# RAPID SCOPING REVIEW

The Effects of the COVID-19 Pandemic on the Three Core Drivers of AMR November 3, 2023



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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 65.

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## **ABBREVIATIONS**

AMR	antimicrobial resistance
AMS	antimicrobial stewardship
AMU	antimicrobial use
CAI	community-associated infection
CRA	carbapenem-resistant Acinetobacter infection
CRPA	carbapenem-resistant Pseudomonas aeruginosa
CRE	carbapenem-resistant Enterobacteriaceae
ESBL	extended spectrum beta-lactamase-producing
HAI	hospital-associated infection
HICs	high-income countries
ESBL	Extended-spectrum beta-lactamases
HIV	human immunodeficiency virus
ICU	intensive care unit
IPAC	infection prevention and control
ITS	interrupted time series
LMICs	low- and middle-income countries
MDR	multidrug resistant
MRSA	methicillin-resistant Staphylococcus aureus
MSSA	methicillin-sensitive Staphylococcus aureus
NOS	Newcastle Ottawa Scale
NPIs	nonpharmaceutical interventions
PPE	personal protective equipment
STI	sexually transmitted infections
STBBI	sexually transmitted and blood borne infection
ТВ	Tuberculosis
VRE	Vancomycin-resistant Enterococcus
WHO	World Health Organization

## **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 contributed to the deaths of close to 5 million people around the world.

In this study, key questions we wanted to answer were (1) if the COVID-19 pandemic changed how antimicrobials are used and (2) 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, Norway, Denmark, and the United States of America (US).

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antimicrobials refers to the antimicrobials used or prescribed inside a hospital or emergency-room setting.

Hospital use of

#### Community use of

antimicrobials refers to the antimicrobials used or prescribed outside of a hospital or emergency-room setting, for example, through community pharmacies.

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, may have impacted AMR, for example, through reduced use of healthcare systems. 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.

#### Why is this study important?

It is important to understand what actions during the COVID-19 pandemic increased or decreased AMR. We can use this information to 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?

• Different countries showed different trends in AMR and we did not consistently find that AMR either increased or decreased because of changes in antimicrobial use during COVID-19. 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 some countries found that AMR increased, while others found it decreased or stayed the same.

- Measures meant to stop the spread of COVID-19, like wearing face masks and lockdowns, reduced AMR.
- Changes to how people used the medical system during the pandemic like reduced diagnostic testing, may have increased resistance of community-associated infections. Changes like higher ICU admission rates may also have increased resistance of hospital-associated infections. Additional studies are needed, since only a few studies examining health system use in either setting were found.

What is needed now?

- 1. More studies to find out how the COVID-19 pandemic has impacted AMR after the initial pandemic wave.
- 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 third 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 <u>first</u> and <u>second</u> editions were published November 2022 and May 2023, respectively.

This third edition includes fifteen new studies, for a total of sixty-three studies and includes updated national surveillance data on AMU and AMR. This report also includes risk of bias assessments for the included studies; most were found to be at high risk of bias. In addition, this report explored national AMR trends across WHO priority pathogens (*Appendix 1, Figure 1*).

National surveillance data shows a significant decrease in AMU in 2020 driven by reductions in community prescribing. Whether, or for how long, these reductions will be sustained remains to be seen: while Canada, England, the European Union, and Norway continued to report lower than pre-pandemic level of community AMU in 2021, the US and Denmark may already be experiencing a return to (or above) pre-COVID-19 levels of community prescribing. 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. Trends in community AMU may become more apparent as 2022 data is released.

Conclusions in this report were consistent with our May 2023 update: changes in AMU were not consistently associated with increasing or decreasing levels of AMR while COVID-19-driven IPAC measures have reduced AMR. Research studies found an increase in AMU in some hospital settings (e.g., ICU or COVID wards), decreases in other hospital settings or when looking at whole hospital AMU, and decreases in community settings. Health system use changed significantly during the COVID-19 pandemic through increased ICU admissions, raised threshold for seeing a general practitioner for symptoms, and shifting inperson appointments to telemedicine ones all of which may have also impacted AMR. However, we found few studies which examined these factors as a driver of AMR. The studies we did find suggest that changes to health system use during the COVID-19 pandemic including limited capacity to provide service delivery and diagnosis for community-associated diseases like human immunodeficiency virus (HIV), tuberculosis (TB), malaria, and STIs, as well as reduced global vaccination coverage may have negatively affected AMR.

IPAC measures in the community, including travel restrictions, lockdowns, social distancing requirements, and mandatory masking, consistently contributed to a reduction in resistant community-associated infections (CAIs). However, impact of hospital IPAC measures on AMR and resistant hospital-associated infections (HAIs) was more varied; studies reporting increasing, decreasing and no change in HAI rates.

The impact of reduced diagnostic testing in the community and an increased number of sick patients in hospital ICUs were generally associated with increasing AMR. However, since few studies were identified, this remains a consistent knowledge gap from the first version of this report that requires further research and investigation. Furthermore, few studies investigated the impact of any COVID-19-driven changes on AMR transmission and emergence. The lack of data about either dimension represents an opportunity area for future research.

The COVID-19 pandemic compounded existing equity challenges at both the individual and global level. COVID-19 disproportionally affected people based on age, income, race or ethnicity, gender and sexual orientation, and migrant status. Many of these populations faced barriers to access testing and other services (eg, reduced access to sexually transmitted and blood borne infection (STBBI)) due to COVID-19. As well, globally, many countries faced limited or reduced access to vaccinations, reduced access to laboratory materials, and reduced staff availability—all of which may drive inequitable AMR transmission. Despite these known impacts, we found no studies included in this study direct mentioned equity or social determinants of health.

Five policy implications emerged from this review:

- 1. Improve AMR surveillance systems. Effective and timely policy decisions require improved AMR surveillance systems to ensure robust data collection during future pandemics, and that AMR trends are identified in an appropriate timeframe.
- 2. Address AMR as part of pandemic preparedness. The COVID-19 pandemic has had profound implications for AMR, and we should expect that future pandemics will also impact and be impacted by AMR. Policymakers working in pandemic preparedness must ensure that AMR is addressed.
- 3. Develop Antimicrobial Stewardship (AMS) programs that evolve alongside changes to health system use. Policymakers can draw important lessons from the changes seen during the COVID-19 pandemic. For example, the decrease in community AMU observed at the start of the pandemic could be maintained by implementing stewardship activities that target outpatient and community prescribing.

- 4. Build stronger links between IPAC and AMS programs. Effective IPAC is key to reducing demand for antimicrobial use and therefore reducing AMR. There is a need to integrate IPAC and AMS programs in settings which influence and inform the development and uptake of preventive measures.
- 5. Determine the inequitable impacts of the pandemic on AMR. This will allow the implementation of effective IPAC measures, particularly for populations disproportionately impacted by AMR (e.g., remote and isolated communities, long-term care residents) by developing, updating and promoting uptake of guidelines/best practices including stewardship programs for human health.

## 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 only accelerated the need for global action to address rising AMR rates (2). In 2019 alone, bacterial AMR contributed to almost 5 million deaths (3). The World Health Organization (WHO) estimates that AMR has caused at least one-third as many deaths as COVID-19 in 2020 (4). Whether the COVID-19 pandemic will have a net negative or positive impact on AMR has been widely debated (5,6).

Historically, AMR has been 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 (7) by concurrently promoting AMR emergence and burden (5). 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 (6). While in hospital IPAC measures may have been negatively impacted by the re-distribution of resources from AMR to control of COVID-19 (8). The COVID-19 pandemic has also compounded existing societal and health inequities, such as limited or reduced access to vaccinations (9), reduced access to laboratory consumables, and reduced staff availability in healthcare systems in low-resource settings, which may in turn drive inequitable AMR transmission (6,8).

## **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, Norway, and the US. The Global Strategy Lab (GSL) completed the data extraction in Excel, and results were descriptively summarized in *Table 1*.

#### What's new?

- Fifteen new studies were included in this report.
- A second reviewer verified the inclusion of studies and risk of bias assessments were completed for all studies.
- National AMR trends were explored for WHO priority pathogens.

#### 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 (10) 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 September 1<sup>st</sup>, 2023 were included in this review.

