COVID-19 and the potential long-term impact on Antimicrobial Resistance

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Summary

The emergence of the SARS-CoV-2 respiratory virus has required an unprecedented response to control the spread of the infection and protect the most vulnerable within society. Whilst the pandemic has focused society on the threat of emerging infections and hand hygiene, certain infection control and antimicrobial stewardship policies may have to be relaxed. It is unclear whether the unintended consequences of these changes will have a net-positive or -negative impact on rates of antimicrobial resistance. Whilst the urgent focus must be on allaying this pandemic, sustained efforts to address the longer-term global threat of antimicrobial resistance should not be overlooked.

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Main text

The emergence of, and subsequent pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has placed an immense strain on healthcare systems.[1,2] This has required unprecedented response(s) to control the spread of infection and protect the most vulnerable.

In response to the pandemic, healthcare systems have rapidly adapted infection control policies to ensure adequate capacity to isolate patients with potential SARS-CoV-2 infection. Societal focus on the threat from this emerging infectious disease has driven a heightened awareness of the importance of personal hygiene, particularly hand hygiene, environmental contamination, and increased use of personal protective equipment (PPE). The pandemic is also likely to require the relaxing of measures to prevent the spread of multi-drug resistant organisms (MDRO), such as screening and isolation in single rooms, and antimicrobial stewardship.

The paucity of available data makes it difficult to predict the impact that this pandemic may have on antimicrobial stewardship programs and long-term rates of antimicrobial resistance (AMR). On one hand, the increased focus on hand hygiene, attempts to limit patient contact, and social distancing may lead to reductions in healthcare associated transmission of disease. On the other hand, due to the prioritization of isolation rooms to COVID patients, the cohorting and/or management in open bays of patients colonized with CPE/VRE/MRSA/*Clostridium difficile* (*C.difficile*), and the inevitable higher workload of healthcare workers may potentially lead to a higher number of hospital transmissions.

The potential propagation of AMR may also be exacerbated by increasing rates of antimicrobial prescribing and potential breakdown in well-established stewardship programs. For example, despite few reports of bacterial co-infection, 62% of patients with COVID-19 had received antimicrobial therapy in the recent International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) report.[3] These prescriptions tend to be broad-spectrum in nature.[4] In addition to excessive and inappropriate antimicrobial prescribing, the spread of other pathogens and MDRO's may also be affected by day-to-day practicalities of an emergency focus on a single primary pathogen which may affect the depth of sampling for other organisms. The redeployment of antimicrobial stewardship teams and laboratory capacity to support the workload associated with SARS-CoV-2 is likely to compound this further.

With predictions that the current pandemic could continue to consume the focus of individual national healthcare systems such as the United Kingdom and United States for up to 18 months,[5] urgent analysis of its impact on AMR is required. This will support the development of contingency interventions to mitigate the potential impact of the pandemic on rates and transmission of AMR. Learning early lessons from countries currently affected will be important in supporting evidence-based guidance for those regions not yet burdened by an exponential rise in COVID-19 cases. In particular, the unintended consequences, whether positive or negative, of these health system changes need to be described, and where negative impacts are identified these must be mitigated against to ensure that sustained efforts to address the long-term and devastating threat of AMR.

Table 1 outlines some of the core antimicrobial stewardship efforts affected by the SARS-CoV-2 pandemic, suggesting potential interventions to help mitigate the impact of the pandemic response on AMR.

With the rapid redeployment of side rooms and PPE to protect patients and staff from respiratory viral infections and saturation of any isolation capacity, the ability to adhere to isolation policies normally deployed to prevent the spread of MDROs is likely to be challenged.(**REF**) Whilst increased hand hygiene may help prevent transmission[6] - pragmatic interventions are required to ensure sustained surveillance for MDRO's in both SARS-CoV-2 positive and negative patient cohorts.

With the disruption to routine services and redeployment of staff to alternative areas, such as critical care, is likely to cause disruption to engrained, top down antimicrobial stewardship programs within hospitals. With the requirement for increased infectious disease support for managing the response to the pandemic, stewardship teams may be redeployed from their primary roles leading to reduced opportunities to optimize antimicrobial therapy in patients. Loss of expert support for antimicrobial decision making, a paucity of evidence-based guidelines for antimicrobial prescribing in SARS-CoV-2, and anxiety of medical colleagues in front of deteriorating patients, may lead to further inappropriate use of antimicrobials. Urgent steps are needed to develop consensus on empirical use of antimicrobials together with clarification on the role of *Watch* and *Reserve* agents in the WHO essential medicines AWaRe criteria.[7] To support the redeployment of stewardship teams, leadership must be developed within local teams managing SARS-CoV-2 patients, supported by the development of evidence-based guidelines for the role of diagnostic tests, such a procalcitonin, to inform appropriate empirical treatment.(**REF**)

Institutions must also focus on behavioral factors and team dynamics that will come under immense pressure as healthcare services respond to the increase in demand associated with the pandemic. Team dynamics, fear, and specialty level cultural norms of practice are major drivers of inappropriate antimicrobial prescribing.[8] These factors must rapidly be assessed and stabilised in the face of a large variations in staffing levels within healthcare systems in the coming months. This will require effective leadership, clear communication across professions, and realigning chains of command in order to accommodate staff from multiple professions and experience. We must learn from existing social science research to be responsive and adaptive to the changing priorities and clinical needs. This cannot be achieved without engagement from across the healthcare multi-professional teams; the very personnel the interventions will target.

The planned implementation of large field-hospitals with a major focus on a primary viral pathogen also presents potential negative drivers for control of AMR. Uncertainty regarding the levels of staffing and support services for such facilities, as well the pressures of clinical practice and patient culture in such a setting do present opportunities for many of relevant MDRO's to spread with or without disease presentation.

