

Review

Threat of antimicrobial resistance among pilgrims with infectious diseases during Hajj: Lessons learnt from COVID-19 pandemic

Abdul Haseeb ¹, Zikria Saleem ^{2,*}, Hani Saleh Faidah ³, Abdullah A. Saati ⁴, Abdullmoin AlQarni ⁵, Muhammad Shahid Iqbal ⁶, Saleh Alghamdi ⁷, Mahmoud E. Elrggal ¹, Manal Algethamy ⁸, Rozan Mohammad Radwan ⁹, Ahmad Jamal Mahrous ⁹, Safa S. Almarzoky Abuhussain ¹, Sarah M Khayyat ¹, Kiran Ibrahim ¹⁰, Brian Godman ^{11,12,13} and Aziz Sheikh ¹⁴

^{1.} Department of Clinical Pharmacy, College of Pharmacy, Umm Al Qura University, Makkah, Kingdom of Saudi Arabia; amhaseeb@uqu.edu.sa, smkhayat@uqu.edu.sa, merggal@uqu.edu.sa, ssmarzoky@uqu.edu.sa

^{2.} Department of Pharmacy Practice, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.; xikria@gmail.com

^{3.} Department of Microbiology, Faculty of Medicine, Umm Al Qura University, Makkah, Saudi Arabia.; hsfaidah@uqu.edu.sa

^{4.} Department of Community Medicine & Pilgrims Healthcare, Faculty of Medicine, Umm Al-Qura University, Makkah 24382, Saudi Arabia. aaasaati@uqu.edu.sa

^{5.} Alnoor Specialist Hospital Makkah, Department of Infectious diseases, Makkah, Kingdom of Saudi Arabia.; abdullmoina@moh.gov.sa

^{6.} Department of Clinical Pharmacy, College of Pharmacy, Prince Sattam bin Abdul Aziz University, 11942, Alkharj, Saudi Arabia; M.javed@psau.edu.sa

^{7.} Department of Clinical Pharmacy, Faculty of Clinical Pharmacy, Al Baha University, Al Baha 57911, Saudi Arabia; Saleh.alghamdi@bu.edu.sa

^{8.} Alnoor Specialist Hospital Makkah, Department of Infection prevention & Control Program, Makkah, Kingdom of Saudi Arabia; mmalgethamy@moh.gov.sa

^{9.} Pharmaceutical Care Department, Alnoor Specialist Hospital Makkah, Department of Infection prevention & Control Program, Makkah, Kingdom of Saudi Arabia; Rmradwan@moh.gov.sa (R.M.R.), ajmahrous@uqu.edu.sa

^{10.} Primary and Secondary healthcare department, DHQ Hospital Khushab, Khushab, Pakistan. kiran_paracha@yahoo.com

^{11.} School of Pharmacy, Sefako Makgatho Health Sciences University, Ga-Rankuwa, Pretoria 0208, South Africa. Email: brian.godman@smu.ac.za

^{12.} Strathclyde Institute of Pharmacy and Biomedical Sciences, Strathclyde University, Glasgow G4 0RE, UK. Email: brian.godman@strath.ac.uk; ORCID Number: 0000-0001-6539-6972

^{13.} Centre of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman 346, United Arab Emirates

^{14.} Usher Institute, The University of Edinburgh, Teviot Place, Edinburgh, EH164UX, UK. Aziz.sheikh@ed.ac.uk

* Correspondence: Author: zikria@bzu.edu.pk

Citation: Haseeb, A.; Saleem, Z.; Faidah, H.S.; Saati, A.A.; AlQarni, A.; Iqbal, M.S.; Alghamdi, S.; Elrggal, M.E.; Algethamy, M.; Radwan, R.M.; et al. Threat of antimicrobial resistance among pilgrims with infectious diseases during Hajj: Lessons learnt from COVID-19 pandemic. *Antibiotics* **2023**, *12*, x. <https://doi.org/10.3390/xxxxx>

Academic Editor(s):

Received: date

Accepted: date

Published: date

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Abstract: Hajj pilgrimage is a large mass gathering global event that may facilitate the spread and emergence of various infectious diseases as well as antimicrobial resistance (AMR) in a local and global scenario. Planning and preparing for these public health issues is a challenging and complex process for the Kingdom of Saudi Arabia (KSA) health authorities. Despite multiple efforts for the prevention and treatment of infectious diseases through longtime funding in education and medical care, the prevalence of infectious disease is still high among Hajj pilgrims. The commonly observed infectious diseases during Hajj include respiratory tract infections (influenza and pneumonia), urinary tract infections and skin infections that may necessitate the use of antimicrobials. Beta-lactams are used as a first-line treatment for hospital acquired infections as well as community acquired infections due to their broad-spectrum activity. However, most of the bacterial isolates such as *Staphylococcus* spp., *Pseudomonas* spp. and *E. coli* are resistant to beta-lactams. Irrational use of antimicrobials, lack of infection prevention practices and suboptimal healthcare access further exacerbate the risk of spreading AMR among Hajj pilgrims. Enhanced collaboration between countries,

sharing of best practices and international cooperation are crucial in addressing AMR threats among pilgrims. Consequently, robust surveillance systems for early detection and monitoring of AMR, collaboration with national as well as international healthcare agencies, effective infection prevention and control measures, public awareness, and rational use of antimicrobials via antimicrobial stewardship programs are required to mitigate the risk of AMR and ensure the health and well-being of pilgrims during Hajj.

Keywords: Antimicrobial resistance; Hajj pilgrims; COVID-19; Preventive measures; Surveillance

1. Introduction

An appreciable number of pilgrims gather from across the world to attend religious events and festivals when they occur [1]. Such gatherings increase the risk of especially communicable diseases that pose challenges to healthcare authorities [2-4]. Mass gatherings have been reported to have a considerable impact on the individual's health, and the subsequent implications, as well as the host's country infrastructure and economy [5-8]. These mass gatherings can result in the dissemination of multi-drug resistant (MDR) strains and the spread of antimicrobial resistance (AMR) on a global scale [3, 9-11]. Inter-sectoral approaches, public health surveillance and global communication are required to mitigate the risks of emerging and re-emerging infectious diseases [12-16]. After the H1N1 influenza pandemic, the first virtual international conference was held in Jeddah, KSA in 2010, where The Lancet Infectious Diseases Series on mass gatherings was introduced. The majority of the national and international medical experts participated in this conference to develop and modify the guidelines for the diagnosis, treatment and prevention of infectious diseases during mass gathering events [17].

The Hajj is one of the biggest religious events hosted by the Kingdom of Saudi Arabia (KSA) every year. One of the obligatory pillars of Islam, Hajj is a pilgrimage to Makkah which is must for every physically fit, healthy Muslim to perform once in a lifetime if he/she can afford it [18]. It is performed from the 8th to 12th of Dhul-Hujjah, the last month of Islamic calendar. Currently, over three million Muslims travel to Saudi Arabia every year to perform Hajj rituals from almost 184 countries [19]. Over-crowded accommodation make an ideal environment for the exacerbation of communicable diseases, many of which are preventable if proper precautionary measures are taken [20]. Pilgrims are at potential risk of acquiring communicable diseases via contaminated food or water, person-to-person contact as well as vector-borne and respiratory transmission of viruses [4, 17, 21-23].

Antimicrobial resistant pathogens are currently prevalent in KSA [24-26]. Hajj pilgrims therefore face the potential risk of acquiring or transmitting these pathogens during their stay in KSA and subsequently spread these pathogens on their return home. A systematic review reported the prevalence and increasing trend of resistant pathogens during Hajj which include methicillin resistant *staphylococcus aureus* (MRSA), 3GC-Enterobacteriaceae, colistin-resistance bacteria and imipenem-resistant bacteria [27]. Several studies conducted between 2002 and 2012 documented that the prevalence of MRSA varied significantly across different countries ranging from 0.06% to 94% [27-29].

The Hajj presents substantial logistic challenges for the protection of both non-residents and residents of KSA as well as the maintenance of local, national and international health security [17, 30]. Infectious diseases including Zika Virus diseases, extensive drug-resistant tuberculosis, (XDR, TB), Middle East Respiratory Syndrome (MERS), seasonal influenza, and severe acute respiratory syndrome coronavirus (SARS-CoV) have all surfaced in recent decades [31-35]. New policies by Saudi Ministry of Health have been implemented to try and reduce the transmission of infectious diseases during the Hajj. Poli-

cies include the administration of vaccines to pilgrims on arrival at KSA among unvaccinated pilgrims as well as decreasing the Hajj quotas for Saudi and non-Saudi pilgrims [36]. However, there is a need to build on current policies especially given concerns with increasing inappropriate antimicrobial use and resistance globally, and the subsequent impact on morbidity, mortality and costs [37-40]. Consequently, we have summarized the available literature on infectious diseases and the use of antimicrobials among pilgrims. This is combined with recommended interventions to prevent possible emergence and transmission of local and global AMR. In addition, highlighted the role of the Hajj pilgrimage in the spread of infectious diseases and AMR globally, and the subsequent imperative to take necessary actions to address these urgent public health issues especially given the recent COVID-19 pandemic. Subsequently make recommendations for the future to key stakeholder groups in KSA and beyond based on the findings from the multiple studies included in this review.

