THE INTERPLAY BETWEEN ANTIMICROBIAL RESISTANCE AND COVID-19

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About EPHA

EPHA is a change agent – Europe's leading NGO alliance advocating for better health. We are a dynamic member-led organisation, made up of public health civil society, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe.

About EPHA's Antimicrobial Resistance advocacy

EPHA has been working on Antimicrobial Resistance (AMR) since 2011 and used it as an example of a serious cross-border threat to healthcare that can only be mitigated by ambitious, coordinated and well-funded action and research as part of a long-term, multi-stakeholder effort.

See more at https://epha.org/antimicrobial-resistance/

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INTRODUCTION

The COVID-19 pandemic has caused immense suffering across the globe, put tremendous pressure on health professionals, and impacted almost all aspects of our lives. As European policymakers are now engaging in a process of building more resilient healthcare systems, it is crucial that we understand the implications that COVID-19 and our response to it will have.

In light of this, the present paper discusses the interplay between COVID-19 and antimicrobial resistance (the ability of microorganisms to resist antimicrobial treatments - AMR). Oftentimes called the silent pandemic, AMR is likely to have been responsible for a third as many deaths as COVID-19 worldwide in 2020.¹ In the EU alone, AMR is responsible for at least 33,000 deaths per year and is estimated to cost the EU €1.5 billion per year in healthcare costs and productivity losses.²

This briefing explores the direct and indirect impacts of responses to the pandemic relevant to AMR, and presents the policy and political reactions they have stimulated so far. The analysis reveals challenges that the system faces but also opportunities for change and improvement.


DIRECT IMPACT

Over-prescription of antibiotics

In the early days of the pandemic, broad-spectrum antibiotics were often prescribed in the context of the novelty of the disease and the resulting lack of information. Unfortunately, uncertainties persisted for a long time: even as late as April 2020, as much as two thirds of physicians admitted to facing a lack of guidelines for antibiotic prescription.

While antibiotics are not effective against SARS-CoV-2, the virus causing the COVID-19 disease, a small percentage of patients do develop secondary infections, in particular bacterial pneumonia. According to the latest WHO guidelines (January 2021), antibiotic treatment is discouraged in patients with mild and moderate COVID-19, unless there is a clinical suspicion of a bacterial infection.

Yet over-prescription of antibiotics remains a major concern. A 2020 rapid review concluded that 72% of hospitalised patients were administered antibiotics despite evidence of a bacterial superinfection being present in only 8% of cases. Other evidence shows that, in Europe, bacterial superinfections develop in 15% of severe COVID-19 cases but antibiotics are used in 75% of these. Although more detailed data on antibiotic use is needed, the existing numbers point to a clear over-prescription problem in this area. While these levels may go down as clearer information and guidelines are made available and disseminated, over-prescription has a damaging impact on our fight against AMR. Furthermore, the spread of new variants of the coronavirus may increase uncertainty and offset previous progress in terms of appropriate prescription of antibiotics.

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Population responses: misuse of antibiotics and behavioural patterns

Self-medication continues to be a problem throughout the world, including Europe. In a recent survey,\(^\text{10}\) 79 to 96% of Europeans taking antibiotics admitted to having taken them inappropriately, hoping to prevent infection. This becomes sadly unsurprising if we consider the Eurobarometer\(^\text{11}\) data from before the pandemic, showing that almost half of Europeans (48%) believed antibiotics could kill viruses.

As antibiotics are being prescribed to treat COVID-19 superinfections or for prophylaxis, the relationship between COVID-19 (and viruses in general) and antibiotics remains blurry for a majority of the public. The pandemic could have been a chance to clearly communicate about the difference between viruses and bacteria, as well as the different possible treatments and courses of action. Unfortunately, although efforts have been made by experts and parts of the media, the benefits remain doubtful as the message reaches an already confused and stressed public.

