

Effectiveness of Antibiotic Use in the Prevention and Treatment of Respiratory Tract Infections

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ABSTRACT

This study aims to analyze the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections. This study uses the Systematic Literature Review (SLR) method. There are three stages carried out in mapping the effectiveness of antibiotic use in the prevention and treatment of respiratory tract infections, namely: 1) harvesting data, 2) screening data, and 3) Data Analysis and Visualization. This study uses a database from Scopus with scientific journals as many as 9 articles from the range of 2021 to 2024. The effectiveness of antibiotic use in the prevention and treatment of respiratory tract infections is influenced by a variety of factors, including patient adherence, duration of therapy, and vaccine availability and use. Excessive or improper use of antibiotics can increase bacterial resistance, so more sustainable strategies, such as vaccination and stricter antibiotic use policies, are needed to improve the effectiveness of prevention and treatment of respiratory tract infections. The implications of this study are expected to be useful for future researchers and can be used in clinical applications

INTRODUCTION

Respiratory tract infections are medical conditions that involve infections of the respiratory tract, which can be divided into upper respiratory tract infections (ISPA) and lower respiratory tract infections (ISPB). Respiratory tract infections (ISPs) are one of the leading causes of morbidity and mortality worldwide, especially among children, the elderly, and individuals with weakened immune systems. Respiratory tract infections are divided into two, namely Upper Respiratory Tract Infections (ISPA) and Lower Respiratory Tract Infections (ISPB). ISPA is generally caused by viruses, with rhinovirus being the most common etiological agent. Symptoms include nasal congestion, sneezing, sore throat, and cough. In children, fever is more common (K et al., 2024). ISPA can cause

complications such as acute otitis media in children and sinusitis or pneumonia in adults (K et al., 2024). Meanwhile, ISPB includes pneumonia, influenza, bronchitis, and bronchiolitis. The disease is often more serious and can lead to death, especially in vulnerable populations such as the elderly and those with chronic medical conditions (Feldman & Shaddock, 2019; Walter & Wunderink, 2017). Viruses such as influenza, respiratory syncytial virus, and metapneumovirus are common causes of ISPB. Bacteria can also be the cause, especially in cases of pneumonia (Derakhshan-Nezhad, 2023; Singh, 2016). ISPB is the leading cause of death from infectious diseases in the world and is often associated with changes in population demographics and antigenic variations of influenza viruses (Feldman & Shaddock, 2019; Walter & Wunderink, 2017)).

The Global burden of respiratory infections that occur is; 1) Lower Respiratory Tract Infections (LRI): In 2021, there were approximately 344 million episodes of LRI with 2.18 million deaths globally. *Streptococcus pneumoniae* is the main pathogen responsible for most episodes and deaths of LRI (Bender et al., 2024; Yu et al., 2024). 2) Upper Respiratory Tract Infections (URIs): URIs are the leading cause of acute disease incidences worldwide, with 12.8 billion new episodes in 2021. Although its incidence has decreased since 1990, URI remains a significant health burden (Sirota et al., 2024). Therefore, respiratory tract infections remain a significant global health challenge, especially in countries with low SDI. Despite the decline in incidence and mortality, continued efforts in vaccination and the development of new therapies are essential to reduce the burden of the disease.

Antibiotics play an important role in the treatment of respiratory tract infections, both caused by bacteria and to prevent further complications. However, its use should be appropriate to avoid antibiotic resistance and unwanted side effects. Most of these infections are caused by viruses, so antibiotics are often not necessary. However, antibiotics can be used in certain cases such as acute otitis media, streptococcal pharyngitis, and epiglottitis (Raghav et al., 2022; Sur & Plesa, 2022). Improper use of antibiotics in ISPA can lead to antibiotic resistance and side effects (Harris et al., 2016; Sur & Plesa, 2022). Antibiotics are more commonly used for ISPBs such as pneumonia and acute exacerbations of chronic obstructive pulmonary disease (COPD). The selection of antibiotics should take into account the most likely pathogens and the level of local resistance (Feldman & Richards, 2018; Huang et al., 2022; Lazareva & Rebrova, 2023). Amoxicillin/clavulanate is often used as the gold standard for community-acquired infections (Legnani, 1997). Improper use of antibiotics, especially broad-spectrum, contributes to increased antibiotic resistance, which is a serious public health threat (Harris et al., 2016; Raghav et al., 2022). Antibiotics can cause side effects ranging from mild to life-threatening, such as *Clostridium difficile* diarrhea which can be fatal (Harris et al., 2016). It is important to distinguish between bacterial and viral infections to avoid unnecessary use of antibiotics. For example, acute bronchitis is usually caused by a virus and does not require antibiotics unless there is a suspicion of pneumonia (Harris et al., 2016; Sur & Plesa, 2022). Antibiotics have an important role in the treatment of respiratory tract infections, especially those caused by bacteria. However, its use should be wise to avoid antibiotic resistance and side effects. Proper education and clinical guidance are needed to ensure the effective and safe use of antibiotics.

Antibiotic resistance is a serious global threat to the effective treatment of bacterial infections. This problem leads to treatment failure, increased morbidity and mortality, and higher healthcare costs (Huemer et al., 2020; Lin et al., 2015; Nwobodo et al., 2022). The Causes and Mechanisms of Resistance are; 1) Bacterial Adaptation:

Bacteria develop resistance through genetic adaptation, including mutations and the acquisition of new genetic material, which allows them to survive exposure to antibiotics (Blair et al., 2014; Munita & Arias, 2016) 2) Spread of Resistance Genes: Resistance genes can be easily transferred between bacteria, including between commensal flora and pathogens, accelerating the spread of resistance (Blair et al., 2014; Urban-Chmiel et al., 2022). 3) Antibiotic Persistence: In addition to resistance, some bacteria can survive despite being susceptible to antibiotics, known as antibiotic persistence, and these often go undetected (Huemer et al., 2020). Therefore, antibiotic resistance is a global health challenge that requires a multi-sectoral approach to control and prevention. Efforts should be focused on developing new antibiotics, controlling antibiotic use, and improving diagnostic methods to effectively address these threats.

The use of antibiotics for viral infections is a significant issue in medical practice, as antibiotics are not effective against viruses and can lead to antimicrobial resistance. Studies have shown that antibiotics are often inappropriately prescribed for respiratory tract infections caused by viruses, posing challenges in public health management. Antibiotics are often prescribed for upper respiratory tract infections (URTI) caused by viruses, although they do not provide clinical benefits and may increase antimicrobial resistance as well as the risk of adverse reactions (Debes et al., 2023; Machado-Duque et al., 2021). Studies show that about 24.8% of patients with viral URTI in Colombia receive antibiotic prescriptions, even though the infection does not require antibiotics (Machado-Duque et al., 2021). In hospitals, 76% of adult patients with viral respiratory tract infections also received antibiotics, although there were no secondary bacterial infections (Debes et al., 2023). Some of the factors that influence antibiotic administration decisions include laboratory results, clinical symptoms, and radiological results (Debes et al., 2023).. In the emergency room, patients with older viral respiratory infections, longer symptoms, or abnormal chest X-rays are more likely to receive antibiotics (Li et al., 2019). In addition, the inability to accurately distinguish between bacterial and viral infections also encourages the improper use of antibiotics (Tanday, 2016). The use of respiratory virus panels such as real-time PCR can help reduce the improper use of antibiotics by accurately identifying viral pathogens (Dass et al., 2023). These rapid diagnostics can guide more precise antibiotic treatment decisions and reduce the duration of antibiotic use (Dass et al., 2023). In addition, a combination of biomarkers such as TRAIL, IP-10, and CRP has been shown to be effective in differentiating bacterial infections from viral, which can reduce the overuse of antibiotics (Kandula & Farrell, 2023; Papan et al., 2021). The improper use of antibiotics for viral infections remains a significant problem, with impacts on antimicrobial resistance and public health. The use of rapid diagnostics and biomarkers can help reduce unnecessary use of antibiotics, but ongoing education and surveillance are needed to transform clinical practice.

