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REVIEW ARTICLE

Factors influencing physicians' antimicrobial prescribing decisions: A systematic review of qualitative studies

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Inappropriate and overuse of antimicrobials is increasing antimicrobial resistance. Understanding physicians' antimicrobial decision-making is essential for developing interventions to optimize prescribing. The aim of this review was to identify the factors that influence physicians' antimicrobial prescribing decisions. A systematic literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Embase, Medline and Scopus were searched from 2014 onwards using three key concepts: antimicrobial, prescribing and attitude. The search identified 11 038 articles for review. Studies were included if they used qualitative methods and obtained data directly from physicians. Factors influencing antimicrobial prescribing were extracted and categorized into physician-related, patient-related, medication- and condition-related, and external factors. A model of the antimicrobial prescribing process was created to illustrate how these factors influence decision-making. Fifty-three articles from 23 countries met the inclusion criteria. Forty factors influencing antimicrobial prescribing were identified, with the most common being time pressures, patient/carer demand for antimicrobials, diagnostic uncertainty, clinical experience, and the use of evidence-based guidelines and diagnostic tests. The harm to the patient and the physician of underprescribing were considered to outweigh the potential population harm of antimicrobial resistance due to overprescribing. Antimicrobial decision making is a complex process influenced by many different types of factors at each point in the prescribing journey. Awareness of these factors is vital for the success of interventions aiming to optimize antimicrobial prescribing. Future interventions should investigate how to balance individual and population harm whilst considering the individual factors that influence prescribing decisions.

KEYWORDS
antimicrobial, antimicrobial resistance, clinical decision making, prescribing behaviour, qualitative, systematic review

1 | INTRODUCTION

Antimicrobials are one of the most significant advances in modern medicine. Theyave saved countless lives by treating life-threatening infections and allowing life-saving medical procedures, such as surgery and organ transplantation, to proceed without excessive risks of post-operative infections.[1,2] However, the overuse and inappropriate use of antimicrobials have increased the rates of antimicrobial resistance, rendering antimicrobials less effective for these life-threatening conditions.[3]

Antimicrobial resistance (AMR) is one of the most important threats to the future of health and the human population globally. It is estimated that resistant infections currently contribute to nearly 5 million deaths globally each year.[4] If no changes to policy are made, AMR-related deaths are predicted to increase to 10 million deaths each year between now and 2050.[5] AMR also carries a significant financial burden to the global economy. The World Bank estimates that AMR could result in US$1 trillion in additional healthcare costs and between US$2 trillion and US$6 trillion in GDP losses globally by 2050.[6]

The World Health Organization has stated that AMR is a critical global issue that requires urgent attention.[7,8] The novel antimicrobial pipeline alone is insufficient to address growing resistance rates,[9] thus ensuring current antimicrobials are used optimally is vital to preserve their effectiveness and minimize growing resistance. Evidence shows that antimicrobial stewardship interventions to optimize antimicrobial use do significantly reduce the incidence of resistance.[10,11] Despite evidence-based guidelines for optimal antimicrobial use, studies have shown that 45% of antimicrobials prescribed in Australia,[12] 64% in Spain[13] and up to 47% in the USA[14] are not prescribed appropriately in concordance with these recommendations. There are clearly factors adversely impacting prescribers following antimicrobial prescribing guidelines, and this has direct impacts on the development of AMR and patient outcomes. Access to information and guidelines alone is not sufficient to achieve optimal antimicrobial prescribing practices, and consideration needs to be given to cultural, contextual and behavioural factors affecting prescribing to optimize antimicrobial use.[15]

Understanding factors that influence decision making when prescribing antimicrobials is essential to develop successful and targeted interventions aimed at optimizing antimicrobial prescribing. Factors influencing antimicrobial prescribing previously reported were patient demand, infection characteristics, physicians' attitudes and time pressures,[16,17] but these factors may have changed in the last decade since publication of these reviews due to increased awareness of AMR, antimicrobial use monitoring, evaluation of antimicrobial treatment outcomes, and antimicrobial prescribing interventions. More recent systematic reviews in this area have focused only on a single setting or type of infection.[18–20] A clear overview of how factors influencing antimicrobial prescribing differ between settings and resourcing of the countries where physicians practice is required. This systematic review therefore aimed to identify the factors that influence physicians' decision making when prescribing antimicrobials and compare these between high-income countries (HICs) and low- and middle-income countries (LMICs) and settings to guide interventions to improve prescribing practices.

2 | METHODS

2.1 | Search strategy

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21]

A literature search was performed up to 16 November 2023 on Embase, Medline and Scopus databases using three key concepts: antimicrobials, prescribing, and attitudes (the complete search strategy is given in Appendix A). The search was limited to research in humans, published in the English language and publication date from 2014 onwards (to provide a more current review on this topic over the last decade).