2. Results and discussion

2.1. Pattern and prevalence of infectious diseases during Hajj

Possible infectious disease patterns during the Hajj pilgrimage include endemic, exported and imported diseases [41]. Inappropriate sanitary facilities, shared shelters, poor hygiene and lack of portable water enhance the transmission of infectious microorganisms. These combined factors have resulted in multiple communicable diseases among pilgrims during Hajj as well as after their return to their home countries [41, 42]. The presence of a large number of pilgrims from different regions of the world in a gathering can increase the risk of spreading infectious diseases across international borders including resistant strains [43]. Climate conditions and air pollution in Makkah also play an important role in the transmission of infectious diseases [44].

Respiratory tract infections (RTIs) have been the predominant health problem among Hajj pilgrims over the past 15 years [45]. The most common pathogens for RTIs are *Klebsiella pneumoniae*, *Haemophilus influenzae*, Coronavirus, Adenovirus, Respiratory syncytial virus (RSV), *Staphylococcus aureus* and *Streptococcus pneumoniae* [46, 47]. According to one estimate, approximately 90% of Hajj pilgrims develop at least one respiratory illness before their return home [48]. Influenza has been the most common respiratory illness among Hajj pilgrims, estimated to be 24,000 cases per year [49]. Pneumonia has been observed as the most common life threatening respiratory illness among pilgrims attending Mina healthcare centers [50] and the leading cause of hospital admissions particularly in intensive care units (ICUs) [51]. Among viral infections, herpes simplex virus (HSV) and adenovirus infections are the most commonly reported. The recent COVID-19 pandemic has also been a serious public health issue globally including in the KSA [52, 53]. The KSA took all precautionary measures to prevent the spread COVID-19 based on typical effective public health measures, and was declared COVID-19 free until March 2nd, 2020, when first COVID-19 case was reported as an Iranian pilgrim [54, 55]. Since then, KSA, the host country of annual Hajj pilgrimage, started witnessing an increasing trend of COVID-19 cases [56].

Moreover, of equal concern, is that tuberculosis (TB) has been reported in three studies [57-59]. The spread and emergence of MDR-TB has further complicated the circumstances, leading to unfavorable therapy outcomes, and imposing an economic burden on patients as well as healthcare systems [57, 60]. It is challenging to assess the exact prevalence of TB among Hajj pilgrims due to limited comprehensive studies targeting this specific group. Consequently, it is essential that the health authorities in KSA seek to implement strategies in the future to help control TB. These could include enhanced surveillance, diagnostics, and treatment programs.

Several studies have, as mentioned, also recently discussed the transmission and acquisition of AMR during Hajj. Among the resistant strains, New Delhi metallo-B-lac-

tamase, extended-spectrum B-lactamase-producing pathogens, SHV-12- producing *Salmonella typhi*, CTX-M-producing *Escherichia Coli*, *Streptococcus pneumoniae* [41] and methicillin-resistant *Staphylococcus aureus* (MRSA) have frequently been reported in Gulf Cooperation Council (GCC) countries especially in KSA [61, 62]. The overall, prevalence of infectious diseases among Hajj pilgrims are described in Table 1. Encouragingly, outbreaks of meningococcal disease during the Hajj have been largely prevented by a mandatory meningococcal vaccination policy for Hajj pilgrims, However, continued surveillance is needed to help prevent future outbreaks [59, 63].

2.2. Patterns of antimicrobial use among Hajj pilgrims

Pilgrims come from different regions of the world, including countries where antimicrobials are typically dispensed without a prescription, which contributes to the spread and emergence of resistance [64-66]. The purchasing of antimicrobials without a prescription is now less of an issue in KSA following tightening of the regulations and the potential for considerable fines for abuse [67]. One of the predominant factors in the dissemination of AMR among Hajj pilgrims is the irrational use of antimicrobials [11, 41]. During the Hajj Pilgrimage, both community-acquired and hospital-acquired infections may necessitate the use of antimicrobials. The selection of antimicrobials is determined by the specific type and severity of the infection. Beta-lactams and cephalosporins are commonly used antibiotics for hospital acquired infections which exhibit efficacy against a wide range of bacteria and are frequently utilized as first-line therapy [68]. However, glycopeptides, e.g., vancomycin, are increasingly being used for the treatment of serious infections caused by resistant pathogens such as MRSA [69]. Similarly, in the case of community-acquired infections, beta-lactams including amoxicillin are the most frequently prescribed antibiotics among outpatients [70]. Fluoroquinolones are also often prescribed for respiratory tract infections, including CAP as a first-line treatment [71]. Moreover, trimethoprim-sulfamethoxazole (TMP-SMX) and macrolides are also utilized for various infections such as respiratory, urinary, and skin infections [34].

As reported in multiple studies, 34.9% of Australian pilgrims, 84% of Malaysian pilgrims, 17% of Pakistani pilgrims, and 58.5% of Irani pilgrims received antimicrobials during Hajj [72-75] (Table 2). In another study, 47.6% of French pilgrims received antimicrobials [76] where beta-lactams (35.0%), macrolides (11.4%) and cephalosporins (2.3%) were the most common antimicrobials given to French pilgrims [76]. A prospective point prevalence study conducted in two referral hospitals in Medina documented that 49.2% of returning Hajj pilgrims were prescribed antibiotics. This included piperacillin-tazobactam (88%), penicillin (20%), and amoxiclav (12%) among Hajj pilgrims [77]. Another study reported that Malaysian pilgrims suffering from community-acquired pneumonia (CAP) acquired during the pilgrimage received levofloxacin (44%), azithromycin (40.7%) and cefuroxime (23.1%) on their return home [78].

The most common AMR isolates reported during the Hajj season are illustrated in Figure 1, based on the findings of Alreeme et al. (2022) [79], with each bar representing the number of organisms resistant to a specific antibiotic class, e.g. macrolides, quinolones and beta-lactams. Among enteric disease-causing pathogens, *E. coli*, *Acinetobacter spp*, *klebsiella spp*, *Pseudomonas spp.*, and *Enterobacter spp*. are the most common AMR isolates found in Hajj pilgrims while respiratory-disease causing AMR isolates include *Staphylococcus spp*, *Streptococcus spp* and *Hemophilus influenzae*. Most of the pathogens are resistant to beta-lactams, followed by aminoglycosides and sulphonamides. Moreover, a study reported that *Mycobacterium tuberculosis* is resistant to streptomycin in 25.9% cases, while isoniazid showed resistance in 11.1% cases [57].

2.3. Interventions and Recommendations

2.3.1. Local and international guidelines and policies for Infection prevention and control

Infection prevention and control is a pivotal component of any healthcare system at a national as well international levels given rising rates of AMR and the implications [37, 38, 80]. Many infectious diseases as well as outbreaks are preventable if proper measures, including educational sessions regarding disease prevention and self-hygiene combined with prophylactic treatment including vaccines, are adopted by pilgrims before arrival to KSA [81]. Collaborative and well-coordinated efforts from all healthcare professionals (HCPs), as well as other key stakeholders and community groups, are needed to reduce future prevalence rates. To help with this, the KSA Ministry of Health provides up-to-date Hajj travel advice and health regulations through international public health organizations such as the Centers for Disease Control and Prevention (CDC), the WHO and Hajj travel agencies [20]. The WHO has published guidelines entitled “communicable disease alert and response for mass gathering” since June 2008 [82], with the recent COVID-19 pandemic focusing minds on key public health measures that can be introduced to stop the spread of infectious diseases. However, in view of continued concerns, it is recommended that Saudi Ministry of Health and public health officials should propose local guidelines for all stakeholders regarding infection prevention and control not for only future Hajj pilgrimages but also other mass gatherings. Table 3 depicts some recommended measures and their potential barriers that should be considered going forward to prevent, or appreciable reduce, infectious diseases during Hajj and their implications to both KSA and beyond.

2.3.2. Restricting the number of Hajj Pilgrims

The Saudi mitigation plan appears to have successfully limited the spread of COVID-19 in KSA as well as contributed to global health security [83]. In 2020, KSA authorities allowed 1000 pilgrims residing within KSA to perform Hajj with strict compliance with infection control measures and public health protocols [84]. No confirmed cases of COVID-19 or notable public health events were recorded during this Hajj season. On the basis of the successful outcomes from the 2020 Hajj experience, Saudi authorities decided to extend the number to 60,000 pilgrims in 2021, presenting the similar results to 2020's experience [85]. The rate of upper respiratory tract infections (URTIs) was 11.6 cases per 100,000 in the recent study compared to 2200 cases per 100,000 in a previous report [83]. Furthermore, a notable decrease in the number in non-communicable diseases (68 cases per 100,000) was reported when compared to previous study that showed the prevalence rate of 1600 per 100,000 cases [83, 86]. The appreciable reduction in the cases of particularly URTIs reflects the effectiveness of adopting health policies and public health measures to restrict the number of Hajj pilgrims thereby ensuring their health to perform Hajj as well as reducing the period of Hajj stay alongside strict implementation of social distancing policies [83, 87].

2.3.3. Provision and implementation of adequate healthcare services

The KSA government provides over 1000 free healthcare facilities for all pilgrims during Hajj. The services include mass vaccination, outbreak investigation, environmental health services, infectious disease surveillance, mass administration of prophylactic medication and health education [30]. Interventions to cope with the dissemination of infectious diseases include non-pharmaceutical and pharmaceutical methods. Non-pharmaceutical methods include surveillance, wearing face masks, hand hygiene, social distancing, travel restrictions and respiratory etiquette, while pharmaceutical approaches include vaccination and the use of antimicrobials [88, 89]. The strategies and policies should be

introduced to improve vaccination coverage among all HCWs, and these strategies should be practiced by all healthcare facilities in Saudi Arabia [90].