#### Eligibility criteria

Studies published in English between March 2020 and September 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 and did not identify any missed studies. 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 (11). Cohort studies were evaluated using the Newcastle Ottawa Scale (NOS) for cohort studies (12). The three environmental sampling studies (no samples from human participants) were evaluated using the Collaboration for Environmental Evidence Critical Appraisal Tool (13).

#### 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 (14) including place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status and social capital. "Plus" factors, include those used to refer to personal characteristics associated with discrimination (e.g., age, disability), features of relationships (e.g., smoking parents, excluded from school) and time-dependent relationships (e.g., leaving the hospital, respite care, other instances where a person may be temporarily at a disadvantage).

#### 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 classified under health system use only 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

#### National trends in AMU

AMU surveillance data from high-income countries (HICs) including Canada (15), Japan (16), Norway (17), England (18), Denmark (19), and other countries in the EU (20) all reported overall decreases in AMU in 2020 due to substantial reductions in community antimicrobial consumption (*Appendix 1, Table 1*) (16,17). Most countries also reported decreased hospital AMU in 2020, though England reported an overall decrease in AMU despite increased hospital prescribing (18). In 2021, the EU (21), Canada (15), Norway (17), England (18) and Denmark (19) continued to report that total AMU remained below 2019 levels. However, the US reported an increase in AMU in 2021 compared with 2019 due to increased community AMU. Surveillance data from 2022 was not available at the time of writing.

Community or outpatient use is the largest contributor to human AMU in most countries (22). The US (23) found an initial decrease in community AMU during 2020 followed by an increase in 2021 to higher than 2019 levels (23) (*Table 1*). In 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 (24). 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 (25). In Norway, community AMU

did not show a significant change between 2020 and 2021 (17). 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 (26). In the European Union, which saw a dramatic decrease in community AMU during 2020, community AMU did not change between 2020 and 2021.

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
European Union	Decreasing	Significant decrease between 2019 and 2020	No change from 2020
Denmark	Decreasing	Significant decrease between 2019 and 2020	Increasing
Norway	Decreasing	Significant decrease between 2019 and 2020	No change from 2020

Table 1. Community AMU trends for countries from before 2020 to 2021

#### National Trends in AMR

Most national surveillance programs track AMR trends in priority pathogens, a list of 12 species of bacteria classified by the WHO as having critical, high, and medium rates of antibiotic resistance (27). Across countries, surveillance data showed increasing, decreasing, and mixed trends in resistance rates among priority pathogens in 2020 and 2021 for countries reporting 2021 data (*Figure 1*).

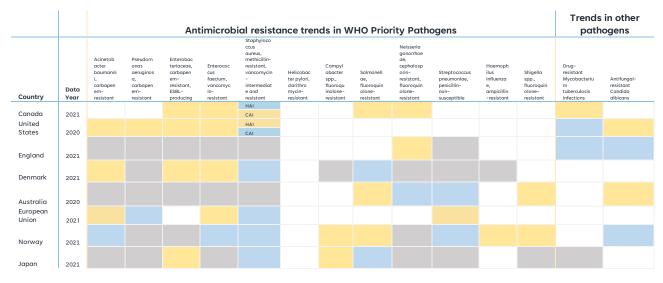


Figure 1. AMR trends for countries for WHO priority pathogens, drug-resistant Mycobacterium tuberculosis and anti-fungal resistant Candida albicans. HAI = Hospital-associated infections; CAI =community-acquired infections.



For 9 of their 18 priority pathogens the US noted a 15% increase in the rates of HAIs in 2020 compared to 2019. Data is currently unavailable for the remining pathogens (23). In 2020, Canada reported an increase in AMR for most priority organisms, except for hospital-associated MRSA infections which have been declining since 2018 (26). England had also observed an increase in AMR burden in key pathogens causing blood stream infections since 2017 before AMR rates fell in 2020. This lower level of resistance was maintained in 2021 (24). The European AMR Surveillance Network found most bacterial species–antimicrobial combinations under surveillance showed either a significantly decreasing trend or no significant trend in AMR rates with the exception being Acinetobacter spp, VRE and Streptococcus pneumonia where resistance significantly increased (20). Denmark (19), Norway (17) and Japan (16) reported variable increasing, decreasing or no change in resistance across their HAI pathogens.

The US reported that community MRSA incidence was decreasing in 2020 compared to 2019 (15,23), but reported increasing resistance among community-associated infections with ESBLproducing Enterobacterales (23). Denmark (19) also reported decreasing incidence of communityassociated MRSA infections. The EU (20), Norway (17) and Japan (16) did not separate MRSA trends into community and hospital but did report overall decreasing MRSA trends. Canada concurrently found that community MRSA was increasing in 2020 compared to 2019 while rates of community-associated Vancomycin-resistant Enterococcus remained consistent during 2019 and 2020 (15), while rates of resistant TB remained unchanged during the pandemic. In Australia(28), resistance to ciprofloxacin and other fluoroquinolones rose in 2020 among isolates from community-associated E.coli infections, while Carbapenem resistance in community Enterobacterales isolates decreased in 2020.

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

Sixty-three studies were identified (*Appendix 1, Table 2*) that collected data on one of the three drivers (*Appendix 1, Table 3*) and AMR (*Figure 2*).

Twenty-four studies explored the link between AMU and AMR burden (30–52), thirty-four studies investigated the link between COVID-19 related changes in IPAC measures and AMR burden (16,41,42,52–79) and six studies considered changes in health system use as a driver of AMR burden (80–85). Two studies collected data on two drivers (IPAC and AMU) and AMR burden (41,52). 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 (86–88) and one that looked at emergence (89). 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 (90). No studies attempted to measure changes in health system use as a driver of AMR transmission or emergence.

Most included studies looked at changes in AMR burden during the first 12 months of the pandemic, starting in March 2020, (2021). Twenty-one studies (30,43,44,53,59,62,66,68–71,73,74,76,78,79,82,83,89–91) explored resistant CAIs; most studies were single-site hospital-based studies focused on HAIs. Eight studies collected data on both HAIs and CAIs (30,44,53,62,66,68,73,80).

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		Risk of Bia	
Setting	Hospital	Community	Hospital	Community	Hospital	Community	Modera	
Antimicrobial Use		•			•	••	Low-ris	
Infection Prevention Control		•	•		•	•		
Health System Issue					••	•		

Figure 2. Map of study classification in accordance with the Knight et al. (29) framework, and risk of bias. Bubble size reflects number of studies while bubble colour reflects risk of bias assessment.

#### AMR burden

The majority (fifty-eight) of studies included in this review explored the impact of COVID-19 drivers on AMR burden (16,30,32–37,39–41,41–57,59–73,76–78,80–84,91–95). Of these, twenty-four studies explored the link between AMU and AMR burden (30–52,91), and thirty two studies investigated the link between COVID-19 related changes in IPAC measures and AMR burden (16,41,42,52–79).

#### AMU and AMR burden

We identified twenty-four studies which explored the link between changes in AMU driven by COVID-19 and the number and nature of infections due to antimicrobial resistant organisms (AMR *burden*) (30–52,91).

#### Community

Four studies (30,43,44,91) looked at the impact of decreasing community-based AMU on AMR burden. In Hong Kong researchers found a decrease in antimicrobial sales in 2020-2021 compared with 2012-2019 that coincided with a significant decrease in community-onset bacteremia caused by Streptococcus pyogenes, Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis as well as scarlet fever and air-borne infections, including tuberculosis and chickenpox, but found increasing rates of community-onset bacteremia due to methicillin-sensitive Staphylococcus aureus (MSSA), MRSA and Escherichia coli (30). In Italy, researchers found overall antibiotic consumption decreased by 28% from 2019 to 2020 while susceptibility to amoxicillin/clavulanate increased among Enterobacterales isolates (43). Similarly in Slovenia, a reduction in resistance to macrolides by 42% and 40% in 2021 and 2022 respectively among invasive pneumococcal diseases was significantly associated with a 20% decrease in the use of macrolides (91). While in Northern Ireland, an analysis of all primary care (community) AMU found a reduction community AMU from 25.56 to 20.53 defined daily doses (DDDs) per 1000 occupied-bed days but no change in hospital AMR or community-associated MRSA pre-pandemic to during the pandemic (44).