2.2 | Inclusion and exclusion criteria

Studies were included if they used qualitative methods and reported on factors that influenced antimicrobial prescribing decisions obtained directly from physicians about their own prescribing practices. All practice settings, antimicrobials and types of infections were included. Studies focusing on antimicrobial knowledge or prescribing patterns based on surveillance or audit data only were excluded. Only studies using qualitative methods were included in this review. Antimicrobial prescribing is a complex and nuanced behaviour, hence qualitative studies were chosen to answer "how" and "why" factors influenced prescribing to understand the motivations and reasons behind prescribing and elicit a deeper understanding of the issue. In studies using both qualitative and quantitative methods, only the qualitative results were extracted and reported. Studies investigating antimicrobial prescribing practices by healthcare professionals other than physicians (eg, pharmacists, nurse practitioners and dentists) were excluded. When studies reported data from physicians and other healthcare professionals, only data from physicians were extracted and included in this review. If it was not possible to extract data from physicians only, then the study was excluded.

2.3 | Screening process

One reviewer (S.R.) completed a title and abstract screen and full-text review of all papers included in this review. A second reviewer (Y.C.K.) independently screened a random 20% sample of the titles and abstracts of the papers captured by the search strategy. Discrepancies were discussed between the two reviewers, and inclusion and exclusion criteria clarified. The inclusion and exclusion criteria of this

review are readily identifiable in the titles and abstracts of screened articles, hence it was not considered necessary for a second reviewer to screen the titles and abstracts of all of the identified papers. All the papers deemed eligible for full-text review were screened by Y.C.K. to confirm the accuracy of screening. Discrepancies were resolved by discussion between S.R. and Y.C.K. Covidence was used to automatically remove duplicates and conduct the screening process (second reviewer protocol in Appendix B).[22]

2.4 | Data extraction and quality assessment

Data extraction and quality assessment were completed by one researcher (S.R.). A second researcher (Y.C.K.) independently conducted a quality assessment and extracted data from 10% of the included articles to confirm the accuracy of the process (second reviewer protocol in Appendix B). The information extracted from each article included study title, year of publication, author, country, physician population and setting, sample size of physicians, patient population (if specified), infection type (if specified), study design, study aim, method of data analysis, and study outcomes and findings. Factors influencing antimicrobial prescribing were categorized into four groups after inductive analysis of the data: patient-related factors, prescriber-related factors, medication- and condition-related factors, and external factors, subcategorised into organizational factors and other factors. Where two or more articles reported data from the same sample of physicians, that factor was only counted once in data analysis. All articles were assessed for quality and risk of bias using the 10-item Joanna-Briggs Institute Critical Appraisal Checklist for Qualitative Research.[23]

3 | RESULTS

3.1 | Studies included

The search identified a total of 11 038 articles. After removal of duplicates, there were 6417 articles for title and abstract screening. A total of 6110 articles were excluded based on title and abstract, and 307 articles underwent a full-text review. Fifty-three articles met the inclusion criteria and were included (Figure 1). The characteristics of the included studies are summarized in Table 1. The World Bank country classifications were used for the definition of HICs and LMICs.[77] All 53 studies demonstrated good methodological quality with respect to their aims, data collection methods, sampling and interpretation of results, thus no studies were excluded from this review based on their quality (outcomes of the quality and risk of bias assessment can be found in Appendix C).

3.2 | Factors influencing antimicrobial prescribing

Forty factors influencing antimicrobial prescribing were identified: 10 prescriber-related factors, seven patient-related factors, nine

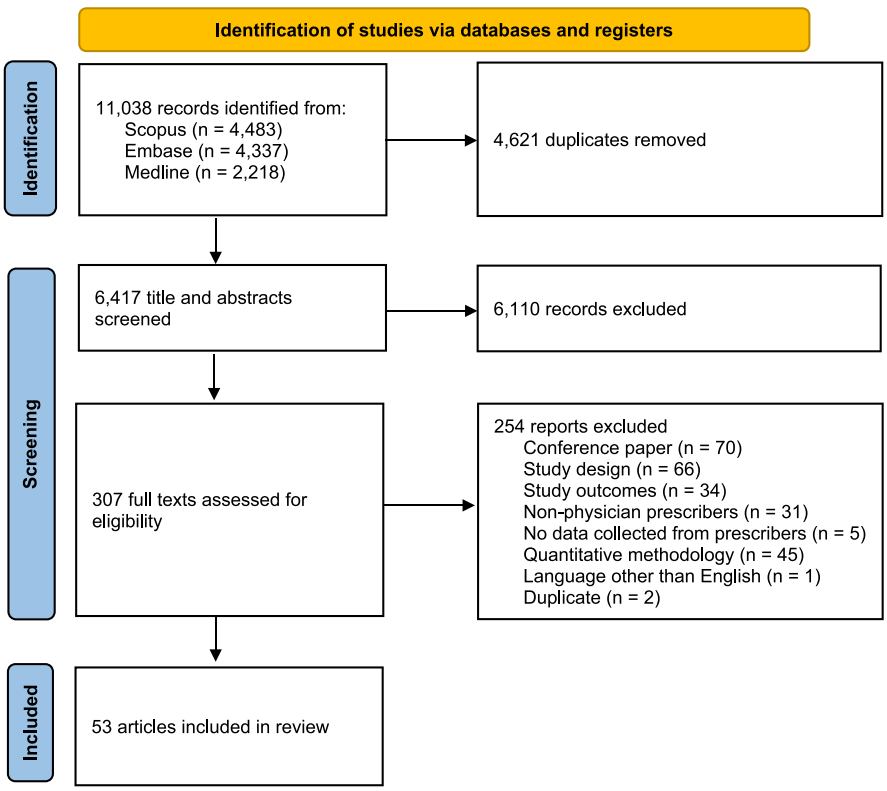

FIGURE 1 PRISMA diagram of search strategy and screening.