Alternative and prevention strategies for respiratory tract infections (RTI) involve a variety of approaches, including nutritional interventions, microbiome modifications, vaccinations, and supplement use. Here are some of the strategies that have been researched: 1) Nutrition and Microbiome Interventions. Synbiotics and Probiotics: Synbiotics, a combination of prebiotics and probiotics, can reduce the incidence of RTI by up to 16% and are more effective in adults than children (C. Chan et al., 2020). Probiotics also show potential in reducing the incidence of acute upper respiratory tract infections (URTI) and antibiotic use (Zhao et al., 2022). Microbiome Modulation: Altering the gut and lung microbiome may be a new strategy for preventing respiratory

tract infections, especially in the face of drug-resistant pathogens (Mindt & DiGiandomenico, 2022) 2) Vaccination and Immunotherapy. Sublingual Vaccine MV130: This vaccine induces trained immunity and has been shown to significantly reduce the incidence of RTI and antibiotic use in children and adults (Montalbán-Hernández et al., 2024). Inhaled Immunotherapy: Using immunomodulatory agents through inhalation can improve the immune response to respiratory pathogens. (Sécher et al., 2019) 3) Supplements and Natural Remedies. Flavonoid Supplements: Supplements containing flavonoids may reduce the incidence of ARTI and the duration of illness without increasing side effects (Yao et al., 2022). Homeopathic Medicine: Although widely used, the evidence for the effectiveness of homeopathy in preventing or treating ARTI in children is inconsistent and generally does not support its use (Hawke et al., 2022; King et al., 2020) . Various RTI prevention strategies involve nutritional approaches, microbiome modifications, vaccinations, and supplement use. Synbiotics and probiotics show potential in reducing the incidence of RTI, while sublingual vaccines and flavonoid supplements are also promising. However, the effectiveness of homeopathy is still questionable. This approach can help reduce dependence on antibiotics and overcome drug resistance. Therefore, the purpose of this study is to analyze the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections.

METHODOLOGY

This study uses the Systematic Literature Review (SLR) method. SLR is a synthesis of literature studies that are carried out systematically, clearly, and thoroughly. SLRs are often used to conduct thematic analysis, identify key themes and subthemes in the existing literature, and explore current trends and developments (Oladimeji et al., 2020). The purpose of this method is to help researchers understand more deeply about the research being studied, including why and how the results can be used as a reference for new research. In this study, researchers analyzed the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections. This study uses a database from Scopus. There are three stages carried out in mapping the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections, namely:

1. *Harvesting Data.* At this stage, the researcher harvested the data by collecting articles that had been published and indexed by the Scopus indexing agency. To collect publications from this Scopus indexing institution, researchers directly went to the Scopus database. The search for publications was carried out using keywords in this study, including: "antibiotic", "AND prevention", "OR treatment", "AND of AND respiratory", "AND tract", "AND infections" with a time span from 2021-2024. In harvesting this data, it is also based on several countries in Southeast Asia, such as Indonesia, Malaysia, and Singapore

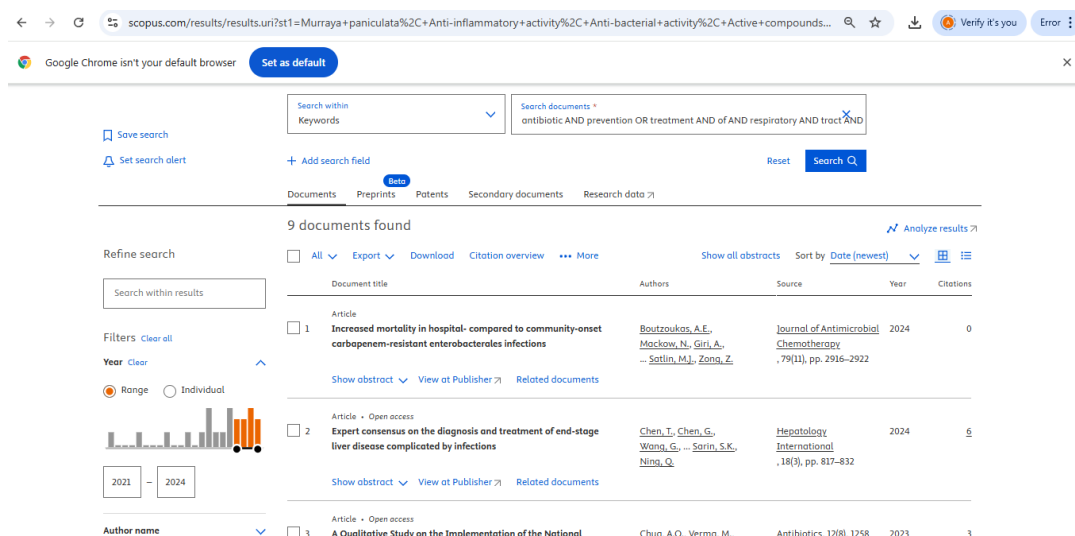


Figure 1. Data harvesting process on scopus data
Source: Data Research

From the results of data harvesting, 9 articles were published. Furthermore, the researcher downloads all scientific papers in the form of RIS. Click "Select All", then click "Export" and select "RIS Format". Then it will go to the page as below

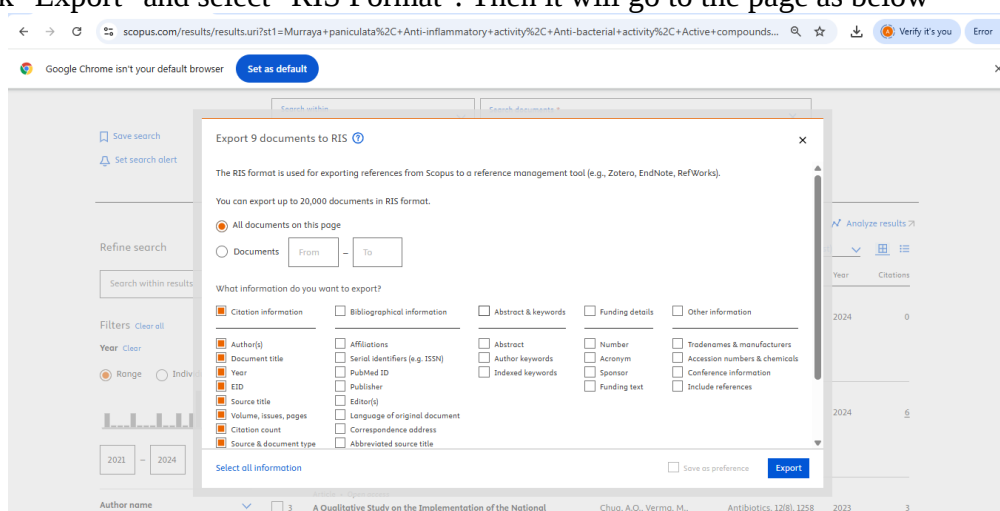


Figure 2. The process of downloading RIS on scopus data
Source: Data Research

Data Screening (Data Screening). Based on the results of data collection obtained from the Scopus indexing agency, there are 9 article publications related to the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections during the 2021-2024 period.