#### Hospital

Hospital-based studies, by contrast, largely found an increase in AMU (31–40,45); however, changes in AMU still did not consistently correspond to higher or lower rates of AMR. Eight of the studies reporting increased AMU are from ICU or COVID-19 referral settings (31,33,34,37,40,42,45,47). For example, studies from a medical centre in Taiwan, which measured change in density of MRSA, VRE, CRA, carbapenem-resistant *Klebsiella pneumonia*, and CRPA (46), an interrupted time series analysis of all hospitals Sao Paulo city in Brazil which looked at change in resistance of MRSA, VRE, CRA, and Enterobacterales (47) and an interrupted time series of a university hospital in the US looking at change in resistance to CRPA, CRA and Enterobacterales (33) all found no change in resistance despite increasing AMU. A study from the US also found that despite an increase antibiotic prescriptions, patients admitted during the pandemic (2020 – 2021) had significantly lower rates of a number of resistant infections including MRSA, VRE, and resistant E.Coli, Klebsiella spp, Enterococcus spp, and *Streptococcus pneumoniae* than those admitted pre-pandemic (2019) (35).

Other studies found an increase in resistant HAIs along increasing AMU during the pandemic. For example a study from an Italian hospital which looked at changes in resistance to MRSA, CRA, and carbapenem-resistant *Klebsiella pneumonia* (42), a study examining resistance in MRSA, VRE, CRE and CRA from four university hospitals in Korea (31), a study looking at extended spectrum beta-lactamase-producing (ESBL) in K. pneumoniae and E. coli and carbapenem-resistant *Klebsiella pneumonia* from an ICU in a university hospital in Turkey (50) and a study using data from 46 laboratories across Mexico looking at MRSA, erythromycin resistance in S. aureus, carbapenem resistance for K. pneumoniae CRA and CRPA (38) all reported increasing resistance incidence. A number of studies also reported increasing resistance in single pathogens including a Brazilian study found an increase of all CRA infections reported to the Parana state health department in 2020 (36). Similarly studies from Chile and Poland found increased AMU was accompanied by an increase in carbapenem-resistant Enterobacteriaceae (CRE) and resistant *Acinetobacter baumannii* infections, respectively (45,49).

Finally, some studies reported different resistance trends among the pathogens they examined. For example, a study from Japan (2018 to 2022) found no change MRSA, but an increase in ESBL Enterobacterales incidence (40). A Columbian study found during the pandemic (2020-2021) resistance significantly decreased for *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, while resistance of *Enterococcus faecium* to vancomycin increased and resistance did not change for MRSA, ESBL and carbapenem-resistant *Escherichia coli* (48). A study from Hong Kong found a significant increase in the trend of carbapenem-resistant Actinetobacter (CRA) infections during the pandemic (2020-2022) compared to before (2017-2020) but no significant increase in the trend of MRSA and ESBL-Enterobacterales infections (52).

A few hospital studies reported reduced or no change in AMU during the pandemic. Three of four of the studies reporting no change or reduced AMU look at whole hospital AMU and aren't focus on ICU or COVID-19 ward settings (32,39,44). A single-center study from a university hospital in Italy found comparable incidence of hospital-associated and multidrug resistant infections pre-2019 and during the pandemic (2020) despite significantly reduced AMU (37). A single center study from a university hospital in the US did not find any change in AMU between 2019 and 2020 (39) but found increases in some AMR pathogen events (vancomycin resistant *Eneteroccocus* (VRE) and CRE) but no difference in others (carbapenem-resistant *Pseudomonas aeruginosa* 

(CRPA), MRSA). A time-series analysis from Northern Ireland from 2015 to 2021, which used data from hospitals capturing 81% of the population also found no significant change in AMU from prepandemic. Although they found *Klebsiella oxytoca* and MSSA cases increased, MRSA cases remained the same during this this period (44). An interrupted time-series analysis from a university hospital in Italy (2015-2021) also found a decrease in antibiotic consumption during the pandemic however the increase in MRSA blood stream infections was not statistically significant (32).

#### IPAC and AMR burden

#### Community

Twelve studies collected data on the impact of IPAC on CAIs (53,59,62,66,68–70,73,74,76,78,79) and most reported a reduction in both CAIs and resistance. Implementation of COVID-19 nonpharmaceutical interventions (NPIs) like physical distancing, face masking, hand hygiene, stay-at-home orders, school closures, closing borders and travel restrictions from April 2020 to March 2021 resulted in significant reductions in both incidence and Macrolide-resistance of *Mycoplasma pneumoniae* rates globally (69). A 2020 interrupted time series analysis from Germany assessed the impact of non-pharmaceutical measures and found drastic reductions in resistant and susceptible CAIs (73). In Taiwan a study (2018-2021) showed reduced incidence of droplet-transmitted infectious diseases including multidrug resistant (MDR)-Tuberculosis (TB) during the pandemic period (71).

In contrast, some studies found less consistent associations between IPAC and community AMR (53,55,66,73,74,78,79). A study from China (2011-2020) looking at the effect of COVID-19 IPAC measures (including vaccination, social distancing, masking, hand hygiene, and environmental disinfection) on pediatric respiratory tract infections found that *Escherichia coli* and *Klebsiella pneumoniae* cephalosporin resistance decreased but carbapenem resistance and rates of MRSA increased (74). 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 in Germany did not result in significant changes in the prevalence of drug-resistant bacterial pathogens despite significantly decreases in CAIs overall (62). Researchers from Taiwan found these same measures had limited efficacy in reducing TB transmission and found no change in MDR-TB trends during the pandemic (76). While in the Netherlands, although lockdowns led to an overall decrease of casual sex partners, resistance of *Neisseria gonorrhoeae* isolates to azithromycin increased while ceftriaxone susceptibility increased (79).

Prevalence of resistant gastrointestinal pathogens may have decreased because of COVID-19 IPAC measures like stay-at-home orders, closed schools and reduced public transport crowding. A decrease in both salmonellosis incidence and proportion of trimethoprim resistance was found in the Netherlands (70) during the pandemic (2016 to 2021). For example a study from Botswana looking at cephalosporin-resistant *Enterobacterales* and CRE carriage found prevalence was significantly reduced post-lockdown (68). Similarly studies from France found reduced ESBL-*E.coli* rates in primary care and nursing home residents (59). A US study found that lifestyle changes, including lockdowns, social distancing, and extensive hygiene practices during the pandemic may have improved human gut bacterial susceptibility (78). However one time series analysis from Japan (2015-2020) reported incidence of CRE was unchanged, despite significant reductions in the incidence of other common infectious diseases which they attributed to mask wearing, handwashing, and avoiding crowded spaces (66).

#### **Hospital**

Counter to the argument that COVID-19 compromised hospital IPAC programs (5), many studies reported that improved IPAC measures during the COVID-19 pandemic corresponded with reduced resistant HAIs. Studies from hospitals in Taiwan (55), Italy (54,65,77,86), Turkey (67), India (63) Portugal (72) and Lebanon (34) identified a significant reduction in multidrug resistant bacterial infections 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 (57). A study from Singapore that also evaluated the impact of a similar multimodal program found that while rates of most HAIs were stable, hospital-wide MRSA acquisition rates declined significantly (56). A study from Japan (41) found that while the use of hand sanitizer and antibacterial drugs increased during COVID-19, the incidence of MRSA blood infections (non-significantly) decreased in all departments.

Some hospital studies reported no change in AMR due to COVID-19 IPAC measures, including a hospital in Turkey (60) and an Australian single-hospital study of surgical patients (58). Other studies found increasing AMR despite universal mask wearing, increased hand sanitizer consumption and improved hand hygiene compliance. This included a single-hospital study from Japan (96) which found the incidence of VRE to be (non-significantly) higher and a study from China which found MRSA incidence increased (97). A study from Hong Kong (52) also found significant increases in CRA infections and non-significant increases in MRSA and ESBL-producing Enterobacterales infections. Another Chinese study found despite community mask wearing, hand hygiene and social distancing, hospital-associated MRSA infections increased (53).