TABLE 1 Characteristics of articles included in this systematic review.

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Abdoler et al (2020)[24]	United States of America (HIC)	Physicians in infectious diseases and hospital medicine from two hospitals	Not specified	Community-acquired pneumonia, cellulitis, urinary tract infections	16	Semi-structured interviews	Investigate decision-making process that underlies physicians' antimicrobial choice	Braun and Clarke's approach to thematic analysis (iterative and inductive)
Alsaleh et al (2021)[25]	Saudi Arabia (HIC)	Physicians in a single tertiary care hospital	Not specified	Not specified	16	Semi-structured telephone interviews	Explore physician perceptions and views about broad-spectrum antibiotics and factors that impact their prescribing decisions	Braun and Clarke's approach to thematic analysis
Arnau-Sánchez et al (2023)[26]	Spain (HIC)	Primary care paediatricians in public health centres	Paediatrics	Not specified	Three focus groups (25 physicians total)	Focus groups	Explore factors influencing inappropriate use of antibiotics in early infancy	Theoretical development proposed by Corbin and Strauss based on the grounded theory
Biezen et al (2017)[27]	Australia (HIC)	Primary care physicians	Paediatrics	Respiratory tract infections	20[a]	Semi-structured interviews	Explore the views, attitude and practices of primary care physicians in the management of respiratory tract infections in infants	Theoretical Domains Framework and COM-B model to determine themes
Biezen et al (2019)[28]	Australia (HIC)	Primary care physicians	Paediatrics	Respiratory tract infections	20[a]	Semi-structured interviews	Compare general practitioners' views on antibiotics for respiratory tract infections in young children	Thematic analysis
Bisgaard et al (2021)[29]	Denmark (HIC)	Primary care physicians	Not specified	Lower respiratory tract infections	7	Semi-structured interviews	Explore Danish general practitioners' considerations and experiences managing patients with acute lower respiratory tract infection symptoms	Systematic text condensation
Broom et al (2014)[30]	Australia (HIC)	Hospital physicians at a single hospital (multiple specialties and seniority)	Not specified	Not specified	30[b]	Semi-structured interviews	Explore doctors' antibiotic decisions and the social relations that generate and perpetuate norms of practice	Thematic analysis
Broom et al (2015)[31]	Australia (HIC)	Hospital physicians at a single hospital (multiple specialties and seniority)	Not specified	Not specified	30[b]	Semi-structured interviews	Develop a better understanding of antibiotic decisions within an evolving interpersonal and professional context	Thematic analysis

(Continues)

TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Broom et al (2017)[32]	Australia (HIC)	Hospital physicians at two teaching hospitals (multiple specialties and seniority)	Not specified	Not specified	64[b]	Semi-structured interviews	Explore views of hospital doctors in Australia around the global significance of antimicrobial resistance and how it impacts decision making in clinical practice	Thematic analysis
Broom et al (2018)[33]	Australia (HIC)	Surgeons and anaesthetists at a single teaching hospital	Not specified	Not specified	20	Semi-structured interviews	Examine interpersonal and cultural influences on surgical prophylaxis by surgeons and anaesthetists	Thematic analysis
Chan et al (2019)[34]	Singapore (HIC)	Emergency department physicians in a large adult tertiary-care hospital	Adults	Upper respiratory tract infections	9	Semi-structured interviews	Understand factors influencing antibiotic prescribing decisions in adults with upper respiratory tract infections among emergency physicians	Thematic analysis
Charani et al (2017)[35]	United Kingdom (HIC)	Physicians from six surgical teams at a teaching hospital in London	Not specified	Not specified	30 ward rounds and 13 interviews	Ethnography (non-participant observation of ward rounds, interviews, documentary analysis)	Investigate antibiotic prescribing decisions during surgical ward rounds	Thematic analysis
Chen et al (2020)[36]	China (LMIC)	Primary care physicians at six rural health facilities	Not specified	Not specified	21 observed consultations and 19 interviews	Direct observation, semi-structured interviews and informal conversations with physicians	Understand the complex relationships between the social drivers of antibiotic use in rural China	Thematic analysis
Christensen et al (2022)[37]	Norway (HIC)	Hospital physicians in a secondary acute care hospital (multiple specialties and seniority)	Not specified	Not specified	14	Semi-structured interviews	Explore factors impacting hospital physicians' antibiotic prescribing practices in a low-resistance country	Thematic analysis
Dallas et al (2014)[38]	Australia (HIC)	General practice registrars at multiple sites	Not specified	Upper respiratory tract infections and acute bronchitis	One focus group (three physicians total) and 14 interviews	Focus groups and semi-structured interviews	Explore attitudes of trainees in general practice towards antibiotic use and resistance	Coded data segments were collated and the relationships between the resultant codes mapped

TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
de Oliveira et al (2018)[39]	Spain (HIC)	General practitioners and geriatric specialists	Not specified	Not specified	25	Semi-structured interviews	Provide contextual knowledge about the decision-making process that physicians use to prescribe antimicrobials	Descriptive analysis
Dempsey et al (2014)[40]	United States of America (HIC)	Primary care physicians in internal medicine from three practice-based research network clinics	Not specified	Acute bronchitis	12	Semi-structured interviews	Understand clinicians' views about antibiotic prescribing in acute bronchitis	Thematic analysis
Dooling et al (2014)[41]	Egypt (LMIC)	Physicians in government hospitals, private hospitals and primary rural healthcare	Not specified	Not specified	20	Semi-structured interviews	Assess the knowledge, attitudes and practices of physicians and pharmacists when treating outpatient acute respiratory infections	Thematic analysis
Duane et al (2016)[42]	Ireland (HIC)	General practitioners	Not specified	Urinary tract infections	15	In-depth interviews	Explore the culture of antibiotic prescribing and consumption in the community for urinary tract infections from the perspective of the general practitioners	Thematic analysis
Geis et al (2023)[43]	Switzerland (HIC)	General practitioners	Not specified	Lower respiratory tract infections	12	Semi-structured interviews	Describe general practitioners process of deciding on an antibiotic for lower respiratory tract infections using procalcitonin and sonography	Grounded theory
Ghiga et al (2023)[44]	Romania (LMIC)	Primary care physicians	Not specified	Not specified	12	Semi-structured interviews	Understand how family doctors perceive antibiotic consumption and antibiotic resistance	Content analysis
Guo et al (2021)[45]	Singapore (HIC)	General practitioners in the public and private sector	Not specified	Not specified	30	Semi-structured interviews	Explore processes underpinning decision-making for antibiotic prescribing in different primary care settings	Thematic analysis
Hampton et al (2021)[46]	United Kingdom (HIC)	Physicians who prescribe for paediatrics in UK emergency departments	Paediatrics	Respiratory tract infections	21	Semi-structured interviews	Explore the barriers and facilitators to antibiotic prescribing for paediatric respiratory illness in emergency departments	Thematic analysis
Hayward et al (2019)[47]	United Kingdom (HIC)	National Health Service general practitioners	Geriatrics	Not specified	28	Semi-structured interviews	Understand the attitudes and beliefs held by general practitioners regarding antibiotic prescribing in older adults	Modified framework approach

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TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Huang et al (2023)[48]	Singapore (HIC)	Emergency department physicians from four acute care hospitals in Singapore	Adults	Not specified	50	Semi-structured interviews	Explore emergency physicians' attitudes and behaviours towards antibiotic prescribing in the context of COVID-19	Deductive-inductive-deductive framework method
Ierano et al (2019)[49]	Australia (HIC)	Surgeons and anaesthetists in one private hospital and two public hospitals	Not specified	Surgical prophylaxis	10 focus groups and one paired interview (56 physicians total)	Focus groups and paired interviews	Identify barriers and enablers of appropriate surgical antibiotic prophylaxis and guideline compliance	Thematic analysis
Khan et al (2021)[50]	India (LMIC)	Consultants and residents at a tertiary teaching hospital	Not specified	Surgical prophylaxis	28 focus groups and 16 paired interviews (184 physicians total)	Focus groups and paired interviews	Assess the knowledge and compliance rate for surgical antimicrobial prophylaxis among consultant and resident physicians	Thematic analysis
Kohut et al (2020)[51]	United States of America (HIC)	Primary care physicians from nine clinics	Not specified	Not specified	25	Semi-structured interviews	Identify how clinicians perceive patient demand for antibiotics and how this impacts prescribing	Thematic analysis
Krishnakumar and Tsopra (2019)[52]	France (HIC)	General practitioners	Not specified	Cystitis, pyelonephritis, prostatitis, pharyngitis, sinusitis, otitis, pneumonia	20	Semi-structured interviews	Understand the rationale used by general practitioners to decide which antibiotic to prescribe in different clinical scenarios	Thematic analysis
Lam et al (2021)[53]	China (LMIC)	Medical interns at nine public hospitals	Not specified	Not specified	Two focus groups with three or four physicians per group	Focus groups	Explore antibiotic prescribing behaviours of the medical interns in Hong Kong	Content analysis approach described by Hsieh and Shannon, coding categories were inductively derived from the text data
Livorsi et al (2015)[54]	United States of America (HIC)	Hospital physicians at two acute care hospitals	Not specified	Not specified	30	Semi-structured interviews	Understand professional and psychosocial factors that influence physicians' antibiotic-prescribing habits	Thematic analysis
Lum et al (2018)[55]	Australia (HIC)	General practitioners	Not specified	Not specified	10	Semi-structured interviews	Establish factors influencing general practitioners' decision-making in antibiotic prescribing in the Australian primary health sector	Deductive and inductive coding then mapping of themes and subthemes

TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Mas-Dalmau et al (2023)[56]	Spain (HIC)	Primary care physicians	Not specified	Respiratory tract infections	Four focus groups and three interviews (25 physicians total)	Focus groups and semi-structured interviews	Explore perceptions and attitudes of primary care physicians regarding use of antibiotics in respiratory tract infections	Inductive thematic analysis
May et al (2014)[57]	United States of America (HIC)	Emergency department physicians at eight hospitals	Not specified	Urinary tract infections, upper respiratory tract infections, skin and soft tissue infections	21 interviews and 10 patient-provider interaction observations	Semi-structured interviews and observation of practice	Examine provider, patient and environmental factors associated with antimicrobial prescribing in the emergency department	Thematic analysis
Micallef et al (2023)[58]	United Kingdom (HIC)	Hospital physicians in haematology, solid organ transplant, respiratory and intensive care unit specialties at a tertiary teaching hospital	Not specified	Fungal infections	21	Qualitative telephone interview	Identify drivers and barriers for antifungal prescribing behaviours across the four clinical specialties	Theoretical Domains Framework and COM-B model to determine themes
Molina-Romera et al (2023)[59]	Spain (HIC)	Medical interns from a university teaching hospital	Not specified	Not specified	Seven focus groups (35 physicians total)	Focus groups	Examine the factors that influence antibiotic use among medical interns	Constructivist Grounded Theory method
Nakwatumbah et al (2017)[60]	Namibia (LMIC)	Hospital physicians at a national referral hospital	Not specified	Not specified	77	Interviewer-administered questionnaire	Determine compliance to guidelines in the prescribing of antibiotics in acute infections	Thematic analysis
O'Doherty et al (2019)[61]	Ireland (HIC)	General practitioners	Not specified	Acute respiratory tract infections	13	Semi-structured interviews	Investigate rationale for Irish general practitioners prescribing antibiotics in acute respiratory tract infections	Thematic analysis
Obucina et al (2023)[62]	Australia (HIC)	Emergency department physicians at two hospitals	Not specified	Not specified	24 physicians observed and 34 physicians in group-reflective sessions	Video-reflexive ethnography	Identify factors that shape clinical decision making on antibiotic prescribing in the emergency department	Braun and Clarke's approach to thematic analysis (reflective)
Pandolfo et al (2022)[63]	United Kingdom (HIC)	Hospital intensive care unit physicians at four hospitals	Not specified	Lower respiratory tract infections	Four focus groups (26 physicians total), 33 interviews and one paired interview	Focus groups and semi-structured interviews	Explore influences of antibiotic decision-making in the intensive care unit	Thematic analysis

(Continues)

TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Peel et al (2020)[64]	Australia (HIC)	Orthopaedic and cardiothoracic surgeons at a quaternary hospital	Not specified	Orthopaedic and cardiothoracic surgical infections	58 observed hours and six interviews	Ethnographic study (observation of practice, semi-structured interviews)	Describe the phenomenon and culture of antimicrobial decision making in surgical teams	Thematic analysis
Poss-Doering et al (2020)[65]	Germany (HIC)	Primary care physicians	Not specified	Not specified	27	Semi-structured interviews	Develop a model that identifies and explains deviations from rational and appropriate antibiotic prescribing	Framework analysis based on the Tailored Implementation for Chronic Disease framework
Pulia et al (2022)[66]	United States of America (HIC)	Emergency department physicians at multiple hospitals	Not specified	Skin and soft tissue infections	20	Semi-structured interviews	Characterize barriers and facilitators to optimal antibiotic use for skin and soft tissue infections	Deductive directed content analysis guided by the Systems Engineering Initiative for Patient Safety framework
Rynkiewich et al (2023)[67]	United States of America (HIC)	Hospital intensive care unit physicians at two teaching hospitals	Not specified	Not specified	56.6 observed hours and 11 interviews	Ethnographic study (observation of practice, semi-structured interviews)	Investigate patterns of antibiotic use among physicians in medical intensive care units	Thematic analysis
Saleem et al (2019)[68]	Pakistan (LMIC)	Physicians in tertiary hospitals at multiple sites (multiple specialities and seniority)	Not specified	Not specified	15	Semi-structured interviews	Assess factors influencing physicians' antibiotic prescribing	Thematic analysis
Saliba-Gustafsson et al (2021)[69]	Malta (HIC)	General practitioners	Not specified	Acute respiratory tract infections	20	Semi-structured interviews	Explore general practitioners' understanding of antibiotic use and their perceived barriers and facilitators to prudent prescribing in respiratory tract infections	Manifest and latent content analysis with an inductive approach
Sharaf et al (2021)[70]	Qatar (HIC)	Primary care physician	Not specified	Not specified	30 physicians	Focus groups	Explore barriers and motivators of appropriate antibiotic prescription by primary care physicians	Constant comparative method, inductive qualitative analysis
Shen et al (2023)[71]	China (LMIC)	Physicians in township hospitals at multiple sites	Not specified	Upper respiratory tract infections	30	Semi-structured interviews	Explore how clinical uncertainty influences the practice of antibiotic prescribing among physicians	Conceptual content analysis and Colaizzi's method to generate qualitative codes and identify themes