2. Data Analysis and Visualization. In this stage of data analysis, the researcher conducted an analysis of the publications obtained from Scopus at the time of data harvesting. There are several data related to the publications that are analyzed, such as the development of publications per year during the 2021-2024 period. Of the three stages, namely the stages of data harvesting, data filtering and data analysis and visualization, can be described as follows:

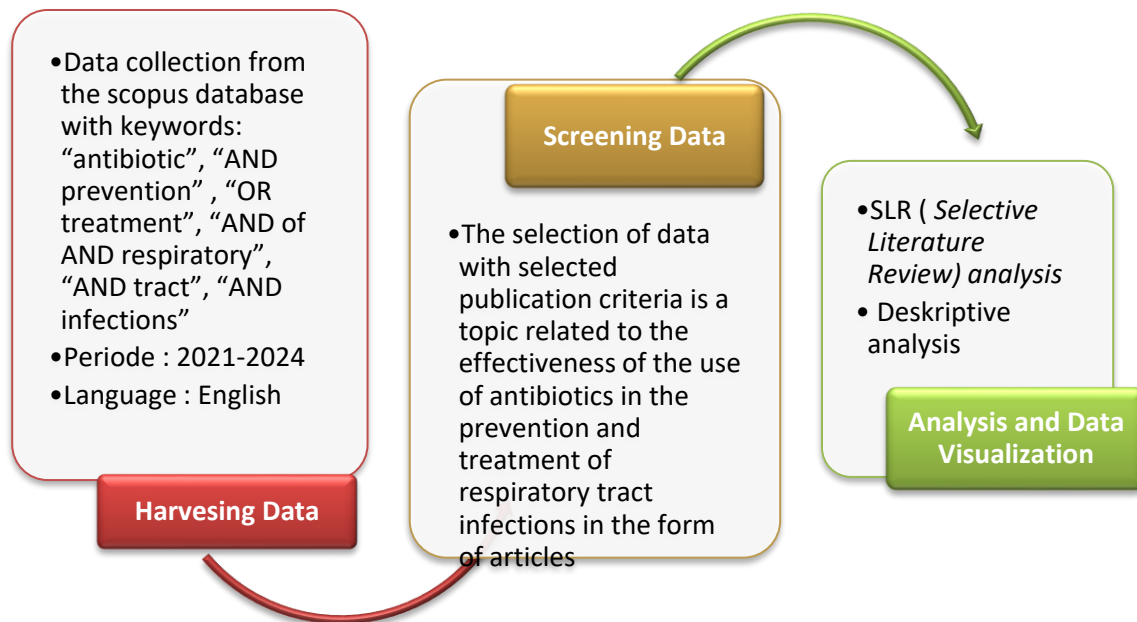


Figure 3. Draft SLR Methodology on Research related to the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections
Source: Data Research

RESULTS AND DISCUSSION

1. Publication Development

Publication developments in the journal Scopus related to the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections during the period 2021-2024. From 2021 to 2022, the number of published Scopus journals has been relatively stable, namely 2 Scopus journals per year. 2023 saw an increase in the number of journal publications, reaching 3 scopus journals, which is the peak of this year. In 2024, the number of Scopus journals will again decrease to 2 Scopus journals, indicating fluctuations in the number of publications.

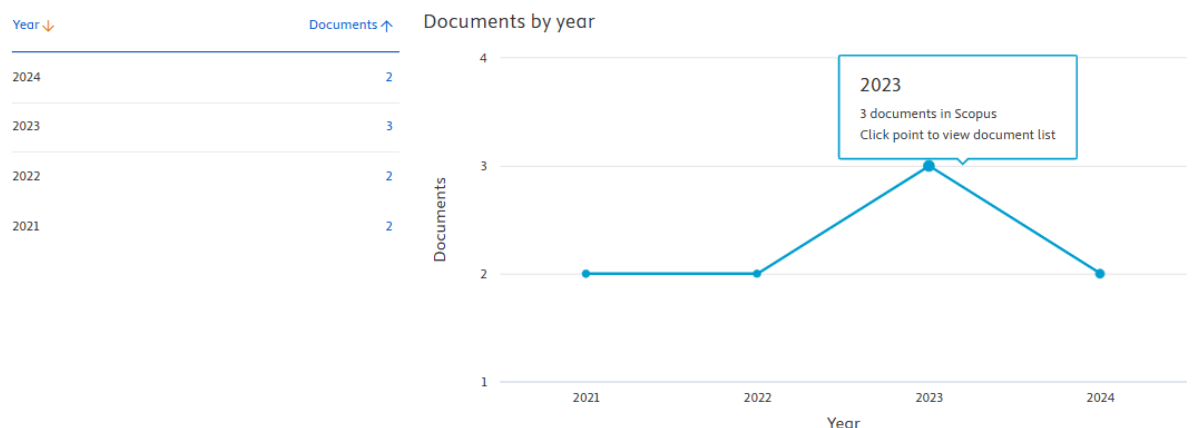


Figure 4. Publication Development Based on Scopus Data for the Period 2021-2024
Source Scopus Data 2025

The graph above explains the list that 2023 was the year with the most publications, namely 3 journals in the Scopus database. This shows the increase and productivity of research that year. After an increase in 2023, the number of scopus journals in 2024 returns to 2 scopus journals. This can be caused by a variety of factors, such as a reduced number of related research, changes in research trends, or different publication policies. Based on the description of the explanation, it can be concluded that the graph shows a fluctuating pattern in the number of publications from year to year. There was a significant increase in 2023, which was then followed by a decline in 2024. This pattern may reflect dynamics within the area of research being analyzed, such as a temporary increase in interest or a peak in research productivity before stabilizing again.

2. Affiliation of the Country Producing Scientific Work

The affiliation of the countries producing this scientific work is within the scope of countries in Southeast Asia, such as Indonesia, Malaysia, and Singapore. Based on the graph produced, it shows the distribution of documents based on affiliation. The institutions with the most publications are; National University of ... (most likely the National University of Singapore) has the highest number of publications, close to 7 documents. Tan Tock Seng Hospital is in second place with the number of publications of more than 3 documents. NUS Yong Loo Lin School of Medicine and National University ... has almost the same number of publications, slightly lower than Tan Tock Seng Hospital.

In addition to major institutions, some universities and hospitals such as The University of Hong Kong, Capital Medical University, Hospital Escuela Oscar Danilo Rosales, Guangzhou Eighth People's Hospital, and Mount Sinai have fewer contributions in publications. Most of the institutions on this list are universities and hospitals that have a focus on medical and health research. This indicates that the research related to the documents being analyzed involves international collaboration or has a global scope.