In terms of behavioural patterns among the general population, the increased hand hygiene practices, together with physical distancing and the use of face masks that have been observed during the pandemic favour a decrease in the general disease burden, thus lowering the AMR threat. Now there is a need to ensure that some of these new behaviors outlast the pandemic, by emphasising the general health benefits they bring. At the same time, however, there is a concern in the scientific community\(^\text{12}\) that the excessive use of biocidal agents will select for resistant bacteria and lead to an increase in AMR. This highlights the need for a balanced approach, which takes into account all consequences of human behaviour.

Vaccine uptake

The issues raised above illustrate a larger information problem, which has received most public attention in recent times, in the context of vaccine hesitancy. Before the pandemic, in 2019, the WHO\(^\text{13}\) already had identified vaccine hesitancy as one of the top ten global health threats in 2019, with AMR also included on the list.

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Despite variations among member states, a 2020 survey\textsuperscript{14} in the EU+UK showed increased confidence in vaccine importance and safety compared to 2018 levels. Overall, 92% of respondents (strongly or tend to) agree that vaccines are important, and 87% believe they are safe. In the case of COVID-19, early data\textsuperscript{15} showed that only an average of 56% of people in 7 European countries wanted to take the vaccine once it became available. A more recent study\textsuperscript{16} reveals vaccine hesitancy levels among adults in the EU to be at over 25%. This may be indicative of a larger underlying societal problem given that there is a correlation\textsuperscript{17} between the level of trust in institutions and the level of vaccine uptake in the EU. Given the crucial role that governments play in informing the public about vaccines and fighting misinformation from other sources, the OECD\textsuperscript{18} has published a paper including policies and best practices that governments can implement to increase public trust in COVID-19 vaccines. More broadly, trust in governments and in the healthcare systems will be essential for a successful common approach to future challenges.\textsuperscript{19}

Vaccines are key in the fight against both COVID-19 and AMR. One direct implication for AMR will be that a decline in (severe) COVID-19 cases will lead to fewer necessary treatments and fewer associated antibiotics prescriptions. There will also be an indirect effect, in that vaccination and prevention practices more broadly are one of the main pillars of fighting AMR. Therefore, the general trend in vaccine trust will also impact the AMR burden. Lastly, there is hope\textsuperscript{20} that the technologies and knowledge used to develop the COVID-19 vaccines hold promises for new vaccines for other diseases, with several projects\textsuperscript{21} exploring this possibility already underway.


INDIRECT IMPACTS

Overburdening healthcare professionals and health systems

Many national health systems were already facing capacity challenges, including lacking the ability to screen for patients who carry resistant bacteria and to isolate them. As the pandemic called for an unprecedented mobilization of all existing resources, some staff were reallocated and many healthcare professionals, including those who continued treating non-communicable diseases (NCDs), faced additional pressures. The extraordinary demands placed on healthcare professionals created tremendous mental health burdens, which may have long term implications. This concern is exacerbated in Eastern Europe by the brain drain that has been affecting the health sector for many years now. A lack of human resources will put additional pressure on systems already facing gaps in infection prevention and control practices, from hand hygiene to isolation capacity for patients with resistant bacteria. This is affecting all aspects of care, and thus negatively impacting AMR.

Non-communicable diseases and air pollution

Among the general population, patients suffering from NCDs are one of the groups most vulnerable to COVID-19. Due to their pre-existing conditions, they are more likely to experience severe symptoms and to die if infected with COVID-19. For many of these diseases, including cancer, cardiovascular diseases and asthma, air pollution is one of the main risk factors. In pre-pandemic times, air pollution was already the fourth most important health risk factor globally, increasing morbidity and mortality. Nowadays, the burden caused by air pollution is even greater, as it is indirectly responsible for worse outcomes of some COVID-19 patients suffering from NCDs. Moreover, indoor air pollution, which has so far received less public and political attention, has grown in importance as people spent more time inside their houses due to quarantines, lockdowns and travel restrictions. While this is still the subject of upcoming and future studies, some existing papers point to a correlation between exposure to air pollution and higher COVID-19 transmission rates or worse health outcomes. In this case, as more people

become sick, more antimicrobials are used for their treatments, and this inevitably drives up antimicrobial resistance in the population.

