RAPID SCOPING REVIEW

The Effects of the COVID-19 Pandemic on the Three Core Drivers of AMR

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Global Strategy Lab

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ABOUT COVID-END

To help Canadian decision-makers as they respond to unprecedented challenges related to the COVID-19 pandemic, COVID-END in Canada is preparing evidence syntheses like this one. This living evidence synthesis was commissioned by the Office of the Chief Science Officer, Public Health Agency of Canada, and was funded by the COVID-19 Evidence Network to support Decision-making (COVID-END) through an investment from the Government of Canada through the Canadian Institutes of Health Research (CIHR). The opinions, results, and conclusions are those of the team that prepared the evidence synthesis, and independent of the Government of Canada, CIHR, and the Public Health Agency of Canada. No endorsement by the Government of Canada, Public Health Agency of Canada or CIHR is intended or should be inferred.

The AMR Policy Accelerator at Global Strategy Lab (GSL) and the Knowledge Synthesis and Application Unit (KSAU) team at the University of Ottawa conducted this living evidence review to explore how (1) antimicrobial use, (2) infection prevention, and (3) health system changes have impacted the emergence, transmission, and burden of AMR during the COVID-19 pandemic (1). For more on the Global Strategy Lab and Knowledge Synthesis and Application Unit project team see page 64.

THIRD-PARTY MATERIALS

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PUBLIC SUMMARY

How did the COVID-19 pandemic impact antimicrobial resistance (AMR)?

What is this study about?

Antimicrobials are medicines meant to treat infections. Antimicrobial resistance (AMR) occurs when bacteria, viruses, and other microbes stop responding to these antimicrobial medicines. AMR is a serious global public health issue. In 2019 alone, AMR was directly responsible for the deaths of 1.27 million people and contributed to the deaths of close to 5 million people around the world.

In this study, we wanted to know if the COVID-19 pandemic changed how antimicrobials are used and if AMR was higher or lower than before the COVID-19 pandemic. To measure this, we looked at data on AMR rates and rates of hospital and community use of antimicrobials before and during the pandemic. Data was used from the following countries: Australia, Canada, England, the European Union (EU), Japan, Korea, Norway, and the United States of America (US). We also looked at whether actions that prevent infection like hand washing, wearing face masks, and lockdowns increased or decreased AMR during the pandemic. Finally, we looked at how changes to how people use medical systems, for example, reduced use of healthcare systems during the COVID-19 pandemic, may have impacted AMR. As part of our analysis, we looked at whether studies collected data on age, race, ethnicity, or other factors to determine how the pandemic and AMR may have impacted different groups of people including different genders, minorities, and equity-seeking groups.

Hospital use of antimicrobials refers to antimicrobials used or prescribed inside a hospital or emergency-room setting.
Community use of antimicrobials refers to antimicrobials used or prescribed outside of a hospital or emergency-room setting; for example, through community pharmacies.

Why is this study important?

It is important to understand what actions during the COVID-19 pandemic increased or decreased AMR. If we can identify how the COVID-19 pandemic impacted AMR, we can provide recommendations to slow down AMR and save lives.

Results: How did COVID-19 impact antimicrobial use?

- In 2020, all countries used fewer antimicrobials than before the start of the pandemic. Some countries used more antimicrobials in hospitals to treat COVID-19 patients. In all countries, there was less community use of antimicrobials.
- We only have information on antimicrobial use from a few countries for 2021. In Denmark, England, and the US, community antimicrobial use increased from 2020 levels. In the US, community antimicrobial use *increased to more than before the pandemic*. In Canada and Norway, the community use of antimicrobials in 2021 did not increase.

Results: How did COVID-19 impact AMR?

- We did not consistently find that AMR either increased or decreased because of changes in antimicrobial use during COVID-19. Different countries showed different trends in AMR. The various ways that countries responded to try to slow the spread of COVID-19, like

lockdowns, travel restrictions, and mandatory face masking, may explain why the results are mixed. Some countries found that AMR increased, while some found it decreased or stayed the same.
- Measures meant to stop the spread of COVID-19, like wearing face masks and lockdowns, may have also reduced AMR.
- Changes to how people used the medical system, like reduced diagnostic testing, may have increased AMR because infections were not recognized and treated early, but more studies are needed.
- Most studies did not collect data on how the pandemic and AMR impacted different groups of people including different genders and minority groups.

What is needed now?

1. More studies to find out how the COVID-19 pandemic has impacted AMR.
2. In all countries, better systems are needed to track antimicrobial use and AMR.
3. More studies on how the pandemic and AMR may have impacted different groups of people including different genders and minority groups.

EXECUTIVE SUMMARY

Antimicrobial resistance (AMR) is a critical threat to global public health. This report is the second edition of a living evidence review aimed at identifying linkages and evidence gaps to determine how three drivers —antimicrobial use (AMU), infection prevention and control (IPAC), and use of healthcare and related systems— have impacted the emergence of new drug-resistant strains (AMR *emergence*), the spread of antimicrobial resistant organisms between hosts (AMR *transmission*), and the number and nature of infections due to antimicrobial resistant organisms (AMR *burden*). The first living evidence review report was published in November 2022.

This second report includes thirty-one new studies, in addition to seventeen studies identified in the first report. This report also includes verification and risk of bias assessments for included studies; most were found to be at high risk of bias. Results were further stratified by setting to look at community- and hospital-associated infections.

Conclusions in this report were consistent with our earlier report: changes in AMU were *not* associated with a positive or negative impact on AMR while COVID-19-driven IPAC measures may be reducing AMR. The few studies that examined health system use during the COVID-19 pandemic found changes such as increased ICU use, reduced health system access and reduced diagnostic testing may be driving AMR, but additional research is needed to substantiate these results.

National surveillance data from the early stages of the pandemic (2020) demonstrated that the impact of COVID-19 on AMR varied across geographic, healthcare, and community settings. The 2020 surveillance data for all included countries showed an initial decrease in AMU driven by reductions in community prescribing, but mixed trends in AMR rates among priority pathogens. A few countries have released 2021 surveillance data, including Denmark, England, and the US, reporting that community and outpatient AMU trended upwards; in Norway and Canada, community AMU did not increase in 2021. The US reported an increase in 2021 community AMU *to*

above pre-pandemic levels. Different community AMU trends may be explained by national differences in timing and speed at which COVID-19 restrictions (like lockdowns and travel restrictions) were eased. Additional trends in community AMU may become apparent as 2022 data is released.

Most of the studies reviewed reported an increase in hospital antibiotic consumption during the pandemic. Changes in AMU, however, were not consistently associated with a positive or negative impact on AMR and studies reported increases, decreases, and no impact on AMR (2–12). We found that community IPAC measures, including travel restrictions, lockdowns, social distancing requirements, and mandatory masking, all consistently contributed to reduced community-associated infections (CAIs) (13–39). However, impact on AMR and hospital-associated infections (HAIs) was more varied. We also found that changes to health system use during the COVID-19 pandemic, including increased ICU admissions, reduced testing, and reduced health system access may be driving AMR. We found only a few studies looking at the impact of COVID-19 on health system use and AMR. This remains a consistent knowledge gap from the first version of this report that requires further research and investigation. Additionally, few studies investigated the impact of any COVID-19-driven changes to the three drivers on AMR transmission and emergence. The lack of data about either dimension represents a significant evidence gap and opportunity for future research.

Different AMR findings across regions and settings likely reflect the interacting, and conflicting, effects the COVID-19 pandemic has had on AMR. For example, improved IPAC measures may have decreased health system use, leading to decreases in AMU and AMR. However, ICUs being over-capacity, hospitals struggling with staffing and protective equipment shortages, and high rates of AMU in COVID-19 patients may have increased AMR rates.

Five policy implications emerged from this review:

1. The lack of available evidence on COVID-19 impacts on AMR underscores the need to strengthen AMR surveillance systems, including improving the timeliness of data collection, strengthening coordination between One Health surveillance systems and enhancing data collection to provide insights on equity considerations and equity seeking groups.
2. Since community prescribing represents a large proportion of AMU in most countries, interventions addressing AMU in this setting should be prioritized.
3. Community IPAC measures like social distancing and hospital IPAC measures such as improved hand hygiene were found to reduce AMR, policymakers working in antimicrobial resistance should ensure they consider IPAC measures in their policy.
4. Even though COVID-19 has disproportionally affected low income, racial, ethnic, gender, minority groups and migrant populations, very few studies collected any data on social determinants of health or evaluated differential AMR outcomes among marginalized populations. Identifying populations with inequitable COVID-19 and AMR effects will allow the development of better and targeted policy initiatives and stewardship programs.
5. We must learn from this pandemic and ensure AMR is a consideration of pandemic preparedness moving forward.

KEY FINDINGS

- The COVID-19 pandemic has produced both positive and negative effects on AMR, likely the result of interactions between three drivers of interest: antimicrobial use (AMU), infection prevention and control (IPAC) and health system use. Different findings across regions and settings reflect these interacting and conflicting effects. *Interpreting these interactions will require more contextual evidence on local COVID-19 dynamics and policies.*
- The impact of COVID-19 on AMR varied across geographic, resource, and healthcare and community settings. Surveillance data from 2020 consistently showed a decrease in community AMU, while changes in AMR rates among priority pathogens varied. Surveillance data from 2021 indicates that community and outpatient AMU trended upwards. Different community AMU trends may be explained by national differences in timing and speed at which COVID-19 restrictions (like lockdowns and travel restrictions) were eased. For example, the US reported an increase in community AMU to above pre-pandemic levels in 2021, which may be because COVID-19 travel restrictions, masking mandates, and social distancing requirements were eased sooner there than in other countries.
- Changes in AMU were not consistently associated with a positive or negative impact on AMR. Studies reported increases, decreases, and no impact on a range of resistant pathogens regardless of changes to AMU. However, many studies included in this report only looked at data from the start of the pandemic (2020 and 2021) and may not have captured the lag between changes in AMU and AMR impacts that may be occurring. Trends may become more apparent as additional data becomes available.
- We found that community IPAC measures such as masking, lockdowns, social distancing, and travel restrictions consistently contributed to reduced CAIs. Impact on AMR and HAIs was more varied.
- A small number of studies showed changes to health system use including increased ICU admissions, reduced diagnostic testing, and reduced health system access, may be driving AMR. However, the full impact of health system use on AMR is a knowledge gap that requires further researched. Studies on AMR emergence and transmission are also needed.
- Most studies included in this review did not collect data on sociodemographic and socioeconomic factors. More research is needed to assess equity and how the pandemic and AMR may have impacted different groups of people including different genders and minority groups.

BACKGROUND

Context

The COVID-19 pandemic has reshaped the landscape of healthcare around the world. Antimicrobial resistance (AMR) was already a critical pre-pandemic issue, and the COVID-19 pandemic has accelerated the need for concerted global action to address rising AMR rates (40). A recent study estimated that, in 2019 alone, bacterial AMR contributed to almost 5 million deaths (41). The World Health Organization estimates that AMR has caused at least one-third as

many deaths as COVID-19 in 2020 (42). However, whether the COVID-19 pandemic would increase or decrease AMR has been widely debated (43,44).

AMR is an evolutionary response accelerated by widespread antimicrobial use (AMU). In the context of COVID-19, the development and spread of AMR has also likely been impacted by changes in infection prevention and control measures (IPAC), and changes to health system use around the world (1). These drivers, including self-medication, handwashing, use of personal protective equipment, and changes to modes of access to healthcare services such as remote prescribing, can affect AMR through different mechanisms. Inappropriate or increased use of antimicrobials to treat secondary or co-infections (with bacterial, fungal, and other viral infections) in COVID-19 patients may directly influence AMR rates (45) by concurrently promoting AMR emergence and burden (43). Policy measures in response to the COVID-19 pandemic, such as reduced travel and improved infection prevention and control practices (in community and across healthcare systems), may have reduced AMR transmission (44). While in hospital IPAC measures may have been negatively impacted by the re-distribution of resources from AMR to control of COVID-19 (46). The COVID-19 pandemic has also compounded existing societal and health inequities, such as limited or reduced access to vaccinations (47), reduced access to laboratory consumables, and reduced staff availability in healthcare systems in low-resource settings, which may in turn drive inequitable AMR transmission (44,46).

METHODS

National surveillance data on AMR and AMU

We conducted a targeted scan of national surveillance reports that were published using data from March 2020 or later to provide background data on AMU and AMR rates. We searched for surveillance reports from key countries identified by the Public Health Agency of Canada: Australia, Canada, England, EU countries, Japan, Korea, Norway, and the US. GSL completed the data extraction in Excel, and results were descriptively summarized in *Table 1*.

What's new?

- Thirty-one new studies were included in this report.
- A second reviewer verified the inclusion and categorization of studies.
- Risk of bias assessments were added for all studies.
- Results were stratified by community- and hospital- associated infections.

The impact of COVID-19 on AMR drivers: AMU, IPAC and health system use

Search strategy

A detailed search strategy was developed in consultation with an information specialist (*Appendix 4*). A PRESS peer review was completed for this search strategy. Electronic searches were carried out using MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews. Studies published to February 24th, 2023 were included in this review.

Eligibility criteria

Studies published in English between March 2020 and February 2023 were eligible for inclusion. Studies that directly measured the impact of the driver on AMR rates (e.g., the impact of COVID-19 IPAC programs on AMR) or that attempted to show an association by measuring changes in

the driver and AMR rates before and during the COVID pandemic (e.g., presenting AMU trends and AMR trends) were included. Non-systematic reviews, case reports, case series, surveys, modelling studies, commentaries, letters, conference abstracts, and qualitative studies were excluded.

Study selection and data extraction

Study selection and data extraction were completed by a single reviewer. The reviewer completed both title and abstract screening and full-text screening. A second reviewer validated 30% of single reviewer screenings. Data extraction and charting was completed in Covidence and Excel, respectively, and results summarized descriptively (*Appendix 1*, *Table 2)*.

Risk of bias assessment

Risk of bias assessments for non-randomized studies (including retrospective data linkage and interrupted time series designs) were completed with the ROBINS-I tool (48). Cohort studies were evaluated using the Newcastle Ottawa Scale (NOS) for cohort studies (49). Risk of bias was not assessed for environmental sampling studies (no samples from human participants); these assessments will be included in a future report update.

Equity: PROGRESS-Plus framework

Health inequities were also considered for each study using the PROGRESS-Plus framework and PROGRESS-Plus factors were extracted for each study (*Appendix 2, Table 1*). The PROGRESS-Plus framework identifies characteristics that stratify health opportunities and outcomes (50) including place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status and social capital. “Plus” factors, including those used to refer to personal characteristics associated with discrimination (e.g., age, disability), features of relationships (e.g., hospital, respite care, other instances where a person may be temporarily at a disadvantage) were also recorded.

Synthesis

Evidence was synthesized using the Knight et al. (1) framework which describes three dimensions of AMR which may have been, and may continue to be, affected by the COVID-19 pandemic. The framework identifies three dimensions of AMR: the emergence of new drug-resistant strains (AMR *emergence*), the spread of antimicrobial resistant organisms between hosts (AMR *transmission*), and the number and nature of infections due to antimicrobial resistant organisms (AMR *burden*). Included studies were classified using this analytic framework (*Figure 1*) according to both the *driver* of AMR measured or reported and the *dimension* of AMR that was considered. Drivers are defined in accordance with Knight et al.’s framework as: AMU; community or hospital IPAC measures such as masking, improved hand hygiene, lockdowns, and travel restrictions; and/or changes to health systems use such as reduced numbers of elective procedures. Studies were classified under transmission only if they included a measure of horizontal transmission. Additionally, studies were only classified under health system use if they considered a measure of health system use, for example a change in admission rates or testing rates.