#### Health system use and AMR burden

We identified six studies that considered the impact of COVID-19 driven changes in health system use on AMR burden (80–85).

#### Community

Three studies explored changes to resistant CAIs (80,82,83). In Nigeria, an exponential increase in incidence of rifampicin resistant TB in 2022 was attributed to reduced testing during 2020 and 2021 (82). In Western Siberia reduced resistant TB incidence was attributed to under-testing, reduced access to resources, and reduced detection rates (83). A study from the UK found community-associated E. coli blood stream infection rates remained below pre-pandemic levels during COVID-19 but began to peak following the easing of lockdown in May 2020. They reported an increase in hospital MRSA infections during the pandemic which they believed was due to increased numbers of critical patients and ICU overcapacity (80).

#### Hospital

An Italian study investigating impact of ICU patient numbers on AMR reported increasing resistance in *Pseudomonas* spp. and *Enterobacterales* spp. (81). A study from Greece found an increasing trend in the incidence of resistant Gram-negative bacteria during COVID-19 from 2020 to 2022 when compared to 2018-2019, which corresponded with reduced number of infectious disease consultations (84). A Mexican study found despite a 36% reduction in total surgeries in 2020 compared to 2019 but no significant change in resistance (95).

#### AMR emergence

Two studies considered the role of COVID-19 in contributing to AMR emergence or the emergence of new drug resistant strains of resistant infections (89,90). Both studies looked at community-associated infections. No studies were identified that looked at the impact of health-system use on AMR emergence. No studies looked one of the three drivers and emergence of AMR in hospital settings.

#### AMU and AMR emergence

A study of antidrug resistant genes from ambient waterways in India (2018-2020) found a significant increase in *E.coli* antidrug resistance during the pandemic which they attributed to higher rates of AMU and antibiotic pollution during the pandemic (90).

#### IPAC and AMR emergence

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. Another Indian study found the prevalence of genes associated with drug resistance decreased by 0.64-fold during COVID lockdown in India (June 2020) suggesting bacteria that re-established during lockdown have lower prevalence of the gene families associated with drug resistance (89).

#### AMR transmission

Three studies considered the role of COVID-19 IPAC measures in reducing AMR transmission (86–88). All three studies investigated HAIs; none looked at community settings. No studies looked at the impact of AMU or health system use on AMR.

#### IPAC and AMR transmission

An Italian single-center study (2019-2020) found significantly reduced transmission of carbapenemase-producing *Klebsiella pneumoniae* in hospitalized patients because of COVID-19 measures including PPE (masking, gloves, gowns), increase hand sanitization, visitor restrictions and reduced ward transfers (86). 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 outbreaks (87). Conversely an interrupted time series, multicenter analysis from Italy, found no change in incidence of colonization and infection with carbapenemase-producing *Enterobacteriaceae* and carbapenem-resistant *Actinobacter* before and during the pandemic (88).

#### Risk of bias assessment

The quality of non-randomized studies judged using the ROBINS-I tool ranged from an overall rating of "moderate" for five studies (30,47,53,68,84) to "serious" (16,31–34,36,38,41,43–46,48,50–52,54–56,59,60,62,64–67,70,71,73,78–80,82,83,85–87,91,97–100) risk of bias for the remainder of the studies (*Appendix 3, Figure 1*). Many studies failed to adjust for potential confounding factors, including time-varying confounding factors before and after the pandemic. For interrupted time series (ITS) studies, most studies failed to adjust for the months/time of year that AMR was assessed (e.g., seasonality). Selection bias was not a large concern in studies that

used linked patient databases, but several studies failed to account for different follow up times between participants. For ITS studies, most studies did not provide a rationale on what date was selected as the interruption point (i.e., when the pandemic period began) or what time was selected to begin follow up to monitor post-pandemic AMR. The surveillance systems or sampling methodologies to obtain data on antimicrobial resistant strains were poorly reported in many studies, although the laboratory methods were generally well-reported. Additionally, the proportion of missing outcome data/participants excluded for missing outcome data was poorly reported across studies, making the potential effect of bias difficult to judge in this domain.

Studies evaluated using the Newcastle Ottawa Scale (35,37,58,63,72) 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.

Finally, we judged the three studies evaluated using the Collaboration for Environmental Evidence Critical Appraisal Tool (61,89,90) to have a high risk of bias (*Appendix 3, Figure 3*). Like the ITS studies, environmental sampling studies failed to control for any confounding factors or to account for other factors that may have changed in the environment unrelated to the pandemic. Risk of Post-Intervention/Exposure Selection Biases was judged to be "low" as sampling areas were reported to remain the same in the pre-pandemic and post-pandemic periods. Although the sampling locations and laboratory procedures appeared to remain the same in both prepandemic and post-pandemic periods across studies, there was insufficient reporting of how the environmental samples were obtained.

#### Equity: PROGRESS-Plus Framework

Most included studies did not collect data on PROGRESS-Plus factors. Twenty-nine of the sixtythree studies (32,35,37,45,50,52,53,57–59,63–65,67–70,72–74,78–82,84–86,91) collected data on at least some PROGRESS-Plus characteristics. Four studies collected data on place of residence (35,59,69,73), one collected race, ethnicity, culture, or language data (80), twenty-six collected gender/sex (32,35,37,52,53,57–59,63–65,67–70,72–74,78–82,86,91,101), while twenty-eight collected personal characteristics associated with disability (e.g., age) (32,35,37,50,52,53,57– 59,63–65,67–70,72–74,78–82,85,86,91,101), and twenty-two collected information on timedependent relationships (e.g., leaving the hospital or time to discharge, risk factors, or other instances where a person may be temporarily at a disadvantage) (35,37,45,50,52,53,57,63– 65,67,68,70,72,78,80,81,86,88,92,95,101). 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 (23) and Denmark (19) 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 England (24), Norway (17) and Canada (26) have not yet seen this rebound in community prescribing. Additional trends in community AMU may become apparent as later data is released. Differences in the implementation of COVID-19

measures such as lockdowns, physical distancing, travel restrictions, and masking — 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 explain why studies did not find AMU was consistently associated with a positive or negative impact on AMR. Although other COVID-19 driven changes including healthcare provisions due to reduced healthcare seeking, reduced secondary care referrals, and reduced diagnostic capacity have been hypothesized to affect AMR (23) additional evidence is needed to substantiate these 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.

#### 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 (eg. when looking at whole hospital AMU) and decreases in community settings. Within the timeframe of these studies, researchers did not find that changes to AMU consistently resulted in negative or positive effects on AMR. As well, some national surveillance data showed increases in the rates of priority pathogens, most notably in the US which observed a 15% increase in the rates of resistant HAIs in 2020 (23).

Inappropriate antibiotic use in milder COVID-19 cases is likely the major contributor to increased AMU in ICU hospital settings (102). 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 beginning (between March and October of 2020) of the pandemic received an antibiotic (7) and in countries such as Liberia and Ghana, prescribing guidelines recommended antibiotics for COVID-19 cases with mild or moderate symptoms (103). This unnecessary prescribing must be addressed in future pandemics through rapid publication of guidelines to prevent antimicrobial misuse and resultant AMR impacts.

Studies tracking environmental indicators of AMR offer an interesting perspective on how these results may be impacted by interactions between AMR drivers. Included studies from India found a reduction in AMR genes in rivers attributed to restrictive IPAC measures like lockdowns (89) and an increase in AMR genes in a different Indian river system attributed to increased AMU and environmental pollution during the pandemic (90). These two examples underline the need to examine driver interactions collectively, since examining them in isolation would provide an incomplete understanding of how environmental AMR emergence has potentially evolved in India

during the COVID-19 pandemic. Examining only a single driver of AMR provides an incomplete picture and additional studies examining interactions between drivers in different settings are needed.

#### COVID-19 and IPAC measures

#### Community

The COVID-19 pandemic saw the 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 droplettransmitted respiratory diseases (71). 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 (104). In Spain, gathering size restrictions and physical distancing measures coincided with the greatest reduction in AMU. Preventative measures such as physical distancing, contact and travel restrictions, and closures of day cares, schools, and restaurants may explain reported reductions in gastrointestinal disease, spread of sexually transmitted infections (STIs), and other diseases (62,66). 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. However, any broad community IPAC measures being considered 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 resources such as STI prevention.