Furthermore, COVID-19 has made it more difficult to keep under control behavioral risk factors for certain NCDs. Unhealthy diets, alcohol consumption, tobacco use, and physical inactivity became more challenging to manage under these conditions of stress, coupled with physical distancing and lockdowns. Moreover, NCDs treatment and management often times require repeated and constant interactions with the healthcare system. As hospitals and practitioners were overwhelmed with the demands of treating COVID-19 patients, many routine checks and medical visits were put on hold.

The disruption in the continuity of care for NCD patients will likely lead to otherwise avoidable complications occurring. This, in turn, will increase the chances that antimicrobials are needed where they could be avoided, driving up antimicrobial resistance over time. Interruptions in treatment can moreover select for resistant bacteria, directly increasing the AMR burden. Besides disease management, diagnoses were affected and delayed due to the pandemic as well. People avoided going to hospitals and medical centres for fear of contracting COVID-19, resulting in diseases in the early stages – with milder symptoms and which usually require less invasive interventions – having gone undiagnosed. Overall, fewer emergency and planned hospital admissions did result in fewer antibiotic prescriptions in hospital settings, an aspect which favours a decrease in AMR in the short term. However, more research is needed to determine overall antibiotic use, as well as the long-term impact of cancelled or delayed hospital visits.

Public communication campaigns on health topics unrelated to COVID-19 were also disrupted, potentially resulting in a higher disease and AMR burden in the future. As the pandemic is brought under control, and routine processes are reinstated, health professionals are expecting a surge in non-COVID-19 patients, and higher levels of mortality.

Cancer care represents a particular case for concern. With suspended screening campaigns and delayed regular checkups, early stage cancer diagnoses have decreased and symptom-based diagnoses are expected


to become more important. However, later diagnosis of cancer generally reduces the chance of positive outcomes and increases the risk of complications. Meanwhile, already diagnosed cancer patients had to interrupt their chemotherapy and other treatments as the presence of COVID-19 in hospitals created a hazardous environment for an already immunocompromised group, for whom COVID-19 posed a very serious life threat. Infections are a common complication among cancer patients, making effective antimicrobials an integral part of the necessary treatment. AMR is thus a major concern for oncologists, who fear that in the future they will no longer be able to use current courses of treatment due to rising antimicrobial resistance. While the EU has developed a comprehensive and multi-pillared Beating Cancer Plan, its success may be threatened if AMR is not fully integrated in this broader approach.

**Telemedicine**

In driving patients away from hospitals and healthcare centres, COVID-19 has led to an uptake in telemedicine practices. While the added flexibility may bring some benefits, such as continuity of care, or eliminating transportation time and costs, several concerning observations have emerged. Firstly, telemedicine encounters appear to result in higher rates of antibiotics prescription. For example, antibiotic prescribing in dentistry in the UK April to July 2020 was 25% higher than during the same period in the previous year. It will be important to see whether this is a trend across telemedicine practices. Secondly, higher patient satisfaction rates have been recorded for encounters that result in prescription of antibiotics. As a causal connection between the two observations appears plausible, this underscores once more that changing patients’ expectations and demand for antibiotics represents a crucial factor in reducing inappropriate use.

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POLITICAL RESPONSES

Experts’ and decision-makers’ responses

While initially dominating the public and health agenda and redirecting resources away from AMR, the pandemic has also exposed and brought attention to the weakness of the European and global health system when faced with cross-border health crises. Furthermore, as experts noted the inappropriate use of antibiotics and the issue gained more attention, the WHO called on the international community to “stop the COVID-19 pandemic from becoming an AMR catastrophe”.37

A number of high-level declarations have echoed this concern. European Commissioner Stella Kyriakides and WHO Director-General Tedros Adhanom Ghebreyesus38 pointed out that the AMR threat has been neglected while all focus was on COVID-19, and warned that the former could have an even higher death toll. Subsequently, they called for a “spirit of global cooperation and a sense of genuine urgency” in tackling AMR. WHO Director-General Tedros Adhanom Ghebreyesus39 reiterated this message in his opening remarks as the second meeting of the Global Leaders Group on AMR, highlighting that the consequences of antimicrobial resistance could dwarf those of Covid-19, while actions aimed at fighting it will offer cross-cutting benefits across several sectors. The OECD had a very similar message, with Secretary-General Angel Gurría40 cautioning, in his remarks on European Antibiotic Awareness Day on 18 November 2020, that AMR risks becoming the COVID-19 of tomorrow. More recently, the declaration of the G20 health ministers,41 following their meeting in September 2021, noted the impact of growing levels of AMR on our ability to reach the Sustainable Development Goals (SDGs), and the importance of the One Health approach.