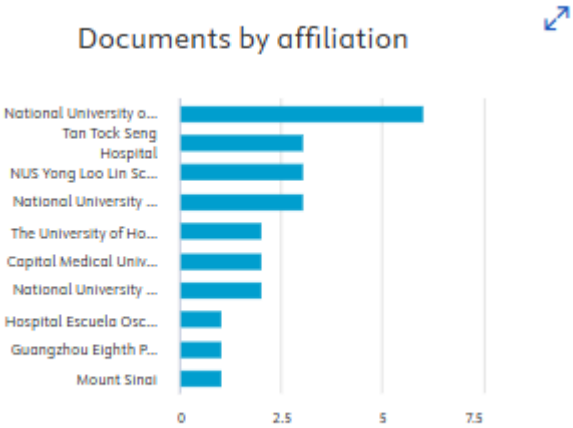


Figure 2. Affiliation of Scientific Paper Producing Countries Based on Scopus Data
Source: Data Scopus 2025

Based on the graph image above, it can be concluded that this graph shows that the National University of Singapore (NUS) and Tan Tock Seng Hospital are the most active institutions in publications related to this field. Singapore's institutional dominance also

indicates that the country has a strong focus on medical and health research. Meanwhile, contributions from other institutions are fairly evenly distributed but in smaller amounts.

3. Most Cited Articles

Based on the results of harvesting data, screening data and data processing on publications related to the effectiveness of antibiotic use in the prevention and treatment of respiratory infections in the Scopus database. During the period 2021 to 2024, there were 9 journal publications related to the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections. From Table 1 below, there are nine journal publications related to the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections.

Tabel 2. Summary of Literatur review

No	Referensi	Judul	Fokus Studi	Metode dan sampel	Hasil
1	(Boutzoukas et al., 2024)	Increased mortality in hospital-compared to community-onset carbapenem-resistant enterobacterales infections	Increased mortality in hospital	Methods: Patients prospectively enrolled in CRACKLE-2 from 56 hospitals in 10 countries between 30 April 2016 and 30 November 2019 with a CRE BSI were eligible	The primary outcome was the desirability of outcome ranking (DOOR) at 30 days. The difference in 30-day mortality was calculated with a 95% CI. Among 891 patients with CRE BSI, 65% (582) were HO. Compared to CO CRE patients, those with HO CRE were younger (median 60 vs. 65 years; $P<0.001$), had fewer comorbidities (median CCI 2 vs. 3; $P=0.002$), and were more acutely ill (Pitt score ≥ 4 : 47% vs. 32%; $P<0.001$). The probability of a better DOOR outcome in CO BSI patients versus HO BSI patients was 60.6% (95% CI: 56.8%–64.3%). The 30-day mortality was higher in HO BSI (33% vs. 21%; $P<0.001$).
2	(Chen et al., 2024)	Expert consensus on the diagnosis and treatment of end-stage liver disease	The diagnosis and treatment of end-stage liver disease	Method type: study literature assembled up-to-date knowledge and experience from	In patients with ESLD, bacterial or fungal infections can trigger or worsen liver decompensation, making them a major cause of disease deterioration. Standardized protocols for early diagnosis and

		complicated by infections		colleagues across the Asia-Pacific region, providing data on the principles as well as evidence-based current working protocols and practices for the diagnosis and treatment of patients with ESLD complicated by infections.	management are urgently needed. The Asia-Pacific region, with the highest ESLD cases due to hepatitis B, alcohol use, and NAFLD, faces significant challenges, as infections contribute to organ failure, high mortality, and increased healthcare burdens.
3.	(Chua et al., 2023)	A Qualitative Study on the Implementation of the National Action Plan on Antimicrobial Resistance in Singapore	Implementation of the National Action Plan on Antimicrobial Resistance	Method : Interviews with 20 participants across the One Health spectrum and Literature study the implementation of the NSAP with guidance from an AMR governance framework	The implementation of AMR-related activities was more advanced in human health than in other sectors, including (1) AMR and AMU surveillance in hospitals, (2) hospital AMS services and legislation for AMU optimization, (3) national vaccination programs for IPC, (4) diverse education and awareness initiatives, and (5) extensive research and collaboration with multiple funding sources.
4.	(Mo et al., 2023)	Implications of reducing antibiotic treatment duration for antimicrobial resistance in hospital settings: A	Implications of reducing antibiotic treatment duration for antimicrobial resistance	Method : A modelling study and meta-analysis, 3 stochastic mechanistic models and a meta-analysis of antibiotic treatment duration trials	The meta-analysis found that each extra day of antibiotic treatment increases resistance carriage risk by 7% (80% credible interval: 3%–11%). However, the limited number of trials monitoring resistant gram-negative bacteria affects estimate precision. While shorter treatment can reduce

		modelling study and meta-analysis			resistance, models also suggest scenarios where it may unexpectedly increase resistance.
5.	(See & Lau, 2023)	Acute management of pneumonia in adult patients	A pneumonia disease	Method: randomized trials and meta-analysis	In pneumonia patients, key organ support includes managing shock, acute respiratory failure, and acute kidney failure. Shock is indicated by delayed capillary refill (>3 seconds) and requires rapid fluid resuscitation, even without hypotension. If hypotension persists after fluid administration, vasopressors such as norepinephrine (0.05 mcg/kg/min) or dopamine (5 mcg/kg/min) may be needed. Acute respiratory failure is identified by oxygen saturation <90% and should be promptly treated with supplemental oxygen before further interventions. Kidney failure may not be immediately apparent and is indicated by oliguria (<0.5 mL/kg/hour).
6.	(E. Y.-H. Chan et al., 2022)	Long-term Efficacy and Safety of Repeated Rituximab to Maintain Remission in Idiopathic Childhood Nephrotic Syndrome: An	Idiopathic Childhood Nephrotic Syndrome	Method: A retrospective cohort study at 16 pediatric nephrology centers from 10 countries in Asia, Europe, and North America included children with FRSDNS who received	Primary outcomes were relapse-free survival and adverse events. Results: 346 children (age 9.8 years, IQR 6.6-13.5; 73% boys) received 1149 rituximab courses. 145, 83, 50, 28, 22, and 18 children received 2, 3, 4, 5, 6 and ≥ 7 courses, respectively. Median follow-up was 5.9 years (IQR, 4.3-7.7). Relapse-free survival differed by treatment courses (clustered log-rank test $p < 0.001$). Compared to the first course

		International Study		≥2 rituximab courses.	(10.0 months, 95% CI, 9.0-10.7), relapse-free period and relapse risk progressively improved following subsequent courses (12.0-16.0 months; HRadj, 0.03-0.13; 95% CI, 0.01-0.18; ps<0.001). B-cell depletion duration remained similar with repeated treatments (6.1 months, 95% CI, 6.0-6.3). Adverse events were mostly mild, most commonly hypogammaglobulinemia (50.9%), infection (4.5%), and neutropenia (3.7%). Side effects did not increase with more treatment courses nor higher cumulative dose. Only 78 of the 353 episodes of hypogammaglobulinemia were clinically significant. Younger age at presentation (2.8 vs 3.3 years; p=0.05) and at first rituximab (8.0 y vs 10.0 years; p=0.01) and history of steroid resistance (28% vs 18%; p=0.01) were associated with significant hypogammaglobulinemia. All 53 infective episodes resolved, except one patient with hepatitis B infection and another with EBV infection. There were 42 episodes of neutropenia, associated with history of steroid resistance (30% vs 20%, p=0.04). Upon last follow-up, 332 children (96%) had normal kidney function.
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7.	(Tan et al., 2022)	Antibiotic expectations of patients attending an emergency department with upper respiratory tract infections: clinical and behavioural determinants of antibiotic use	clinical and behavioural determinants of antibiotic use	Methods: A cross-sectional study was undertaken of 717 patients attending the ED at Tan Tock Seng Hospital for URTIs between June 2016 and November 2018	Results: Most patients were young (mean age 40.5 ± 14.7 years), had no comorbidities (66.5%), and sought care within a week of symptoms (62.9%). The majority (79.1%) did not meet the CDC's influenza-like illness (ILI) criteria. Key behavioral factors included non-compliance with prescribed antibiotics, self-medication with unprescribed antibiotics, and discontinuation due to adverse effects. Patients with ILI (OR 1.73, 95% CI 1.15–2.59; $P=0.008$) or who self-medicated with unprescribed antibiotics (OR 1.28, 95% CI 1.04–1.57; $P=0.021$) were more likely to expect antibiotics at the ED. Vaccination against bacterial and viral pathogens, such as pneumococcal and influenza vaccines, helps reduce infections and antibiotic use.
8.	(Tambyah, 2021)	Future role of vaccines on antibacterial resistance	antibacterial resistance	Method : Observational studies and clinical trials	Results: Most patients were young (mean age 40.5 ± 14.7 years), had no comorbidities (66.5%), and sought care within a week of symptoms (62.9%). The majority (79.1%) did not meet the CDC's influenza-like illness (ILI) criteria. Key behavioral factors included non-compliance with prescribed antibiotics, self-medication with unprescribed antibiotics, and discontinuation due to adverse effects. Patients with ILI (OR 1.73, 95% CI 1.15–2.59; $P=0.008$) or who