2.3.3.1 Vaccination

Vaccination is the most effective way to prevent the acquisition and transmission of infectious diseases [91]. The WHO has estimated that approximately 2.5 million individuals are prevented from catching various infectious diseases through vaccination every year [92]. In addition, vaccines can not only protect individuals from serious disease but also unvaccinated individuals through the concept of herd immunity [93]. Moreover, several studies have supported the idea that administration of viral and bacterial vaccines help to control the emergence and spread of AMR [94-96]. Vaccine administration and acceptability can be promoted through the implementation of effective strategies including educating HCWs and pilgrims about vaccination as a prerequisite for acquiring a Hajj visa [19]. Such strategies are endorsed by the fact that the prevalence of influenza-like symptoms was lower in vaccinated pilgrims than in unvaccinated pilgrims [97].

In view of studies such as these, the Saudi Ministry of Health has recommended influenza and meningococcal vaccination as mandatory for all pilgrims entering KSA for the Hajj to reduce the risk of transmission of RTIs [98]. During the current COVID-19 pandemic, the Saudi healthcare authorities has also made COVID-19 vaccination a mandatory requirement for all pilgrims participating in Hajj rituals before leaving for KSA.

2.3.3.2 Hand hygiene

Hand hygiene is one of the simple, primary and effective preventive measures recommended by various healthcare organization for the prevention of cross-contamination of pilgrims especially during pandemics [99, 100]. A survey of Australian and French pilgrims during 2013-14 reported that 94% and 50% of their pilgrims respectively practiced various hand hygiene techniques including washing and sanitizing [19]. Generally, the use of alcoholic sanitizer is one of the essential hand hygiene practices to prevent infectious diseases. However, Muslim pilgrims are denied using them because alcohol is prohibited in Islam [101]. This is a concern as compliance with recommended hand hygiene was reported in US (67.2%) and Turkish (57%) pilgrims, and was significantly associated with low risk of RTIs [102, 103]. According to one study, the knowledge and attitude of Hajj pilgrims regarding the importance of hand hygiene was poor; however, compliance with hand washing was good [104]. Encouragingly, a recent study has reported a significantly lower incidence of RTIs among Hajj pilgrims during the COVID-19 pandemic after adopting hand hygiene practices [105].

2.3.3.3 Social distancing and contact avoidance

According to the CDC, social distancing and contact avoidance with people are the best ways to minimize the transmission of infectious diseases [106]. During COVID-19 pandemic, whilst no Hajj pilgrimage was performed in 2020 apart from 1000 KSA residents, in 2021 the Saudi healthcare authorities allowed the return of pilgrims. However, there were restrictions regarding social distancing of approximately 5 feet during prayers in the mosques and holy sites [107]. According to multiple surveys conducted among the wider pilgrim community, 48% of Turkish, 73% of Australian, 82% of Arab, and 86% of French pilgrims believed that contact avoidance with sick people was a key element that would have reduced the transmission of infections [19].

2.3.3.4 Face Masks

Proper utilization of face masks has proven an effective preventive strategy to curb the aerosol spread of airborne infectious diseases [108]. The effectiveness of face masks depends on its type, design and quality [109]. A study reported that Malaysian pilgrims

used N-95 masks and surgical masks performing Hajj rituals [109]. However, the effectiveness of N-95 masks over surgical masks among HCWs from the prevention of communicable diseases is still unknown [110].

A meta-analysis study documented that the wearing face masks did not reduce the chances of catching influenza in 2009 [111]. Conversely, a systematic review reported that the prevalence of COVID-19, SARS and influenza was decreased to 96%, 74% and 45% by wearing facemasks [112]. In April 2020, the CDC recommended the use of cloth face mask to curtail community-based transmission [113], which should be adhered to for future mass gatherings.

2.4. Impact of antibiotic prescribing patterns during COVID-19 pandemic on AMR

The irrational use of antibiotics during the recent COVID-19 pandemic may result in the emergence of AMR through appreciable over-prescribing across sectors despite limited evidence of bacterial infections or co-infections [11, 114–119]. Usually, a large proportion of Hajj pilgrims consist of older people, with multiple chronic comorbidities. Currently, patients with COVID-19 may receive antimicrobials for two main reasons. Firstly, the symptoms of the bacterial infectious disease resemble COVID-19. However, in order to differentiate between viral and bacterial infection, the ratio of CRP (mg/l) to 2-5A synthetase (pmole/dl) $\times 10$ is used as a differential index. The index values in viral infections ranged from 0 to 0.9 and were lower than the values in bacterial infections, which ranged from 3.9 to 50 [120]. Diagnostic tests may though not be that effective with detection and can be time-consuming when immediate therapy is required [121]. Secondly, patients with COVID-19 may have bacterial co-infections that require antimicrobial therapy; however, this is rare in practice [117–119, 122].

Consequently, comprehensive data is still required to have a better understanding of the occurrence of co-infections and pathogens involved, alongside the impact of underlying patient risk factors. Furthermore, standardized definitions and diagnostic criteria should be used to perform an in-depth analysis of microbiological resistance and antimicrobial usage where diagnostic laboratory infrastructure exists [123]. However, in the meantime, guidelines based on the AWaRe Book can be used to guide patient management of infectious diseases based on the balance of risks and benefits to reduce inappropriate prescribing and dispensing of antibiotics [124, 125].

This is especially important in regions where gram-negative pathogens are resistant to carbapenems. We are aware that antimicrobials with less favorable safety profiles such as colistin, a 'Reserve' antibiotic, are recommended as empiric therapy for suspected gram-negative infections [126]. This needs to be avoided in the future. Similarly in countries such as Pakistan, 'Watch' and 'Reserve' antibiotics are being routinely dispensed in the community without a prescription driving up resistance rates [65], which is a concern. On the other hand, if antimicrobial treatment is not tailored to local AMR prevalence, patients with co-infections may receive ineffective therapy, which results in increased mortality rates and healthcare costs [122]. This situation can be avoided by developing local guidelines based on the AWaRe book and subsequently monitoring antibiotic usage through antimicrobial stewardship programmes [127–129].

We are aware of a number of limitations with this study. Firstly, we restricted sourced papers to English language only for the reasons documented. Secondly, we utilized a limited number of databases including Scopus, PubMed and ScienceDirect, to retrieve articles; however, we believe these databases did capture most relevant papers of scientific interest. Thirdly, we did not assess the cause of irrational use of antibiotics that resulted in an increase in AMR as such studies have been conducted before. Despite these limitations, we believe our findings are robust providing direction to key stakeholders in KSA and beyond to reduce the extent of communicable diseases during Hajj.

Table 1. Prevalence of infectious diseases among Hajj pilgrims.

Author year	Geographical origin	Study design	Sample size	Prevalence of infection	Top 3 infections			Findings
					1	2	3	
Mahdi et al., 2022 [130]	Makkah	Cross-sectional study	476	2.3%	RTIs (2.3%)	-	-	Low prevalence of RTIs among pilgrims was observed as compared to those documented in pre-pandemic studies.
Mahdi et al., 2022 [105]	Makkah	Cohort study	445	4.7%	RTIs (4.7%)	-	-	Hand hygiene practice could play an important role to reduce the prevalence of RTIs.
Alasmari et al., 2021 [131]	Jeddah	Cross-sectional study	2973	4.6%	Neisseria meningitidis (4.6%)	-	-	Vaccination is required to prevent meningococcal disease outbreaks during and after Hajj.
Al-Hayani et al., 2021 [58]	Makkah	Cross-sectional study	472	100%	Pulmonary tuberculosis (91.7%)	-	-	Epidemiological studies are needed to validate the findings.
Sambas et al., 2020 [57]	Makkah	Cross-sectional study	158	100%	Tuberculosis (100%)	-	-	TB control programs are required to prevent emergence and spread of MDR TB.
AboEl-Magd et al., 2020 [132]	Makkah	Cohort study	614	39.2%	Pneumonia (39.2%)	-	-	Upgradation of antibiograms is required to enable selection of appropriate antibiotic.
Raja et al., 2017 [133]	Makkah, Madina, Jeddah	Descriptive, cross-sectional study	184496	30.0%	RTIs (29%)	-	-	Structured policies and legislation, training sessions of HCWs should be introduced to prevent the spread of infections.
Yezli et al., 2017 [59]	Makkah	Cross-sectional study	1063	1.4%	Tuberculosis (1.4%)	-	-	Undiagnosed TB poses a risk to other pilgrims. Consequently, proactive screening is needed.
Shirah et al., 2017 [43]	Madina	Retrospective study	1059	23%	Pneumonia (23%)	-	-	Specific adjustment in the guidelines is required for the treatment of pneumonia.
Dhfar et al., 2016 [134]	Makkah	Descriptive, observational study	217	-	RTIs (12.9%)	Skin and soft tissue infections (9.2%)	-	Policies and legislation are required to improve the quality life of patients.
Hashim et al., 2016 [97]	Makkah, Arafat	Cross-sectional study	468	93.4%	-	-	-	Preventive measures should be practiced.