RESULTS

The impact of COVID-19 on AMR and AMU: National trends

AMR and AMU surveillance data from high-income countries (HICs) including Canada (51), Japan (13), Norway (52), England (53), Denmark (54), and other countries in the EU (55) all reported overall decreases in AMU in 2020 due to substantial reductions in community antimicrobial consumption (*Appendix 1, Table 1)* (13,52). Overall decreases in AMU were seen in the UK (53) and the EU (55) despite increased in-patient prescribing. Most other countries reported decreased hospital AMU.

Community or outpatient use is the largest contributor to human AMU in most countries (56). The US (57) found an initial decrease in community AMU during 2020 followed by an increase in 2021 to higher than 2019 levels (57) (*Table 1*). In the England total antibiotic consumption had been decreasing prior to the COVID-19 pandemic, and a sharp decrease was seen during the COVID-19 pandemic (between 2019 and 2020). Between 2020 and 2021, overall AMU in England saw only a minor reduction; hospital inpatient, hospital outpatient and community AMU increased while dental prescribing decreased(58). Denmark also reported a substantial decrease in AMU during the first wave of the COVID-19 pandemic (March-May 2020) and into 2021. However, AMU slowly increased from August 2021, following the lifting of COVID-19-related restrictions in the country and rose to similar levels seen in corresponding months in 2018 and 2019 (59). In Norway community AMU did not show a significant change between 2020 and 2021 (52). In Canada between 2017 and 2021, a decrease in community antimicrobial consumption was observed which was most pronounced during the COVID-19 pandemic (2019 to 2021). In 2021 antimicrobial consumption in the community sector in Canada continued to decline from 2020, remaining below pre-pandemic levels (60).

Table 1. Community AMU trends for countries from before 2020 to 2021 (for countries that have released 2021 data)

Country	Pre-2020 AMU trend	2020 AMU trend	2021 AMU trend
Canada	Decreasing	Significant decrease between 2019 and 2020	Decreasing
United States	Decreasing	Significant decrease between 2019 and 2020	Increasing
England	Decreasing	Significant decrease between 2019 and 2020	Minor decrease
Denmark	Decreasing	Significant decrease between 2019 and 2020	Increasing
Norway	Decreasing	Significant decrease between 2019 and 2020	No change from 2020

AMR trends

Most countries track AMR trends in priority pathogens, which typically include 12 species of bacteria classified as having critical, high, and medium rates of antibiotic resistance (61). The most critical include bacteria commonly associated with bloodstream infections in hospitals like A*cinetobacter*, *Pseudomonas* and various *Enterobacteriaceae*. Increasing, decreasing and mixed trends in AMR rates were seen among priority pathogens in 2020 and 2021. The US noted a 15% increase in the rates of resistant hospital-associated infections in 2020 compared to 2019, despite

delayed or unavailable data for 9 of their 18 priority pathogens (57). England had observed an increase in AMR burden in key pathogens causing blood stream infections since 2017 before AMR rates fell in 2020. This decline was maintained in 2021 (58). The European AMR Surveillance Network found an increase in reported invasive isolates for all bacterial species under surveillance except for *Streptococcus pneumoniae*, which saw a decrease overall and for resistant isolates between 2019 to 2020 (55). In 2020, Canada reported an increase in AMR for most priority organisms between 2016 and 2020 (60). Surveillance data pointed to a decreasing incidence of resistant *Klebsiella pneumoniae* in Denmark from 2019 to 2020 (54), *Streptococcus pneumoniae* in the EU (55) and in Japan (13) from 2019 to 2020, methicillin-resistant *Staphylococcus aureus* (MRSA) in Norway (52) from 2019 to 2021, and extended spectrum beta-lactamase producing *Escherichia coli* in Australia (62) and Norway (52) between 2019 and 2021. However, an increase in tuberculosis infections classified as multidrug resistant was reported from 2019 to 2020 in England (58) and 2019 to 2021 in Norway (52).

The impact of COVID-19 driven changes in AMU, IPAC and health system use on AMR emergence, transmission and burden

Forty-eight studies were identified (*Appendix 1, Table 2*) that collected data on the impacts of COVID-19-related changes to AMU, IPAC, or health system use (*Appendix 1, Table 3*) on AMR (*Figure 1*). Fourteen studies explored the link between AMU and AMR burden (2–12,28,33,63), twenty-seven studies investigated the link between COVID-19 related changes in IPAC measures and AMR burden (13–39) and four studies considered changes in health system use as a driver of AMR burden (64–67). One study collected data on two drivers (IPAC and AMU) and AMR burden (28). Significantly fewer studies looked at the impact of COVID-19 related changes in relation to AMR transmission and emergence; we identified three studies that looked at changes in IPAC measures as a driver of AMR transmission (68–70) and one that looked at emergence (71). We found no studies that looked at change in AMU as driver of AMR transmission and only one that considered AMU as a driver of AMR emergence (72). No studies attempted to measure changes in health system use as a driver of AMR transmission or emergence. The majority of included studies looked at changes in AMR burden during the first 12 months of the pandemic, starting in March 2020. Seventeen studies (2,14,20,23,27,30–32,34,36,37,39,63,66,67,71,72) explored resistant community-associated infections (CAIs); most remaining studies were single-site hospital-based studies focused on hospital-associated infections (HAIs).

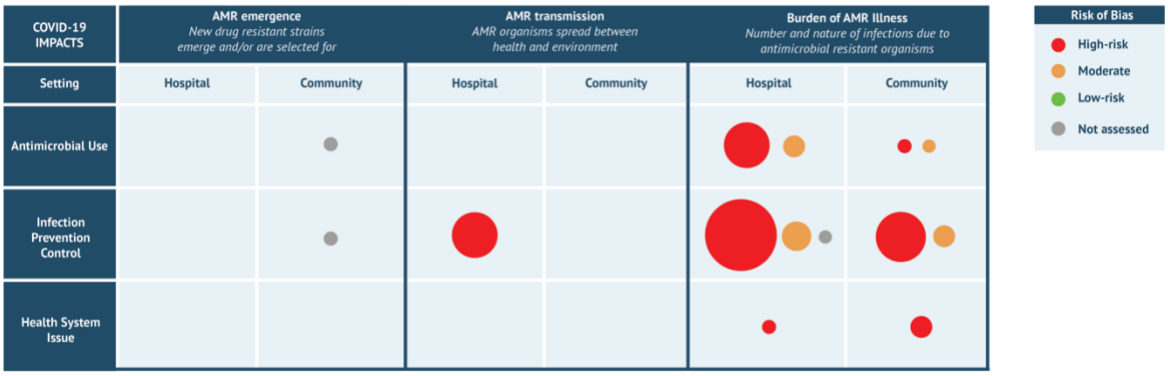

Figure 1. Map of study classification in accordance with the Knight et al. (73) framework, and risk of bias. Bubble size reflects number of studies while bubble colour reflects risk of bias assessment.

AMR burden

Forty-three studies explored AMR burden (2,4–9,11–18,20–28,28–36,39,63–67,74,75).

AMU and AMR burden

We identified fourteen studies that explored the link between AMU and AMR burden (2–12,28,33,63). Most did not directly evaluate the impact of changes in AMU on AMR, but instead measured changes in trends in both AMU and AMR, before and during the COVID-19 pandemic.

Community

Only two studies (2,63) considered community-based AMU. The first from Hong Kong, reported a decrease in antimicrobial sales in 2020-2021 compared with 2012-2019. Decreases in antimicrobial sales coincided with a significant decrease in the incidence of community-onset bacteremia due to *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Haemophilus influenzae,* and *Neisseria meningitidis* but a significant increase in community-onset bacteremia due to methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli* (2). The second study, from Italy, measured antibiotic consumption and AMR patterns of Enterobacterales cultured from urine samples in the community during 2019 and 2020. Researchers found overall antibiotic consumption decreased by 28% from 2019 to 2020 (although from March to April 2020 azithromycin use increased) and correspondingly susceptibility rate of amoxicillin/clavulanate increased among Enterobacterales isolates (63).

Hospital

Hospital-based studies largely found an increase in AMU (3–12); however, changes in AMU did not consistently correspond to higher or lower rates of AMR. A single-center study from Japan using 2018 to 2022 data found no change MRSA, but an increase in extended spectrum beta-lactamase-producing Enterobacterales incidence and consumption of intravenous antimicrobials during the pandemic (12). In the US (5), a single center study found that although AMU was higher, the incidence of resistant organisms did not significantly change during the early stages of

the pandemic. Similarly, a multicenter analysis from the US found patients admitted during the pandemic (March 2020 – October 2021) had significantly lower AMR rates but significantly higher rates of antibiotic prescriptions compared with those admitted pre-pandemic (2019 – February 2020) (7). A study from a South Korean hospital identified an increase in both antibiotic use and incidence of multidrug resistant infections including MRSA, vancomycin-resistant *Enterococcus* (VRE), carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) from March 2020 to September 2021 when compared to the same period pre-pandemic in 2018 to 2019 (3). Studies from Italy (33), Brazil (8), and Mexico (10) also found an increase in multidrug resistant infections along with an increase in antibiotic use during the pandemic.

Some studies reported reduced AMU during the pandemic. For example an interrupted time-series analysis from a university hospital in Italy from 2015 to 2021 found a decrease in antibiotic consumption during the pandemic while MRSA blood stream infections increased, albeit not significantly (4). Another single-center study from Italy found comparable incidence of both hospital-associated and multidrug resistant infections pre-2019 and during the pandemic (2020) despite the fact that hospital AMU was significantly less during the pandemic period than before (9). A single-center study from the US comparing 2019 and 2020 data (11) found increases in monthly number of some AMR pathogen events (CRE, VRE) but no differences in others (CRPA, MRSA). They also did not find any significant difference in hospital antibiotic use between two time periods.

IPAC and AMR burden

Twenty-seven studies investigated the link between COVID-19 related changes in IPAC measures and AMR burden (13–39).

Community

Ten of these studies collected data on CAIs (14,20,23,27,30–32,36,37,39). Most studies measuring CAIs reported an overall reduction in both CAIs and resistance. For example, a study from Botswana looking at extended-spectrum cephalosporin-resistant *Enterobacterales* and CRE carriage found prevalence was significantly higher pre-lockdown versus post-lockdown (30). An investigation of global *Mycoplasma pneumoniae* incidence after implementation of COVID-19 nonpharmaceutical interventions (NPIs) including physical distancing measures, personal protective measures like face masking and improved hand hygiene, stay-at-home orders, school and day-care closures, closing borders and travel restrictions from April 2020 to March 2021 found significant reductions in both M. pneumonia and Macrolide-resistant Mycoplasma *pneumoniae* rates (31). A decrease in both salmonellosis incidence and proportion of trimethoprim resistance was found in the Netherlands (32) pre- and intra-pandemic (2016 to March 2021). A 2020 interrupted time series analysis from Germany which assessed the impact of the pandemic and COVID-19 non-pharmaceutical IPAC measures on HAIs and CAIs found CAIs drastically decreased while resistant-HAIs like carbapenem-non-susceptible *Acinetobacter* and Methicillin-resistant *Staphylococcus aureus* invasive infections also reduced (although less dramatically) (36). In Taiwan there was reduced incidence of twelve of fourteen different airborne/droplet-transmitted notifiable infectious diseases between the pandemic period and the pre-pandemic period (2018-2021) including a decrease in MDR-TB (34). Another study from Taiwan investigated whether facial masking and social distancing during the COVID-19 pandemic reduced TB transmission. A study from France found reduction in ESBL-*E.coli* carriage rates in both primary

care and nursing home residents which they attributed to improved community IPAC due to stay at home orders, closed school or daycare centers, and reduced public transport crowding during lockdown (20).

By contrast, five studies found less consistent associations between IPAC and AMR in the community (14,16,27,36,37). A study from China looking at the effect of COVID-19 IPAC measures including vaccination, implementation of isolation measures and social distance, strengthening of personal protective measures, aseptic operation of invasive medical treatment, hand hygiene, and environmental disinfection on resistance in pediatric lower respiratory tract infections (LRTI) using data from 2011 to 2020 found that *Escherichia coli* and *Klebsiella pneumoniae* third generation cephalosporin resistance decreased but carbapenem resistance and rates of MRSA increased from 2018 to 2020 (37). Another Chinese study examining the effects of community epidemic prevention and control requirements including like wearing masks, hand hygiene and social distancing found hospital-acquired MRSA infections increased (14). A similar study from a German hospital in 2020 found no significant changes in the prevalence of drug-resistant bacterial pathogens were seen, although virus-associated respiratory and gastrointestinal diseases significantly decreased because of public IPAC measures like contact and travel restrictions, distance rules, mandatory face masks, cancellation of mass events, and closures of day-cares, schools, restaurants and shops (23). A time series analysis from Japan using data from 2015 to 2020 found that the incidence of CRE showed the same trends as that over the previous 5 years, despite significant reductions in the incidence of other common infectious diseases which they attributed to community IPAC measures implemented for COVID-19 like wearing masks, handwashing, and avoiding crowded spaces (27). Researchers from Taiwan found that facial masking and social distancing likely had limited efficacy in reducing TB transmission and found no change in MDR-TB trends during the COVID-19 pandemic (39).

Hospital

Counter to the argument that COVID-19 compromised hospital IPAC programs (43), many studies examining hospital-associated infections reported that improved IPAC measures introduced during the COVID-19 pandemic corresponded with reduced AMR. A Portuguese study found enhanced IPAC measures did not reduce postoperative infection rates but did significant decrease the rate of drug resistant infections during this period (35). Studies from hospitals in Italy (15), Turkey (29), and Lebanon (6) also identified a significant reduction in multidrug resistant bacterial infection incidence attributed to pandemic-related infection prevention and control measures including improved personal protective equipment (PPE) (masking, face shields, or disposable gowns) and improved hand hygiene (hand washing and hand sanitizer use). A COVID-19 IPAC program in Mexico resulted in a significant reduction in multidrug-resistant *Pseudomonas aeruginosa* but no other AMR pathogens (18). A similar evaluation in Taiwan examined the impact of universal face masking of hospital staff and enhanced hand hygiene on hospital acquired infection incidence and found overall lower incidence density of multidrug resistant organisms, driven by a lower incidence of CRAB and VRE in 2020 compared to 2018 and 2019 (16). A study from Singapore that also evaluated the impact of a multimodal IPAC strategy designed for the containment of COVID-19 on hospital acquired infection rates found rates were mostly stable, but that hospital-wide MRSA acquisition rates declined significantly during the pandemic (17). A study from India looking at neonatal sepsis epidemiology, found lower incidence of resistant sepsis during lockdown than before or after (24). An interrupted time series from Italy (26) found that robust adherence to hygiene measures and distance restrictions in an ICU reduced the

transmission of multiple drug resistant pathogens and infections less frequently exhibited multidrug-resistant. A study from a hospital in Japan (28) which measured two drivers, both AMU and IPAC and found that while the use of hand sanitizers and antibacterial drugs tended to increase during COVID-19, the incidence of MRSA blood cultures (non-significantly) decreased in all departments.

