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## Comment on: Global consumption of antimicrobials: impact of the WHO Global Action Plan on Antimicrobial Resistance and 2019 coronavirus pandemic (COVID-19)

Giorgia Sulis <sup>1</sup>, Madhukar Pai<sup>1</sup> and Sumanth Gandra<sup>2\*</sup>

<sup>1</sup>Department of Epidemiology, Biostatistics and Occupational Health, School of Population and Global Health, McGill University, Montreal, Canada; <sup>2</sup>Division of Infectious Diseases, Washington University School of Medicine in St. Louis, St. Louis Missouri, USA

\*Corresponding author. E-mail: [gandras@wustl.edu](mailto:gandras@wustl.edu)

We read with interest the article by Khouja *et al.*<sup>1</sup> who examined the impact of the COVID-19 pandemic on antimicrobial consumption in 66 countries. This work is much awaited as there is uncertainty on the impact of COVID-19 on antibiotic use worldwide, especially in low- and middle-income countries (LMICs). The authors report that antibiotic sales significantly increased in both high-income countries (HICs) and LMICs in March 2020 compared with March 2019. This is attributed to antibiotic use for COVID-19 patients early in the pandemic owing to uncertainties in the management of such cases. As evidence accumulated that the rates of bacterial co-infections and secondary infections among COVID-19 patients are low, this trend reversed quickly, as observed in several HICs.<sup>2</sup> Subsequently, antibiotic sales decreased significantly between April and August 2020 despite the growing spread of COVID-19.

Khouja *et al.*<sup>1</sup> state that this decrease in antibiotic sales post-March 2020 in both HICs and LMICs is encouraging and suggests that antimicrobial stewardship efforts have not been largely derailed. We disagree with this interpretation that such efforts were not negatively affected, particularly in LMICs. In fact, we examined the impact of the epidemic surge in antibiotic sales in India and estimated that 216.4 million (95% CI: 68.0–364.8 million) excess doses of non-paediatric formulations of antibiotics and 38.0 million (95% CI: 26.4–49.2 million) excess doses of non-paediatric formulations of azithromycin were sold nationally during the first COVID-19 wave (June to December 2020), likely attributable to COVID-19.<sup>3</sup> Our estimates of excess azithromycin treatment courses suggest that a large number of mild COVID-19 cases were treated with antibiotics despite the WHO and Indian national treatment guidelines discouraging this choice for mild and moderate COVID-19. Our findings were corroborated by a multicentre study that reported inappropriate use of

broad-spectrum antibiotics for hospitalized COVID-19 patients during the first epidemic wave in India.<sup>4</sup> Similar observations were reported in Bangladesh, where across twelve tertiary level hospitals 77% of patients with mild COVID-19, and 94% of those with moderately severe infections, received an antibiotic on admission.<sup>5</sup> A multicentre prevalence survey in Pakistan reported that, in April 2021, antibiotics were widely prescribed for COVID-19 patients, with 85% of these prescriptions having prophylactic purposes.<sup>6</sup> To our knowledge, there are no published primary studies examining antibiotic use among COVID-19 patients in Africa; however, the fact that national COVID-19 treatment guidelines from ten African countries include antibiotics in the routine management of COVID-19 cases is a matter of concern.<sup>7</sup> Moreover, several LMICs approved drugs such as hydroxychloroquine and used ivermectin during the pandemic, and this also needs to be factored in.<sup>8</sup>

There is ample evidence of antibiotic misuse among presumptive and confirmed COVID-19 cases in several LMICs. The observed reduction in overall antibiotic sales between April and August 2020 in both HICs and LMICs mainly reflects a decline in community transmission or serious under-testing of infections other than COVID-19 attributable to public health measures (e.g. social distancing, widespread face mask wearing, remote schooling and working policies), or diversion of testing services to COVID-19. For this reason, it is not surprising that the observed decrease in antibiotic prescribing/dispensing has been more pronounced for paediatric versus adult patients. Additionally, changes in healthcare-seeking behaviours, access to care, and cancellation of elective surgeries and dental procedures likely contributed to this downward trend. Although these factors played a role irrespective of the country income level, Khouja *et al.*<sup>1</sup> reported a lower reduction in antibiotic sales in LMICs (–16.8% versus –28% in HICs), partly attributable to the greater extent of antibiotic misuse among COVID-19 cases in LMICs. To better understand the misuse of antibiotics during the ongoing pandemic, Khouja *et al.*<sup>1</sup> could have examined trends in sales of individual antibiotics/classes as overall antibiotic use alone can be misleading. As we noted in our study in India,<sup>3</sup> select antibiotics (such as azithromycin, +34.4% in June to September 2020 versus the same trimester of 2019) have been affected more than others, with important stewardship implications. This is consistent with reports from other settings. For instance, while the total antibiotic consumption in Jordan declined by 5.5% in 2020 compared with 2019, the use of lincosamides (+106%), macrolides (+57%) and carbapenems (+52%) rose significantly.<sup>9</sup> Similarly, substantial increases in azithromycin sales were reported in Brazil during the pandemic period (monthly change: +5.8%; 95% CI: 1.8%–10.0%), whereas the use of other antibiotics fell (e.g. amoxicillin and cefalexin).<sup>10</sup>

Considering the evidence summarized above indicating the widespread use of antibiotics in several LMICs, likely attributable to COVID-19, we would suggest caution in interpreting aggregate global trends in antibiotic consumption that do not capture the nuances of prescribing and dispensing practices at the country-

level and could lead to underestimation of what is indeed a major problem. We cannot let our guard down when it comes to antibiotic resistance and the importance of promoting and implementing stewardship interventions at all levels of care.

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## Transparency declarations

None to declare.

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