Bakhsh et al., 2015 [135]	Makkah	Observational study	1008	-	RTIs (17.6%)	Skin and soft tissues infections (15.7%)	-	Improvement in healthcare facilities during Hajj is required.
Memish et al., 2014 [136]	Makkah and Madina	Observational study	38	68.4%	CAP (68.4%)	-	-	Improved respiratory tract infection surveillance is needed.
Memish et al., 2013 [137]	Makkah and Madina	Observational study	1103	100%	Invasive meningococcal disease (100%)	-	-	The number of cases has declined. Regular monitoring is necessary to monitor the trends during upcoming hajj seasons.
Barasheed et al., 2014 [138]	Makkah, Mina	Randomized controlled trial	1038	38%	Rhinovirus (25%)	Influenza (2%)	Adenovirus (2%)	Appropriate vaccination and infection control are required to reduce the risk of transmission of respiratory virus.
Alzahrani et., 2012 [139]	Mina	Descriptive study	4136	67%	RTIs (60.8%)	Infectious skin diseases (4.7%)	UTIs (1.5%)	Best possible healthcare service should be given to Hajj pilgrims by Saudi healthcare authorities.
Mandourah et., 2012 [140]	Mina, Makkah, Arafat, Madina	Cohort study	452	27.2%	CAP (66.7%)	Aspiration-related pneumonia (25.2%)	Tuberculosis (4.9%)	Increased efforts for the prevention of infectious diseases among Hajj pilgrim is required.
Alherabi et al., 2011 [141]	Makkah	Cross-sectional study	3087	92%	Pharyngitis (45.7%)	URTIs (42.1%)	Influenza (2.5%)	Misuse of antimicrobials should be discouraged by guiding pilgrims regarding rational use of antimicrobials.
Al-Ghamdi et al., 2011 [104]	Mina, Arafat	Cohort study	160	57%	Pneumonia (39.4%)	URTIs (3.3%)	-	Structured policies and strategies regarding infection prevention and control should be initiated.
Baharoon et al., 2009 [142]	Makkah	Cross-sectional study	165	71%	CAP (54.8%)	Intra-abdominal source (16.6%)	Skin and soft issue infection (14.3%)	Initiation and implementation of infection prevention and control programs are required.
Ibrahim et al., 2008 [143]	Mina	Cross-sectional study	248	-	RTIs (29.8%)	UTIS (1.6%)	-	Intensified health education campaigns should be conducted for all pilgrims in their home countries and KSA.
Madani et al., 2007 [144]	Mina, Arafat	Cross-sectional Study	140	26.4%	Pneumonia (22%)	Sepsis (4.3%)	-	Cost-effective and optimal healthcare services are urgently needed for Hajj pilgrims.

Madani et al., 2006 [145]	Mina, Arafat	Cross-sectional study	808	36.4%	Pneumonia (19.7%)	URTIs (3.3%)	Cellulitis (1.6%)	Cost-effective and optimal healthcare services are urgently needed for Hajj pilgrims.
Memish et al., 2006 [61]	Mina	Cohort study	411	20.6%	-	-	-	Susceptibility testing should be performed so that antimicrobials could be used when needed.
Balkhy et al., 2004 [49]	Mina	Cross-sectional study	500	10.8%	Influenza (55.6%)	HSV (24.1%)	RSV (12.9%)	Vaccination should be required for every Hajj pilgrim.
Karima et al., 2003 [146]	Makkah	Cross-sectional study	105	100%	Meningitis (64%)	Meningococemia (36%)	-	Quadrivalent Vaccine is required for all pilgrims before coming to KSA.

RTIs; Respiratory tract infections, UTIs; Urinary tract infections, CAP; Community-acquired pneumonia, HSV; Herpes simplex virus

Table 2. Prevalence of antimicrobial use among Hajj pilgrims.

Author year	Study Population (N)	Study Design	Prevalence of antimicrobial use	Top 3 antimicrobials			Findings
				1	2	3	
Harimurti et al., 2021 [147]	Indonesian pilgrims (N=813)	Prospective longitudinal study	47.8%	-	-	-	Pneumococcal vaccine should be administered before departure to KSA.
Alahmadi et al., 2020 [77]	Pilgrims from 7 different countries (N=675)	Prospective point prevalence survey	49.18%	Penicillin (20%)	Amoxiclav (12%)	Pipercillin-tazobactam (88.0%)	The rational use of antimicrobial should be assessed by standardized methodology.
Hoang et al., 2019 [76]	French pilgrims (N=783)	Prospective cohort study	47.6%	Beta-lactams (35.0%)	Macrolides (11.4%)	Cephalosporins (2.3%)	Educational training and sessions are required to control the irrational use of antimicrobials.
Alqahtoni et al., 2019 [148]	Pilgrims (N=344)	Cross-sectional study	6%	-	-	-	Pre-travel education training related with health and use of preventive measure should be addressed.
Dzaralay et al., 2017 [78]	Malaysian Pilgrims (N=91)	Cross-sectional study	100%	Levofloxacin (44%)	Azithromycin (40.7%)	Cefuroxime (23.1%)	The proper guidelines regarding antimicrobial use for the pilgrims with CAP should be introduced to improve healthcare services during Hajj.

Hashim et al., 2016 [97]	Malaysian pilgrims (N=468)	Cross-sectional study	61.8%	-	-	-	Preventive measures including social distancing, wearing face mask, hand hygiene should be practice to prevent the spread of infectious diseases.
Metanat et al., 2015 [74]	Irani pilgrims (N=422)	Prospective, cross-sectional study	58.5%	-	-	-	The meningococcal vaccine was effective in reducing the number of carriers among pilgrims after travel.
Azeem et al., 2014 [72]	Australian pilgrims (N=229)	Cross-sectional study	34.9%	-	-	-	Educational sessions and campaign regarding rational use of antimicrobials is required.
Alborzi et al., 2008 [149]	Irani pilgrims (N=674)	-	58.2%	-	-	-	The administration of vaccine was effective for reduction the number of carriers among pilgrims.
Mustafa et al., 2003 [73]	Malaysian pilgrims (N=820)	Cohort study	84%	-	-	-	Immunization programs for Hajj pilgrims should be supported by KSA government
Qureshi et al., 2000 [75]	Pakistani pilgrims (N=100)	Randomized blinded study	17%	-	-	-	Influenza vaccination should be recommended for the pilgrims before arrival to KSA.

KSA= Kingdom of Saudi Arabia.

Table 3. Recommended strategies and their potential barriers to prevent infection during Hajj.

Strategies	Potential barriers
Public Awareness	Language barriers. Illiteracy. Scarcity of resources for educational programs. Concerns with misinformation from authorities
Adequate sanitation facilities	Limited access to clean water and sanitation facilities. Overcrowding. Insufficient availability of handwashing stations. Lack of awareness of hand hygiene.
Respiratory Etiquettes	Culture norms. Lack of awareness about respiratory hygiene practices.
Vaccination campaign	Limited access to vaccines. Vaccines hesitancy. Inadequate healthcare infrastructure.
Infectious Disease surveillance	Lack of resources for surveillance. Delays in reporting and response.
Crowd management and planning	Lack of infrastructure for crowd control.

	Logistical challenges.
Food Safety Measures	Poor food handling practices. Lack of proper food inspection and regulation.
Healthcare Services availability	Insufficient healthcare facilities and personnels. Overwhelmed healthcare systems.

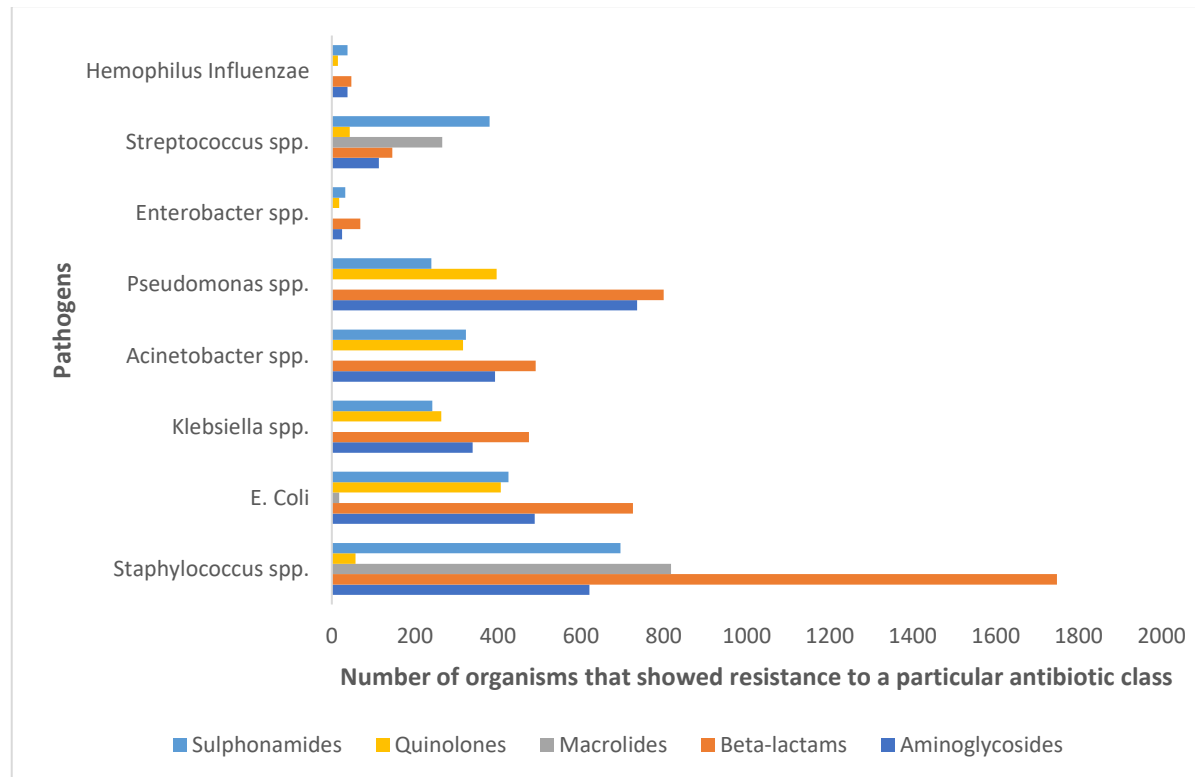


Figure 1. The most common AMR isolates reported during Hajj

3. Materials and Methods

This study is basically a narrative review of relevant published articles building on similar studies undertaken by some of the co-authors before in high priority areas including infectious diseases [128, 150-154]. However, whilst there is no relevant formal reporting guidelines for narrative reviews, we built on guidance from the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2020 checklist PRISMA to enhance the structure and content of our paper (Figure 2) [155].