Some hospital studies reported no change or increased AMR due to COVID-19 IPAC measures, including one from a hospital in Turkey (21) and an Australian single-hospital study of surgical patients (19). An Italian study found decreasing carbapenemase-producing *Klebsiella pneumoniae* trends in hospitalized patients (68). A single-hospital study from Japan found the incidence of VRE to be (non-significantly) higher in 2020 than 2018 and 2019, in spite of universal mask waring and increased hand sanitizer consumption in 2020 (76). A study from China found that MRSA detection increased with elevated concentration and frequency of disinfection during the pandemic (77).

Health system use and AMR burden

We identified four studies that considered the impact of COVID-19 driven changes in health system use on AMR burden (64–67). These studies found that changes to health system use during the COVID-19 pandemic including increased ICU admissions, reduced testing, and reduced health system access may be driving AMR, but additional studies are needed to substantiate these results.

Community

Three studies considered changes to resistant CAIs (64,66,67). As seen in Nigeria, for example, where incidence of rifampicin resistant tuberculosis rose exponentially in 2022 because of reduced testing during 2020 and 2021 (66) and in Western Siberia where reduced TB incidence was attributed to under-testing, reduced access to resources, and reduced detection rates (67). A study from the UK found community-acquired E. coli blood stream infection rates remained below pre-pandemic levels during COVID-19 waves but began to peak following lockdown easing in May 2020 and authors also found hospital-associated MRSA infection had the largest increase among all causative pathogens compared to pre-COVID-19 figures which they credited to increased numbers of critically ill patients and ICU overcapacity (64).

Hospital

An Italian study investigating impact of ICU patient numbers on AMR found a significant increase in resistance of *Pseudomonas* spp. to carbapenems and piperacillin/tazobactam and *Enterobacterales* spp. for piperacillin/tazobactam (65).

AMR emergence

Two studies considered the role of COVID-19 in contributing to AMR emergence or the emergence of new drug resistant strains of CAIs (71,72). One study considered impact of IPAC measures (71) and the other looked at AMU (72). No studies were identified that looked at the impact of health-system use on AMR emergence.

AMU and AMR emergence

A study of antidrug resistant genes from ambient waterways in India found a significant increase in *E.coli* antidrug resistance in 2020 during the pandemic compared to 2018, which they attributed to higher rates of AMU and thus pollution during the COVID-19 pandemic (72).

IPAC and AMR emergence

In India, religious mass bathing events attract millions of pilgrims from India and other countries each year and these events have been linked to increased drug resistant genes among river bacteria. Using pre-pandemic data from 2015 as a baseline, the study found the prevalence of genes associated with drug resistance decreased by 0.64-fold during a COVID lockdown in India (June 2020) suggesting the bacterial communities that were re-established during lockdown have lower prevalence of the gene families associated with drug resistance (71).

AMR transmission

Three studies considered the role of COVID-19 IPAC measures in reducing AMR transmission (68–70). All three studies investigated HAIs. No studies were identified that looked at the impact of AMU or health system use on AMR.

IPAC and AMR transmission

An Italian single-center study found significantly reduced horizontal transmission of carbapenemase-producing *Klebsiella pneumoniae* in hospitalized patients in 2020 compared to 2019 because of COVID-19 measures employed (68). Similarly a Danish study investigating the impact of IPAC measures set up to curb COVID-19 spread on VRE Eneteroccocus faecium outbreaks reported a 10-fold decrease in outbreak patients (69). An interrupted time series, multicenter analysis from Italy, however found no change incidence of colonization and infection with carbapenemase-producing *Enterobacteriaceae* and carbapenem-resistant *Actinobacter* before and during the pandemic (70).

Risk of bias assessment

The quality of non-randomized studies judged using the ROBINS-I tool ranged from an overall rating of “moderate” (2,14,30) to “serious” (3–6,8,10,13,15–17,20,21,23,25–29,32,34,36,63,64,66–69,77,78). Most studies were judged to be at serious risk of bias. For studies evaluated using the ROBINS-I tool, many studies failed to adjust for potential confounding factors, including time-varying confounding (*Appendix 3, Figure 1*). For interrupted time series designs, not all studies adjusted for the months or time of year that AMR was recorded. Selection bias was not a large concern in studies that used linked patient databases due to the inclusion of all available participant data in most cases, but several studies failed to adjust for varying follow-up times between participants. For interrupted time series designs, most studies did not provide rationale on what date was selected as the interruption point and what time was selected to begin follow-up for post-pandemic AMR monitoring. Reporting processes and sampling methodologies for obtaining antimicrobial resistant strains were poorly reported in many studies. Additionally, the proportion of missing outcome data/participants excluded for missing outcome data was also poorly reported across studies, making the potential effect of bias difficult to judge. Studies evaluated using the Newcastle Ottawa Scale (7,9,19,24,35) were judged to have moderate risk of bias (*Appendix 3, Figure 2*). The primary concerns noted were regarding the

representativeness of the exposed cohort, demonstration that outcomes of interest were not present at start of study, and the length of follow-up.

Equity: PROGRESS-Plus Framework

Most included studies did not collect data on PROGRESS-Plus factors. Twenty-one of the forty-eight studies (4,7,9,14,18–20,24–26,29–32,35–37,64–66,68) collected data on at least some PROGRESS-Plus characteristics. Four studies collected data on place of residence (7,20,31,36), one collected race, ethnicity, culture or language data (64), twenty-one collected gender/sex and personal characteristics associated with disability (e.g., age) (4,7,9,14,18–20,24–26,29–32,35–37,64–66,68) and sixteen collected information on time-dependent relationships (e.g., leaving the hospital or time to discharge, risk factors, or other instances where a person may be temporarily at a disadvantage) (7,9,13,14,18,19,24,25,29,30,32,35,64,65,68,70). No studies directly mentioned equity or social determinants of health.

DISCUSSION

Most national surveillance data reported significant reductions in AMU in 2020 driven primarily by decreases in community-prescribing. Whether, or for how long, these reductions will be sustained remains to be seen: more recent data from the US (57), Denmark (54), and England (58) suggest that some countries may already be experiencing a return to pre-COVID-19 levels of community prescribing or even higher. However, some countries, including Norway (52) and Canada (60) have not yet seen this rebound in community prescribing. Additional trends in community AMU may become apparent as 2022 data is released. International policy responses to COVID-19 and implementation of community IPAC measures such as lockdowns, physical distancing, travel restrictions, and masking varied widely. Differences in the implementation of these measures — as well as the timing and speed of their removal —may explain observed differences in community AMU trends between countries.

In contrast to AMU trends, AMR rates varied across priority pathogens and geographic, resource, healthcare, and community settings. These observed differences reflect that the COVID-19 pandemic has produced both positive and negative effects on AMR. For example, increased AMU and misuse in COVID-19 patients and reduced IPAC measures (e.g., staffing shortages, reduced access to PPE) may have increased AMR rates in some settings, while reductions in elective procedures and overall improvements in IPAC measures (e.g., face masking, improved hand hygiene) may have decreased AMR rates in others. These interacting, and conflicting effects may explain why the included studies did not find a consistent link between changes in AMU and changes in AMR. While other associations —including healthcare provisions due to reduced healthcare seeking, reduced secondary care referrals and GP testing, and reduced diagnostic capacity— have been hypothesized to affect AMR (57) we found insufficient evidence to substantiate the hypotheses.

Impact of drivers on AMR

The framework developed by Knight *et al.* provides an opportunity to assess the positive and negative effects of COVID-19 on AMR through the lens of AMU, IPAC, and health system use. Only looking at a single driver of AMR provides an incomplete picture and additional studies examining

interactions between drivers in different settings: hospital, community, and in the environment are needed.

AMU and AMR burden

Included studies found an increase in AMU in some hospital settings (e.g., ICU or COVID wards), decreases in other hospital settings (e.g., surgical wards) and decreases in community settings. Within the timeframe of these studies, researchers did not consistently find that changes to AMU resulted in changes to AMR rates. However, some national surveillance data does show increases in the rates of several priority pathogens, most notably in the US which observed a 15% increase in the rates of resistant hospital-associated infections in 2020, despite delayed or unavailable data for 9 of their 18 priority pathogens (57).

Inappropriate antibiotic use in milder COVID-19 cases is likely the major contributor to increased AMU in ICU hospital settings (79). Although many patients were in critical condition and developed secondary infections that required antibiotics, antibiotics were also widely used for mild cases of COVID-19. One review found about 75% of hospitalized COVID-19 patients admitted during the initial part of the pandemic (between March and October of 2020) received an antibiotic (45) and in countries such as Liberia and Ghana, prescribing guidelines recommended antibiotics for COVID-19 cases with mild or moderate symptoms (80). This unnecessary prescribing must be addressed in future pandemics through rapid publication and updates of AMU guidelines to prevent antimicrobial overuse and misuse and resultant AMR impacts.

Studies tracking environmental indicators of AMR offer an interesting perspective on the interactions between AMR drivers. Included studies from India found a reduction in AMR genes in rivers attributed to restrictive IPAC measures like lockdowns (71) and an increase in AMR genes in a different Indian river system attributed to increased AMU and environmental pollution during the pandemic (72). Interpreting each of these studies in isolation would provide an incomplete understanding of how environmental AMR emergence has potentially evolved in India during the COVID-19 pandemic. These two examples underline the need to examine driver interactions collectively — only examining IPAC would have suggested a reduction in AMR in this case while only examining AMU would have suggested an increase in AMR.

COVID-19 and IPAC measures

Community

The COVID-19 pandemic saw the unprecedented implementation of infection and prevention control measures (like physical distancing, lockdowns, and masking) in both community and healthcare settings. Although preventative measures such as mandatory face masking and physical distancing rules targeted the spread of COVID-19, they likely also contributed to reductions in airborne or droplet-transmitted respiratory diseases (34). For example, in New Zealand, IPAC measures like social distancing and restricting gathering sizes and travel changed health system use: ICU admission rates decreased by almost 40% in 2021 compared with the past 5 years (81). In Spain, gathering size restrictions and physical distancing measures coincided with the greatest reduction in AMU. Better community preventative measures across the board can be an important tool to mitigate transmission of resistant CAIs. Preventative measures such as physical distancing, contact and travel restrictions, no mass gatherings, and closures of day cares, schools, restaurants, and the retail sector may explain reported reductions in gastrointestinal disease, spread of STIs, and other diseases (23,27). Most of the studies identified in this review

focused on hospital settings in high-income countries, so studies from community settings and low-income countries are needed to fill these knowledge gaps. While many of these preventative measures could not be replicated outside of an emergency, some community IPAC measures such as improved hand hygiene and mandatory masking in certain settings may be feasible for AMR mitigation. Broad community IPAC measures should be carefully reviewed to identify any unintended and inequitable consequences – for example, lockdown measures during the COVID-19 pandemic made it difficult for some communities to access key resources such as sexually transmitted infection prevention, testing and treatment services, as well as harm reduction and substance use and treatment services.

Hospital

While some types of resistant hospital-associated infections appear to have increased during the COVID-19 pandemic (82,83) others have decreased (82). The anticipated reasons for both can be informative as countries navigate ongoing challenges in their healthcare systems. Improved IPAC measures implemented in hospitals because of COVID-19 (such as improved hand hygiene, PPE and masking) may have contributed to reduced transmission of HAIs between patients (68,69). However, the reduced transmission of HAIs may also be attributed to changes in health system use during the pandemic: restrictions saw fewer patients in secondary care and reduced elective surgical interventions (84). It is unlikely the reductions seen during acute phases of the COVID-19 pandemic would be replicable outside a pandemic, however, focusing on achievable targets such as improving IPAC would likely result in long term benefits for AMR and other infections. The COVID-19 pandemic also underlined the secondary effects of critical gaps in resourcing of healthcare systems, such as lack of PPE and staffing shortages. These factors may have negatively affected antimicrobial stewardship (AMS) and the success of IPAC measures (85). Given these factors are likely to remain present beyond the attention of the COVID-19 pandemic, their contributions to AMR must continue to be monitored.

COVID-19 and health system use

Health system use changed significantly during the COVID-19 pandemic through increased ICU admissions and efforts to increase ICU capacity at the beginning of the pandemic, changing health-seeking behaviour, raising the threshold for seeing a general practitioner for symptoms, and shifting in-person appointments to telemedicine ones (86) all of which may have also impacted AMR. However, we found little research evidence examining these factors as a driver of AMR. Other pandemic related challenges, including limited capacity to provide service delivery and diagnosis for community-acquired diseases like human immunodeficiency virus (HIV), tuberculosis (TB), malaria, and sexually transmitted infections (STIs), as well as reduced global vaccination coverage (87–89) may have negatively affected AMR. Decreases in availability and access of these resources is well documented but additional evidence is needed to clearly link these challenges to AMR. For example, the World Health Organization estimated that because 1.4 million fewer people received care for tuberculosis (TB) in 2020 than in 2019 (90), there may be significant repercussions for AMR given that TB is the greatest contributor to global AMR burden (41).

Equity impacts of COVID-19

The COVID-19 pandemic compounded existing equity challenges, such as limited or reduced access to vaccinations, reduced access to laboratory materials, and reduced staff availability—all

of which may be driving inequitable AMR transmission (44,46). The COVID-19 pandemic has also inequitably impacted the ability of countries to develop and maintain strategies to address and mitigate AMR (81). These impacts were particularly felt by low- and middle-income countries: high-income countries, overwhelmed by COVID-19, reduced their capacity to support AMR partnerships and reduced funding to programs in low- and middle-income countries (46). Since AMR is a borderless threat, all countries must share the responsibility of addressing it.

Around the globe, COVID-19 has disproportionally affected people on the basis of age, income (91), race or ethnicity(92), gender and sexual orientation (93), and migrant status (94). Many of these groups have also been identified as being at higher risk of AMR(95) and many of these populations faced barriers to access testing and other services due to COVID-19. In Canada, for example, COVID-19 and related measures compromised access to sexually transmitted and blood borne infection (STBBI) prevention, testing and treatment services, as well as, harm reduction services and substance use and treatment services for key populations at higher risk of AMR-STBBIs, such as men who have sex with men and people who use drugs (96). Addressing the existing research gap on equity and the social dimensions of COVID-19 and AMR will be vital for designing future pandemic strategies that address inequity. More targeted research on the effects of diminished capacity in HICs to support AMR partnerships, AMS initiatives, and funding to LMICs should be a priority to inform future pandemic preparedness and emergency management.

Limitations

This was a rapid scoping review with screening conducted by a single reviewer which increases the risk that relevant studies may be missed, however a second reviewer validated 30% of single reviewer screenings. Most studies included in this review were also observational single-site studies. Risk of bias assessment found many of the included were assessed as at a “serious” risk of bias, which may affect our certainty in data synthesized from these studies. Future high-quality research with clear reporting and appropriate adjustment for confounding factors is required to increase our confidence in the conclusions drawn from these studies.