					self-medicated with unprescribed antibiotics (OR 1.28, 95% CI 1.04–1.57; P=0.021) were more likely to expect antibiotics at the ED. Vaccination against bacterial and viral pathogens, such as pneumococcal and influenza vaccines, helps reduce infections and antibiotic use.
9.	(Rousseau et al., 2021)	Epidemiology, treatment and outcome of patients with lower respiratory tract infection presenting to emergency departments with dyspnoea (AANZD EM and EuroDEM studies)	lower respiratory tract infection	Methods: We conducted a prospective cohort study with three time points in Europe and Oceania/SEA	Results: A total of 1,389 patients were included (773 in Europe, 616 in SEA). European patients had more comorbidities and higher inflammatory marker levels, while hypercapnia was more common in SEA. Antibiotic use was higher in SEA (72.2% vs. 61.8%, P < 0.001), whereas Europe had higher use of diuretics, non-invasive, and invasive ventilation. ICU admission was 9.9% in Europe and 3.4% in SEA. ED mortality was 1%, and overall in-hospital mortality was 8.7%, with no regional differences.

Based on table 2, it shows the explanation in each journal that; 1) Infection by Carbapenem Resistant Enterobacterales (CRE) in Hospital vs. Community (Boutzoukas et al., 2024) Hospital (HO) CRE infection has a higher mortality rate (33%) compared to infection in the community (CO) (21%). Patients with HO CRE are younger but more acutely ill than CO CRE. 2) Diagnosis and Treatment of Complicated Late-Stage Liver Disease Infection (Chen et al., 2024) Bacterial and fungal infections exacerbate liver decompensation. Better diagnostic and early management standards are needed, especially in the Asia Pacific region. 3) Implementation of the National Action Plan on Antimicrobial Resistance in Singapore (Chua et al., 2023) The management of antimicrobial resistance is more advanced in the human health sector than any other sector. There is a surveillance system, an antibiotic use optimization policy, a vaccination program, and extensive research. 4) Duration of Antibiotic Treatment against Antimicrobial Resistance (Mo et al., 2023) Each additional day of antibiotic therapy increases the risk of resistance by 7%. Reducing the duration of antibiotics can help reduce resistance, but there are certain conditions where this reduction actually increases

resistance. 5) Management of Acute Pneumonia in Adult Patients (See & Lau, 2023) The main focus is organ support such as recovery from shock, respiratory failure, and acute kidney failure. Treatment involves oxygenation, vasopressor therapy, and strict hemodynamic monitoring. 6) Long-Term Effectiveness of Rituximab in Pediatric Nephrotic Syndrome (Chan et al., 2022) Patients who received rituximab more than twice had an increased relapse-free period. The main side effects were hypomaglobulinemia, infection, and neutropenia, but without increased risk with more doses. 7) Patient Behavior Towards Antibiotic Use in the Emergency Room (Tan et al., 2022) Patients with upper respiratory tract infections often have hope of receiving antibiotics even though they are not always needed. Behavioral factors include non-adherence to antibiotic regimens, nonprescription use of antibiotics, and self-discontinuation due to side effects. 8) The Role of Vaccines against Antibacterial Resistance (Tambyah, 2021) Vaccination against bacteria and viruses has been shown to reduce the need for antibiotic use by preventing infection from the start. For example, pneumococcal and influenza vaccines reduce infections that often require antibiotics. 9) Epidemiology and Treatment of Lower Respiratory Tract Infections in the Emergency Department (Rousseau et al., 2021) Patients in Europe have more comorbidities than patients in Southeast Asia and Oceania. Antibiotic use is higher in Southeast Asia (72.2% vs. 61.8% in Europe). The mortality rate in the emergency room was low (1%) but the total mortality during hospitalization reached 8.7

DISCUSSION

Reducing the duration of antibiotic use may reduce resistance, but it should be adapted to the clinical condition.

Reducing the duration of antibiotic use can help reduce antimicrobial resistance, but it should be tailored to the patient's clinical condition. Some studies have shown that reducing the duration of antibiotic therapy may reduce the level of bacterial resistance, although results vary depending on the clinical context and the type of bacteria involved. Studies show that reducing the duration of antibiotic therapy can reduce bacterial resistance, especially in settings with high transmission rates (Marra et al., 2009; Mo et al., 2023; Spellberg & Rice, 2019). However, in some cases, duration reduction can increase resistance if resistant bacteria grow rapidly under the pressure of antibiotic selection (Mo et al., 2023). Short-term antibiotic therapy often provides the same clinical outcomes as long-term therapy, with lower levels of resistance and fewer side effects (Shahanenko et al., 2023; Spellberg & Rice, 2019). The effectiveness of reducing the duration of antibiotics can vary depending on the type of infection and the patient's condition (Bassetti et al., 2022; Rice, 2008). Based on several such sources, it can be concluded that reducing the duration of antibiotic use can be an effective strategy to reduce antimicrobial resistance, but it must be adapted to specific clinical conditions. The use of biomarkers and an individualized approach to therapy can increase the effectiveness of these strategies. However, more research is needed to fully understand the impact of reducing the duration of antibiotics in a variety of clinical contexts.

Vaccination has an important role in reducing infections and the need for antibiotics.

Vaccination plays an important role in reducing infections and the need for antibiotics, which in turn helps reduce antibiotic resistance. Vaccines can prevent infections that often require antibiotic treatment, thereby reducing antibiotic use and associated resistance. Direct and Indirect Impacts of Vaccination; 1) Direct Impact:

Vaccines such as pneumococcal conjugate vaccines (PCVs) directly reduce the prevalence of antibiotic-resistant diseases by targeting specific strains of bacteria that carry resistant genes (Klugman & Black, 2018; Villegas et al., 2021). Studies show that PCV vaccines can reduce the incidence of invasive diseases resistant to penicillin by up to 67% (Klugman & Black, 2018; Villegas et al., 2021).. 2) Indirect Impacts: Influenza vaccines, for example, can reduce antibiotic use by 13-50% by preventing febrile illnesses that are often treated with antibiotics (Klugman & Black, 2018; Villegas et al., 2021).