#### Hospital

While some types of resistant HAIs appear to have increased during the COVID-19 pandemic (105), others have decreased (106). The COVID-19 pandemic 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 (107). 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. Conversely, 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 (86,87). Reduced transmission may also be attributed to changes in health system use during the pandemic: restrictions saw fewer patients in secondary care and reduced elective surgeries (108). It is unlikely the reductions seen during acute phases of the COVID-19 pandemic would be replicable outside a pandemic, so focusing on achievable targets such as improving IPAC would likely result in long term benefits for AMR and other infections.

#### COVID-19 and health system use

Health system use changed significantly during the COVID-19 pandemic through increased ICU admissions, raised threshold for seeing a general practitioner for symptoms, and shifting inperson appointments to telemedicine ones (109) all of which may have also impacted AMR. However, we found few studies which examined these factors as a driver of AMR. The studies we did find suggest that changes to health system use during the COVID-19 pandemic including limited capacity to provide service delivery and diagnosis for community-associated diseases like human immunodeficiency virus (HIV), tuberculosis (TB), malaria, and STIs, as well as reduced global vaccination coverage (110–112) may have negatively affected AMR. Decreases in availability and access to these resources is well documented but additional evidence is needed to clearly link these challenges to AMR. For example, the WHO estimated that because 1.4 million fewer people received care for TB in 2020 than in 2019 (113), there may be significant repercussions for AMR given that TB is the greatest contributor to global AMR burden (3). Other changes to health system use like changes in the number of consults, the swap to telemedicine consults or the reduction in elective surgeries have unknown effects on AMR and additional research investigating this is needed.

#### Equity impacts of COVID-19

The COVID-19 pandemic compounded existing equity challenges at both the individual and global level. COVID-19 disproportionally affected people on the basis of age, income (114), race or ethnicity (115), gender and sexual orientation (116), and migrant status (117). Many of these populations have also been identified as being at higher risk of AMR (118) and 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 (119). Despite these known impacts, no studies included in this study direct mentioned equity or social determinants of health.

Globally, some countries faced limited or reduced access to vaccinations, reduced access to laboratory materials, and reduced staff availability—all of which may drive inequitable AMR transmission (6,8). These impacts were particularly felt by low- and middle-income countries (LMICs): HICs, overwhelmed by COVID-19, reduced their capacity to support AMR partnerships and reduced funding to programs in LMICs (8). The COVID-19 pandemic also inequitably impacted the ability of countries to develop and maintain strategies to address and mitigate AMR (104). Since AMR is a borderless threat, all countries must share the responsibility of addressing it.

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 research is needed that specifically accounts and evaluates for these equity impacts. More targeted research on the effects of diminished capacity in HICs to support and fund AMR initiatives in 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 using data collected in 2020 during the early stages of the COVID-19 pandemic. Risk of bias assessment found many of the included studies were assessed as at a "serious" risk of bias, which may affect the certainty of data synthesized from these studies. Future high-quality research with clear reporting and appropriate adjustment for confounding factors is required to increase confidence in the conclusions drawn from these studies. Data from later stages of the pandemic (beyond 2020) are likely to show different results. Later studies may be forthcoming, or may reflect a change in research focus during the later stages of the pandemic. 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.

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 the reduced number of referrals provided by general practitioners (120). Similarly in many countries, laboratory capacity was overwhelmed by COVID-19 testing resulting in reduced reagents and staff availability to perform cultures (8,121).

Key research gaps include a complete lack of evidence on the impact of COVID-19 on healthsystem use as a driver of AMR emergence or transmission, and a lack of evidence on AMU as a driver of AMR transmission (*Figure 1*). More studies investigating all three drivers on AMR emergence and transmission are needed. Most studies focused on hospital settings in HICs, 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 (81) despite the fact that there have been multiple reports of increased antifungal use (122) and selection for fluconazole resistant *C. parapsilosis* during the COVID-19 pandemic (123). 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 (124). Investigations focusing on fungal resistance are needed.

## **POLICY CONSIDERATIONS AND IMPLICATIONS**

Antimicrobial use (AMU) and antimicrobial resistance (AMR) surveillance data lags by 18-24 months and therefore reflects an earlier phase of the COVID-19 recovery. Population research data, which typically relies on this surveillance data, lags even further. For example, most studies included in this report contain data from 2020 or 2021, meaning policymakers are using data that is outdated. It is possible that the AMU and AMR trends reported from the US in 2021 — 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 (125) — earlier than Canada and most other countries (126). Acting now to reinforce antimicrobial stewardship may be critical to avoiding the increased AMU seen in the US.

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

#### Improve 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.

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 must also 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 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 ensure the development of successful mitigation and stewardship strategies during future pandemics.

#### Address AMR as part of 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. It should be expected 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 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.

## 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, and restricted reimbursement are all effective in reducing community prescribing (127,128). An additional consideration is that since spring 2023, Canadian pharmacists now have prescribing rights for minor ailments in all provinces, as a result AMS programs should also include pharmacists in audit and feedback programs, community stewardship initiatives, and pledge programs (129,130).

#### 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 in particular, like social distancing, face masking and lockdowns were 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. Effective IPAC is key to reducing demand for antimicrobial use and therefore reducing AMR (131). There is a need to integrate IPAC and AMS programs in settings which influence and inform the development and uptake of preventive measures.

#### Determine the inequitable impacts of the pandemic on AMR.

Although COVID-19 has impacted access to community infection prevention measures like supervised consumption sites, sexually transmitted and blood borne infection (STBBI) clinics that may reduce AMR infections in key populations, few research studies collected data on demographic or equity related PROGRESS-Plus factors, limiting our ability to assess the extent to which the 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 and treatment for AMR infections. Identifying populations with inequitable COVID-19 and AMR effects will allow also allow for the implementation of effective IPAC measures, particularly for populations disproportionately impacted by AMR (e.g., remote and isolated communities, long-term care residents) by developing, updating and promoting uptake of guidelines/best practices including stewardship programs for human health.

## CONCLUSIONS

The COVID-19 pandemic has changed the landscape of AMR in ways we still do not fully grasp. COVID-19 has impacted AMU, IPAC measures, and health system use differently, impacting AMR emergence, transmission, and burden. However, differences in the implementation of COVID-19 measures across countries and settings are reflected in the substantial variability in the reported impact of COVID-19 on AMR. Most results are from early in the COVID-19 pandemic and as later data becomes available longer-term impacts and trends in AMR may be identified. To ensure evidence-informed AMR policy solutions, additional research, especially high-quality studies, are needed to fully elucidate the impact of COVID-19 driven changes in AMU, IPAC, and health-system on AMR.

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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 <i>Streptococcus pneumoniae</i> 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.	A 15% overall increase was noted key hospital-associated pathogen-antimicrobial combinations including: carbapenem-resistant <i>Acinetobacter</i> , extended-spectrum beta-lactamase- producing Enterobacterales, and vancomycin-resistant <i>Enterococcus</i> . Antifungal-resistant <i>Candida spp</i> . 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.
		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.		
England, 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	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	English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2021 to 2022

		to be highest in general practice (72.1%), with a marginal reduction seen in this setting. 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.	increase in rate of BSI caused by key pathogens. However, rates of Escherichia coli and Streptococcus pneumoniae 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. <i>Escherichia coli</i> caused about 49% of bacteraemias with <i>Staphylococcus aureus</i> 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.	There was an overall increase of 26.8% in critical antimicrobial resistances reported in 2019 compared with 2018. However, in 2020, there was a 21.3% decrease in reports compared with 2019. Reports of carbapenemase- producing Enterobacterales decreased by 27% in 2020 compared to 2019. Multidrug-resistant Shigella species, and Azithromycin- or ceftriaxone-non-susceptible Neisseria gonorrhoeae also decreased. Vancomycin-, linezolid- or daptomycinnonsusceptible Staphylococcus aureus was the only critical antimicrobial resistances reported to have increased in 2020.	Fourth Australian report on antimicrobial use and resistance in human health: AURA 2021

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. In 2021, the EU/EEA population-weighted means for total consumption and community consumption stabilised after unprecedented reductions between 2019 and 2020.