At the policy level, the EU AMR One Health Network activities in 2020 illustrate the initial response and redirecting of resources. While the Network normally holds bi-annual meetings, there were no sessions organized in 2020.42 Similarly, according to the Commission’s progress report,43 the EU Health Security Committee (HSC) meetings were focused

on COVID-19 “during the pandemic” although the 2017 European One Health Action Plan against Antimicrobial Resistance specifically calls for making increased use of the EU HSC, “to strengthen coordination and to share information”.

Nonetheless, as the initial shock of the COVID-19 pandemic subsided, AMR initiatives have become one of the key components in the emerging EU architecture aimed at responding to global health threats. By way of example, the Pharmaceutical Strategy for Europe, published towards the end of 2020, was shaped by the pandemic and includes AMR – developing new antibiotics, prudent use, etc. Moreover, tackling AMR has been included as a policy priority in the EU4Health Programme. In the aftermath of the COVID-19 pandemic, effective stakeholder coordination will be crucial given that one of the lessons learnt from the crisis was that Europe is lacking a well-organised, harmonised surveillance and response mechanism. AMR remains one of the most serious cross-border health threats: a simultaneous COVID-19 and AMR crisis could crush already weakened health systems in Europe and globally.

Population responses: political attitudes

Despite a temporary pause in international travel and attempts early on in the pandemic to implement protectionist measures, it soon became apparent that the pandemic requires international cooperation and global solutions. As much of the population in high income countries has been vaccinated or has access to vaccines, experts continue to warn that no one is safe until everyone is safe. At the same time, the pandemic may have sensitized the public to cross-border health threats. A parallel can easily be drawn to the threat of AMR, which also knows no borders. Having seen the initial inability of national health systems to manage the COVID-19 crisis, there should be a potential for increased public support in favour of global action on health issues including AMR.

Regarding the potential for larger scale change, many have pointed out that COVID-19 recovery plans can be an opportunity to rethink our ways of life from the local to the global level: policy priorities, financial incentives, but also public mobility practices and city planning.

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For example, during lockdown periods, there was a dramatic decrease in carbon dioxide emissions,\textsuperscript{50} air pollution\textsuperscript{51} and noise levels, and there was a general public desire\textsuperscript{52} to maintain better air quality in cities. Many local governments\textsuperscript{53} rolled out plans to build more bike lanes and created temporary ones. However, the long-term impact remains to be seen as these measures have not always been integrated into a broader systemic effort to rethink the use of public space.


CONCLUSIONS

The long-term impact of COVID-19 on AMR, as well as on all aspects of our health and lives, remains to be fully uncovered. While there is still considerable uncertainty, a few directions can be teased out and some lessons to be learned are already emerging. These include the importance of access to vaccines, antibiotics, and medicines generally, as well as access to accurate and reliable information regarding their uses and effects. Furthermore, the strain put on healthcare systems did not only negatively impact COVID-19 patients, but also challenged society’s ability to respond in a way that takes into account broader implications of reactions to the crisis. Global coordination and cooperation have played important roles in alleviating this pressure, by sharing information and resources, and should continue to be further developed with a view to strengthening health systems. Just like COVID-19, AMR is a “problem without a passport” and requires the same concerted international efforts for a sustainable and equitable solution.

The threat of AMR has been well-known in expert circles for a long time but that has not always translated into political momentum or public awareness. Yet incremental progress has been made and should serve as the backbone for real systemic change, on the backdrop of broader transformations prompted by the pandemic.