Initially, a scoping review was undertaken on Google Scholar to search available published literature as well as search keywords or key terms to structure a comprehensive search in potential databases. Box 1 contains the key terms used.

Subsequently, the identified key terms were entered in 3 databases. These were Google Scholar, PubMed and ScienceDirect to search for relevant articles. We were only interested in publications published in English as this is the internationally accepted scientific language. Potential publications were searched from January 2000 until September 2022 to provide the most recent data as concerns with the transmission of infectious diseases has grown following the COVID-19 pandemic alongside fears with increasing AMR and the implications. Potential studies for inclusion in the review were divided among the co-authors using specifically designed data collection forms. The findings from identified papers were accumulated and assembled, and the results were summarized in the form of tables and descriptions by the principal author (ZS). This approach, as mentioned, aligns with similar studies undertaken by the co-authors across Africa and beyond, in giving future guidance for managing infectious diseases and broader approaches, and in accordance with institutional guidance [16, 128, 150-154].

Box 1. Retrieval strategy and search results from Databases.

#	Search terms
1	(Haji) OR (Pilgrims) - [MeSH Terms]*[Text Word]
2	(Antimicrobial resistance) OR (Antimicrobial sensitivity) - [MeSH Terms] *[Text Word]
3	(Infectious diseases) AND (Antimicrobial use) - [MeSH Terms] *[Text Word]
4	(COVID) - [MeSH Terms] *[Text Word]
5	#1 AND #2
6	#1 AND #3
8	#2 AND #3
9	#1 AND #2 AND #3 AND #4

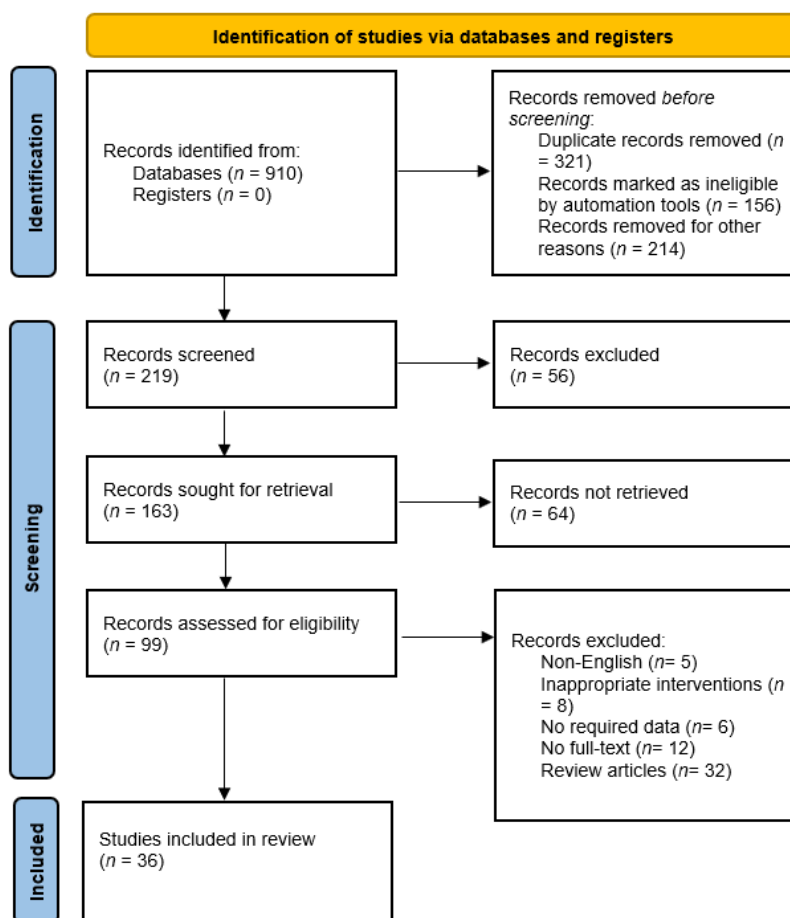


Figure 2. Flow chart of included studies.

4. Conclusion

Hajj pilgrimage contributes towards the transmission of communicable diseases around the globe. This narrative review highlights the importance of intersectoral government collaboration for educational sessions regarding the rational use of antimicrobials before and during Hajj pilgrimage. This is essential given rising concerns with AMR globally. Alongside this, the need for vaccination against target viruses among pilgrims including COVID-19, influenza and meningococcus, as well as acknowledging the need for personal hygiene (face masks, hand hygiene) and social distancing during Hajj to minimize the risk of transmission of various infectious diseases and the risk of AMR is essential. This requires co-ordination among key stakeholder groups in KSA, including educational activities, as well as international collaboration and strategies. These include expanded AMR surveillance, increased laboratory diagnostic testing and infection prevention and control programs. In addition, educational and other programs to address vaccine hesitancy where this occurs. These coordinated efforts are required to overcome this global public health concern and ensure Hajj pilgrims return home safely without any infectious diseases. These are research projects for the future.

Author Contributions: Conceptualization, A.H., Z.S., and H.S.F.; methodology, A.H. and M.S.I.; software, -; validation, Z.S., H.S.F., and A.A.S.; formal analysis, -; investigation, A.H., A.A.S., and A.J.M.; resources, -; data curation, A.H., M.A., and R.M.R.; writing—original draft preparation, Z.S., H.S.F., and A.H.; writing—review and editing, Z.S., B.G., and A.S.; visualization, Z.S., S.A., and S.M.K.; supervision, B.G. and A.S.; project administration, -; All authors have read and agreed to the published version of the manuscript.

Funding: The authors extend their appreciation to the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia for funding this research work through the project number IFP22UQU4290073DSR133

Institutional Review Board Statement: Not Applicable

Informed Consent Statement: Not Applicable

Data Availability Statement: No data are available. All data relevant to the study are included in the article or uploaded as supplemental information.

Acknowledgments: None

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Yezli, S. and B.M.J.S.m.j. Alotaibi, *Mass gatherings and mass gatherings health*. 2016. **37**(7): p. 729.
2. Coltart, C.E. and R.H. Behrens, *The new health threats of exotic and global travel*. 2012, British Journal of General Practice.
3. Saleem, Z. and M.A. Hassali, *Travellers take heed: Outbreak of extensively drug resistant (XDR) typhoid fever in Pakistan and a warning from the US CDC*. *Travel Med Infect Dis*, 2019. **27**: p. 127.
4. Hoang, V.-T. and P. Gautret, *Infectious diseases and mass gatherings*. *Current infectious disease reports*, 2018. **20**: p. 1-12.
5. Bokhary, H., et al., *The rise of antimicrobial resistance in mass gatherings*, in *Handbook of Healthcare in the Arab World*. 2021, Springer. p. 1199-1214.
6. Shafi, S., et al., *Infectious diseases threats at the Arba'een—a neglected but one of the largest annually recurring mass gathering religious events*. *International Journal of Infectious Diseases*, 2022. **123**: p. 210-211.
7. Lami, F., et al., *Real-time surveillance of infectious diseases, injuries, and chronic conditions during the 2018 Iraq Arba'een mass gathering*. *Health security*, 2021. **19**(3): p. 280-287.
8. Sweileh, W.M., *Health-related research publications on religious mass gatherings of Muslims: a bibliometric analysis (1980–2020)*. *Tropical diseases, travel medicine and vaccines*, 2022. **8**: p. 1-10.
9. Alshammari, S.M., et al. *Disease spread simulation to assess the risk of epidemics during the global mass gathering of Hajj pilgrimage*. in *2019 Winter Simulation Conference (WSC)*. 2019. IEEE.
10. Haseeb, A., et al., *Antimicrobial resistance among pilgrims: a retrospective study from two hospitals in Makkah, Saudi Arabia*. *International Journal of Infectious Diseases*, 2016. **47**: p. 92-94.
11. Haseeb, A., et al., *Antimicrobial Usage and Resistance in Makkah Region Hospitals: A Regional Point Prevalence Survey of Public Hospitals*. *International Journal of Environmental Research and Public Health*, 2022. **19**(1): p. 254.
12. Memish, Z.A., et al., *Emergence of medicine for mass gatherings: lessons from the Hajj*. 2012. **12**(1): p. 56-65.
13. Haseeb, A., et al., *Evaluation of a Multidisciplinary Antimicrobial Stewardship Program in a Saudi Critical Care Unit: A Quasi-Experimental Study*. *Frontiers in pharmacology*, 2021. **11**: p. 2222.
14. Haseeb, A., et al., *Evaluation of Antimicrobial Stewardship Programs (ASPs) and their perceived level of success at Makkah region hospitals, Kingdom of Saudi Arabia*. *Saudi Pharmaceutical Journal*, 2020. **28**(10): p. 1166-1171.
15. Degeling, C., et al., *Implementing a One Health approach to emerging infectious disease: reflections on the socio-political, ethical and legal dimensions*. *BMC Public Health*, 2015. **15**(1): p. 1-11.
16. Saleem, Z., et al., *Progress on the national action plan of Pakistan on antimicrobial resistance (AMR): A narrative review and the implications*. *Expert review of anti-infective therapy*, 2022. **20**(1): p. 71-93.
17. Memish, Z.A., et al., *Mass gatherings medicine: public health issues arising from mass gathering religious and sporting events*. *The Lancet*, 2019. **393**(10185): p. 2073-2084.
18. Mantoro, T., M.F.M. Aris, and M.A. Ayu. *Hajjlocator: A hajj pilgrimage tracking framework in crowded ubiquitous environment*. in *2011 International Conference on Multimedia Computing and Systems*. 2011. IEEE.