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). 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 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. OECD 2022

Antimicorbial consumption in the EU/EEA (ESAC-Net) – Annual Epidemiologica Report for 2021

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 carbapenemaseproducing 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).

Norway, 2021 2013 to 2021\*

Japan, 2022 2019 to 2020 (AMR data 2013-2019

2019 to 2020In 2020, usage of antimicrobial agents in Japan based(AMR dataon total yearly sales fell by 29.9% from 2013. Oral2013-2019antimicrobial agents accounted for 91.5% of total sales,unless specified)with cephalosporins, fluoroquinolones, and macrolidesaccounting for the highest shares. The three mostfrequently used antimicrobial classes have alsodecreased in use by 42.7%, 41.3%, and 39.3%,respectively, compared to 2013. Injectableantimicrobial agents have also decreased by 1.1%compared to 2013.

Data is only available for some pathogens to 2020 so additional data is needed to determine trends during COVID-19. Carbapenem resistance rate in Enterobacteriaceae, particularly Escherichia coli and Klebsiella pneumoniae has remained below 1% to 2019, despite its global increase in human isolates. Resistance rates to third generation cephalosporins and fluoroquinolones in E. coli were increasing in 2019. Carbapenem resistance in Pseudomonas aeruginosa is on a decreasing trend. Vancomycin (VCM) resistance in Enterococcus faecium was 1.4% in 2020 and it has been increasing in recent years, including increasing widespread hospital outbreaks due to VCM-resistant E. faecium were observed in some regions. Percentage of methicillinresistant Staphylococcus aureus (MRSA) has been declining since 2011 but levels remain high.

Nippon AMR One Health Report (NAOR) 2021. The AMR One Health Surveillance Committee 2023.

#### \*Data is available from 2021 on AMU

Hospital-associated infections (HAIs), community-associated 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* (CRA), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), fluconazole-resistant *Candida parapsilosis* (FRCP), *Neisseria gonorrhoeae* (GC), *Clostridial difficile* infections (CDI), MDR (multidrug resistant)

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.	(82)
Aldeyab 2023	Northern Ireland	Interrupted Time Series	Data was collected on antibiotic use and Gram- positive and Gram-negative pathogens from primary and secondary health care settings in Northern Ireland for the period before and during the pandemic.	2015-2020	Community and Hospital	In the hospital setting, the mean total hospital antibiotic consumption did not change during pandemic. The number of hospital Klebsiella oxytoca and methicillin-susceptible Staphylococcus aureus cases increased. MRSA cases remained the same. In primary care, the mean total antibiotic consumption during the COVID-19 pandemic was lower than before the COVID-19 pandemic. There was an increase in the number of community Pseudomonas aeruginosa cases. The incidence of Gram- positives (including MRSA) did not change.	(44)
Allel 2023	Chile	Interrupted Time Series	Evaluated intravenous antibiotic use and frequency of carbapenem- resistant Enterobacterales (CRE) pre and post COVID- 19 at a tertiary hospital in Santiago, Chile.	2018-2022	Hospital	Compared with pre-pandemic, antibiotic use significantly increased after the pandemic onset, for broad-spectrum β-lactams, carbapenems, and colistin, respectively. The frequency of CP- CRE increased during the pandemic.	(45)
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.	(35)
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 ( <i>p</i> < 0.05). Significantly higher incidence of MDR bacterial infections in COVID-19 departments compared with other medical departments.	(54)

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

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.	(33)
Bussolati 2022	ltaly	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).	(37)
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- <i>E. faecium</i> BSI decreased by 34%. There was a significant decrease of 80% in antibiotic isolates ( <i>p</i> -value < 0.0001).	(34)
Chang 2023	Taiwan	Retrospective observational	Measured usage of antimicrobial agents, and HAI density of five major MDR bacteria at a medical center in Taiwan pre and during COVID-19.	2017-2021	Hospital	Antibiotics consumption was significantly increased during pandemic period. There was no significant change of HAI density in MRSA, VRE, CRA, CRKP, and CRPA, comparing the pandemic to the pre-pandemic period. Strict infection prevention measures for COVID-19 precautions and sustained antimicrobial stewardship probably bring these effects.	(46)
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 <i>P</i> < 0.05), but there were no significant changes in infections by VRE, CRE, CRA, or CRPA.	(53)
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, <i>p</i> = 0.001).	(30)

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.	(62)
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	CRA 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 CRA or COVID-19 incidence density, presumably due to empirical and untargeted prescribing.	(36)
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. <i>baumannii</i> and MDR sepsis, which persisted during unlocking.	(63)

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 <i>S. pneumoniae</i> 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.	(16)
Freire 2023	Brazil	Interrupted Time Series	Analyzes HAI rates and antimicrobial consumption in Sao Paulo city before and during the COVID-19 pandemic.	2017-2020	Hospital	HAI increased during COVID-19. The microorganisms' susceptibility profile did not change with the pandemic, but there was a disproportionate increase in large-spectrum antimicrobial drug use.	(47)
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, butsignificantly 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.	(64)
Gaspari 2021	Italy	Interrupted time series	Investigated whether behavioral precautions adopted during the COVID- 19 pandemic also influenced the spreading and MDR of <i>E. faecium</i> , <i>S.</i> <i>aureus</i> , <i>K. pneumoniae</i> , <i>A.</i> <i>baumannii</i> [AB], <i>P.</i> <i>aeruginosa</i> , <i>Enterobacter</i> <i>spp. and E. Coli</i> , [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).	(65)
Gisselø 2022	Denmark	Prospective observational	Outbreak data set were collected prospectively from April 2, 20142014, to August 13, 2020 on VRE <i>E</i> .	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 <i>E</i> .	(87)

			<i>faecium</i> at Copenhagen University Hospital Bispebjerg, Denmark.			<i>faecium</i> outbreak patients and median outbreak duration decreased from 56 to 7 days (88%).	
Guven 2021	Turkey	Retrospective observational	Evaluated the nosocomial infection rates over the first 3 months of the COVID-19 compared to the same time frame of the previous year.	2019 - 2020	Hospital (oncology ward)	The rate of nosocomial infections caused by MDR bacteria was similar between periods (p = 0.677).	(60)
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.	(66)
Hosseini 2023	United States	Retrospective observational	To examine the potential effects of pandemic-related lifestyle changes on the metabolically relevant small bowel microbiome.	2019-2021	Community	The COVID-19 pandemic altered lifestyle through lockdowns, social distancing, altered food consumption and exercise patterns, and extensive hygiene practices. These changes may have affected the human gut microbiome. There were no significant changes in duodenal microbial alpha diversity in the intra-pandemic vs. pre-pandemic group, but beta diversity was significantly different. The RA of several Gram- negative taxa and the RA of potential disruptor genera (E. coli, Shigella) were significantly lower during COVID-19. Lower RA may indicate shift towards more balanced composition with improved susceptibility.	(78)
Hurtado 2023	Columbia	Retrospective observational	Assessed changes in antibiotic resistance of eight of the World Health Organization priority bug- drug combinations and consumption of six antibiotics in Valle del Cauca, Colombia.	2018-2021	Hospital	While resistance significantly decreased for four selected bug-drug combinations (Klebsiella pneumoniae, extended spectrum beta lactamase ESBL-producing, K. pneumoniae, carbapenem- resistant, Pseudomonas aeruginosa, carbapenem-resistant, Acinetobacter baumannii, carbapenem-resistant) the level of resistance for Enterococcus faecium to vancomycin significantly increased. There was no change in resistance for the remaining three combinations (Staphylococcus aureus, methicillin-resistant; Escherichia coli, ESBL-producing; E. coli,	(48)

						carbapenem-resistant). Consumption of all antibiotics increased.	
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 <i>S. aureus</i> 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.	(41)
lpek 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 <i>K. pneumoniae</i> while <i>P. aeruginosa, E.</i> <i>faecium</i> , and <i>E. faecalis</i> 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%.	(67)
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.	(89)
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.	(31)
Kastrin 2023	Solvenia	Retrospective observational	Aimed to investigate the impact of the COVID-19 pandemic on community antibiotic consumption and the resistance of invasive Streptococcus pneumoniae to penicillin in Slovenia.	2015-2022	Community	During the pandemic in 2020 and 2021, the total use of antibiotics for systemic use decreased (due to reduced penicillin and macrolide use). The incidence of invasive pneumococcal diseases in Slovenia had a large decline during the pandemic. Decreased resistance to macrolides was significantly associated with decreased use	(91)

of macrolides, while for penicillin the correlation could not be statistically confirmed.