Methodological and analytical heterogeneity across studies presented challenges to establishing a rigorous comparative assessment. The scientific community researching pandemics and the effects of the COVID-19 pandemic on other pandemics and healthcare systems should develop standardized methods for reporting AMR trends (using existing methodological and analytic expertise) that account for potential biases like the reduced reporting and testing seen during COVID-19.

Most research to date has relied on data collected in 2020 during the early stages of the COVID-19 pandemic. Later studies may be forthcoming, or this may reflect a change in research focus during the later stages of the pandemic. Data from later stages of the pandemic are likely to show different results based on changes in AMU, IPAC practices, and health system access as governments relaxed the restrictions and public health measures that were imposed in 2020.

Finally, reduced laboratory capacity and a decrease in the total number of tested patients during the pandemic (due to reduced referrals and testing) may be underestimating reported AMR trends for most included papers. The US, the EU, England, and Norway all reported a decrease in numbers of culture and sensitivity tests performed during the COVID-19 pandemic compared to previous years as a potential confounder to their reported AMR trends. This reduction in cultures is

likely due to a reduced number of elective procedures or chronically ill patients being admitted, the higher threshold of infection needed during COVID-19 for patients to seek medical care and reduced number of referrals provided by general practitioners (97). Similarly in many countries, laboratory capacity was overwhelmed by COVID-19 testing resulting in reduced reagents and consumable availability and staff availability to perform cultures (46,98).

Key research gaps include a complete lack of evidence on the impact of COVID-19 on health-system use as a driver of AMR emergence or transmission, as well as a lack of evidence on AMU as a driver of AMR transmission (*Figure 1*). More studies investigating all three drivers, AMR emergence and transmission are needed. Most studies focused on hospital settings in high-income countries, so studies from community settings and low-income countries are needed to fill these knowledge gaps. Finally, only a single study looked at the impact of any of the three drivers on fungal resistance (65) despite the fact that there have been multiple reports of increased antifungal use (99) and selection for fluconazole resistant *C. parapsilosis* during the COVID-19 pandemic (100). Antifungal resistance is chronically neglected as a threat to public health even though global mortality rate for fungal diseases is greater than that for malaria or breast cancer (101). Investigations focusing on fungal resistance are needed.

POLICY CONSIDERATIONS AND IMPLICATIONS

Antimicrobial use (AMU) and antimicrobial resistance (AMR) surveillance data, which in most countries lags 18-24 months, are already out of date and reflect an earlier phase of the COVID-19 recovery. Population research data, which typically relies on this surveillance data, lags even further. As such, it is possible that the AMU and AMR trends reported from the US last year — showing a rebound in antimicrobial prescribing and rising resistance rates — may be a signal of future trends for countries that removed pandemic restrictions more slowly. Many states in the US lifted their pandemic-related restrictions by the summer of 2021 (102) — earlier than many other countries (103). In other words, given that Canada lifted restrictions later than the US, we cannot operate from the assumption that Canada's 2021 data, which suggests AMU is still decreasing, is still accurate in the spring of 2023. Acting now to reinforce antimicrobial stewardship may be critical to avoiding the scale of increased AMU witnessed in the US.

Included below are additional policy considerations based on the results of this scoping review and our analysis for Canada:

We need improved AMR surveillance systems.

Effective and timely policy decisions require improved AMR surveillance systems. Improving Canadian surveillance systems should be a priority to allow policymakers to draw from real time evidence when making decisions. Improved surveillance systems will ensure robust data collection during future pandemics, and that AMR trends are identified in an appropriate timeframe. Most studies included in this report contain data from 2020 or 2021, meaning policymakers are using data that is already outdated and reflects a fundamentally different stage of the COVID-19 recovery.

Rapid identification of AMR trends will also support the development of antimicrobial stewardship programs and guidelines that ensure antimicrobial stewardship is maintained across healthcare

settings. Our findings suggest conflicting forces may be acting on AMR in different settings. Additional data will help policymakers target settings with potential higher contributions for stewardship activities. Surveillance systems should be strengthened to ensure adequate data is collected to address equity issues affecting AMR.

While further comparative analysis of national AMR trends can be useful, Canada needs targeted research to understand the context-specific conditions of the trends *as they presented in this country* and the underlying conditions that were exacerbated by the COVID-19 pandemic and our responses to it. Developing this baseline understanding is vital because future pandemics will not necessarily mimic trends observed during the COVID-19 pandemic. Robust surveillance systems are needed to identify trends and to develop successful mitigation and stewardship strategies for future pandemics.

We must consider AMR in pandemic preparedness.

Policymakers working in pandemic preparedness must ensure that AMR is addressed. The impacts of the COVID-19 pandemic on AMU, infection prevention and control (IPAC), and the use of healthcare and related systems have had profound implications for AMR. We should expect that future pandemics will also impact and be impacted by AMR.

Lessons learned from the COVID-19 pandemic may be useful for slowing AMR outside of the pandemic response. For example, IPAC programs implemented during COVID-19 had significant impacts on susceptible and resistant community-associated infections (CAIs). Policymakers should preserve these programs in settings where they can and preserve the capacity, resources, and infrastructure needed to use them for future pandemics. Reduced access to testing and health services because of the COVID-19 pandemic negatively impacted AMR. Policy that ensures these services can be maintained during future pandemics—while governments address the acute stages of a future pandemic—will be essential.

We must develop Antimicrobial Stewardship (AMS) programs that evolve alongside changes to health system use.

Policymakers can draw important lessons from the significant decrease in community AMU observed at the start of the pandemic by implementing stewardship activities that target outpatient and community prescribing. Community prescribing constitutes the largest proportion of AMU in most countries, including Canada. Interventions addressing AMU in this setting are key to preventing community prescribing from rebounding to above pre-pandemic levels as has already been reported in the US. AMS programs focused on primary care, such as educational programs and feedback targeting physicians, electronic health record interventions, delayed prescriptions, development of guidelines and restricted reimbursement are all effective in reducing community prescribing (104,105).

As of spring 2023, pharmacists will have prescribing rights for minor ailments in all provinces; AMS programs should also include them in audit and feedback programs, as well as community stewardship initiatives, and pledge programs (106,107).

We need to build stronger links between IPAC and AMS programs.

IPAC measures showed a consistent impact on AMR trends with both heightened community and hospital IPAC measures contributing to decreased AMR. Community IPAC measures like social distancing, face masking and lockdowns were especially associated with reduced numbers of susceptible and resistant CAIs.

Policymakers responsible for AMS programs must ensure IPAC measures are addressed; and if a gap exists, consider what measures are needed to address it. IPAC measures are often unaddressed by AMS programs even though strong IPAC measures are one of the most cost-effective approaches for controlling AMR (108). Although the WHO's core components for IPC programs are a useful starting point for national and facility IPAC programs (109), IPC programs tailored to specific settings have the best efficacy against AMR spread (110).

We need to determine the inequitable impacts of the pandemic on AMR.

Although COVID-19 has impacted access to community infection prevention measures that may reduce AMR infections in key populations such as men who have sex with men and people who inject drugs, few research studies have collected data on PROGRESS-Plus factors which limits our ability to assess the extent to which the COVID-19 pandemic exacerbated AMR-related inequalities.

Surveillance systems must collect data on socioeconomic, sociodemographic, social and structural determinants of health to allow us to identify and address the potential inequitable AMR impacts including impacts on AMR prevention, AMR burden, care, and treatment for AMR infections. Identifying populations with inequitable COVID-19 and AMR effects will allow the development of community-led prevention and health programs, policy initiatives and stewardship programs.

CONCLUSIONS

The COVID-19 pandemic has changed the landscape of AMR in ways we still do not fully grasp. We know that COVID-19 impacted AMU, IPAC measures, and health system use differently across countries in many ways, impacting AMR emergence, transmission, and burden. This scoping review synthesized current literature and national AMR surveillance data results. These results show substantial variation in the reported impact of COVID-19 on AMR, which seems expected given the variation in response to COVID-19 that was seen across countries and settings. Most results from the period of the COVID-19 pandemic are still preliminary and as additional data becomes available longer-term impacts and trends in AMR may also be identified. Additional research, however, especially high-quality studies, is needed to fully elucidate the impact of COVID-19 driven changes in AMU, IPAC, and health-system on AMR to ensure evidence-informed AMR policy solutions.

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APPENDIX 1

Table 1. Overview of national surveillance data on antimicrobial use trends, trends in key pathogen-antimicrobial combinations and the potential contributors to these reported trends during the COVID-19 pandemic

Country, publication year	Data collection interval	Antimicrobial use (AMU) trends	Antimicrobial resistance (AMR) trends in key pathogen-antimicrobial combinations	Name of report
Canada, 2022	2017 to 2021* (AMU trends) 2016 to 2020 (AMR trends except GC rates which are from 2016 to 2019)	Between 2017 and 2021, a decrease in antimicrobial consumption was observed in all Canadian jurisdictions, most pronounced during the COVID-19 pandemic (2019 to 2021). In 2021, overall antimicrobial consumption in the community sector remained below pre-pandemic levels. Antimicrobial prescribing in the community during the first 8 months of COVID-19 pandemic was lower than previous years due to pandemic-driven changes in health system use and remain lower the pre-pandemic levels.	The incidence of MRSA associated BSI is shifted from hospital-associated infections (down by 2.3%) to community-associated infections (up by 75.0%). Both hospital and community associated VRE BSI in hospitalized patients appeared to have plateaued during the pandemic. Rate of hospital-associated CPE infection in hospitalized patients appears to have decreased during COVID-19. Following a sustained decrease from 2016 to 2019, hospital-associated rates of CDI increased in 2020 during the pandemic. Multidrug resistant vaccine-preventable invasive *Streptococcus pneumoniae* diseases rates are increasing. Incidence of GC continues to increase in Canada (2016-2019), while TB rates remain stable.	Canadian antimicrobial resistance surveillance system report 2022
United States, 2022	2019 to June 14, 2021*	A significant decrease in community AMU was noted during the first year of the pandemic. Antibiotic use in the community dropped significantly in 2020 but rebounded in 2021 to be 3% higher than pre-COVID-19 levels. Antibiotic use in nursing homes spiked during the pandemic but was 5% lower than 2019 in 2021, which may be due to fewer nursing home residents. Reduced ability to follow IPAC measures as a result of COIVD-19 pandemic may have contributed to the increase in antimicrobial-resistant hospital infections. More and sicker patients during the pandemic may have also contributed. Long-term care facilities were significantly affected by COVID-19 outbreaks, burdens, and staffing shortages. Health-seeking behaviour and access to outpatient clinics was limited.	A 15% overall increase was noted key hospital-acquired pathogen-antimicrobial combinations including: carbapenem-resistant *Acinetobacter,* extended-spectrum beta-lactamase- producing Enterobacterales, and vancomycin-resistant *Enterococcus.* Antifungal-resistant *Candida spp.* increased by 26%. There is a lack of data available on community-spread pathogens (e.g., drug-resistant gonorrhea).	CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2022.
United Kingdom, 2021 to 2022	2017 to 2021*	Total antibiotic consumption had been decreasing prior to the COVID-19 pandemic (4.3% reduction between 2017 and 2019). A sharp decrease was seen during the COVID-19 pandemic, with consumption declining by 10.9% between 2019 and 2020. Data remained similar from 2020 to 2021, with only a slight further decline in consumption of 0.5%. Antibiotic prescribing continued to be highest in general practice (72.1%), with a marginal reduction seen in this setting.	The overall burden of antimicrobial resistance (AMR), decreased by 4.2% between 2017 and 2021, although the trend varied by key pathogen. The AMR burden in BSI had been steadily increasing since 2017 before falling in 2020. This decline has been maintained in 2021 and remains predominantly driven by the reduction in the incidence of E. coli BSI. Between 2017 and 2021 there was a slight increase in rate of BSI caused by key pathogens. However, rates of Escherichia coli and Streptococcus pneumoniae	English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2021 to 2022

		Hospital inpatient, hospital outpatient and other community settings have shown an increase in consumption between 2020 and 2021. This may be a result of an increase in routine healthcare activities following the pandemic. Consumption in dental practices has declined (-7.1%) following the large increase seen during 2020, although it has not returned to pre-pandemic levels.	sustained the decline seen in 2020 into 2021; most likely due to the multifactorial effects of the SARS-CoV-2 (COVID-19) pandemic. The decrease in BSI was likely due to multifactorial effects of the SARS-CoV-2 (COVID-19) pandemic such as reduction in person-to-person contact and improvements in IPAC and reduced international travel. Reduced healthcare provision may have also contributed. Increased in-patient antibiotic prescription is likely due to more acutely ill patients being admitted while elective procedures were cancelled.	
Denmark, 2022	2012-2021*	Total antimicrobial consumption in Denmark was the same in 2021 as in 2020 but 18% lower than 10 years ago in 2012. The drop in total antimicrobial consumption observed seems to show that the lower levels of consumption observed during the COVID-19 pandemic in 2020 continued. Analysis of monthly antimicrobial consumption data showed that consumption increased from August 2021, i.e., following the lifting of almost all COVID-19-related restrictions, to similar levels seen in corresponding months in 2018 and 2019.	The total number of invasive infections (blood or cerebrospinal fluid isolates) caused by the surveyed bacteria has been increasing steadily over the past ten years. *Escherichia coli* caused about 49% of bacteraemias with *Staphylococcus aureus* being the second most causative organism with 20%. Resistance in K. pneumoniae has been decreasing over the last ten years. Resistance levels in E. coli are decreasing with the notable exception of piperacillin-tazobactam resistance that has increased over the last four years. Carbapenem-resistance is still very low, but increasing numbers of isolates are observed. In 2021, 16% more CREs were identified compared to 2020. The percent of vancomycin-resistant E. faecium isolates increased to 10.2% after being stable at 9.4% since 2018. The number of S. aureus bacteraemias has increased continuously over the past ten years, a 75% and 4.8% increase compared to 2012 and 2020, respectively. The number of MRSA regardless of clinical status (infection or colonisation) dropped during the COVID-19 pandemic, presumably due to related restrictions.	Summary DANMAP 2021: Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark
Australia, 2022	2015 to April 2020 (AMR data), November 2015 to October 2020 (AMU data)	The number of systemic antibiotic prescriptions decreased from 2.3 million in March 2020 to 1.4 million in April 2020 – a fall of 40%. Longer term data is not available yet. The COVID-19 pandemic may have affected the reporting and analysis of results of AMR data through changes in access to community-based health care, hospital admission patterns and the range of hospital services offered such as outpatient clinics and elective surgery, antimicrobial prescribing practices, and movement of people into and within Australia.	Overall, a mild decrease in ESBL *E. coli* from all settings was reported between 2020 and 2021. During COVID-19 to 2021 there was an increase in ESBLs in aged care home residents.	Fourth Australian report on antimicrobial use and resistance in human health: AURA 2021 Australian Passive Antimicrobial Resistance Surveillance: Third-generation cephalosporin resistance in *Escherichia coli* and *Klebsiella pneumoniae*: prevalence of extended-spectrum β-lactamase (ESBL) phenotype