19. Goni, M.D., et al., *Health Education Intervention as an Effective Means for Prevention of Respiratory Infections Among Hajj Pilgrims: A Review*. 2020. **8**: p. 449.
20. Shafi, S., et al., *The annual Hajj pilgrimage—minimizing the risk of ill health in pilgrims from Europe and opportunity for driving the best prevention and health promotion guidelines*. 2016. **47**: p. 79-82.
21. Razavi, S.M., M. Mardani, and P.J.A.o.C.I.D. Salamati, *Infectious Diseases and Preventive Measures During Hajj Mass Gatherings: A Review of the Literature*. 2018. **13**(3).
22. Almeleebia, T.M., et al., *Regulating antimicrobial sales in Saudi Arabia: Achievements and challenges*. International Journal of Clinical Practice, 2021. **75**(4): p. e13833.
23. Petersen, E., et al., *Transmission of respiratory tract infections at mass gathering events*. Current opinion in pulmonary medicine, 2020. **26**(3): p. 197-202.
24. Yezli, S., et al., *Prevalence and antimicrobial resistance among Gram-negative pathogens in Saudi Arabia*. J Chemother, 2014. **26**(5): p. 257-72.
25. Yezli, S., et al., *Antimicrobial resistance among Gram-positive pathogens in Saudi Arabia*. J Chemother, 2012. **24**(3): p. 125-36.
26. Zowawi, H.M., et al., *β -Lactamase production in key gram-negative pathogen isolates from the Arabian Peninsula*. Clinical microbiology reviews, 2013. **26**(3): p. 361-380.
27. Leangapichart, T., et al., *Emergence of drug resistant bacteria at the Hajj: A systematic review*. Travel Medicine and Infectious Disease, 2017. **18**: p. 3-17.
28. Yousef, S.A., S.Y. Mahmoud, and M.T. Eihab, *Prevalence of methicillin-resistant Staphylococcus aureus in Saudi Arabia: systemic review and meta-analysis*. African journal of clinical and experimental microbiology, 2013. **14**(3): p. 146-154.
29. Nazeer, A. and J.A. Al-Tawfiq, *Methicillin-resistant Staphylococcus aureus metrics for patients in Saudi Arabia*. The Journal of Infection in Developing Countries, 2012. **6**(03): p. 223-233.
30. Memish, Z.A., et al., *Hajj: infectious disease surveillance and control*. 2014. **383**(9934): p. 2073-2082.
31. Alotaibi, B.M., et al., *Strengthening health security at the Hajj mass gatherings: characteristics of the infectious diseases surveillance systems operational during the 2015 Hajj*. 2017. **24**(3): p. taw087.
32. Gautret, P., et al., *The spectrum of respiratory pathogens among returning Hajj pilgrims: myths and reality*. 2016. **47**: p. 83-85.
33. Krutika Kuppali, S.M., *Emerging Infectious Diseases During COVID-19*. Contagion, 2021. **6**(1).
34. Alhifany, A.A., et al., *Employment of mapping technology in antimicrobial resistance reporting in Saudi Arabia*. Geospatial Health, 2020. **15**(1).
35. Muniz Junior, R.L., et al., *Consumer willingness to pay for a hypothetical Zika vaccine in Brazil and the implications*. Expert review of pharmacoeconomics & outcomes research, 2019. **19**(4): p. 473-482.
36. Aldossari, M., A. Aljoudi, and D.J.E.M.H.J. Celentano, *Health issues in the Hajj pilgrimage: a literature review*. 2019. **25**(10): p. 744-753.
37. Murray, C.J., et al., *Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis*. The Lancet, 2022.
38. Dadgostar, P., *Antimicrobial resistance: implications and costs*. Infection and drug resistance, 2019: p. 3903-3910.
39. Cassini, A., et al., *Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis*. The Lancet infectious diseases, 2019. **19**(1): p. 56-66.
40. Pulingam, T., et al., *Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome*. European Journal of Pharmaceutical Sciences, 2022. **170**: p. 106103.
41. Al-Tawfiq, J., Z.J.C.M. Memish, and Infection, *Potential risk for drug resistance globalization at the Hajj*. 2015. **21**(2): p. 109-114.
42. Leangapichart, T., et al., *Acquisition of a high diversity of bacteria during the Hajj pilgrimage, including Acinetobacter baumannii with blaOXA-72 and Escherichia coli with blaNDM-5 carbapenemase genes*. 2016. **60**(10): p. 5942-5948.

43. Shirah, B.H., et al., *Mass gathering medicine (Hajj Pilgrimage in Saudi Arabia): The clinical pattern of pneumonia among pilgrims during Hajj*. 2017. **10**(3): p. 277-286.
44. Simpson, I.J., et al., *Air quality in Mecca and surrounding holy places in Saudi Arabia during Hajj: initial survey*. 2014. **48**(15): p. 8529-8537.
45. Gautret, P., et al., *Hajj-associated viral respiratory infections: a systematic review*. 2016. **14**(2): p. 92-109.
46. van Doorn, H.R. and H. Yu, *Viral respiratory infections*, in *Hunter's Tropical Medicine and Emerging Infectious Diseases*. 2020, Elsevier. p. 284-288.
47. Dauda Goni, M., et al., *Assessment of Knowledge, Attitude and Practice towards Prevention of Respiratory Tract Infections among Hajj and Umrah Pilgrims from Malaysia in 2018*. *Int J Environ Res Public Health*, 2019. **16**(22).
48. Alfelali, M., et al., *Influenza vaccination among Saudi Hajj pilgrims: Revealing the uptake and vaccination barriers*. 2018. **36**(16): p. 2112-2118.
49. Balkhy, H.H., et al., *Influenza a common viral infection among Hajj pilgrims: time for routine surveillance and vaccination*. 2004. **11**(2): p. 82-86.
50. Benkouiten, S., et al., *Clinical respiratory infections and pneumonia during the Hajj pilgrimage: A systematic review*. 2019. **28**: p. 15-26.
51. Dzaraly, N.D., et al., *Patterns of communicable and non-communicable diseases in Pilgrims during Hajj*. 2014. **7**(9): p. 12.
52. Algaissi, A.A., et al., *Preparedness and response to COVID-19 in Saudi Arabia: Building on MERS experience*. *Journal of Infection and Public Health*, 2020. **13**(6): p. 834-838.
53. Shang, W., et al., *Global excess mortality during COVID-19 pandemic: a systematic review and meta-analysis*. *Vaccines*, 2022. **10**(10): p. 1702.
54. Shabrawishi, M., et al., *Clinical, radiological and therapeutic characteristics of patients with COVID-19 in Saudi Arabia*. 2020. **15**(8): p. e0237130.
55. Ayouni, I., et al., *Effective public health measures to mitigate the spread of COVID-19: a systematic review*. *BMC public health*, 2021. **21**(1): p. 1-14.
56. Atique, S., R.J.I. Itumalla, disease, and health, *Hajj in the Time of COVID-19*. 2020. **25**(3): p. 219-221.
57. Sambas, M.F.M.K., et al., *Prevalence and determinants of multidrug-resistant tuberculosis in Makkah, Saudi Arabia*. *Infection and Drug Resistance*, 2020: p. 4031-4038.
58. Al-Hayani, A.M., et al., *Drug resistance to anti-tuberculosis drugs: A cross-sectional study from Makkah, Saudi Arabia*. *Cureus*, 2021. **13**(8).
59. Yezli, S., et al., *Undiagnosed Active Pulmonary Tuberculosis among Pilgrims during the 2015 Hajj Mass Gathering: A Prospective Cross-sectional Study*. *Am J Trop Med Hyg*, 2017. **97**(5): p. 1304-1309.
60. Yezli, S. and Z.A. Memish, *Tuberculosis in Saudi Arabia: prevalence and antimicrobial resistance*. *Journal of Chemotherapy*, 2012. **24**(1): p. 1-5.
61. Memish, Z.A., et al., *Carriage of Staphylococcus aureus among Hajj pilgrims*. 2006. **27**(9): p. 1367.
62. Al-Saleh, A., et al., *Trends in methicillin-resistant Staphylococcus aureus in the Gulf Cooperation Council countries: antibiotic resistance, virulence factors and emerging strains*. *Eastern Mediterranean Health Journal*, 2022. **28**(6): p. 434-443.
63. Yezli, S., et al., *Meningococcal disease during the Hajj and Umrah mass gatherings*. *International Journal of Infectious Diseases*, 2016. **47**: p. 60-64.
64. Zowawi, H.M.J.S.m.j., *Antimicrobial resistance in Saudi Arabia: An urgent call for an immediate action*. 2016. **37**(9): p. 935.
65. Saleem, Z., et al., *Sale of WHO AWaRe groups antibiotics without a prescription in Pakistan: a simulated client study*. *Journal of pharmaceutical policy and practice*, 2020. **13**(1): p. 1-8.