In community practice, primary and secondary care has rapidly shifted towards telemedicine.[9] This is a vital step in protecting both healthcare workers and patients, but currently has limited data to support its potential to reduce or propagate suboptimal antimicrobial prescribing, and therefore AMR.[10,11] Limited evidence suggests that telemedicine is associated with increased rates of antimicrobial use.[10,11] Currently, there is little guidance and support for colleagues practicing telemedicine for the management of infection. With primary care being the biggest prescriber of antimicrobials, there is an urgent need for education and training, development of risk stratification, and guidance that is specific for telemedicine consultations. Community pharmacy roles must be urgently developed to support appropriate stewardship of antimicrobials prescribed by this route.

In summary, before the outbreak of SARS-CoV-2 in December 2019, major national and international interventions had begun to focus on reducing the potential future impact of AMR on society. The consequences of the current pandemic have the potential to stretch well into the post-COVID19 era. With increased societal sensitization towards emerging threats from infectious diseases and the concept of transmission and acquisition of disease, this may subsequently drive greater engagement with the problem of AMR. However, the current pandemic may also have a greater impact on society through the unintended propagation of AMR. Whilst, undoubtedly the main focus of healthcare must be on controlling the spread of SARS-CoV-2 and mitigating immediate impact on individual patients, we must not lose sight of the longer-term threat of AMR if our current structures and stewardship programs are completely disrupted during this unprecedented time.

Additional information

Transparency declarations

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Table 1. Potential impacts of healthcare system adaption during the COVID-19 pandemic on antimicrobial resistance.

Effected area	Potential impact	Potential interventions
Increased focus on hand hygiene in hospitals	Reduction in the spread of AMR within healthcare settings.	Ensure adequate resources and equipment available to support increase in demand (e.g. hand sanitizer). Ensure that routine surveillance systems remain in place to monitor rates of AMR within healthcare settings.
Social distancing in the community	Reduction in antimicrobial seeking behaviours by members of the public, leading to reductions in antimicrobial prescribing.	Reinforcement through public engagement.
Less opportunity for isolation of infective / MDRO patients	Potential spread of MDRO. Potential for suboptimal management of other public health challenges (e.g. tuberculosis).	Hand hygiene and barrier nursing. Sustaining MDRO surveillance. Staff and patient education & training. Clustered cohorting of patients by risk-factor (e.g. COVID-19 & CPE, COVID-19 & MRSA).
Pre-emptive discharge of patients and cancellation of routine procedures to enhance bed capacity	Reduction in patients carrying MDRO, such as CPE, within the hospital environment.	Stringent surveillance systems to detect and track the spread of AMR on reintroduction of these patients to healthcare services.
Diversion of all PPE for SARS-CoV-2 patients	Potential spread of MDRO.	Hand hygiene and barrier nursing. Sustaining MDRO surveillance. Staff and patient education & training. Appropriate stratification of PPE for different indications in line with evidence-based guidelines.
Increased rates of empirical antimicrobial therapy for patients presenting with respiratory symptoms	Potentiation of AMR.	Clear guidelines for empirical therapy in suspected SARS-CoV-2 patients. Specifically delineating the requirement for anti-pseudomonal and / or atypical coverage. Education and emphasis on local stewardship within all healthcare workers. Re-establishment of AMS oversight as soon as possible. Upskilling of staff within the organisation (e.g nurses and

		pharmacy technicians) to take on broader roles and responsibilities. Development of rapid diagnostics to support prescribing decisions. Including a clear role for the use of procalcitonin to detect bacterial infection. Ensuring that pandemic preparedness is part of future IPC and AMS strategy.
Increased rate of telemedicine within primary and secondary care and outpatient services	Possible increase in community rates of antimicrobial prescribing as part of safety netting. Possible reduction in community antimicrobial prescriptions due to social distancing and reduced access to pharmacies.	Need for education and specialist support to develop AMS strategies for telemedicine. Engagement with community-based pharmacies, who may not be confident in screening secondary care medicines. Need for development in technology to support risk stratification.
Redeployment of antimicrobial stewardship teams to deal with healthcare strain due to pandemic	Loss of developed stewardship frameworks within local healthcare environments.	Focus on education and responsibility of individual teams for promotion of appropriate antimicrobial usage. Addressing current social hierarchies within healthcare and upskilling of staff within the organisation (e.g nurses and pharmacy technicians) to provide routine AMS services. Integration of AMS / IPC teams.
Maintenance of institutional memory and team dynamics within organisations experiencing rapid reorganization and recruitment of staff	Loss of best practice and leadership within local team environments.	Education and training. Focus on fostering positive behaviours towards antimicrobials and infection control. Ensuring that structures are agile enough to absorb new individuals with minimal impact of process and patient care.
Overcrowding associated with overloading of healthcare systems	Major driver for the transmission of AMR.	Stringent surveillance systems to detect and track the spread of AMR. Ensuring that routine MDRO screening still takes place in the face of increased viral screening. Cohorting of high-risk patients. Contingency plans for rapidly responding to detected outbreaks.

Depletion of structural resources	Loss of side room capacity leading to propagation of SARS-CoV-2 infection due to cohorting of positive and negative patients.	Stringent pathways for segregation of cases. Rapid diagnostics to facilitate rapid identification.

Legend: AMR = antimicrobial resistance; AMS = antimicrobial stewardship; CPE = carbapenemase producing enterobacteriaceae; COVID-19 = novel coronavirus 2019; IPC = infection prevention and control; MDRO = multi-drug resistant organism; MRSA = meticillin resistant Staphylococcus aureus; PPE = personal protective equipment; SARS-COV-2 = severe acute respiratory distress coronavirus 2