The impact of the COVID-19 pandemic on antimicrobial resistance: a debate

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The coronavirus disease 2019 (COVID-19) pandemic is having an enormous impact on public health. Infection with SARS-CoV-2 has become a leading cause of morbidity and mortality in many regions around the world. As many COVID-19 patients are treated with antibiotics, there is concern regarding an associated rise in rates of antimicrobial resistance (AMR). On the other hand, social distancing, isolation and reduced travel may result in decreased spread of AMR. In this issue of *JAC-Antimicrobial Resistance*, we present a PRO/CON debate on the question of the potential impact of COVID-19 on AMR rates.

In December 2019, a cluster of patients infected with a novel coronavirus was recognized in Wuhan, China.¹ This novel coronavirus was found to be similar to the Severe Acute Respiratory Syndrome (SARS)-coronavirus (CoV) and was named SARS-CoV-2. The associated disease was named coronavirus disease 2019 (COVID-19). COVID-19 spread rapidly worldwide and at the time of writing over 6 000 000 cases have been confirmed, with over 300 000 deaths.² The impact of the COVID-19 pandemic on antimicrobial resistance (AMR) remains unclear.

Antibiotic use, often to treat presumed secondary bacterial coinfection, is common in patients infected with SARS-CoV-2. This is despite the relatively low rates of these infections. Furthermore, early reports of the possible activity of hydroxychloroquine in COVID-19 when used in combination with azithromycin led to substantial use of the latter.³ Another important feature of this disease is the prolonged dependence on invasive mechanical ventilation of patients with severe infection. In a large cohort, 12% of hospitalized patients in New York State required mechanical ventilation.⁴ In a smaller Boston cohort of COVID-19 patients who were managed with invasive mechanical ventilation, the median duration was 16 days (IQR: 10.0-21.0 days).⁵ These prolonged intensive care stays, high mortality rate, diagnostic and prognostic uncertainty and concern for secondary bacterial infections has led to frequent empiric antibacterial use. In Chinese randomized trials evaluating remdesivir and lopinavir/ritonavir, over 90% of patients were treated with antibacterials.^{6,7} In an analysis of published literature, Rawson et al.⁸ report that while only 8% of patients included in publications had reported bacterial or fungal coinfection, 72% of patients were treated with antibiotics. This frequent use of empiric antibiotics, often broad spectrum or in combination, has led to concerns over increased AMR rates, with an attendant call not to neglect antimicrobial stewardship, which perhaps now has an even more important role. $^{9}\,$

On the other hand, the COVID-19 pandemic has resulted in unprecedented changes in society that may actually result in decreased AMR rates. Social distancing, a focus on isolation and reductions in national and international travel may decrease the spread of AMR pathogens and associated AMR genes. International travel has been consistently reported as an important risk factor for acquisition of AMR pathogens.¹⁰ In April 2020, the number of travellers going through US checkpoints was reduced by 95% compared with 2019.¹¹ In addition, social distancing measures to limit the spread of SARS-CoV-2 has impacted prevalence of other infectious diseases, most notably influenza.¹² These measures may similarly impact the spread of AMR.

In this issue of JAC-Antimicrobial Resistance, we have invited international thought leaders for a PRO/CON debate regarding the impact of COVID-19 on AMR. Clancy and colleagues¹³ argue in favour of the premise that COVID-19 will result in an overall increase in AMR rates. They argue that while overall hospital attendance may have decreased, the patients who are admitted during the pandemic have a higher likelihood of being treated with broadspectrum antibiotics, as well as being exposed to procedures, such as invasive mechanical ventilation, that are known risk factors for AMR development. In addition, many shared risk factors exist for patients who are at risk of COVID-19 requiring hospitalization and those at risk of AMR. Collignon and Beggs¹⁴ argue that COVID-19 will not lead to increased AMR rates. They present several important arguments, ranging from factors that impact transmission in healthcare and community settings, to the impact of decreased international travel. They also emphasize that control of AMR

© The Author(s) 2020. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/ by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited. requires control of the spread of AMR pathogens, in addition to antimicrobial stewardship.

The impact of COVID-19 on AMR rates remains to be determined and is likely to be heterogeneous due to variation in healthcare practices, such as in the specific antimicrobials used and infection prevention and control interventions during the pandemic. It is clearly an important area for future systematic studies.

Transparency declarations

D.v.D. reports being on the advisory Board for Allergan, Achaogen, Qpex, Shionogi, Tetraphase, Sanofi-Pasteur, T2 Biosystems, NeuMedicine, Roche, MedImmune, Astellas and Merck. D.N. and G.B.: none to declare.

References

1 Huang C, Wang Y, Li X *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

2 Johns Hopkins University. Coronavirus Resource Center. https://corona virus.jhu.edu/.

3 Rodrigo C, Fernando SD, Rajapakse S. Clinical evidence for repurposing chloroquine and hydroxychloroquine as antiviral agents: a systematic review. *Clin Microbiol Infect* 2020; doi: 10.1016/j.cmi.2020.05.016.

4 Richardson S, Hirsch JS, Narasimhan M *et al.* Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020; doi: 10.1001/jama.2020.6775.

5 Ziehr DR, Alladina J, Petri CR *et al.* Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. *Am J Respir Crit Care Med* 2020; doi: 10.1164/rccm.202004-1163LE.

6 Cao B, Wang Y, Wen D *et al*. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med* 2020; **382**: 1787–99.

7 Wang Y, Zhang D, Du G *et al*. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020; **395**: 1569–78.

8 Rawson TM, Moore LSP, Zhu N *et al*. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis* 2020; doi: 10.1093/cid/ ciaa530.

9 Huttner BD, Catho G, Pano-Pardo JR *et al.* COVID-19: don't neglect antimicrobial stewardship principles! *Clin Microbiol Infect* 2020; doi: 10.1016/ j.cmi.2020.04.024.

10 Frost I, Van Boeckel TP, Pires J *et al.* Global geographic trends in antimicrobial resistance: the role of international travel. *J Travel Med* 2019; **26**: taz036.

11 Airlines for America. Impact of COVID-19. https://www.airlines.org/data set/impact-of-covid19-data-updates/#.

12 Noh JY, Seong H, Yoon JG *et al*. Social distancing against COVID-19: implication for the control of influenza. *J Korean Med Sci* 2020; **35**: e182.

13 Clancy CJ, Buehrle DJ, Nguyen MH. PRO: the COVID-19 pandemic will result in increased antimicrobial resistance rates. *JAC Antimicrob Resist* 2020; doi: 10.1093/jacamr/dlaa049.

14 Collignon P, Beggs JJ. CON: COVID-19 will NOT result in increased AMR prevalence. *JAC Antimicrob Resist* 2020; doi: 10.1093/jacamr/dlaa051.