Vaccination in children in low- and middle-income countries has been shown to significantly reduce antibiotic consumption. Pneumococcal and rotavirus vaccines, for example, prevent millions of episodes of the disease treated with antibiotics each year (Lewnard et al., 2020; Stower, 2020). Vaccination can reduce the transmission of resistant bacteria in hospital-like environments, which often have a higher proportion of resistant strains (Jit & Cooper, 2020; Mullins et al., 2023). Existing and ongoing vaccines, such as for *Streptococcus pneumoniae* and *Haemophilus influenzae*, show great potential in reducing antibiotic resistance (Jit & Cooper, 2020; Micoli et al., 2021). The development of new vaccines and the expansion of vaccination programs can further reduce antibiotic use and emerging resistance (Lipsitch & Siber, 2016; Smith, 2021). Based on some of the above sources, it can be concluded that vaccination is an important tool in reducing infections and the need for antibiotics, which ultimately helps reduce antibiotic resistance. By preventing infection and reducing the use of antibiotics, vaccination contributes significantly to combating antimicrobial resistance. Efforts to increase vaccination coverage and develop new vaccines are critical to addressing these global challenges.

CONCLUSION

Based on research with the SLR method that has been conducted, it can be concluded that the effectiveness of the use of antibiotics in the prevention and treatment of respiratory tract infections is influenced by various factors, including patient adherence, duration of therapy, and vaccine availability and use. Excessive or improper use of antibiotics can increase bacterial resistance, so more sustainable strategies, such as vaccination and stricter antibiotic use policies, are needed to improve the effectiveness of prevention and treatment of respiratory tract infections.

Research Implications

The research implications is;

1. For Researchers

This research can enrich insights in the fields of pharmacology and biomedicine, especially in understanding the mechanism of action of active compounds against inflammatory processes and bacterial infections. It can be the basis for further research related to the optimization of drug formulations based on natural compounds to improve the effectiveness of therapy.

2. In Clinical Applications

If proven effective, the compounds studied could be developed into alternative or supportive therapies in the treatment of diseases caused by chronic inflammation and bacterial infections. Potential reduction of dependence on synthetic antibiotics, which can help address the problem of antibiotic resistance.

LITERATURE

- Bassetti, S., Tschudin-Sutter, S., Egli, A., & Osthoff, M. (2022). Optimizing antibiotic therapies to reduce the risk of bacterial resistance. *European Journal of Internal Medicine*. <https://doi.org/10.1016/j.ejim.2022.01.029>
- Issusilaningtyas E, Rochmah NN, Azmi SD, Fadhila N (2024). Effectiveness of Soursop Leaf Extract in Reducing Glucose Levels in Diabetes Mellitus Patients: Literature Study. *Journal of Pharmacopoeia: Jurnal Farmasi*. <https://nawalaeducation.com/index.php/JP/article/view/558/1127>
- Bender, R., Sirota, S. B., Swetschinski, L., Dominguez, R.-M. V., Novotney, A., Wool, E., Ikuta, K., Vongpradith, A., Rogowski, E., Doxey, M., Troeger, C., Albertson, S., Jianing, He, J., Maass, K. L., A.F.Simões, E., Abdoun, M., Aziz, J. A., Abdulah, D. M., ... Kyu, H. (2024). Global, regional, and national incidence and mortality burden of non-COVID-19 lower respiratory infections and aetiologies, 1990–2021: a systematic analysis from the Global Burden of Disease Study 2021. *The Lancet. Infectious Diseases*, 24, 974–1002. [https://doi.org/10.1016/S1473-3099\(24\)00176-2](https://doi.org/10.1016/S1473-3099(24)00176-2)
- Blair, J., Webber, M., Baylay, A., Ogbolu, D., & Piddock, L. (2014). Molecular mechanisms of antibiotic resistance. *Nature Reviews Microbiology*, 13, 42–51. <https://doi.org/10.1038/nrmicro3380>
- Boutzoukas, A. E., Mackow, N., Giri, A., Komarow, L., Hill, C., Chen, L., Doi, Y., Satlin, M. J., Arias, C., Wang, M., Moreo, L. M., Herc, E., Cober, E., Weston, G., Patel, R., Bonomo, R. A., Fowler, V., van Duin, D., Banerjee, R., ... Zong, Z. (2024). Increased mortality in hospital- compared to community-onset carbapenem-resistant enterobacterales infections. *Journal of Antimicrobial Chemotherapy*, 79(11), 2916–2922. <https://doi.org/10.1093/jac/dkae306>
- Chan, C., Tao, J., Chan, O., Li, H., & Pang, H. (2020). Preventing Respiratory Tract Infections by Synbiotic Interventions: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Advances in Nutrition*. <https://doi.org/10.1093/advances/nmaa003>
- Chan, E. Y.-H., Yu, E. L. M., Angeletti, A., Arslan, Z., Basu, B., Boyer, O., Chan, C.-Y., Colucci, M., Dorval, G., Dossier, C., Drovandi, S., Ghiggeri, G. M., Gipson, D. S., Hamada, R., Hogan, J., Ishikura, K., Kamei, K., Kemper, M., Ma, A. L.-T., ... Tullus, K. (2022). Long-term Efficacy and Safety of Repeated Rituximab to Maintain Remission in Idiopathic Childhood Nephrotic Syndrome: An International Study. *Journal of the American Society of Nephrology*, 33(6), 1193–1207. <https://doi.org/10.1681/ASN.2021111472>
- Chen, T., Chen, G., Wang, G., Treeprasertsuk, S., Lesmana, C. R. A., Lin, H.-C., Al-mahtab, M., Chawla, Y. K., Tan, S.-S., Kao, J.-H., Yuen, M.-F., Lee, G.-H., Alcantara-Payawal, D., Nakayama, N., Abbas, Z., Jafri, W., Kim, D.-J., Choudhury, A., Mahiwall, R., ... Ning, Q. (2024). Expert consensus on the diagnosis and treatment of end-stage liver disease complicated by infections. *Hepatology International*, 18(3), 817–832. <https://doi.org/10.1007/s12072-023-10637-3>
- Chua, A. Q., Verma, M., Villanueva, S. Y. A., Roxas, E., Hsu, L. Y., & Legido-Quigley, H. (2023). A Qualitative Study on the Implementation of the National Action Plan on Antimicrobial Resistance in Singapore. *Antibiotics*, 12(8). <https://doi.org/10.3390/antibiotics12081258>
- Dass, A., Diaz-Cardona, Y., & Patel, S. (2023). 2619. Impact of Positive Real-Time Polymerase Chain Reaction Respiratory Viral Panel on the Duration of