Korea, 2021	March 2018 to September 2021 (AMU data), August 2016 and July 2020 (AMR data)	Overall, a 14-30% reduction in antibiotic use adjusting for respiratory tract infections was reported, with the largest reduction seen in pediatric populations. The reduction in antibiotic use may be due to reduced respiratory infections as a result of stringent public health interventions including social distancing measures. Changes in health-seeking behavior during the outbreak in South Korea may have reduced the propensity of individuals to seek care for symptoms consistent with upper respiratory symptoms that were not COVID-19.	National surveillance data is not yet available. A study looking at incidence of multidrug resistant infections from 2018 to 2021 in 4 hospitals found that during the COVID-19 pandemic the prevalence of hospital-associated infections increased (including MRSA, VRE, CRE, and CRPA).	Sukhyun Ryu, Youngsik Hwang, Sheikh Taslim Ali, Dong-Sook Kim, Eili Y Klein, Eric H Y Lau, Benjamin J Cowling, Decreased Use of Broad-Spectrum Antibiotics During the Coronavirus Disease 2019 Epidemic in South Korea, *The Journal of Infectious Diseases*, Volume 224, Issue 6, 15 September 2021, Pages 949–955. Jeon, K.; Jeong, S.; Lee, N.; Park, M.-J.; Song, W.; Kim, H.-S.; Kim, H.S.; Kim, J.-S. Impact of COVID-19 on Antimicrobial Consumption and Spread of Multidrug-Resistance in Bacterial Infections. Antibiotics 2022, 11, 535.
EU, 2022	2011 to December 2020	Between 2014-2020, a 23% decrease in the total consumption of antibiotics was observed for the EU/EEA, with most of this decrease happening between 2019 and 2020. Most EU countries reported decreases in antibiotic consumption for both the community and the hospital sector, with a larger decrease in community sector. However, if the total number of hospitalised patients decreased the apparent decrease in hospital antibiotic consumption expressed in 'defined daily doses (DDD) per 1 000 inhabitants per day' could actually become an increase, if expressed in 'DDD per 100 bed days'. Interpret changes with caution. Interventions to curb the COVID-19 pandemic affected antibiotic consumption including infectious disease epidemiology (decreases in groups of antibiotics prescribed for respiratory infections and to the youngest age groups); non-pharmaceutical interventions (restrictions on movement, physical distancing, respiratory etiquette, hand hygiene and travel restrictions), reduced use of and difficulties in accessing primary care services, leading to a decrease in inappropriate prescribing for milder and self-limiting infection. COVID-19 also put pressures on hospitals (demand for intensive care beds, fewer elective surgery or chronic diseases admittances).	For all bacterial species under surveillance by the European Antimicrobial Resistance Surveillance Network (EARS-Net), except for *Streptococcus pneumoniae*, the number of reported bacterial invasive isolates increased in 2020 compared to 2019 (Including *Acinetobacter spp*. and *Enterococcus faecium)*. For *S. pneumoniae,* the number of reported invasive isolates decreased by 44%, with large decreases of 20% or more being reported in all but one EU/EEA country. Reduced testing and reduced laboratory capacity may affect AMR percentages and make the observed changes in AMR percentages difficult to interpret.	Antimicrobial Resistance in the EU/EEA: A One Health Response Antimicrobial resistance surveillance in Europe 2022 (2020 data)

Norway, 2021	2013 to 2021*	In 2021, the total sales of antibacterial agents for use in humans decreased. Since 2012 there has been a decline in total antibiotic use of 33%. Reduction in antibiotics may be due to reduced use of antibiotics indicated for respiratory tract infections in primary care	There was a mild reduction in 2021 and 2020 in MRSA infections. Extended spectrum beta-lactamases (ESBL) prevalence including of E. coli and Klebsiella spp. has decreased. The number of patients with carbapenemase-producing P. aeruginosa remained unchanged whereas Acinetobacter spp. notifications decreased. The proportion of MDR tuberculosis isolates increased in 2021. COVID-19 IPAC measures may have decreased the incidence of infections, and the threshold for seeing a general practitioner for symptoms of infections may have been raised. Travel restrictions may have also critically reduced the number of travel-associated infections.	NORM/NORM-VET 2021. Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway. Tromsø / Oslo 2022. ISSN:1502-2307 (print) / 1890-9965 (electronic).
Japan, 2022	2019 to 2020	Reported a reduction in antimicrobial sales in 2020 compared with preceding years (20% reduction).	Incidence of *Streptococcus pneumoniae* dramatically decreased from April 2020 onward, probably due to stringent non-pharmaceutical interventions against COVID-19. The incidence of hospital-associate *S. aureus* and *E. coli* did not show a change after the start of the COVID-19 pandemic. Decrease in the incidence of microbial infections in 2020 compared with 2019 may have been driven primarily by a reduction in bed occupancy.	Endo A, Asai Y, Tajima T, Endo M, Akiyama T, Matsunaga N, Ishioka H, Tsuzuki S, Ohmagari N. Temporal trends in microbial detection during the COVID-19 pandemic: analysis of the Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE) database. Journal of Infection and Chemotherapy. 2022 Sep 14.

*Data is available from 2021 on AMU

Hospital-associated infections (HAI), community-acquired infections (CAIs) central-line–associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), bloodstream infections (BSI), Vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenemase-producing *Klebsiella pneumoniae* (KPC-KP), extended-spectrum beta-lactamase (ESBL) , carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), fluconazole-resistant *Candida parapsilosis* (FRCP), *Neisseria gonorrhoeae* (GC), *Clostridial difficile* infections (CDI), MDR (multidrug resistant)

Table 2. Characteristics of studies included in analysis of the impact of COVID-19 on AMR.

Author, Year	Country or region	Type of study	Brief description of study itself	Dates of data collection	Setting	Pathogen type(s) reported, measure of AMR reported and change to AMR	Reference
Alao 2022	Nigeria	Retrospective observational	Determine the trends in rifampicin-resistant TB between the pre-COVID and COVID era in a resource-constrained setting.	2016 - 2022	Community	The annual prevalence of Mycobacterium TB rose from 2016 to 2019, followed by a decline in 2020 and in 2022 (COVID-19 era) (p = <0.001). The incidence of RR was higher during pre-COVID-19 than the COVID-19 era (p = <0.001). The incidence of RR-TB declined substantially from 2016 to 2021 but rose exponentially in 2022.	(66)

Bauer 2022	United States	Retrospective cohort analysis	This multicenter, retrospective cohort analysis from 271 US facilities evaluated rates of AMR events, before (1 July 2019–29 February 2020) and during (1 March 2020–30 October 2021) the SARS-CoV-2 pandemic.	2019 - 2021	Hospital	AMR rates per 1000 admissions among community-onset infections during the pandemic were lower versus pre-pandemic levels (26.1 vs 27.6 p<.0001); whereas AMR rates for hospital-onset infections were higher (8.6 vs 7.7; P<.0001), driven largely by SARS-CoV-2–positive admissions. Overall AMR rates did not substantially increase from pre-pandemic levels.	(7)
Bentivegna 2021	Italy	Retrospective case–control	Examined the incidence of MDR infections while using pandemic-related preventive measures (from 2017 to 2020) in St. Andrea Hospital, Rome.	2017 - 2020	Hospital	A significant reduction in the incidence of total MDRO infections was observed during the pandemic compared to in pre-pandemic years ($p < 0.05$). Significantly higher incidence of MDR bacterial infections in COVID-19 departments compared with other medical departments.	(15)
Bork 2020	United States	Interrupted time series	Examined MDR gram-negative acquisition relative to COVID-19 at an academic hospital.	2019 - 2020	Hospital	MDR gram-negative incidence did not differ significantly during the 2020 post-onset period compared to the same period in 2019.	(5)
Bussolati 2022	Italy	Retrospective observational	Compared HAIs and antibiotic use to a cohort of acute respiratory failure (ARF) patients admitted to the ICU the year before the pandemic during the same period.	February 2019 - April 2020	Hospital	Found a comparable incidence of HAIs 62.2% vs. 65.8%, p = 0.74) and MDR isolations (44.4% vs. 36.8% p= 0.48) in the two groups. The year of ICU admission was not independently associated with an increased risk of developing HAIs (OR = 0.35, 95% CI 0.16–1.92, p = 0.55).	(9)
Chamieh 2021	Lebanon	Retrospective observational	Analyzed the trends of the overall isolates, the antimicrobial susceptibilities of blood isolates (BSI), BSI, CRE BSI, and restricted antimicrobial consumption as daily-defined-dose/1000 patient-days from 1 January 2015-31 December 2020.	January 2015 - December 2020	Hospital	The isolation density of CRE BSI/1000 patient-days decreased by 64% from 2019 to 2020, VRE-*E. faecium* BSI decreased by 34%. There was a significant decrease of 80% in antibiotic isolates (p-value < 0.0001).	(6)
Chen 2021	China	Retrospective observational	Examined the effect of the COVID-19 prevention and control requirements (implemented May 2020) on HAI and CAI in China during 2018, 2019, and 2020.	2018 - 2020	Community and hospital	Analysis of HAI by MDROs indicated MRSA infections were more common in 2020 than in 2018 and 2019 (both $P < 0.05$), but there were no significant changes in infections by VRE, CRE, CRAB, or CRPA.	(14)

Cheng 2022	Hong Kong	Retrospective observational	Data of blood cultures of patients admitted to public hospitals collected by the Hospital Authority in Hong Kong for the last 10 years, were analyzed.	2012 - 2021	Community and hospital	Mean episodes of community-onset bacteremia due to MRSA per year was higher during two pandemic years (2020, 2021) then pre-pandemic years (2012-2019) (1154 vs. 1288, $p = 0.001$).	(2)
Dapper 2022	Germany	Retrospective observational	Analyzed the impact of infection control measures implemented in public (e.g., contact and travel restrictions, distance rules, mandatory face masks, cancellation of mass events, closures of day-cares, schools, restaurants and shops, changes in demand or access to health care) on infectious diseases in Marburg University Hospital from January 2019 to June 2021.	June 2019 - June 2021	Community and hospital	Significant changes were detected for virus-associated respiratory and gastrointestinal diseases. No significant changes were detected in the prevalence of susceptible and drug-resistant bacterial pathogens. In particular, the detection rates of MRSA isolates or MDR and extended drug resistant (XDR) bacteria remained constant, although the consumption of hand disinfectants and protective equipment increased.	(23)
de Carvalho Hessel Dias 2022	Brazil	Retrospective observational	The incidence density trend of the carbapenem-resistant Gram-negative bacteria was analysed in device-associated infections and antimicrobial consumption in 99 critical care facilities in a low/middle-income country, between January 2019 and December 2020.	January 2019 - December 2020	Hospital	CRAB per 1000 patient-days increased in 2020 and this finding had a strong positive correlation with the incidence density of COVID-19. Polymyxin consumption also increased in 2020 but without significant correlation with CRAB or COVID-19 incidence density, presumably due to empirical and untargeted prescribing.	(8)
Dutta 2022	India	Retrospective observational	We compared the hospital-based epidemiology of neonatal sepsis after the coronavirus disease 2019 lockdown (LD) versus historical epochs and the LD period versus phases of unlocking.	March 2019 - September 2020	Hospital	Groups pre-LD and corres-LD had higher proportion of MDR/extreme drug resistance/pan drug resistance sepsis than LD [77%, 77% and 44%, respectively (P values of both groups vs. LD = 0.01)]. From LD 1.0 to unlock 4.0, there were fewer episodes of MDR sepsis. Lockdown favorably impacted the epidemiology of neonatal sepsis in a hospital setting, with less *A. baumannii* and MDR sepsis, which persisted during unlocking.	(24)

Endo 2022	Japan	Retrospective observational	Assessed the temporal changes in AMR-related metrics before and after the start of the COVID-19 pandemic.	January 2019 - January 2021	Hospital	Found that an apparent decrease in the incidence of microbial infections in 2020 compared with 2019 may have been driven primarily by a reduction in bed occupancy (although the incidence showed a constant or even slightly increasing trend after adjusting for bed occupancy). The incidence of *S. pneumoniae* dramatically decreased from April 2020 onward, probably due to stringent non-pharmaceutical interventions against COVID-19. AMU showed a weak increasing trend, while the use of hand sanitizer increased by about 50% in 2020 compared with 2019.	(13)
Fukushige 2022	Japan	Retrospective observational	Investigated the burden and patient characteristics of hospital-associated VRE infections in 2018, 2019 and 2020, when multiple preventive measures for COVID-19 were taken.	2018 - 2020	Hospital	The incidence density of both VRE HAIs and VRE hospital-associated bloodstream infections (HABSI) did not change significantly but was higher in 2020 than that in 2018 and 2019. This was in spite of universal mask waring and increased consumption of 75% alcohol in 2020. Increased prescriptions of broad-spectrum cephalosporins might partially explain the increase of VRE infection.	(25)
Gaspari 2021	Italy	Interrupted time series	Investigated whether behavioral precautions adopted during the COVID-19 pandemic also influenced the spreading and MDR of *E. faecium, S. aureus, K. pneumoniae, A. baumannii* [AB], *P. aeruginosa, Enterobacter spp. and E. Coli,* [EC] (ESKAPEEc pathogens) among IICU patients during the COVID-19 period and in the corresponding pre-pandemic period.	June 2019 - February 2021	Hospital	These findings suggest that a robust adherence to hygiene measures with human contact restrictions in a COVID-19 free ICU might also restrain the transmission of ESKAPEEc pathogens. In comparison with the pre-pandemic period, no AB was recorded during COVID-19 period, ($p = 0.017$), while extended spectrum beta-lactamase-producing EC infections significantly decreased ($p = 0.017$). Overall, the ESKAPEEc isolates during pandemic less frequently exhibited MDR ($p = 0.014$).	(26)
Gisselø 2022	Denmark	Prospective observational	Outbreak data set were collected prospectively from April 2, 2014, to August 13, 2020 on VRE *E. faecium* at Copenhagen University Hospital Bispebjerg, Denmark.	2014 - 2020	Hospital	When comparing the first 5 months of the COVID-19 pandemic with the corresponding period in 2019, there was a 10-fold decrease in VRE *E. faecium* outbreak patients and median outbreak duration decreased from 56 to 7 days (88%).	(69)
Guven 2021	Turkey	Retrospective observational	Evaluated the nosocomial infection rates over the first 3 months of the COVID-19	2019 - 2020	Hospital (oncology ward)	The rate of nosocomial infections caused by MDR bacteria was similar between periods ($p = 0.677$).	(21)

			compared to the same time frame of the previous year.				
Hibiya 2022	Japan	Interrupted time series	Examined the incidence of common infectious diseases in Japan during the COVID-19 pandemic.	2015 - 2020	Community and Hospital	CRE, exanthema subitum showed the same trend as that over the previous 5 years. A time-series of disease counts of common infectious diseases and COVID-19 found the weekly number of cases of measles, rotavirus, and several infections transmitted by droplet spread, was negatively correlated with the weekly number of cases of COVID-19. Activity of influenza and rubella was significantly lower starting from the second week in 2020 than that in 2015–2019. Only legionellosis was more frequent throughout the year than in 2015–2019.	(27)
Imoto 2022	Japan	Retrospective observational	Investigated the effects of COVID-19 on daily medical practices at a tertiary hospital in Japan by comparing the use of hand sanitizers, the detection of bacteria from blood cultures, and the amount dose of antibacterial drugs used for one year before and after COVID-19 admissions began.	April 2019 - March 2021	Hospital	The use of hand sanitizers increased by 1.4–3 times during the year after COVID-19 admissions began; the incidence of MSSA and all *S. aureus* detected in blood cultures reduced in all departments. No decrease was observed in the usage of all antibacterial drugs; rather, the usage of all antibacterial drugs tended to increase in all departments. No significant change was observed in the detection of drug-resistant bacteria and the trends of antibacterial drug use.	(28)
Ipek 2022	Turkey	Retrospective observational	Investigate the change of nosocomial infection factors in equivalent historical periods in pediatric patients before and during the pandemic in the pediatric intensive care unit. Hand hygiene compliance rates of healthcare workers were evaluated.	April 2019 - September 2020	Hospital	During the pandemic, there were decreased cases of *K. pneumoniae* while *P. aeruginosa, E. faecium*, and *E. faecalis* were not seen. Prior to the pandemic, the hand hygiene compliance rate was 94.83%, and during the pandemic, it was found to be 99.44%.	(29)
Jani 2021	India	Retrospective observational	Examined the impact of lockdowns and travel restrictions on changes in antibiotic-resistant strains of bacteria the Godavari River in India.	2015 - 2020	Community	Functional profiling found a reduction in infection and drug resistance genes by−0.71-fold and−0.64-fold, respectively.	(71)