TABLE 1 (Continued)

Author (year)	Country (HIC or LMIC)[#]	Physician population and setting	Patient population	Type of infection	Completed sample size	Study design	Study aim	Data analysis method
Simeoni et al (2022)[72]	Canada (HIC)	Family physicians	Not specified	Upper respiratory tract infections	20	Semi-structured interviews	Identify the determinants of antibiotic prescribing behaviour among family physicians	Deductive and inductive analytical processes using the Theoretical Domains Framework
Thaulow et al (2023)[73]	Norway (HIC)	General practitioners	Not specified	Acute sinusitis	Five focus groups (25 physicians total)	Focus groups	Identify factors influencing general practitioners' decisions to prescribe antibiotics to patients with acute sinusitis	Thematic cross-case analysis
Tillekeratne et al (2017)[74]	Sri Lanka (LMIC)	Outpatient physicians at a tertiary care hospital	Not specified	Acute respiratory tract infections	5	Semi-structured interviews	Assess Sri Lankan physicians' knowledge and attitudes towards antibiotic use in respiratory tract infections	Structural coding followed by thematic coding
Van Buul et al (2014)[75]	Netherlands (HIC)	Physicians at five nursing homes and two residential care homes (multiple specialties and seniority)	Geriatrics	Not specified	13	Semi-structured interviews	Examine factors that influence antibiotic prescribing in long-term care facilities	Iterative analysis
Yin et al (2019)[76]	China (LMIC)	Physicians in village clinics	Not specified	Not specified	15	Semi-structured interviews	Assess factors related to antibiotic prescribing by village doctors	Illustrative quotations were extracted using manifest content analysis

[#]Abbreviations: HIC, high-income country; LMIC, low- and-middle income country.
[a]The 20 primary care physicians in Biezen et al. (2017) and Biezen et al. (2019) form the same sample.
[b]The 30 hospital physicians in Broom et al. (2014), Broom et al. (2015) and 30 of the 64 hospital physicians in Broom et al. (2017) form the same sample.