- Antimicrobials. Open Forum Infectious Diseases, 10. <https://doi.org/10.1093/ofid/ofad500.2232>
- Debes, S., Haug, J., De Blasio, B., Lindstrøm, J., Jonassen, C., & Dudman, S. (2023). Antibiotic Consumption in a Cohort of Hospitalized Adults with Viral Respiratory Tract Infection. *Antibiotics*, 12. <https://doi.org/10.3390/antibiotics12040788>
- Derakhshan-Nezhad, E. (2023). An Overview of Bacterial Respiratory Tract Infections and their Etiologies. *Journal of Medical Bacteriology*. <https://doi.org/10.18502/jmb.v11i1-2.14373>
- Feldman, C., & Richards, G. (2018). Appropriate antibiotic management of bacterial lower respiratory tract infections. *F1000Research*, 7. <https://doi.org/10.12688/f1000research.14226.1>
- Feldman, C., & Shaddock, E. (2019). Epidemiology of lower respiratory tract infections in adults. *Expert Review of Respiratory Medicine*, 13, 63–77. <https://doi.org/10.1080/17476348.2019.1555040>
- Harris, A., Hicks, L., & Qaseem, A. (2016). Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. *Annals of Internal Medicine*, 164, 425–434. <https://doi.org/10.7326/M15-1840>
- Hawke, K., King, D., Van Driel, M., & Mcguire, T. (2022). Homeopathic medicinal products for preventing and treating acute respiratory tract infections in children. *The Cochrane Database of Systematic Reviews*, 12. <https://doi.org/10.1002/14651858.cd005974.pub6>
- Huang, Y., Wei, W., Correia, D. F., Ming, B. H., Tang, A., Yeoh, E., Wong, S. Y. S., Ip, M., & Kwok, K. (2022). Antibiotic use for respiratory tract infections among the older adults living in long term care facilities: a systematic review and meta-analysis. *The Journal of Hospital Infection*. <https://doi.org/10.1016/j.jhin.2022.09.016>
- Huemer, M., Shambat, S. M., Brugger, S., & Zinkernagel, A. (2020). Antibiotic resistance and persistence—Implications for human health and treatment perspectives. *EMBO Reports*, 21. <https://doi.org/10.15252/embr.202051034>
- Jit, M., & Cooper, B. (2020). The role of vaccines in combating antimicrobial resistance. *European Journal of Public Health*. <https://doi.org/10.1017/9781108864121.009>
- K, V. S., K, S., Jk, V., P, N., Y, R., & Y, P. C. (2024). A review on upper respiratory tract infection. *Asian Journal of Hospital Pharmacy*. <https://doi.org/10.38022/ajhp.v4i4.93>
- Kandula, M., & Farrell, J. (2023). 867. Diagnostic test accuracy of TRAIL, IP-10 and C-RP biomarker combination (MeMed BV test) for discrimination of viral vs. bacterial infections among Emergency Department patients with febrile illness: A Systematic Review and Meta-analysis. *Open Forum Infectious Diseases*, 10. <https://doi.org/10.1093/ofid/ofad500.912>
- King, D., Hawke, K., Mcguire, T., & Van Driel, M. (2020). Homeopathic preparations for preventing and treating acute upper respiratory tract infections in children: A systematic review and meta-analysis. *Academic Pediatrics*. <https://doi.org/10.1016/j.acap.2020.07.016>
- Klugman, K., & Black, S. (2018). Impact of existing vaccines in reducing antibiotic resistance: Primary and secondary effects. *Proceedings of the National Academy of Sciences*, 115, 12896–12901. <https://doi.org/10.1073/pnas.1721095115>

- Lazareva, N., & Rebrova, E. (2023). Advantages of instant forms of antibiotics in the treatment of lower respiratory tract infections. *Meditsinskiy Sovet = Medical Council*. <https://doi.org/10.21518/ms2023-296>
- Legnani, D. (1997). Role of oral antibiotics in treatment of community-acquired lower respiratory tract infections. *Diagnostic Microbiology and Infectious Disease*, 27 1-2, 41–47. [https://doi.org/10.1016/S0732-8893\(97\)00019-9](https://doi.org/10.1016/S0732-8893(97)00019-9)
- Lewnard, J., Lo, N., Arinaminpathy, N., Frost, I., & Laxminarayan, R. (2020). Childhood vaccines and antibiotic use in low- and middle-income countries. *Nature*, 581, 94–99. <https://doi.org/10.1038/s41586-020-2238-4>
- Li, J., Kang-Birken, S., Mathews, S., Kenner, C., & Fitzgibbons, L. (2019). Role of rapid diagnostics for viral respiratory infections in antibiotic prescribing decision in the emergency department. *Infection Control & Hospital Epidemiology*, 40, 974–978. <https://doi.org/10.1017/ice.2019.166>
- Lin, J., Nishino, K., Roberts, M., Tolmasky, M., Aminov, R., & Zhang, L. (2015). Mechanisms of antibiotic resistance. *Frontiers in Microbiology*, 6. <https://doi.org/10.3389/fmicb.2015.00034>
- Lipsitch, M., & Siber, G. (2016). How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem? *MBio*, 7. <https://doi.org/10.1128/mBio.00428-16>
- Machado-Duque, M., García, D. A., Emura-Vélez, M. H., Gaviria-Mendoza, A., Giraldo-Giraldo, C., & Machado-Alba, J. (2021). Antibiotic Prescriptions for Respiratory Tract Viral Infections in the Colombian Population. *Antibiotics*, 10. <https://doi.org/10.3390/antibiotics10070864>
- Marra, A., De Almeida, S., Corrêa, L., Silva, M., Martino, M., Silva, C., Cal, R., Edmond, M., & Santos, O. Dos. (2009). The effect of limiting antimicrobial therapy duration on antimicrobial resistance in the critical care setting. *American Journal of Infection Control*, 37 3, 204–209. <https://doi.org/10.1016/j.ajic.2008.06.008>
- Micoli, F., Bagnoli, F., Rappuoli, R., & Serruto, D. (2021). The role of vaccines in combatting antimicrobial resistance. *Nature Reviews. Microbiology*, 19, 287–302. <https://doi.org/10.1038/s41579-020-00506-3>
- Mindt, B., & DiGiandomenico, A. (2022). Microbiome Modulation as a Novel Strategy to Treat and Prevent Respiratory Infections. *Antibiotics*, 11. <https://doi.org/10.3390/antibiotics11040474>
- Mo, Y., Oonsivilai, M., Lim, C., Niehus, R., & Cooper, B. S. (2023). Implications of reducing antibiotic treatment duration for antimicrobial resistance in hospital settings: A modelling study and meta-analysis. *PLoS Medicine*, 20(6 June). <https://doi.org/10.1371/journal.pmed.1004013>
- Montalbán-Hernández, K., Cogollo-García, A., De Velasco-Sada, P. G., Caballero, R., Casanovas, M., Subiza, J., & Conejero, L. (2024). MV130 in the Prevention of Recurrent Respiratory Tract Infections: A Retrospective Real-World Study in Children and Adults. *Vaccines*, 12. <https://doi.org/10.3390/vaccines12020172>
- Mullins, L., Mason, E., Winter, K., & Sadarangani, M. (2023). Vaccination is an integral strategy to combat antimicrobial resistance. *PLOS Pathogens*, 19. <https://doi.org/10.1371/journal.ppat.1011379>
- Munita, J., & Arias, C. (2016). Mechanisms of Antibiotic Resistance. *Microbiology Spectrum*, 4. <https://doi.org/10.1128/microbiolspec.vmbf-0016-2015>
- Nwobodo, D. C., Ugwu, M., Anie, C. O., Al-Ouqaili, M., Ikem, J. C., Chigozie, U. V., & Saki, M. (2022). Antibiotic resistance: The challenges and some emerging