66. Saleem, Z., et al., *Antimicrobial dispensing practices and determinants of antimicrobial resistance: a qualitative study among community pharmacists in Pakistan*. Family Medicine and Community Health, 2019.
67. Alrasheedy, A.A., et al., *The impact of law enforcement on dispensing antibiotics without prescription: a multi-methods study from Saudi Arabia*. Expert review of anti-infective therapy, 2020. **18**(1): p. 87-97.
68. Alyamani, E.J., et al., *The occurrence of ESBL-producing Escherichia coli carrying aminoglycoside resistance genes in urinary tract infections in Saudi Arabia*. Annals of Clinical Microbiology and Antimicrobials, 2017. **16**(1): p. 1.
69. Marglani, O.A., et al., *Acute rhinosinusitis during Hajj season 2014: Prevalence of bacterial infection and patterns of antimicrobial susceptibility*. Travel Medicine and Infectious Disease, 2016. **14**(6): p. 583-587.
70. Yezli, S., et al., *Medication utilization pattern among outpatients during the Hajj mass gathering*. Saudi Pharmaceutical Journal, 2020. **28**(9): p. 1122-1128.
71. Memish, Z.A., et al., *Management and Prevention Strategies for Community-Acquired Pneumonia in the Gulf Corporation Council*. Journal of Chemotherapy, 2007. **19**(sup1): p. 33-46.
72. Azeem, M., et al., *Knowledge, Attitude and Practice (KAP) Survey Concerning Antimicrobial Use among Australian Hajj Pilgrims*. Infect Disord Drug Targets, 2014. **14**(2): p. 125-32.
73. Mustafa, A.N., et al., *A case-control study of influenza vaccine effectiveness among Malaysian pilgrims attending the Haj in Saudi Arabia*. International Journal of Infectious Diseases, 2003. **7**(3): p. 210-214.
74. Metanat, M., et al., *Pharyngeal carriage rate of Neisseria meningitidis before and after the Hajj pilgrimage, in Zahedan (southeastern Iran), 2012*. Turk J Med Sci, 2015. **45**(6): p. 1317-20.
75. Qureshi, H., et al., *The incidence of vaccine preventable influenza-like illness and medication use among Pakistani pilgrims to the Haj in Saudi Arabia* ☆☆☆This study was funded in part by Aventis Pasteur (formerly Pasteur Mérieux Connaught), a producer of influenza vaccine. Vaccine, 2000. **18**(26): p. 2956-2962.
76. Hoang, V.-T., et al., *Respiratory tract infections among French Hajj pilgrims from 2014 to 2017*. 2019. **9**(1): p. 1-8.
77. Yaser, M., et al., *A prospective antibiotic point prevalence survey in two primary referral hospitals during and after pilgrims stay in Madinah, Saudi Arabia*. 2020. **19**(2): p. 391-399.
78. Dzaraly, D., et al., *Antibiotic therapy of choice for community-acquired pneumonia in Malaysian Hajj pilgrims: the pattern and associated factors*. 2017. **33**(3): p. 199-207.
79. Alreeme, S., H. Bokhary, and A.T. Craig, *Transmission of Antimicrobial Resistant Bacteria at the Hajj: A Scoping Review*. International Journal of Environmental Research and Public Health, 2022. **19**(21): p. 14134.
80. Sukhmeet Minhas, A.K., SM, and Mandeep Singh, VSM, *Infection Control in Health Care Facilities*. Medical Journal of Armed Forces India, 2011. **67**(1): p. 7-8.
81. Shafi, S., et al., *Hajj: Health lessons for mass gatherings*. Journal of Infection and Public Health, 2008. **1**(1): p. 27-32.
82. Organization, W.H., *Communicable disease alert and response for mass gatherings*. 2008.
83. Alahmari, A.A., et al., *Hajj 2021: Role of Mitigation Measures for Health Security*. Journal of Infection and Public Health, 2022.
84. Jokhdar, H., et al., *COVID-19 mitigation plans during Hajj 2020: a success story of zero cases*. Health security, 2021. **19**(2): p. 133-139.
85. Basahel, S., A. Alsabban, and M. Yamin, *Hajj and Umrah management during COVID-19*. International Journal of Information Technology, 2021. **13**(6): p. 2491-2495.
86. Alamri, F.A., et al., *Common Health Complains Among Pilgrims during Manasik El Hajj; Season 1439H (2018)*. 2020.
87. Aljohani, A., et al., *E-government and logistical health services during Hajj season*. Bulletin of the National Research Centre, 2022. **46**(1): p. 1-8.
88. Abolfotouh, M.A., et al., *Behavior Responses and Attitude of the Public to COVID-19 Pandemic During Movement Restrictions in Saudi Arabia*. Int J Gen Med, 2021. **14**: p. 741-753.

89. Haworth, E., et al., *Prevention of influenza at Hajj: applications for mass gatherings*. 2013. **106**(6): p. 215-223.
90. Haridi, H.K., et al., *Influenza vaccine uptake, determinants, motivators, and barriers of the vaccine receipt among healthcare workers in a tertiary care hospital in Saudi Arabia*. *Journal of Hospital Infection*, 2017. **96**(3): p. 268-275.
91. Abd El Ghany, M., H. Sharaf, and G.A.J.I.J.o.I.D. Hill-Cawthorne, *Hajj vaccinations—facts, challenges, and hope*. 2016. **47**: p. 29-37.
92. Riedmann, E.M., *Report: State of the worlds vaccines and immunization*. 2010, Taylor & Francis.
93. Andre, F.E., et al., *Vaccination greatly reduces disease, disability, death and inequity worldwide*. 2008. **86**: p. 140-146.
94. Dagan, R. and K.P.J.P.V.T.I.o.C.V. Klugman, *Impact of conjugate pneumococcal vaccine on antibiotic resistance*. 2008: p. 369-385.
95. Cohen, R.J.T.P.i.d.j., *Approaches to reduce antibiotic resistance in the community*. 2006. **25**(10): p. 977-980.
96. Kwong, J.C., et al., *The effect of universal influenza immunization on antibiotic prescriptions: an ecological study*. 2009. **49**(5): p. 750-756.
97. Hashim, S., et al., *The prevalence and preventive measures of the respiratory illness among Malaysian pilgrims in 2013 Hajj season*. 2016. **23**(2).
98. Badahdah, A.-M., et al., *Mandatory meningococcal vaccine, and other recommended immunisations: uptake, barriers, and facilitators among health care workers and trainees at Hajj*. 2018. **6**(16): p. 1128.
99. Prevention, I.J.G.W.H.O., *Control of Epidemic-and Pandemic-Prone Acute Respiratory Infections in Health Care*. 2014.
100. Nieradko-Iwanicka, B.J.R., *Hygiene—gold standard not only in prevention of COVID-19 infection*. 2020. **58**(4): p. 191.
101. Ahmed, Q.A., et al., *Muslim health-care workers and alcohol-based handrubs*. 2006. **367**(9515): p. 1025-1027.
102. Balaban, V., et al., *Protective practices and respiratory illness among US travelers to the 2009 Hajj*. 2012. **19**(3): p. 163-168.
103. Sahin, M.K., S. Aker, and E.K.J.E. Tuncel, *Knowledge, attitudes and practices concerning Middle East respiratory syndrome among Umrah and Hajj pilgrims in Samsun, Turkey, 2015*. 2015. **20**(38): p. 30023.
104. Al-Ghamdi, A.S. and I.A.J.S.M.J. Kabbash, *Awareness of healthcare workers regarding preventive measures of communicable diseases among Hajj pilgrims at the entry point in Western Saudi Arabia*. 2011. **32**(11): p. 1161-7.
105. Mahdi, H.A., et al., *Syndromic surveillance of respiratory-tract infections and hand hygiene practice among pilgrims attended Hajj in 2021: A cohort study*. 2022.
106. Sen-Crowe, B., M. McKenney, and A.J.T.A.j.o.e.m. Elkbuli, *Social distancing during the COVID-19 pandemic: Staying home save lives*. 2020. **38**(7): p. 1519-1520.
107. Sayed, A.A.J.I.J.o.E.R. and P. Health, *The Progressive Public Measures of Saudi Arabia to Tackle Covid-19 and Limit Its Spread*. 2021. **18**(2): p. 783.
108. Sim, S.W., K.S.P. Moey, and N.C.J.S.m.j. Tan, *The use of facemasks to prevent respiratory infection: a literature review in the context of the Health Belief Model*. 2014. **55**(3): p. 160.
109. Mohamed Yusof, S.A., et al., *The issues of facemask among hajj pilgrims: a critical review*. 2014. **3**(4): p. 1528-1534.
110. Smith, J.D., et al., *Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis*. *Cmaj*, 2016. **188**(8): p. 567-574.
111. Saunders-Hastings, P., et al., *Effectiveness of personal protective measures in reducing pandemic influenza transmission: A systematic review and meta-analysis*. *Epidemics*, 2017. **20**: p. 1-20.
112. Liang, M., et al., *Efficacy of face mask in preventing respiratory virus transmission: A systematic review and meta-analysis*. *Travel Med Infect Dis*, 2020. **36**: p. 101751.
113. Coclite, D., et al., *Face mask use in the Community for Reducing the Spread of COVID-19: a systematic review*. 2020.
114. Getahun, H., et al., *Tackling antimicrobial resistance in the COVID-19 pandemic*. 2020. **98**(7): p. 442.
115. Bednarčuk, N., et al., *Antibiotic Utilization during COVID-19: Are We Over-Prescribing?* *Antibiotics*, 2023. **12**(2): p. 308.
116. Hsu, J., *How covid-19 is accelerating the threat of antimicrobial resistance*. *Bmj*, 2020. **369**.

