GARDP
Global Antibiotic Research & Development Partnership

Why a pandemic instrument should include antimicrobial resistance within its scope.

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit organization developing and providing access to lifesaving treatments for drug-resistant infections that pose the greatest threat to health. GARDP was created by the World Health Organization (WHO) and the Drugs for Neglected Diseases *initiative* (DNDi) in 2016 to ensure that everyone who needs antibiotics receives effective and affordable treatment, no matter where they live. GARDP welcomes the effort of WHO and Member States to negotiate a WHO Convention, Agreement, or other international instrument on pandemic prevention, preparedness, and response (WHO CAII).

As an organization focused on supporting global efforts to prepare and respond to antimicrobial resistance (AMR), a pandemic of drug-resistant infections, we would like to share three critical challenges that should encourage Member States to include AMR within the scope of the WHO CAII, including provisions that encourage governments to cooperate globally and across regions to ensure timely research and development as well as sustainable access to antimicrobials.

Timely and sustainable access to appropriate antibiotics is and will be an important component of preparedness and response to future viral pandemics.

Future viral pandemics could carry a significant risk of hospitalization and secondary bacterial infections, which increases the risk of severe morbidity and/or mortality. To reduce this risk, health systems require timely access to effective antibiotics (and diagnostics), much as there is recognition health systems also require sustained access to oxygen and critical care.

The COVID-19 pandemic illustrated the critical importance of timely access to antibiotics. A systematic review of 148 studies (362,976 patients with COVID-19), found that 18.4% of those individuals developed a secondary bacterial infection.[1] A previous systematic review found that between 16% and 28% of adults hospitalized for COVID-19 also had a bacterial infection, and that these patients stayed in the hospital twice as long, were four times more likely to require mechanical ventilation, and had a three times greater likelihood of dying compared to people only with COVID-19.[2] Smaller studies also illustrated that secondary bacterial infections, which are often multi-drug resistant, were a leading cause of death amongst patients with COVID-19. One study of patients in the United States, demonstrated that nearly half of patients who required mechanical ventilation developed a bacterial pneumonia, and that secondary bacterial pneumonia that did not resolve was a key driver of death in COVID-19 patients (potentially such deaths exceeded death rates from the viral infection itself).[3]

Furthermore, bacterial co-infections are also common during influenza epidemics. For example, in the 2009 H1N1 influenza epidemic 18-34% of ICU patients had bacterial co-infections.[4]

There is a substantial risk of antibiotic misuse and inadequate infection prevention and control throughout a viral pandemic that can fuel antibiotic resistance.

During a viral pandemic, there may be a substantial increase in the use of antimicrobials, especially before new or repurposed treatments are developed or identified. This was the case during the COVID-19 pandemic. One study estimated that while bacterial co-infections occurred in less than 10% of patients, antibiotics were prescribed to an estimated 75% of patients with COVID-19.[5] In addition to this use of antibiotics, there were other reasons that the COVID-19 pandemic may have increased the number of antibiotic resistant infections, including, as noted in a U.S. government report, difficulty in healthcare facilities to follow infection prevention and control (IPC) guidance.[6] Appropriate policies and investments, enumerated in a pandemic instrument, can ensure governments and health systems will be well-prepared to prevent misuse of antibiotics, and to ensure other preventive measures, such as appropriate IPC, can be sustained.

AMR is a pandemic of drug-resistant infections that merits appropriate prevention, preparedness, and response.

While AMR is often framed as a 'silent pandemic', recent figures demonstrate that this is not accurate, especially considering morbidity and mortality associated with AMR in low- and middle-income countries. According to the Global Burden of Bacterial Antimicrobial resistance (GRAM) study, published in the Lancet, 1.27 million people died of drug-resistant infections in 2019, and a further ~5 million died with a drug-resistant infection. More than half of bacterial-infection related deaths were caused by just five pathogens. There are many bacterial pathogens that have caused outbreaks and so have pandemic potential. Spikes in prevalence and rapid global spread of drug-resistant bacterial infections has occurred, usually associated with travel, as with other pandemic infections. For example, carbapenem-resistant Enterobacteriaceae (CRE) such as *Escherichia coli* and *Klebsiella pneumoniae* due to New Delhi metallo-β-lactamase or other carbapenemases have rapidly spread from a limited geography worldwide. These cause life-threatening infections including sepsis that are hard to treat. Consequently, drug-resistant infections require an aggressive and focused response, while acknowledging that spread can either be progressive and predictable or occur in sudden leaps.

References

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