healthcare systems in co-managing multiple infectious disease threats as resources for monitoring and detecting, and conducting research on antimicrobial resistance have been compromised during the pandemic. The increased awareness of the importance of infectious diseases, clinical microbiology and infection control and lessons learnt during the COVID-19 pandemic should be exploited to ensure that emergence of future infectious disease threats, including those related to AMR, are minimised. Harnessing the public understanding of the relevance of infectious diseases towards the long-term pandemic of AMR could have major implications for promoting good practices about the control of AMR transmission.

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1. Introduction

The COVID-19 (coronavirus disease 2019) pandemic is predicted to impact the transmission of bacterial infections and the emergence of antimicrobial resistance (AMR). The likely positive influence on AMR of social distancing, increased awareness and the use of interventions to prevent the transmission of COVID-19 could be counteracted by the reported excessive use of broad-spectrum antibiotics to treat patients infected with SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). Antimicrobial stewardship programmes and AMR-focused research activities must remain active during the COVID-19 and future pandemics in order to safeguard against an uncontrolled rise in AMR.

2. Antibiotic use in the COVID-19 pandemic

The priority during the COVID-19 pandemic has been treating patients and avoiding the acquisition of SARS-CoV-2 by healthcare personnel whilst maintaining the functionality of healthcare systems. Within healthcare, there has been a need to redirect personnel, resources and attention to COVID-19 diagnosis and management. AMR surveillance and screening programmes to detect colonisation by resistant organisms have been compromised due to a shortage of personnel and the need to redirect molecular diagnostic platforms, reagents, tracking and tracing from AMR surveillance to COVID-19 diagnostics.

It has been reported that only 7–8% of hospitalised COVID-19 patients were diagnosed with a bacterial or fungal infection [1–3], while antibiotic use in COVID-19 patients has been considerably high at 71.9% (95% confidence interval 56.1–87.7%) [3]. Further studies using molecular techniques on samples from ventilated and non-ventilated COVID-19 patients are needed. Whether new or evolving AMR in COVID-19 patients will emerge in areas with low previous rates should be examined in retrospective and prospective clinical and microbiological studies.

3. Simultaneously managing the acute COVID-19 pandemic and escalating antimicrobial resistance

COVID-19 has illustrated the vulnerability of our healthcare systems. This is even more noticeable in low- and middle-income countries (LMICs) and in resource-constrained settings less prepared to deal with pandemics or other emergencies [4–6]. Local, national and international scale resistance data are needed to help researchers better understand potential disruptions in stewardship and surveillance efforts and to highlight the early emergence of resistance due to antibiotic use linked to COVID-19 and secondary infections.

Co-managing multiple infectious disease threats simultaneously is a further challenge for LMICs. Laboratory infrastructure, surveillance and diagnostic capacity both for COVID-19 and AMR are often unreliable, and infection prevention and control policies, practice and personnel are suboptimal and/or unsustainable [7]. Regulated antibiotic use is difficult to enforce where there is poor access to antibiotics overall, while sociobehavioural interventions such as physical distancing and hand hygiene can be limited, especially in areas with high population densities with limited access to clean water and sanitation services. Thus, an exit strategy from COVID-19 for many LMICs may not be pharmacologically based in the short-term and more community-based strategies are currently being explored [8].

4. Impact of the COVID-19 pandemic on antimicrobial resistance research

A critical lesson from the COVID-19 pandemic is the importance of embedding research in the response. Supporting good-quality implementation research could help understand not only what has worked, but also how and why an intervention was successful. While research on COVID-19 has progressed during the pandemic, research in other fields including AMR has been deprioritised, delayed or even halted. Delays limit the possibilities for scientists to meet deadlines and targets within projects, as well as restrict sharing of information and networking activities. Funding agencies across the globe have given research grant extensions; however, the long-term impact on AMR research is yet to be understood and factors such as the effect on early career researchers may take years to manifest. As solidarity pledges emerge to address COVID-19, so too must efforts to openly share research and data on AMR, including surveillance data from the pharmaceutical industry, as incentivised by the Access to Medicine Foundation's AMR Benchmark. In order to ensure that AMR research continues to be adequately supported, it is important to prioritise funds for AMR research both at national and international levels.

The COVID-19 pandemic has led to an unprecedented awareness of the importance of infectious diseases, clinical microbiology and infection control. The AMR research community is in an ideal position to raise the awareness of the topic of AMR and to build on community engagement in the importance of sanitary infrastructures [9], handwashing, disinfection, social distancing when ill, and avoiding unnecessary use of antibiotics. Harnessing public understanding of the relevance of infectious diseases towards the long-term pandemic of AMR could have major implications for promoting good practices about the control of AMR transmission.

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Competing interests

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Ethical approval

Not required.

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References

- [1] Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis* 2020;71:2459–68, doi:<http://dx.doi.org/10.1093/cid/ciaa530>.
- [2] Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clin Microbiol Infect* 2020;26:1622–9, doi:<http://dx.doi.org/10.1016/j.cmi.2020.07.016>.
- [3] Garcia-Vidal C, Sanjuan G, Moreno-García E, Martínez JA, Puerta-Alcáde P, Garcia-Pouton N, et al. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. *Clin Microbiol Infect* 2021;27:83–8, doi:<http://dx.doi.org/10.1016/j.cmi.2020.07.041>.
- [4] Access to Medicine Foundation. Antimicrobial Resistance Benchmark 2020. https://accesstomedicinefoundation.org/media/uploads/downloads/5e270aa36821a_Antimicrobial_Resistance_Benchmark_2020.pdf. [Accessed 2 March 2021].
- [5] Lai CC, Wang CY, Wang YH, Hsueh SC, Ko WC, Hsueh PR. Global epidemiology of coronavirus disease 2019 (COVID-19): disease incidence, daily cumulative index, mortality, and their association with country healthcare resources and economic status. *Int J Antimicrob Agents* 2020;55:105946, doi:<http://dx.doi.org/10.1016/j.ijantimicag.2020.105946>.
- [6] Bong CL, Brasher C, Chikumba E, McDougall R, Mellin-Olsen J, Enright A. The COVID-19 pandemic: effects on low- and middle-income countries. *Anesth Analg* 2020;131:86–92, doi:<http://dx.doi.org/10.1016/j.anane.0000000000004846>.
- [7] Dubbink JH, Branco TM, Kamara KB, Bangura JS, Wehrens E, Falama AM, et al. COVID-19 treatment in sub-Saharan Africa: if the best is not available, the available becomes the best. *Travel Med Infect Dis* 2020;37:101878, doi:<http://dx.doi.org/10.1016/j.tmaid.2020.101878>.
- [8] Walker PGT, Whittaker C, Watson OJ, Baguelin M, Winskill P, Hamlet A, et al. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. *Science* 2020;369:413–22, doi:<http://dx.doi.org/10.1126/science.abc0035>.
- [9] Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. *Lancet Planet Health* 2018;2:e398–405, doi:[http://dx.doi.org/10.1016/S2542-5196\(18\)30186-4](http://dx.doi.org/10.1016/S2542-5196(18)30186-4).