Jeon 2022	South Korea	Retrospective observational	Examined the prevalence of MDR bacteria during the COVID-19 pandemic (March 2020 to September 2021) compared to in the pre-pandemic period (March 2018 to September 2019) in four university hospitals.	2018 - 2021	Hospital (ICU and wards)	The prevalence of MRSA (4.7%), VRE (49.0%), CRE (22.4%), and CRPA (20.1%) isolated in clinical samples from the ward and VRE (26.7%) and CRE (36.4%) isolated from the ICU were significantly increased. Only CRE (38.7%) in surveillance samples increased in the wards.	(3)
Kumar 2021	India	Retrospective observational	To assess the effect of imprudent consumption of ABS during the COVID-19 pandemic by comparing the 2020 prevalence of antidrug resistance (ADR) of *E. coli* with results from 2018 in Ahmedabad, India using SARS-CoV-2 gene detection as a marker of ABS usage.	2018 - 2020	Community	Found a significant ADR increase in 2020 compared to 2018 in ambient water bodies, harbouring a higher incidence of ADR *E.coli* towards non-fluoroquinolone drugs.	(72)
Lemenand 2021	France	Interrupted time series	Compared ESBL-*E.coli* rates of patients in primary care and nursing home residents before and after the general lockdown in March 2020.	January 2019 - December 2020	Community	In primary care, 3.1% of *E. coli* isolates from clinical samples were producing ESBL before March 2020 and 2.9% since May 2020 ($p < 0.001$). In nursing home, the ESBL-*E.coli* rate was 9.3% before March 2020 and 8.3% since May 2020 ($p < 0.001$).	(20)
Lin 2023	Taiwan	Retrospective observational	Examined whether obligatory facial masking and reduced health-care capacity because of COVID-19 may substantially influence TB transmission in Taiwan	2010-2021	Community	The incidence of TB in countries with a high TB burden sharply declined in 2020 but rebounded immediately in 2021. In Taiwan, TB incidence (and MDR-TB incidence) declined gradually from 2010 to 2021 even during the COVID19 pandemic. TB mortality increased globally because of delayed diagnosis and treatment; nevertheless, this increase in TB mortality was not observed in Taiwan. Did not attribute reduced incidence to facial masking; facial masking and social distancing may prevent COVID-19 transmission but exhibit limited efficacy in reducing TB transmission.	(39)
Lo 2020	Taiwan	Retrospective observational	Investigated the impact of IPAC measures on the incidence rates of HAI and MDRO in a Taiwan medical center.	2018 - 2020	Hospital	Incidence density of MDRO was significantly lower in 2020. CRAB and VRE were significantly lower in 2020 than in 2018 and 2019 ($p = 0.011$, $p = 0.005$ respectively), and MRSA or CRPA incidence slightly decreased with no statistically significant difference.	(16)

Lopez-Jacome 2022	Mexico	Retrospective observational	Aimed to assess the changes in antimicrobial resistance among some critical and high-priority microorganisms collected previously and during the coronavirus disease 2019 (COVID-19) pandemic in Mexico.	2019 - 2020	Hospital	Antimicrobial resistance increased in Mexico during the COVID-19 pandemic. The increase in oxacillin resistance for *S. aureus* and carbapenem resistance for *K. pneumoniae* and an increase in erythromycin resistance in *S. aureus* was detected, which may be associated with high azithlromycin use. In general, for *A. baumannii* and *P. aeruginosa*, increasing resistance rates were detected. An increase in carbapenem use was reported during the first wave of the COVID-19 pandemic; the increase in carbapenem resistance may be associated with the increased consumption of these antibiotics.	(10)
Mannathoko 2022	Botswanna	Retrospective observational	Determined the prevalence of ESCrE and CRE colonization in hospitals, outpatient clinics, and community settings in Botswana to evaluate the changes in colonization prevalence coincident with the national response to the SARS-CoV-2 pandemic.	2020	Community and Hospital	ESCrE and CRE prevalence varied substantially across regions and was significantly higher pre-lockdown versus post-lockdown. For both ESCrE and CRE, there were significant decreases in colonization prevalence after a two-month countrywide lockdown to address the COVID-19 pandemic.	(30)
Meschiari 2022	Italy	Interrupted time series	Evaluated the impact of COVID-19 on AMR in the University Hospital of Modena from January 2015 to October 2021.	2015 - 2021	Hospital	Significant increase only in the level of BSIs due to CRPA (p = 0.032). MRSA had a non-significant increase in resistance.	(4)
Meyer Sauteur 2022	Global	Retrospective observational	Investigated global *M. pneumoniae* incidence after implementation of NPIs against COVID-19 in March 2020 from thirty-seven sites from 21 countries in Europe, Asia, America and Oceania.	April 2020 - March 2021	Community	In all countries, *M. pneumoniae* incidence by direct test methods declined significantly after implementation of NPIs with a mean of 1.69% (SD ±3.30) compared with 8.61%(SD ±10.62) in previous years (p<0.01). Also, a decrease in Macrolide-resistant *M. pneumoniae* (MRMp) rates in April 2020 to March 2021 was observed. The MRMp rates before the COVID-19 pandemic were lower in Europe than in America or Asia, consistent with previous reports	(31)
Micozzi 2021	Italy	Retrospective observational	Evaluated the potential effects of IPAC measures against COVID-19 on KPC-KP transmission in Italy.	November 2019 - August 2020	Hospital	During March–August 2020, 15.5% of hospitalized patients were KPC-KP positive, compared with 52.5% in November 2019–February 2020 (P < 0.0001).	(68)

Mughini-Gras 2021	Netherlands	Retrospective observational	This study assessed the impact of COVID-19 pandemic public health measures on human salmonellosis in the Netherlands until March 2021.	2016-2021	Community	Salmonellosis incidence decreased significantly after March 2020: in the second, third and fourth quarters of 2020, and in the first quarter of 2021. The decrease was strongest among travel-related cases. Other significant changes were: increased proportion of cases among older adults and increased proportion of invasive infections, decreased proportion of trimethoprim resistance and increased proportion of serovar Typhimurium monophasic variant vs. Enteritidis (decreased contributions of laying hens and increased contributions of pigs and cattle as sources of human infections).	(32)
Ochoa-Hein 2021	Mexico	Retrospective observational	HAI rates were compared before (January 2019-February 2020) and after (April-July 2020) the COVID-19 hospital surge capacity response.	2019 - 2020	Hospital	MRSA, CPE, ESBL producers, ampicillinase C (AmpC) producers and CRE showed no significant changes while MDR *P. aeruginosa* showed a significant reduction (p=0.004) between these two periods.	(18)
Pascale 2022	Italy	Interrupted time series	Assessed the incidence of colonization and infection with CPE and carbapenem-resistant *Acinetobacter* (CR-Ab) using a multi-center, before-and-after, cross-sectional study design during 2 study periods, period 1 (January–April 2019) and period 2 (January–April 2020).	2019 - 2020	Hospital	Found no difference in the IRRs of colonization and infection with CPE during the pre-COVID-19 period and the COVID-19 period, whereas the incidence rate ratio (IRR) of CR-Ab increased significantly during the COVID-19 period. However, there was a change in the mechanisms of resistance with a decrease in the prevalence of KPC in favour to OXA-48– and VIM–producing strains.	(70)
Santos 2022	United States	Retrospective observational	Measured facility-wide antimicrobial use/antimicrobial resistance ratios from 2019 to 2020 for specific antimicrobial agents and corresponding adverse reaction (AR) events, and compared median monthly AU/AR ratios between March 2019 through December 2019 (pre-COVID period) and March 2020 through December 2020 (COVID period).	2019 - 2020	Hospital	Intravenous vancomycin was the most commonly used antibiotic but it and linezolid, ceftolozane–tazobactam, and colistin did not differ significantly in use between two time periods. Significant decreases were seen in meropenem and daptomycin use and increases in ceftazidime–avibactam. ESBL Enterobacterales events significantly increased during COVID-19 (p = .001). Increases in the median monthly number of CRE events (p = .031) and VRE events (p = .001) were also observed between periods. No differences were observed in the median monthly number of events for CNA, MRSA, and MDR *P. aeruginosa* between periods.	(11)

Sasaki 2022	Japan	Retrospective observational	Assessed antimicrobial consumption, MDRO incidence, and the CAUTI rate in a small Japanese hospital actively receiving patients with COVID-19 during and before the pandemic.	2018 - 2022	Hospital	Although we found no change in the incidence of MRSA, we detected an increase in the ESBL-E incidence during the pandemic. The consumption of intravenous antimicrobials, especially antipseudomonal antimicrobial agents, and third generation cephalosporins increased significantly. The use of all intravenous antimicrobials as measured by DOT showed a significantly decreasing trend before the pandemic.	(12)
Shbaklo 2022	Italy	Retrospective observational	The objective of this study was to describe the incidence of MDR HAIs and antibiotic consumption during the three waves of COVID-19 and to compare it to the period before the outbreak at Molinette Hospital in Italy.	2019 - 2021	Hospital	Demonstrated an increase in MDR infections: particularly in KPC-Kp, *A. baumannii*, and MRSA. Fluoroquinolone use showed a significant increasing trend in the pre-COVID period but saw a significant reduction in the COVID period. The use of fourth- and fifth-generation cephalosporins and piperacillin–tazobactam increased at the beginning of the COVID period.	(33)
Tang 2022	Taiwan	Retrospective observational	Compare the number of cases of airborne/droplet-transmitted notifiable infectious disease (NID) between the pandemic period (defined as from January 2020 to December 2021) and the pre-pandemic period (defined as the period from January 2018 to December 2019) for fourteen airborne/droplet-transmitted NIDs including MDRTB.	2018 - 2021	Hospital	The case number of influenza with severe complications had the largest reduction from the pre-pandemic period to the pandemic period, followed by TB (−2904), IPD (−490), mumps (−292), measles (−292), pertussis (−57), MDRTB (−43), rubella (−35), Q fever (−20), varicella (−12), meningococcal meningitis (−5), invasive *H. influenzae* type B (−4). In contrast, the case number of legionellosis and hantavirus syndrome also increased during the pre-pandemic period.	(34)
Tedeschi 2023	Italy	Retrospective observational	The aim of this study was to assess antibiotic consumption and antibiotic resistance at the community level in an Italian province before and after the beginning of the COVID-19 pandemic.	2019-2020	Community	Overall antibiotic consumption decreased by 28% from 2019 to 2020 and in 2020 strains of *Enterobacterales* showed increasing susceptibility to amoxicillin/clavulanate among isolated from primary and long-term care.	(63)
Teixeira 2022	Portugal	Retrospective observational	Aimed to compare the rate of postoperative infection and drug-resistant organism (DRO) before and during the COVID-19	2018 - 2020	Hospital	Postoperative infection rates were not significantly reduced during the COVID-19 pandemic, despite the adoption of enhanced infection preventive measures. There was, however, a decrease in the rate of DROs during this period, suggesting a secondary benefit to	(35)

			pandemic in urology departments.			enhanced infection prevention practices adopted during the COVID-19 era.	
Tham 2022	Australia	Retrospective cohort	Determined the effect of the COVID-19 pandemic-related escalation in IPAC measures on the incidence of HAI in surgical patients in a low COVID-19 environment in Australia.	April 2019 - June 2020	Hospital (surgical)	There were no major changes in the types of microorganisms involved in HAI across the two study periods. Counts of MDRO including MRSA and ESBL *E. coli* were similar across both time periods.	(19)
Ullrich 2021	Germany	Interrupted time series	Assessed the impact of the pandemic and COVID-19 NPIs affecting healthcare seeking behaviour, access to healthcare, test strategies, disease notification and workload at public health authorities, on other notifiable infectious diseases under surveillance in Germany.	2020	Community and Hospital	The number of cases decreased most for respiratory diseases, gastro-intestinal diseases and imported vector-borne diseases p<005), except for tick-borne encephalitis, which increased (+58%). Less affected infections were hospital associated pathogens (from -43% colonisation with CNA, to -28% for MRSA invasive infection) and sexually transmitted and blood-borne diseases (from -28% for hepatitis B to -12% for syphilis).	(36)
Vyazovaya 2022	Russia	Retrospective observational	Examined how counteracting factors imposed by the pandemic (undertesting, reduced resources, reduced detection rate) could influence changes in the local *M. tuberculosis* population.	2019-2021	Community	No change was observed in the *M. tuberculosis* population structure in the survey area in Western Siberia during the Covid-19 pandemic in 2020–2021 compared to the pre-pandemic collection but there was a decrease of the Beijing genotype and an increase in the proportion and diversity of the non-Beijing isolates. Both pre-pandemic and pandemic samples are still heavily dominated by the Beijing genotype isolates (95% and 88%) which are mostly MDR (80 and 68%).	(67)
Wee 2021	Singapore	Retrospective observational	Evaluated the impact of a multimodal IPAC COVID-19 strategy on the rates of HAI from February-August 2020 across a large health care campus in Singapore.	2018 - 2020	Hospital	No increase in CP-CRE acquisition, and rates of other HAIs were stable. Hospital-wide MRSA acquisition rates declined significantly during the pandemic (incidence-rate-ratio = 0.54, 95% CI = 0.46-0.64, *P*< .05).	(17)
Yang 2021	China	Retrospective observational	MRSA detection rates in medical institutions and exposure rates to environmental disinfectants were measured before and	2016 - 2020	Hospital	The MRSA detection rate increased with elevated concentration and frequency of disinfection, with 1,000 or 500 mg/L two times per day since January in 2020 vs. 500 mg/L 2–3 times per week in 2016–2019.Overall, the MRSA detection was augmented with the increase in disinfection	(77)

