

Comment for submission to The Lancet

Title:

Globalisation of antibiotic-resistant bacteria at recurring mass gathering events

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Keywords: Mass Gatherings, religious, Gay festivals, MSM, Kumbh Mela, Hajj, Arba'een, Antimicrobial resistance, MDR bacteria

Word count: 946 words

Figure: 1

References: 14

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Comment

Antimicrobial resistance is associated with an estimated 4.95 million deaths annually and is currently a leading cause of death worldwide.¹ Despite numerous global initiatives to control the surge of antimicrobial resistance, at the current rate of increase, annual deaths from antimicrobial resistance are estimated to rise to 10 million by 2050. This puzzling conundrum indicates that there are unknown factors that continue to increase antimicrobial resistance at a global scale and that identifying them will be crucial in controlling the ongoing antimicrobial resistance pandemic. There are also scarce data about the geographical distribution and evolution of antimicrobial resistance over time in settings outside of health-care facilities,^[2,3] and more accurate scientific evidence is required to promote optimal policies to combat antimicrobial resistance.

Opportunities for reviewing knowledge gaps and refocusing scientific, political, and funder attention on priority antimicrobial resistance research will arise during World Antimicrobial Awareness Week, Nov 18–24, 2022. During World Antimicrobial Awareness Week, the quadripartite organisations— WHO, the Food and Agriculture Organization of the UN, the UN Environment Programme, and the World Organisation for Animal Health—will promote the multisectoral approach of preventing antimicrobial resistance together. Although the focus will be on conventional antimicrobial resistance agendas, the neglected issue of the globalisation of antimicrobial resistance through mass gathering religious and pride festival events⁴ must now be a priority agenda at the upcoming World Antimicrobial Awareness Week, given that these events could yield substantial exacerbating factors driving the antimicrobial resistance pandemic. Over the past two decades, individual case and small cohort reports indicate transmission of various pathogens in both symptomatic and asymptomatic travellers from across the world attending recurring mass gathering events (figure).^[4–11] These findings expose huge scientific knowledge gaps on the cryptic carriage, transmission dynamics, and ongoing evolution of antimicrobial resistance genes in people who attend mass gathering events, and their eventual effect on amplifying the global spread of antimicrobial resistance.^[5–7,10,11]

The Kumbh Mela (India), Arba'een (Iraq), Hajj (Saudi Arabia), Grand Magal of Touba (Senegal), and global gay pride events attract millions of people to the host countries from across the world.^{4–7} Attendees of mass gathering events live and interact together, generating a vast amount of biological waste, such as faeces, urine, sweat, and sputum, with billions of microorganisms contaminating the environment, water, food, surfaces, and skin. Thus, mass gathering events create ideal conditions for transmission between

attendees, organisers, and local residents of a range of pathogens, including multidrug-resistant bacteria that affect the respiratory tract, gastrointestinal tract, and genitalia.^{4,7} Men who have sex with men (MSM) are known to be at increased risk of acquiring multidrug-resistant enteric pathogens and other sexually transmitted infections through close contact and exchange of secretions and excreta during unprotected anal, oral, and other sexual practices.^{8,9} Repeated and frequent courses of antibiotic treatments in MSM with recurrent sexually transmitted infections drive antimicrobial resistance further, diminishing antibiotic treatment options.^[8–10] Clinico-epidemiological studies over the past decade have reported *Neisseria gonorrhoea*, *Mycoplasma genitalium*, *Giardia intestinalis*, HIV-1, and multidrug-resistant strains of foodborne gut pathogens *Shigella sonnei* and *Campylobacter coli* in MSM populations across diverse geographical locations.^[6,8–10]