117. Alshaikh, F.S., et al., *Prevalence of bacterial coinfection and patterns of antibiotics prescribing in patients with COVID-19: A systematic review and meta-analysis*. PLoS One, 2022. **17**(8): p. e0272375.
118. Langford, B.J., et al., *Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis*. Clinical microbiology and infection, 2021. **27**(4): p. 520-531.
119. Saleem, Z., et al., *Point prevalence survey of antimicrobial use during the COVID-19 pandemic among different hospitals in Pakistan: Findings and implications*. Antibiotics, 2022. **12**(1): p. 70.
120. Sasaki, K., et al., *Differentiating between bacterial and viral infection by measuring both C-reactive protein and 2' -5' -oligoadenylate synthetase as inflammatory markers*. Journal of infection and chemotherapy, 2002. **8**(1): p. 76-80.
121. Sproston, N.R. and J.J.F.i.i. Ashworth, *Role of C-reactive protein at sites of inflammation and infection*. 2018. **9**: p. 754.
122. Knight, G.M., et al., *Antimicrobial resistance and COVID-19: Intersections and implications*. 2021. **10**: p. e64139.
123. Egyir, B., N. Obeng-Nkrumah, and G.B. Kyei, *COVID-19 pandemic and antimicrobial resistance: Another call to strengthen laboratory diagnostic capacity in Africa*. Afr J Lab Med, 2020. **9**(1): p. 1302.
124. Sharland, M., et al., *Encouraging AWaRe-ness and discouraging inappropriate antibiotic use—the new 2019 Essential Medicines List becomes a global antibiotic stewardship tool*. The Lancet Infectious Diseases, 2019. **19**(12): p. 1278-1280.
125. Sharland, M., et al., *The WHO essential medicines list AWaRe book: from a list to a quality improvement system*. Clinical Microbiology and Infection, 2022. **28**(12): p. 1533-1535.
126. Torres, A., et al., *International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT)*. 2017. **50**(3).
127. Nathwani, D., et al., *Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review*. Antimicrobial Resistance & Infection Control, 2019. **8**(1): p. 1-13.
128. Saleem, Z., et al., *Ongoing efforts to improve antimicrobial utilization in hospitals among African countries and implications for the future*. Antibiotics, 2022. **11**(12): p. 1824.
129. Siachalinga, L. and W. Mufwambi, *Impact of antimicrobial stewardship interventions to improve antibiotic prescribing for hospital inpatients in Africa: A systematic review and meta-analysis*. Journal of Hospital Infection, 2022.
130. Mahdi, H.A., et al. *Low Prevalence of Syndromic Respiratory Tract Infections among Returning Hajj Pilgrims Amidst the COVID-19 Pandemic: A Post-Hajj Survey*. Tropical Medicine and Infectious Disease, 2022. **7**, DOI: 10.3390/tropicalmed7080182.
131. Alasmari, A., et al., *Meningococcal carriage among Hajj pilgrims, risk factors for carriage and records of vaccination: a study of pilgrims to Mecca*. 2021. **26**(4): p. 453-461.
132. AboEl-Magd, G.H., et al., *The prevalence and pattern of pneumonia among Hajj pilgrims: a study of two successive Hajj seasons*. 2020. **69**(2): p. 407.
133. Raja, W., et al., *Disease patterns among Hajj pilgrims attending medical facilities of Pakistan Hajj medical mission 2016 (1437 HJRI)*. 2017. **67**(5): p. 825-31.
134. Dhafar, K.O., et al., *DISEASE PATTERN OF PATIENTS ADMITTED DURING HAJJ TIME AND PROVISION OF HEALTH SERVICE TO FULFILL THE NECESSARY PILLARS OF HAJJ*. 2016. **1**(1): p. 0.4.
135. Bakhsh, A.R., et al., *Diseases pattern among patients attending Holy Mosque (Haram) medical centers during Hajj 1434 (2013)*. 2015. **36**(8): p. 962.
136. Memish, Z.A., et al., *Etiology of severe community-acquired pneumonia during the 2013 Hajj—part of the MERS-CoV surveillance program*. International Journal of Infectious Diseases, 2014. **25**: p. 186-190.
137. Memish, Z., et al., *Laboratory-confirmed invasive meningococcal disease: effect of the Hajj vaccination policy, Saudi Arabia, 1995 to 2011*. Eurosurveillance, 2013. **18**(37): p. 20581.

138. Barasheed, O., et al., *Pilot randomised controlled trial to test effectiveness of facemasks in preventing influenza-like illness transmission among Australian Hajj pilgrims in 2011*. 2014. **14**(2): p. 110-116.
139. Alzahrani, A.G., et al., *Pattern of diseases among visitors to Mina health centers during the Hajj season, 1429 H (2008 G)*. 2012. **5**(1): p. 22-34.
140. Mandourah, Y., et al., *Clinical and temporal patterns of severe pneumonia causing critical illness during Hajj*. 2012. **12**(1): p. 1-8.
141. Alherabi, A.Z.J.S.M.J., *Impact of pH1N1 influenza A infections on the otolaryngology, head and neck clinic during Hajj 2009*. 2011. **32**(9): p. 933-938.
142. Baharoon, S., et al., *Severe sepsis and septic shock at the Hajj: Etiologies and outcomes*. *Travel Medicine and Infectious Disease*, 2009. **7**(4): p. 247-252.
143. Ibrahim, N.K.J.J.E.P.H.A., *Epidemiological pattern of diseases and risk behaviors of pilgrims attending mina hospitals, hajj 1427 h (2007 g)*. 2008. **83**(1-2): p. 15-33.
144. Madani, T.A., et al., *Causes of admission to intensive care units in the Hajj period of the Islamic year 1424 (2004)*. 2007. **27**(2): p. 101-105.
145. Madani, T.A., et al., *Causes of hospitalization of pilgrims during the Hajj period of the Islamic year 1423 (2003)*. 2006. **26**(5): p. 346-351.
146. Karima, T.M., et al., *Clinical and microbiological spectrum of meningococcal disease in adults during Hajj 2000: an implication of quadrivalent vaccination policy*. *JOURNAL-PAKISTAN MEDICAL ASSOCIATION*, 2003. **53**(1): p. 3-7.
147. Harimurti, K., et al., *Streptococcus pneumoniae carriage and antibiotic susceptibility among Indonesian pilgrims during the Hajj pilgrimage in 2015*. 2021. **16**(1): p. e0246122.
148. Alqahtani, A.S., et al., *Saudi Hajj pilgrims' preparation and uptake of health preventive measures during Hajj 2017*. 2019. **12**(6): p. 772-776.
149. Alborzi, A., et al., *Meningococcal carrier rate before and after hajj pilgrimage: effect of single dose ciprofloxacin on carriage*. 2008.
150. Godman, B., et al., *Evidence-based public policy making for medicines across countries: findings and implications for the future*. *Journal of comparative effectiveness research*, 2021. **10**(12): p. 1019-1052.
151. Mwita, J.C., et al., *Key issues surrounding appropriate antibiotic use for prevention of surgical site infections in low-and middle-income countries: a narrative review and the implications*. *International Journal of General Medicine*, 2021. **14**: p. 515.
152. Godman, B. and M. Haque, *Ongoing strategies to improve the management of upper respiratory tract infections and reduce inappropriate antibiotic use particularly among lower and middle-income countries: findings and implications for the future*. 2019: p. 1.
153. Godman, B., et al., *Tackling antimicrobial resistance across sub-Saharan Africa: Current challenges and implications for the future*. *Expert Opinion on Drug Safety*, 2022. **21**(8): p. 1089-1111.
154. Godman, B., et al., *Strategies to improve antimicrobial utilization with a special focus on developing countries*. *Life*, 2021. **11**(6): p. 528.
155. Page, M.J., et al., *The PRISMA 2020 statement: an updated guideline for reporting systematic reviews*. *Bmj*, 2021. **372**.

Disclaimer

The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.