			during the COVID-19 pandemic.			concentration and frequency during the COVID-19 epidemic, suggesting that highly-concentrated and highly-frequent preventive long-term disinfection is not recommended without risk assessment.	
Zaveri 2021	India	Retrospective observational	Surveilled for AMR pathogens from critically essential wards, at three tertiary care hospitals of Ahmedabad between the years April 2017 until July 2020.	2017 - 2020	Hospital	Carbapenem-resistant genes decreased pre and post pandemic. The prevalence of pathogenic (*Klebsiella spp., E. coli,* and *Pseudomonas spp.)* and non-pathogenic (*S. aureus* and *Bacillus spp.*) strains in healthcare setups decreased drastically. This change could be due to frequent cleaning of various surfaces and hands using sanitizers and disinfectants or minimal access to the patients.	(22)
Zhu 2022	United Kingdom	Retrospective observational	Examined community- and hospital-acquired BSIs in coronavirus disease 2019 (COVID-19) and non–COVID-19 patients across 2 epidemic waves.	2020 - 2021	Hospital and community	Community-acquired *E. coli* BSIs remained below pre-pandemic level during COVID-19 waves but peaked following lockdown easing in May 2020. The hospital-acquired BSI rate was 100.4 per 100 000 patient-days across the pandemic, increasing to 132.3 during the first wave and 190.9 during the second, with significant increase in elective inpatients. Hospital-acquired BSI caused by MRSA had the largest increase among all causative pathogens in both COVID-19 and non–COVID-19 patients, compared to pre–COVID-19 figures. The overall rates of community-acquired BSI caused by gram-negative bacteria and MRSA were lower than the pre–COVID-19 level.	(64)
Zhu 2022	China	Retrospective observational	Measured distribution and drug resistance of bacterial pathogens associated with lower respiratory tract infection (LRTI) in children in Chengdul from 2011 to 2020 and impact of COVID-19 measures like improved vaccination, implementation of isolation measures and social distance, strengthening of personal protective measures, aseptic operation of invasive medical treatment, hand hygiene, and environmental	2011 - 2020	Community	Since 2011, the resistance of *E. coli* and *K. pneumoniae* to third-generation cephalosporins has increased, peaking in 2017, and has decreased after 2018, years after which carbapenem resistance has increased significantly, corresponding to an increase in the detection rate of CRE. In the past three years, 73% of *S. aureus* detected in the lower respiratory tract of children were MRSA and the detection rate of MRSA showed an increasing trend year by year with the increase of oxacillin resistance.	(37)

			disinfection measures on these measures.				
Zuglian 2022	Italy	Retrospective observational	Compared the prevalence and the antibiotic profile of bacterial and fungal species of patients with COVID-19, hospitalized in ICUs from 22nd February 2020 to 31st May 2020 (Period 1), and without COVID-19, from 22nd February 2019 to 31st May 2019 (Period 2).	2019 - 2020	Hospital (ICU)	The prevalence of *Pseudomonas spp.* increased significantly, the prevalence of Gram negative non fermenting bacteria (GN-NFB), *H. infuenzae* and *S. pneumoniae* reduced. There was a statistically significant increase in resistance of *Pseudomonas spp.* to carbapenems and piperacillin/tazobactam and *Enterobacterales spp.* for piperacillin/tazobactam, in COVID-19 positive patients compared to patients without COVID-19. We did not observe significant changing in fungal respiratory isolates.	(65)

Multidrug-resistant (MDR), multidrug-resistant organisms (MDRO), hospital-associated infections (HAI), bloodstream infection (BSI), community-acquired infections (CAIs), central-line–associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), bloodstream infections (BSI), Vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *Staphylococcus aureus* (MSSA), carbapenemase-producing *Klebsiella pneumoniae* (KPC-KP), extended-spectrum beta-lactamase (ESBL), carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-non-susceptible *Acinetobacter* (CNA), extended-spectrum cephalosporin-resistant *Enterobacterales* (ESCrE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), fluconazole-resistant *Candida parapsilosis* (FRCP), non-pharmaceutical interventions (NPI), infection prevention and control (IPAC)

Table 3. Included studies classified in accordance with Knight et al.'s framework (2021). Columns reflect AMR dimensions which may be affected by the COVID-19 pandemic (AMR emergence, AMR transmission and AMR burden). Rows reflect COVID-19 drivers of AMR (antimicrobial use (AMU); community or hospital infection prevention and control (IPAC); or changes to health systems use).

COVID-19 Impacts	**AMR emergence (New drug resistant strains emerge and/or are selected for)**		**AMR transmission (AMR organisms spread between health and environment)**		**Burden of AMR Illness (Number and nature of infections due to antimicrobial resistant organisms)**	
Setting	**Hospital**	**Community**	**Hospital**	**Community**	**Hospital**	**Community**
Antimicrobial use		Kumar 2021			Bauer 2022, Bork 2020, Bussolati 2022, Chamieh 2021, de Carvalho Hessel Dias 2022, Imoto 2022, Jeon 2022, Lopez-Jacome 2022, Meschiari 2022, Santos 2022, Sasaki 2022, Shbaklo 2022	Cheng 2022, Tedeschi 2023

Infection prevention and control		Jani 2021	Micozzi 2021, Gisselo 2022, Pascale 2022		Bentivegna 2021, Dutta 2022 (Moderate), Endo 2023, Fukushige 2022, Gaspari 2021, Guven 2021, Ipek 2022, Imoto 2022, Lo 2020, Ochoa-Hein 2021, Teixeira 2022, Tham 2022, Wee 2021, Yang 2021, Zaveri 2021, Zhu 2022 (China)	Chen 2021, Dapper 2022, Hibiya 2022, Lemenand 2021, Lin 2023, Mannathoko 2022, Meyer Sauteur 2022, Mughini-Gras 2021, Tang 2022, Ullrich 2021,
Health system use					Zuglian 2022	Zhu 2022 (UK), Alao 2022, Vyazovaya 2022

APPENDIX 2

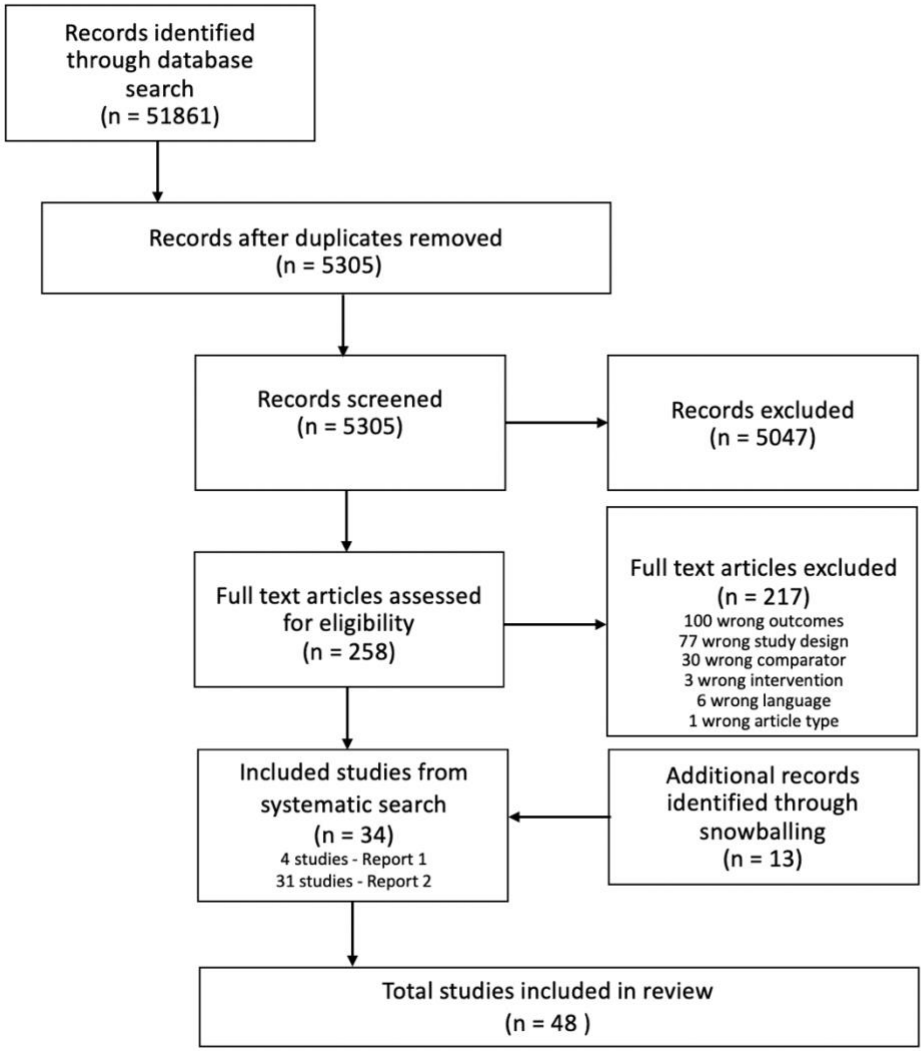
Records identified through database search (n = 51861)
Records after duplicates removed (n = 5305)
Records screened (n = 5305)
Records excluded (n = 5047)
Full text articles assessed for eligibility (n = 258)
Full text articles excluded (n = 217)
100 wrong outcomes
77 wrong study design
30 wrong comparator
3 wrong intervention
6 wrong language
1 wrong article type
Included studies from systematic search (n = 34)
4 studies - Report 1
31 studies - Report 2
Additional records identified through snowballing (n = 13)
Total studies included in review (n = 48)

Figure 1. Study selection process for review

Table 1. PROGRESS-Plus factors for each study

Study author, year	PROGRESS								PLUS		
	Place of residence	Race, ethnicity, culture, or language	Occupation	Gender or sex	Religion	Education	Socioeconomic status	Social capital	Personal characteristics associated with discrimination (e.g., age, disability)	Features of relationships (e.g., smoking parents, excluded from school)	Time-dependent relationships (e.g., leaving the hospital, respite care, other instances where a person may be temporarily at a disadvantage)
Alao 2022	no	no	no	yes	no	no	no	no	yes	no	no
Bauer 2022	yes	no	no	yes	no	no	no	no	yes	no	yes
Bentivegna 2021	no	no	no	no	no	no	no	no	no	no	no
Bork 2020	no	no	no	no	no	no	no	no	no	no	no
Bussolati 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Chamieh 2021	no	no	no	no	no	no	no	no	no	no	no
Chen 2021	no	no	no	yes	no	no	no	no	yes	no	yes
Cheng 2022	no	no	no	no	no	no	no	no	no	no	no
Dapper 2022	no	no	no	no	no	no	no	no	no	no	no
de Carvalho Hessel Dias 2022	no	no	no	no	no	no	no	no	no	no	no
Dutta 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Endo 2023	no	no	no	no	no	no	no	no	no	no	no
Fukushige 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Gaspari 2021	no	no	no	yes	no	no	no	no	yes	no	yes
Gisselo 2022	no	no	no	no	no	no	no	no	no	no	no
Guven 2021	no	no	no	no	no	no	no	no	no	no	no
Hibiya 2022	no	no	no	no	no	no	no	no	no	no	no
Imoto 2022	no	no	no	no	no	no	no	no	no	no	no
Ipek 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Jani 2021	no	no	no	no	no	no	no	no	no	no	no
Jeon 2022	no	no	no	no	no	no	no	no	no	no	no
Kumar 2021	no	no	no	no	no	no	no	no	no	no	no
Lemenand 2021	yes	no	no	yes	no	no	no	no	yes	no	no
Lin 2023	no	no	no	no	no	no	no	no	no	no	no
Lo 2020	no	no	no	no	no	no	no	no	no	no	no
Lopez-Jacome 2022	no	no	no	no	no	no	no	no	no	no	no
Mannathoko 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Meschiari 2022	no	no	no	no	no	no	no	no	no	no	no
Meyer Sauteur 2022	yes	no	no	yes	no	no	no	no	yes	no	no
Micozzi 2021	no	no	no	yes	no	no	no	no	yes	no	yes
Mughini-Gras 2021	no	no	no	yes	no	no	no	no	yes	no	yes
Ochoa-Hein 2021	no	no	no	yes	no	no	no	no	yes	no	yes

Pascale 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Santos 2022	no	no	no	no	no	no	no	no	no	no	no
Sasaki 2022	no	no	no	no	no	no	no	no	no	no	no
Shbaklo 2022	no	no	no	no	no	no	no	no	no	no	no
Tang 2022	no	no	no	no	no	no	no	no	no	no	no
Tedeschi 2023	no	no	no	no	no	no	no	no	no	no	no
Teixeira 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Tham 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Ullrich 2021	yes	no	no	yes	no	no	no	no	yes	no	no
Vyazovaya 2022	no	no	no	no	no	no	no	no	no	no	no
Wee 2021	no	no	no	no	no	no	no	no	no	no	no
Yang 2021	no	no	no	no	no	no	no	no	no	no	no
Zaveri 2021	no	no	no	no	no	no	no	no	no	no	no
Zhu 2022 (UK)	no	yes	no	yes	no	no	no	no	yes	no	yes
Zhu 2022 (China)	no	no	no	yes	no	no	no	no	yes	no	no
Zuglian 2022	no	no	no	yes	no	no	no	no	yes	no	yes

APPENDIX 3

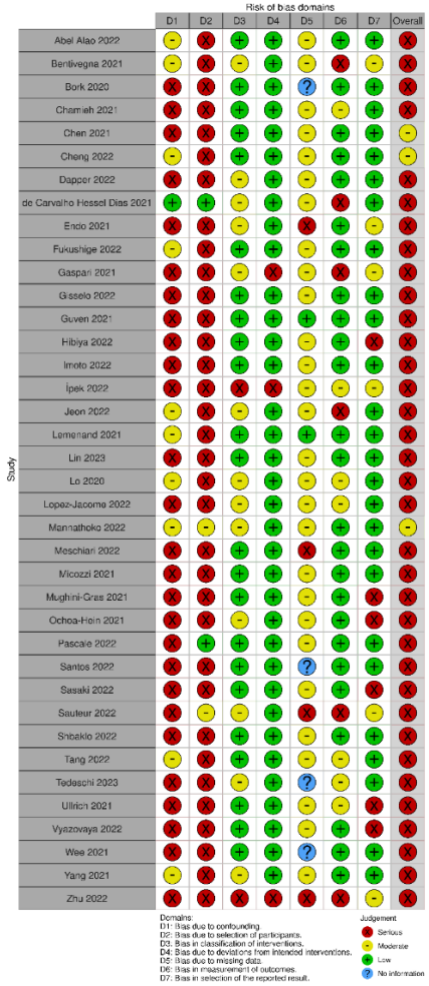

Figure 1. Summary of risk of bias and applicability concerns evaluated using the ROBINS-I quality assessment tool for non-randomized studies.

Study	Risk of bias (NOS)			
	S	C	O	F
Bauer 2022	**	**	*	5/9 stars (Moderate Risk of Bias)
Bussolati 2022	**	*	*	5/9 stars (Moderate Risk of Bias)
Dutta 2022	**	*	*	4/9 stars (Moderate Risk of Bias)
Teixeira 2021	**	**	*	5/9 stars (Moderate Risk of Bias)
Tham 2022	***	**	*	6/9 stars (Moderate Risk of Bias)

S = selection; C = comparability; O = outcome; F = final overall rating

Figure 2. Summary of risk of bias and applicability concerns evaluated using the Newcastle Ottawa Scale (NOS) for cohort studies.