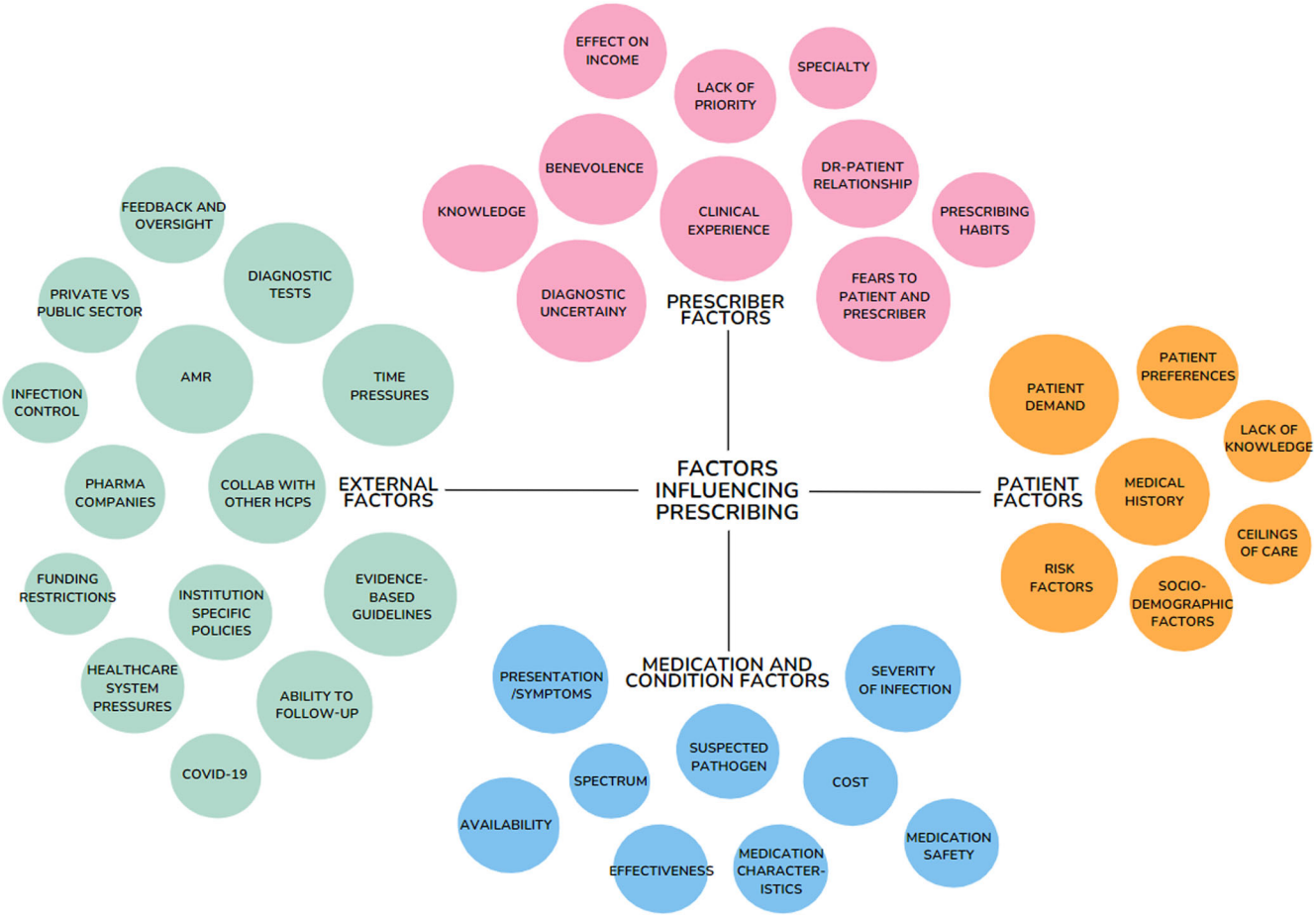

FIGURE 2 Factors influencing antimicrobial prescribing decisions. The size of the bubble correlates to the number of studies mentioning the factor. Collab, collaboration; HCP, healthcare professional; Dr, doctor.

medication- and condition-related factors, eight organizational factors, and six other external factors. A summarized list of factors influencing antimicrobial prescribing can be seen in Figure 2, where the size of the bubble correlates to the number of studies referencing the factor (complete list in Appendix D).

3.3 | Prescriber-related factors

Prescriber-related factors influencing antimicrobial decision making were identified as diagnostic uncertainty, clinical experience, fears of adverse consequences to the patient and the physician, knowledge, benevolence, physician-patient relationship, effect on income, prescribing habits, lack of priority and responsibility for antimicrobial prescribing, and the physicians' specialty.

Diagnostic uncertainty, related to both the diagnosis itself and the progression of the condition, was the most common prescriber-related factor, reported in 27 studies (Appendix D). Diagnostic uncertainty was mentioned more by physicians working in community setting and rural areas, and by those from HICs when compared with LMICs. It was more common when treating patients with respiratory tract infections and in paediatric and geriatric patients when compared with adult patients.

Diagnostic uncertainty led to overprescribing of antimicrobials due to fears of the consequences of underprescribing (for the patient and the prescriber) and the desire to act benevolently. Fear of adverse patient outcomes influenced prescribing in 17 studies (Appendix D). This included missing an infection (six studies), the development of a severe or complicated infection, prolonged or recurrent infection, hospitalization, treatment failure and death. Fears for the prescriber included fear of reputational damage (14 studies), fear of losing patients to other physicians (10 studies) and fear of litigation (seven studies) (Appendix D). Reputational damage could occur if physicians were uncertain about the diagnosis or best treatment approach, resulting in decreased patient confidence if a patient's desire for antimicrobials were not met, or if antimicrobials were underprescribed, resulting in adverse patient outcomes. There was no fear of reputational damage reported for overprescribing antimicrobials when they were not necessary. Likewise, fear of litigation only occurred in scenarios where antimicrobials were underprescribed, not when they were overprescribed if they were not required. Fear of losing patients to other physicians occurred when patients' desire for antimicrobials

were not met. Fear of reputational damage and litigation were more prevalent factors in the hospital setting, whilst fear of losing patients was more common in the community. Fear of adverse patient outcomes and litigation had a greater influence on antimicrobial prescribing in HICs compared with LMICs, whilst fear of reputational damage and losing patients had a greater influence on antimicrobial prescribing in LMICs compared with HICs.

Furthermore, prescribers demonstrated a desire to act benevolently as a factor influencing antimicrobial prescribing decisions in HICs in 11 studies (Appendix D). They felt a responsibility to provide immediate therapeutic options and that providing an antimicrobial prescription would satisfy patients and demonstrate care and concern by the physician. Biezen et al found a parent's satisfaction with a consultation was not dependent on receiving an antimicrobial for their child.[28]

The prescriber-patient relationship was an important factor influencing antimicrobial prescribing decisions in 10 studies (Appendix D). Having a relationship with a patient made it easier to understand and interpret their symptoms, improved continuity of care, gave more opportunity to provide education on prudent antimicrobial use, and gave more weight to the physician's expertise and recommendations, including the decision not to prescribe an antimicrobial. Prescribers shared how denying antimicrobials to a patient who demanded them was difficult when there was no established relationship due to lack of trust, such as in the emergency department or an after-hours service.

Prescribers made decisions about antimicrobials based on the potential effects on their income in seven studies (Appendix D). This was closely linked with the fear of losing patients and reputational damage, and was particularly prevalent in the private sector. Some physicians have described how prescribing an antimicrobial was more time efficient than providing education, resulting in the ability to see more patients in a day and generate more income. In China, providing medical services such as prescribing and administering antimicrobials was an important source of income.[36,71,76] A conflict existed between the physicians' medical and ethical duty to practice evidence-based medicine and the need to generate income.