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 <i>E. coli</i> with results from 2018from 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 <i>E.coli</i> towards non-fluoroquinolone drugs.	(90)
Lemenand 2021	France	Interrupted time series	Compared ESBL- <i>E.coli</i> 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 <i>E. coli</i> isolates from clinical samples were producing ESBL before March 2020 and 2.9% since May 2020 (p < 0.001). In nursing home, the ESBL- <i>E.coli</i> rate was 9.3% before March 2020 and 8.3% since May 2020 (p < 0.001).	(59)
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.	(76)
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. CRA and VRE were significantly lower in 2020 than in 2018 and 2019 ( <i>p</i> = 0.011, <i>p</i> = 0.005 respectively), and MRSA or CRPA incidence slightly decreased with no statistically significant difference.	(55)

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 <i>S. aureus</i> and carbapenem resistance for <i>K. pneumoniae</i> and an increase in erythromycin resistance in <i>S. aureus</i> was detected, which may be associated with high azithlromycin use. In general, for <i>A. baumannii</i> and <i>P. aeruginosa</i> , 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.	(38)
Maczynska 2023	Poland	Retrospective observational	The present study aims to analyze changes in antimicrobial use and change in the drug resistance of Gram- negative Pseudomonas aeruginosa and Acinetobacter baumannii infections.	2017-2022	Hospital	The highest antibiotic use was observed in the hospital between 2020 and 2022, most probably due to the COVID-19 pandemic and the higher number of patients in severe conditions requiring hospitalization. The number of multi resistant strains of A. baumannii was successively increasing; related to increased use, especially during the pandemic period, of broad-spectrum antibiotics, mainly penicillins, third-generation cephalosporins and carbapenems.	(49)
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.	(68)
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 ( <i>p</i> = 0.032). MRSA had a non-significant increase in resistance.	(32)
Meyer Sauteur 2022	Global	Retrospective observational	Investigated global <i>M.</i> <i>pneumoniae</i> 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, <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> (MRMp) rates in April 2020 to March 2021 was observed. The MRMp rates before the COVID-19 pandemic	(69)

						were lower in Europe than in America or Asia, consistent with previous reports	
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).	(86)
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).	(70)
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 <i>P. aeruginosa</i> showed a significant reduction (p=0.004) between these two periods.	(57)
Onal 2023	Turkey	Retrospective observational	This study aimed to evaluate the effects of the COVID-19 pandemic on healthcare-associated infections (HAIs), antibiotic resistance and consumption rates in intensive care units (ICUs).	2018-2021	Hospital	BSI incidence rates were significantly increased in all ICUs during the COVID-19 pandemic. In addition, meropenem, teicoplanin and ceftriaxone consumptions were increased in all ICUs after the start of the COVID-19 pandemic. Although we found an increase of ESBL rates in HAIs for the isolates of K. pneumoniae and E. coli it was not statistically significant. Also found an increase in carbapenem and colistin resistance for the isolates of K. pneumoniae in HAIs, but was also not significant.	(50)
Pascale 2022	Italy	Interrupted time series	Assessed the incidence of colonization and infection with CPE and carbapenem- resistant <i>Acinetobacter</i> (CR-Ab) using a multi- center, before-and-after, cross-sectional study design during 2 study periods, period 1 (January–	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.	(88)

#### April 2019) and period 2 (January–April 2020).

Pereira 2023	Brazil	Retrospective observational	Aimed to evaluate the impact of the first year of the COVID-19 pandemic on antibiotic dispensation and resistance rates in three Brazilian hospitals.	2018 to 2021	Hospital	Reduced antibiotic dispensation occurred during 2020 in all hospitals. However, azithromycin dispensation increased in all hospitals in 2020. Macrolide- resistant bacterial isolates rose from 66.6% in 2019 to 77.1% in 2020 and 88.3% in 2021.	(51)
Petrakis 2023	Greece	Retrospective observational	Evaluated the incidence of antimicrobial resistance and the management of bloodstream infections before and during the COVID-19 pandemic.	2018 to 2022	Hospital	An increasing trend was reported compared to the pre-pandemic period in the incidence of resistant Gram-negative bacteria, particularly in ICUs. In the pre-pandemic period 2018–2019, a total of 246 infectious disease consultations were carried out, while during the period 2020–2022, the number was 154, with the percentage of telephone consultations 15% and 76%, respectively.	(84)
Russotto 2023	Italy	Retrospective observational	This study evaluated the potential COVID-19 pandemic impact on HH practices and rate of healthcare-associated infections.	2017 to 2021	Hospital	A significant increase in alcohol hand rub consumption was seen. A significant decrease in MRSA rates (but not CRE) were seen in 2021 compared to 2017–2019. A significant Spearman's correlation between alcohol hand rub consumption and decreasing CRE rates (but not MRSA) was also found.	(77)
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 <i>P.</i> <i>aeruginosa</i> between periods.	(39)

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-generationthird generation cephalosporins increased significantly. The use of all intravenous antimicrobials as measured by DOT showed a significantly decreasing trend before the pandemic.	(40)
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, <i>A. baumannii</i> , 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-generationfifth generation cephalosporins and piperacillin– tazobactam increased at the beginning of the COVID period.	(42)
Soto Hernandez 2023	Mexico	Retrospective observational	Retrospectively evaluated the impact of the COVID-19 pandemic at a neurosurgical reference center in Mexico City.	2019-2022	Hospital	In 2020 the total number of surgeries was reduced by 36% compared to 2019. The rate of neurosurgical infections increased however no significant differences were found for patterns of resistance to antibiotics.	(85)
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 <i>H.</i> <i>influenzae</i> type B (–4). In contrast, the case number of legionellosis and hantavirus syndrome also increased during the pre-pandemic period.	(71)
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	2019-2020	Community	Overall antibiotic consumption decreased by 28% from 2019 to 2020 and in 2020 strains of <i>Enterobacterales</i> showed increasing susceptibility to amoxicillin/clavulanate among isolated from primary and long-term care.	(43)

			after the beginning of the COVID-19 pandemic.				
Teixeira 2022	Portugal	Retrospective observational	Aimed to compare the rate of postoperative infection and drug-resistant organism (DRO) before and during the COVID-19 pandemic in urology departments.	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 enhanced infection prevention practices adopted during the COVID-19 era.	(72)
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 <i>E. coli</i> were similar across both time periods.	(58)
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).	(73)
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 <i>M. tuberculosis</i> population.	2019- 2021	Community	No change was observed in the <i>M. tuberculosis</i> 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%).	(83)
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, <i>P</i> < .05).	(56)

Wong 2023	Hong Kong	Retrospective observational	Aimed to study the epidemiology of MDRO and antibiotic use before and during the COVID-19 pandemic in Hong Kong.	2016-2022	Hospital	Found a significant increase in the trend of CRA infections, while there was no significant increase in MRSA and ESBL-producing Enterobacterales infections. significant increase in the trend of carbapenems, extended-spectrum beta-lactam- beta-lactamase inhibitor combinations and fluoroquinolones consumption was observed. Increased compliance of hand hygiene per year was maintained.	(52)
Yang 2021	China	Retrospective observational	MRSA detection rates in medical institutions and exposure rates to environmental disinfectants were measured before and during the COVID-19 pandemic.	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 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.	(97)
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 ( <i>Klebsiella spp., E. coli</i> , and <i>Pseudomonas spp.</i> ) and non-pathogenic ( <i>S. aureus</i> and <i>Bacillus spp.</i> ) 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.	(61)
Zhu 2022	United Kingdom	Retrospective observational	Examined community- and hospital-associated BSIs in coronavirus disease 2019 (COVID-19) and non– COVID-19 patients across 2 epidemic waves.	2020 - 2021	Hospital and community	Community-associated <i>E. coli</i> BSIs remained below pre-pandemic level during COVID-19 waves but peaked following lockdown easing in May 2020. The hospital-associated 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-associated 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-associated BSI caused by gram-negative bacteria and MRSA were lower than the pre–COVID-19 level.	(80)
Zhu 2022	China	Retrospective observational	Measured distribution and drug resistance of bacterial	2011 - 2020	Community	Since 2011, the resistance of <i>E. coli</i> and <i>K. pneumoniae</i> to third-generationthird generation	(74)
			a.a.g. constance of sacterial	2020		prisaria generationania generation	