APPENDIX 4

Search Strategy
Covid-19 – Antimicrobial Resistance
Final Strategies
2022 Dec 19

Search saved as: COVID - Antimicrobial Resistance - Multifile
Final - Post-PRESS - 2022 Dec 19 - Remove duplicates and download by database MEDALL EMCZD COCH CCTR

Ovid Multifile

Database: Embase Classic+Embase <1947 to 2022 December 16>, Ovid MEDLINE(R) ALL <1946 to December 16, 2022>, EBM Reviews - Cochrane Central Register of Controlled Trials <November 2022>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to December 14, 2022>
Search Strategy:
---
1 COVID-19/ (272610)
2 SARS-CoV-2/ (169494)
3 Coronavirus/ (14858)
4 Betacoronavirus/ (39932)
5 Coronavirus Infections/ (56651)
6 (COVID-19 or COVID19).tw,kw,kf. (601297)
7 ((coronavirus* or corona virus*) and (hubei or wuhan or beijing or shanghai)).tw,kw,kf. (13884)
8 (wuhan adj5 virus*).tw,kw,kf. (833)
9 (2019-nCoV or 19nCoV or 2019nCoV).tw,kw,kf. (4565)
10 (nCoV or n-CoV or "CoV 2" or CoV2).tw,kw,kf. (234065)
11 (SARS-CoV-2 or SARS-CoV2 or SARSCoV-2 or SARSCoV2 or SARS2 or SARS-2 or severe acute respiratory syndrome coronavirus 2).tw,kw,kf. (237842)
12 (2019-novel CoV or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or (coronavirus* and pneumonia)).tw,kw,kf. (59479)

13 (novel coronavirus* or novel corona virus* or novel CoV).tw,kw,kf. (27082)
14 ((coronavirus* or corona virus*) adj2 "2019").tw,kw,kf. (120389)
15 ((coronavirus* or corona virus*) adj2 "19").tw,kw,kf. (17858)
16 ("coronavirus 2" or "corona virus 2").tw,kw,kf. (65337)
17 (OC43 or NL63 or 229E or HKU1 or HCoV* or Sars-coronavirus*).tw,kw,kf. (10003)
18 COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os. (19107)
19 (coronavirus* or corona virus*).ti,kw,kf. (110557)
20 COVID.ti,kw,kf. (517646)
21 ("B.1.1.7" or "B.1.351" or "B.1.617" or "B.1.427" or "B.1.429").tw,kw,kf,rx,px,ox. (3546)
22 ("BA.1" or "BA.2" or "BA.3" or "BA.4" or "BA.5" or "BA.2.75" or "BA.4.6" or "BA.2.3.20" or "XBB").tw,kw,kf,rx,px,ox. (11090)
23 ("P.1" and (Brazil* or variant?)).tw,kw,kf,rx,px,ox. (4706)
24 (((alpha or beta or delta or eta or gamma or iota or kappa or lambda or omicron or zeta) adj3 variant?) and (coronavirus* or corona virus* or covid*)).tw,kw,kf. (9714)
25 or/1-24 [COVID-19] (723180)
26 exp Drug Resistance, Microbial/ (393502)
27 ((antibiotic? or anti-biotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (324394)
28 (AMR adj10 resistan*).tw,kw,kf. (9794)
29 ((multidrug? or multi-drug? or multiple drug?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (181848)
30 ((betalactam* or beta-lactam* or b-lactam* or blactam*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (28274)
31 (cephalosporin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (11879)
32 ((penicillin* or ampicillin* or methicillin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (125933)
33 (carbapenem* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (27808)
34 (chloramphenicol* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10755)
35 (daptomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (2117)
36 ((fluoroquinolone* or ciprofloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or gatifloxacin* or gemifloxacin* or levofloxacin* or moxifloxacin* or norfloxacin* or ofloxacin* or pefloxacin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (34276)
37 ((macrolide* or ado-trastuzumab emtansine* or everolimus* or fidaxomicin* or lucensomycin* or maytansine* or mepartricin* or miocamycin* or natamycin or nystatin* or oleandomycin* or oligomycin* or rutamycin* or sirolimus* or tacrolimus* or troleandomycin* or tylosin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (13936)
38 ((erythromycin* or azithromycin* or clarithromycin* or ketolide* or roxithromycin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (23588)
39 (kanamycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (7947)

40 ((polymyxin* or poly-myxin* or colistin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10679)
41 (rifampicin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10011)
42 (tetracycline* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (22980)
43 (trimethoprim* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (8581)
44 (vancomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (26464)
45 Antimicrobial Stewardship/ (12229)
46 ((antibiotic? or anti-biotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (custodian* or guardian* or oversee* or oversight* or safeguard* or safe guard* or steward* or watchdog? or watch dog?)).tw,kw,kf. (24623)
47 or/26-46 [AMR] (765724)
48 25 and 47 [COVID-19 - AMR] (4875)
49 limit 48 to yr="2020-current" [DATE LIMIT] (4426)
50 49 use medall [MEDLINE RECORDS] (1872)
51 coronavirus disease 2019/ (487541)
52 severe acute respiratory syndrome coronavirus 2/ (224399)
53 Coronavirinae/ (6402)
54 Betacoronavirus/ (39932)
55 coronavirus infection/ (57539)
56 (COVID-19 or COVID19).tw,kw,kf. (601297)
57 ((coronavirus* or corona virus*) and (hubei or wuhan or beijing or shanghai)).tw,kw,kf. (13884)
58 (wuhan adj5 virus*).tw,kw,kf. (833)
59 (2019-nCoV or 19nCoV or 2019nCoV).tw,kw,kf. (4565)
60 (nCoV or n-CoV or "CoV 2" or CoV2).tw,kw,kf. (234065)
61 (SARS-CoV-2 or SARS-CoV2 or SARSCoV-2 or SARSCoV2 or SARS2 or SARS-2 or severe acute respiratory syndrome coronavirus 2).tw,kw,kf. (237842)
62 (2019-novel CoV or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or (coronavirus* and pneumonia)).tw,kw,kf. (59479)
63 (novel coronavirus* or novel corona virus* or novel CoV).tw,kw,kf. (27082)
64 ((coronavirus* or corona virus*) adj2 "2019").tw,kw,kf. (120389)
65 ((coronavirus* or corona virus*) adj2 "19").tw,kw,kf. (17858)
66 ("coronavirus 2" or "corona virus 2").tw,kw,kf. (65337)
67 (OC43 or NL63 or 229E or HKU1 or HCoV* or Sars-coronavirus*).tw,kw,kf. (10003)
68 (coronavirus* or corona virus*).ti,kw,kf. (110557)
69 COVID.ti,kw,kf. (517646)

70 ("B.1.1.7" or "B.1.351" or "B.1.617" or "B.1.427" or "B.1.429").tw,kw,kf. (3503)
71 ("BA.1" or "BA.2" or "BA.3" or "BA.4" or "BA.5" or "BA.2.75" or "BA.4.6" or "BA.2.3.20" or "XBB").tw,kw,kf. (11036)
72 ("P.1" and (Brazil* or variant?)).tw,kw,kf. (4669)
73 (((alpha or beta or delta or eta or gamma or iota or kappa or lambda or omicron or zeta) adj3 variant?) and (coronavirus* or corona virus* or covid*)).tw,kw,kf. (9714)
74 or/51-73 [COVID-19] (739570)
75 exp antibiotic resistance/ (393502)
76 antifungal resistance/ (6177)
77 antiviral resistance/ (9688)
78 ((antibiotic? or antibiotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (324368)
79 (AMR adj10 resistan*).tw,kw,kf. (9794)
80 ((multidrug? or multi-drug? or multiple drug?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (181848)
81 ((betalactam* or beta-lactam* or b-lactam* or blactam*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (28274)
82 (cephalosporin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (11879)
83 ((penicillin* or ampicillin* or methicillin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (125933)
84 (carbapenem* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (27808)
85 (chloramphenicol* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10755)
86 (daptomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (2117)
87 ((fluoroquinolone* or ciprofloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or gatifloxacin* or gemifloxacin* or levofloxacin* or moxifloxacin* or norfloxacin* or ofloxacin* or pefloxacin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (34276)
88 ((macrolide* or ado-trastuzumab emtansine* or everolimus* or fidaxomicin* or lucensomycin* or maytansine* or mepartricin* or miocamycin* or natamycin or nystatin* or oleandomycin* or oligomycin* or rutamycin* or sirolimus* or tacrolimus* or troleandomycin* or tylosin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (13936)
89 ((erythromycin* or azithromycin* or clarithromycin* or ketolide* or roxithromycin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (23588)
90 (kanamycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (7947)
91 ((polymyxin* or poly-myxin* or colistin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10679)
92 (rifampicin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (10011)
93 (tetracycline* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (22980)
94 (trimethoprim* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (8581)
95 (vancomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).tw,kw,kf. (26464)
96 antimicrobial stewardship.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, sh, kw, tx, ct] (20611)

97 ((antibiotic? or antibiotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (custodian* or guardian* or oversee* or oversight* or safeguard* or safe guard* or steward* or watchdog? or watch dog?)).tw,kw,kf. (24622)
98 or/75-97 [AMR] (776935)
99 74 and 98 [COVID-19 - AMR] (5312)
100 limit 99 to yr="2020-current" [DATE LIMIT] (4869)
101 100 use emczd [EMBASE RECORDS] (2960)
102 COVID-19/ (272610)
103 SARS-CoV-2/ (169494)
104 Coronavirus/ (14858)
105 Betacoronavirus/ (39932)
106 Coronavirus Infections/ (56651)
107 (COVID-19 or COVID19).ti,ab,kw. (599342)
108 ((coronavirus* or corona virus*) and (hubei or wuhan or beijing or shanghai)).ti,ab,kw. (13709)
109 (wuhan adj5 virus*).ti,ab,kw. (810)
110 (2019-nCoV or 19nCoV or 2019nCoV).ti,ab,kw. (4313)
111 (nCoV or n-CoV or "CoV 2" or CoV2).ti,ab,kw. (206245)
112 (SARS-CoV-2 or SARS-CoV2 or SARSCoV-2 or SARSCoV2 or SARS2 or SARS-2 or severe acute respiratory syndrome coronavirus 2).ti,ab,kw. (235807)
113 (2019-novel CoV or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or (coronavirus* and pneumonia)).ti,ab,kw. (57271)
114 (novel coronavirus* or novel corona virus* or novel CoV).ti,ab,kw. (26519)
115 ((coronavirus* or corona virus*) adj2 "2019").ti,ab,kw. (116746)
116 ((coronavirus* or corona virus*) adj2 "19").ti,ab,kw. (16148)
117 ("coronavirus 2" or "corona virus 2").ti,ab,kw. (61868)
118 (OC43 or NL63 or 229E or HKU1 or HCoV* or Sars-coronavirus*).ti,ab,kw. (9923)
119 (coronavirus* or corona virus*).ti,kw. (104607)
120 COVID.ti,kw. (450177)
121 ("B.1.1.7" or "B.1.351" or "B.1.617" or "B.1.427" or "B.1.429").ti,ab,kw. (3475)
122 ("BA.1" or "BA.2" or "BA.3" or "BA.4" or "BA.5" or "BA.2.75" or "BA.4.6" or "BA.2.3.20" or "XBB").ti,ab,kw. (10989)
123 ("P.1" and (Brazil* or variant?)).ti,ab,kw. (4612)
124 (((alpha or beta or delta or eta or gamma or iota or kappa or lambda or omicron or zeta) adj3 variant?) and (coronavirus* or corona virus* or covid*)).ti,ab,kw. (9481)
125 or/102-124 [COVID-19] (721737)

126 exp Drug Resistance, Microbial/ (393502)
127 ((antibiotic? or anti-biotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (306824)
128 (AMR adj10 resistan*).ti,ab,kw. (9392)
129 ((multidrug? or multi-drug? or multiple drug?) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (175149)
130 ((betalactam* or beta-lactam* or b-lactam* or blactam*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (27748)
131 (cephalosporin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (11701)
132 ((penicillin* or ampicillin* or methicillin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (124476)
133 (carbapenem* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (26649)
134 (chloramphenicol* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (10698)
135 (daptomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (2077)
136 ((fluoroquinolone* or ciprofloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or gatifloxacin* or gemifloxacin* or levofloxacin* or moxifloxacin* or norfloxacin* or ofloxacin* or pefloxacin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (33932)
137 ((macrolide* or ado-trastuzumab emtansine* or everolimus* or fidaxomicin* or lucensomycin* or maytansine* or mepartricin* or miocamycin* or natamycin or nystatin* or oleandomycin* or oligomycin* or rutamycin* or sirolimus* or tacrolimus* or troleandomycin* or tylosin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (13739)
138 ((erythromycin* or azithromycin* or clarithromycin* or ketolide* or roxithromycin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (23313)
139 (kanamycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (7923)
140 ((polymyxin* or poly-myxin* or colistin*) adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (10449)
141 (rifampicin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (9937)
142 (tetracycline* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (22900)
143 (trimethoprim* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (8561)
144 (vancomycin* adj5 (resistan* or nonsusceptib* or non-susceptib*)).ti,ab,kw. (26153)
145 Antimicrobial Stewardship/ (12229)
146 ((antibiotic? or anti-biotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or anti-microbial? or antiviral? or anti-viral? or bacterial? or microbial?) adj5 (custodian* or guardian* or oversee* or oversight* or safeguard* or safe guard* or steward* or watchdog? or watch dog?)).ti,ab,kw. (21963)
147 or/126-146 [AMR] (753702)
148 125 and 147 [COVID-19 - AMR] (4649)
149 202*.up. (44809373)

150 148 and 149 (4511)
151 limit 148 to yr="2020-current" (4239)
152 150 or 151 (4511) [DATE LIMITS]
153 152 use coch [CDSR RECORDS] (1)
154 152 use cctr [CENTRAL RECORDS] (39)
155 50 or 101 or 153 or 154 [ALL DATABASES] (4872)
156 remove duplicates from 155 (3418) [TOTAL UNIQUE RECORDS]
157 156 use medall [MEDLINE UNIQUE RECORDS] (1858)
158 156 use emczd [EMBASE UNIQUE RECORDS] (1533)
159 156 use cctr [CENTRAL UNIQUE RECORDS] (26)
160 156 use coch [CDSR UNIQUE RECORDS] (1)

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ABOUT THE KNOWLEDGE SYNTHESIS AND APPLICATION UNIT

The Knowledge Synthesis and Application Unit (KSAU) is located at the University of Ottawa and led by Drs. David Moher, Melissa Brouwers and Julian Little. The KSAU specializes in conducting high quality evidence syntheses and advancing scholarship to optimize methods, usability, and applicability of evidence to inform healthcare and public health decision-making.

ABOUT THE GLOBAL STRATEGY LAB

Based at York University and University of Ottawa, the Global Strategy Lab (GSL) uses an intensely interdisciplinary approach to undertake innovative research to advise governments and public health organizations on how to design laws, policies and institutions that address transnational health threats and make the world a healthier place for everyone. GSL's policy division provides specialized evidence-based advisory services to governments and civil society organizations.

The AMR Policy Accelerator

The AMR Policy Accelerator advises the world's governments, public health institutions and decision-makers on effective and equitable policies to ensure sustainable antimicrobial use for everyone. We undertake rigorous research, develop practical resources and tailor custom advisory services to comprehensively support equitable, evidence-informed policymaking on antimicrobial resistance at the national and global level. The AMR Policy Accelerator is a Wellcome-funded initiative hosted at Global Strategy Lab.