- strategies for tackling a global menace. *Journal of Clinical Laboratory Analysis*, 36. <https://doi.org/10.1002/jcla.24655>
- Oladimeji, O., Cross, J., & Keathley-Herring, H. (2020). System dynamics applications in performance measurement research: progress and challenges. *Management Decision*. <https://doi.org/10.1108/md-11-2019-1596>
- Papan, C., Argentiero, A., Porwoll, M., Hakim, U., Farinelli, E., Testa, I., Pasticci, M., Mezzetti, D., Perruccio, K., Etshtein, L., Mastboim, N., Moscoviz, E., Ber, T., Cohen, A., Simon, E., Boíco, O., Shani, L., Gottlieb, T., Navon, R., ... Tenenbaum, T. (2021). A host signature based on TRAIL, IP-10, and CRP for reducing antibiotic overuse in children by differentiating bacterial from viral infections: A prospective, multicentre cohort study. *Clinical Microbiology and Infection: The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases*. <https://doi.org/10.1016/j.cmi.2021.10.019>
- Raghav, H., Tayal, P., Das, R., & Mehta, D. (2022). Appropriate use of antibiotics for the management of respiratory tract infections. *Infectious Disorders Drug Targets*. <https://doi.org/10.2174/1871526522666220118122516>
- Rice, L. (2008). The Maxwell Finland Lecture: for the duration-rational antibiotic administration in an era of antimicrobial resistance and clostridium difficile. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 46 4, 491–496. <https://doi.org/10.1086/526535>
- Rousseau, G., Keijzers, G., van Meer, O., Craig, S., Karamercan, M., Klim, S., Body, R., Kuan, W. S., Harjola, V.-P., Jones, P., Verschuren, F., Holdgate, A., Christ, M., Golea, A., Capsec, J., Barletta, C., Graham, C. A., Garcia-Castrillo, L., Laribi, S., & Kelly, A.-M. (2021). Epidemiology, treatment and outcome of patients with lower respiratory tract infection presenting to emergency departments with dyspnoea (AANZDEM and EuroDEM studies). *EMA - Emergency Medicine Australasia*, 33(1), 58–66. <https://doi.org/10.1111/1742-6723.13567>
- Sécher, T., Mayor, A., & Heuzé-Vourc'h, N. (2019). Inhalation of Immuno-Therapeutics/-Prophylactics to Fight Respiratory Tract Infections: An Appropriate Drug at the Right Place! *Frontiers in Immunology*, 10. <https://doi.org/10.3389/fimmu.2019.02760>
- See, K. C., & Lau, Y. H. (2023). Acute management of pneumonia in adult patients. *Singapore Medical Journal*, 64(3), 209–216. <https://doi.org/10.4103/singaporemedj.SMJ-2022-050>
- Shahanenko, R., Kozii, N., Shahanenko, V., Avramenko, N., & Taranuha, S. (2023). Influence of antibiotic treatment duration on the development of antibiotic resistance. *Naukovij Visnik Veterinarnoi Medicini*. <https://doi.org/10.33245/2310-4902-2023-180-1-113-124>
- Singh, S. (2016). Respiratory Viral Infections. *Seminars in Respiratory and Critical Care Medicine*, 37, 485–486. <https://doi.org/10.1055/s-0036-1584802>
- Sirota, S. B., Doxey, M., Dominguez, R.-M. V., Bender, R., Vongpradith, A., Albertson, S., Novotney, A., Burkart, K., Carter, A., Abdi, P., Abdoun, M., Abebe, A., Abegaz, K. H., Aboagye, R., Abolhassani, H., Abreu, L. G., Abualruz, H., Abu-Gharbieh, E., Aburuz, S., ... Kyu, H. (2024). Global, regional, and national burden of upper respiratory infections and otitis media, 1990–2021: a systematic analysis from the Global Burden of Disease Study 2021. *The Lancet. Infectious Diseases*, 25, 36–51. [https://doi.org/10.1016/s1473-3099\(24\)00430-4](https://doi.org/10.1016/s1473-3099(24)00430-4)

- Smith, O. (2021). Vaccines and antibiotic resistance. *Science*. <https://doi.org/10.1126/science.373.6556.754-f>
- Spellberg, B., & Rice, L. (2019). Duration of Antibiotic Therapy: Shorter Is Better. *Annals of Internal Medicine*, 171, 210–211. <https://doi.org/10.7326/M19-1509>
- Stower, H. (2020). Vaccination combats antimicrobial resistance. *Nature Medicine*, 26, 822. <https://doi.org/10.1038/s41591-020-0957-6>
- Sur, D., & Plesa, M. (2022). Antibiotic Use in Acute Upper Respiratory Tract Infections. *American Family Physician*, 106, 6, 628–636. <https://consensus.app/papers/antibiotic-use-in-acute-upper-respiratory-tract-sur-plesa/1b812dd7450054e1b7ac3ab40e5ff9ac/>
- Tambyah, P. A. (2021). Future role of vaccines on antibacterial resistance. *International Journal of Antimicrobial Agents*, 58. <https://doi.org/10.1016/j.ijantimicag.2021.106420.44>
- Tan, R., Huang, Z., Guo, H., Weng, Y., & Chow, A. (2022). Antibiotic expectations of patients attending an emergency department with upper respiratory tract infections: clinical and behavioural determinants of antibiotic use. *International Journal of Antimicrobial Agents*, 59(2). <https://doi.org/10.1016/j.ijantimicag.2021.106511>
- Tanday, S. (2016). Resisting the use of antibiotics for viral infections. *The Lancet. Respiratory Medicine*, 4 3, 179. [https://doi.org/10.1016/S2213-2600\(16\)00060-6](https://doi.org/10.1016/S2213-2600(16)00060-6)
- Urban-Chmiel, R., Marek, A., Stępień-Pyśniak, D., Wiczorek, K., Dec, M., Nowaczek, A., & Osek, J. (2022). Antibiotic Resistance in Bacteria—A Review. *Antibiotics*, 11. <https://doi.org/10.3390/antibiotics11081079>
- Villegas, G., Jauregui, L., Moreno, B., Nunez, H., & Kannan, S. (2021). Genesis of Antibiotic Resistance LXVIII: Effective Vaccination (Campaigns) Decrease Antibiotic Consumption Consequent Antibiotic-Resistance (AR) Pandemic(ARP) – The exception that proves the rule. *The FASEB Journal*, 35. <https://doi.org/10.1096/FASEBJ.2021.35.S1.02202>
- Walter, J., & Wunderink, R. (2017). Severe Respiratory Viral Infections: New Evidence and Changing Paradigms. *Infectious Disease Clinics of North America*, 31 3, 455–474. <https://doi.org/10.1016/j.idc.2017.05.004>
- Yao, J., Zhao, J., Wen, J., Yang, Z.-J., Lin, Y.-P., Sun, L., Lu, Q., & Fan, G. (2022). Flavonoid-containing supplements for preventing acute respiratory tract infections: A systematic review and meta-analysis of 20 randomized controlled trials. *Complementary Therapies in Medicine*, 102865. <https://doi.org/10.1016/j.ctim.2022.102865>
- Yu, X., Wang, H., Sheng, Chen, W., Sun, L., & Zou, Z. (2024). Estimating the global and regional burden of lower respiratory infections attributable to leading pathogens and the protective effectiveness of immunization programs. *International Journal of Infectious Diseases : IJID : Official Publication of the International Society for Infectious Diseases*, 107268. <https://doi.org/10.1016/j.ijid.2024.107268>
- Zhao, Y., Dong, B., & Hao, Q. (2022). Probiotics for preventing acute upper respiratory tract infections. *The Cochrane Database of Systematic Reviews*, 8. <https://doi.org/10.1002/14651858.CD006895.pub4>