Antimicrobial resistance is also a neglected but important issue at the Kumbh Mela and requires proper scientific definition. Kumbh Mela is the world's largest religious mass gathering event⁷ and is held every 4 years at locations across India, with over 100 million pilgrims from across all continents bathing together in the holy rivers of Ganga, Godavari, Kshipra, and Sangam. The Kumbh Mela thus carries the combined risk of antimicrobial resistance transmission from the carriage of bacteria in the skin, urinary, genital, or gastrointestinal tracts of pilgrims during mass communal worshipping that involves bathing together in contaminated river water under poor sanitary conditions. In 2021, a spatiotemporal meta-analysis of bacterial communities detected in water samples from the Godavari River showed anthropogenic multidrug-resistant bacterial strains generating in real time during the Kumbh Mela.¹² The 2022 Indian Council of Medical Research Antimicrobial Resistance Surveillance Network annual report¹³ showed an upward trajectory of antimicrobial resistance across India. Resistance of *Escherichia coli* to imipenem increased from 14% in 2016 to 36% in 2021; methicillin-resistant *Staphylococcus aureus* rates increased from 28.4% in 2016 to 42.6% in 2021. Whether the Kumbh Mela contributes to exacerbating antimicrobial resistance within India and globally remains to be defined by case-controlled cohort studies of pilgrims. The disruptions to regular health care in India and across the world because of COVID-19 appear to have worsened challenges with antimicrobial resistance control worldwide.¹⁴

During World Antimicrobial Awareness Week, in addition to advancing a multisectoral, transdisciplinary approach that recognises the connection between people and their shared environments, the organisations and international stakeholders must prioritise and emphasise the urgent need for more political and funder investments in antimicrobial resistance research at mass gathering events. Coordinated action must be inclusive, and

mass gatherings must be incorporated into the global antimicrobial resistance research agenda and more broadly in action plans, to prevent antimicrobial resistance. Given that millions of people from across the world attend recurring religious and gay pride events, they provide unique cohorts for taking forward a range of research and operational studies, such as defining the prevalence of antimicrobial resistance; risk factors for the evolution of antimicrobial resistance genes; transmission between participants; globalisation after the event; efficacy of infection control measures; antibiotic stewardship; and trials of new rapid diagnostics, vaccines, antibiotics, and novel therapeutic agents. Although the initiation and coordination of these studies might appear a logistical nightmare that is seemingly impossible, as the unprecedented but successful COVID-19 response illustrated, stakeholder support is required to take forward these studies.

Overcoming these challenges will require increased political will; approval by the governments of countries hosting mass gathering events; adequate resources, including funding, to establish cross-continental networks, coordinate, and conduct these studies; developing common study and ethics protocols; and the availability of interventions at an affordable cost. To advance optimal participation by attendees of religious and gay pride events in research studies will be to avoid indirect or direct anti-religious, homophobic and racist stereotypes. This will require human-rights-based study protocols, developed with full engagement of representatives from relevant religious, gay pride communities and host countries organisers, to avoid stigmatization, and use of unacceptable, prejudicial language, and content.

At the UN General Assembly on Sept 22, 2022, an important side event addressed antimicrobial resistance; heads of government and state, government ministers, and relevant stakeholders declared that urgent action is required to stop the spread of antimicrobial resistance. Antimicrobial resistance is a consistent agenda item in G7 and G20 presidencies. With such strong political support, the quadripartite organisations and relevant stakeholders need to take up strategic organisational and visionary leadership, create capability and capacity, and generate the required funding to advance research through cross-continental networks. This process could be underpinned by adapting, repurposing, and utilising the extensive existing research infrastructures, including genomics, epidemiological, communication, and data management expertise developed across the world for COVID-19. The quadripartite organisations must act now to find the missing data to formulate more effective policies than we have currently and avoid another global pandemic that could cause millions of deaths from antimicrobial resistance. The time is now ripe for global public authorities to discuss ways in which to invest strategically in high-quality research for obtaining an accurate evidence base and share data and experiences to reduce AMR

transmission at MG events. This will be critical for developing effective prevention, surveillance, and management protocols and help WHO and host countries develop evidenced-based planning for reducing transmission and spread of MDR pathogens at all MG events.

Author declarations:

All authors declare no conflicts of interest. The views expressed are those of the authors and not necessarily of their respective institutions.

Acknowledgements:

Avinash Sharma is DBT Wellcome Trust Fellow.

Sir Alimuddin Zumla is co-principal investigator of The Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET, CANTAM-3 and EACCR-3) funded by the European and Developing Countries Clinical Trials Partnership, supported by the EU Horizon 2020 Framework Programme. Sir Zumla is in receipt of an UK-NIHR Senior Investigator award and is a Mahathir Science Award and EU-EDCTP Pascoal Mocumbi Prize Laureate.

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Legend to Figure 1

Antibiotic resistant pathogens detected at Hajj, Kumbh Mela and Arba'een Religious Mass Gatherings over time.