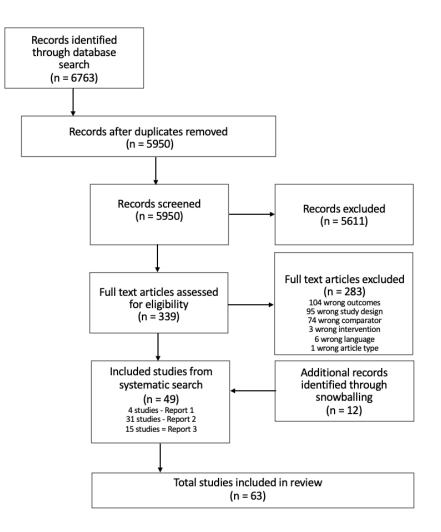
			pathogens associated with lower respiratory tract infection (LRTI) in children in Chengdul from 2011 to 2020 and impact of COVID- 19 measures.			cephalosporins has increased, peaking in 2017, and has decreased after 2018, years after which carbapenem resistance has increased significantly, corresponding to an increase in the detection rate of CRE. In the past three years, 73% of <i>S. aureus</i> 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.	
Zondag 2023	Amsterdam	Retrospective observational	This study investigated the effect of COVID-19 on the genotypic and phenotypic distribution of Neisseria gonorrhoeae (Ng) isolates.	2020	Community	Phenotypic data showed an increase in low- level azithromycin resistance and ceftriaxone susceptibility during the lockdown, and this remained after the study period. The diversity in sequence types (STs) decreased slightly during the lockdown. These findings reflect restricted travel and the change in sexual behaviour such as distancing measures during the COVID- 19 lockdown led to a temporary decrease of casual sex partners affecting gonorrhoeae isolates.	(79)
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 <i>Pseudomonas spp.</i> increased significantly, the prevalence of Gram negative non fermenting bacteria (GN-NFB), <i>H. infuenzae</i> and <i>S. pneumoniae</i> reduced. There was a statistically significant increase in resistance of <i>Pseudomonas spp.</i> to carbapenems and piperacillin/tazobactam and <i>Enterobacterales</i> <i>spp.</i> for piperacillin/tazobactam, in COVID-19 positive patients compared to patients without COVID-19. We did not observe significant changing in fungal respiratory isolates.	(81)

Multidrug-resistant (MDR), multidrug-resistant organisms (MDRO), hospital-associated infections (HAIs), bloodstream infection (BSI), community-associated 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* (CRA), 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			Aldeyab 2023, Allel 2023, Bauer 2022, Bork 2020, Bussolati 2022, Chamieh 2021, Chang 2023, de Carvalho Hessel Dias 2022, Freire 2023, Hurtado 2023, Imoto 2022, Jeon 2022, Lopez-Jacome 2022, Maczynska 2023, Meschiari 2022, Onal 2023, Pereira 2023, Santos 2022, Sasaki 2022, Shbaklo 2022, Wong 2023	Aldeyab 2023, Cheng 2022, Kastrin 2023, 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, Russotto 2023, Teixeira 2022, Tham 2022, Wee 2021, Wong 2023, Yang 2021, Zaveri 2021, Zhu 2022 (China)	Chen 2021, Dapper 2022, Hibiya 2022, Hosseini 2023, Lemenand 2021, Lin 2023, Mannathoko 2022, Meyer Sauteur 2022, Mughini-Gras 2021, Tang 2022, Ullrich 2021, Zondag 2023		
Health system use					Petrakis 2023, Soto Hernandez 2023, Zuglian 2022	Zhu 2022 (UK), Alao 2022, Vyazovaya 2022		

## **APPENDIX 2**



#### Figure 1. Study selection process for review

#### Table 1. PROGRESS-Plus factors for each study

PROGRESS	PLUS

Study author, year	Place of residence	Race, ethnicity, culture, or language	Occupation	Gender or sex	Religion	Educat ion	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
Aldeyab 2023	no	no	no	no	no	no	no	no	no	no	no
Allel 2023	no	no	no	no	no	no	no	no	no	no	yes
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
Chang 2023	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
Freire 2023 Fukushige 2022	no	no	no	no	no	no	no	no	no	no	no
Gaspari 2021	no	no	no	yes yes	no	no no	no no	no	yes yes	no	yes 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
Hosseini 2023	no	no	no	yes	no	no	no	no	yes	no	yes
Hurtado 2023	no	no	no	no	no	no	no	no	no	no	no
Imoto 2022	no	no	no	no	no	no	no	no	no	no	no
lpek 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
Kastrin 2023	no	no	no	yes	no	no	no	no	yes	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
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
Maczynska 2023	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 Meyer Sauteur 2022	no	no	no	no	no	no	no	no	no	no	no
Micozzi 2021	yes	no	no	yes	no	no	no	no	yes	no	no
Mughini-Gras 2021	no	no	no	yes yes	no no	no no	no no	no	yes yes	no	yes yes
Ochoa-Hein 2021	no	no	no	yes	no	no	no	no	ves	no	ves
Onal 2023	no	no	no	no	no	no	no	no	yes	no	yes
Pascale 2022	no	no	no	yes	no	no	no	no	yes	no	yes
Pereira 2023	no	no	no	no	no	no	no	no	no	no	no
Petrakis 2023	no	no	no	yes	no	no	no	no	yes	no	yes
Russotto 2023	no	no	no	no	no	no	no	no	no	no	no
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
Soto Hernandez 2023	no	no	no	no	no	no	no	no	yes	no	yes
Tang 2022	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
Wong 2023	no	no	no	yes	no	no	no	no	yes	no	yes
Yang 2021 Zaveri 2021	no	no no	no no	no no	no no	no no	no	no no	no no	no	no
Zhu 2022 (China)	no	no	no	yes	no	no	no	no	yes	no	no
Zhu 2022 (UK)	no	yes	no	yes	no	no	no	no	yes	no	yes
Zondag 2023	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 ID			Risk of bias (NOS)	
	S	С	0	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

Study ID	Criterion 1: Risk of Confounding Biases	Criterion 2: Risk of Post- Intervention/ Exposure Selection Biases	Criterion 3: Risk of Misclassified Comparison Biases	Criterion 4: Risk of Performance Biases	Criterion 5: Risk of Detection Biases	Criterion 6: Risk of Outcome Reporting Biases	Criterion 7: Risk of Outcome Assessment Biases	Overall risk of bias
Jani 2021	High risk of bias	Medium risk of bias	Low risk of bias	Not applicable	Low risk of bias	Medium risk of bias	Medium risk of bias	High
Zaveri 2021	High risk of bias	Low risk of bias	Low risk of bias	Not applicable	Low risk of bias	Medium risk of bias	Medium risk of bias	High
Kumar 2021	High risk of bias	Low risk of bias	Low risk of bias	Not applicable	Low risk of bias	Medium risk of bias	Medium risk of bias	High

Figure 3. Summary of risk of bias concerns evaluated using the Collaboration for Environmental Evidence Critical Appraisal Tool for environmental sampling 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)

AMR Policy Accelerator

- 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 antimicrobial? 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 nonfloxacin\* 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 nonsusceptib\*)).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 antimicrobial? 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)

((antibiotic? or antibiotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or antimicrobial? 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 nonsusceptib\*)).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 antimicrobial? 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)

((antibiotic? or anti-biotic? or abx or antibacterial? or anti-bacterial? or antifungal? or anti-fungal? or antimicrobial? or antimicrobial? 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 nonsusceptib\*)).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 nonsusceptib\*)).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 antimicrobial? 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 -current" (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)

\*\*\*\*\*

# 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.