Physicians valued their clinical experience when making decisions about antimicrobials in 25 studies (Appendix D). Their experience increased confidence in prescribing decisions and was often more highly regarded than recommendations in evidence-based guidelines. Four studies explicitly stated that prescribers' clinical experience would override guideline and infectious diseases expert recommendations.[25,49,59,65] Experience was influenced by the prescribers' knowledge (14 studies) and prescribing habits (eight studies). There was a general view that prescribers lacked sufficient knowledge of antimicrobials and that greater knowledge increased confidence in decision-making and appropriateness of antimicrobial use. For example, some prescribers opted to use broad-spectrum antimicrobials due to limited knowledge of the coverage of narrower spectrum antimicrobials.[32,37]

Physicians in six studies did not make antimicrobial prescribing a priority and were unwilling to accept responsibility for these decisions (Appendix D). This phenomenon was only reported in hospital physicians, the vast majority of which were surgeons. An Australian study demonstrated this also occurred during overnight shifts where after-hours physicians did not want to take responsibility for the patient, which resulted in prescribing antimicrobials as the safest decision.[30] In surgical patients, there was sometimes discourse between surgeons and anaesthetists over who would take ownership of antimicrobial prescribing decisions.[33,35]

Prescriber specialty was mentioned in three studies as a factor that influenced antimicrobial decisions (Appendix D). All three of these studies were conducted on surgeons. It was evident that surgeons prioritized good surgical technique over optimal antimicrobial prophylaxis to prevent surgical site infections. Increased risk of litigation and consequences if patients developed surgical site infections often resulted in overprescription of antimicrobial prophylaxis rather than considered judicious antimicrobial use.

3.4 | Patient-related factors

Patient factors that influenced antimicrobial prescribing were demand for antimicrobials, medical history, risk factors for infections and infection-related complications, patient preferences, sociodemographic factors, lack of knowledge of antimicrobials and ceilings of care.

Patient or carer demand for antimicrobials was a highly prevalent factor influencing prescribing identified in 29 studies (Appendix D). It resulted in antimicrobial prescriptions when not clinically indicated due to patient pressure, physician exhaustion, and a desire to avoid confrontation and to end the consultation. All four of the studies conducted in paediatric patients mentioned parental demand for antimicrobials as a factor that promoted prescribing. Furthermore, demand was highly prevalent in patients presenting with respiratory tract infection symptoms and in the community setting when compared with the hospital setting. Delayed antimicrobial prescribing was a method some prescribers employed to satisfy patients' demand for antimicrobials when it was felt they were not necessary at the time. This involved providing the patient with a prescription and advising them not to fill it unless symptoms worsened or did not improve within a designated time frame.

Prescribers assessed the patients' medical history when making decisions about antimicrobials, including comorbidities (13 studies), age (12 studies), frailty/vulnerability (five studies), allergies (four studies), prior infections (four studies), prior antimicrobial use (four studies), immunosuppression (three studies), general health (two studies), ability to take oral medications (one study), mobility (one study), if the patient had already commenced an antimicrobial course (one study), family history (one study), and current medications (one study) (Appendix D). In particular, there was a lower threshold for antimicrobial prescribing in patients with comorbidities or immunosuppression to avoid complications of infection. Some physicians considered patients' comorbidities in the context of the possibility of unusual pathogens or adverse drug reactions. Prescribers in 14 studies assessed a patients' risk profile to determine the likelihood of an infective cause of their symptoms, likely responsible pathogen

(including risk factors for unusual or resistant pathogens) and the potential for complications or progression of illness (Appendix D). These risk factors included the patients age, smoking status, occupation, hygiene level and exposure history. Generally, paediatric and geriatric patients were considered more vulnerable and were more likely to be prescribed an antimicrobial, and for a prolonged duration, including as prophylactic therapy. Some prescribers avoided certain antimicrobials due to a patients' old age.[24] Exposure history, including place of residence, was used to assess risk of unusual or resistant pathogens. Prescribers considered patients' occupation and were more likely to prescribe antimicrobials if the patient travelled for prolonged periods for work. Overall, increased risk of infection or complications resulted in an increased likelihood of extended duration broad-spectrum intravenous (IV) antimicrobials being prescribed.

Prescribers in six studies from HICs took patient preference into account when making decisions about antimicrobial therapy (Appendix D), including the decision to prescribe an antimicrobial or not and which antimicrobial to prescribe. Prescribers from a study on antifungal treatment decisions sought patient input for decisions around antifungal prophylaxis but not active infection treatment.[58] General practitioners (GPs) from Spain stated some patients expressed a desire not to take antimicrobials due to fears of adverse effects or to reduce pill burden.[39] Furthermore, prescribers would adjust the type of antimicrobial, formulation, and route of administration in an effort to improve adherence. Sometimes patient preferences would override clinician judgement and guideline recommendations.

A broad range of sociodemographic factors were considered by prescribers to inform antimicrobial decisions in 11 studies (Appendix D). These included patient finances (four studies), geographical remoteness (three studies), education level (three studies), culture or background (one study), and other complex social situations more broadly (one study). A patient's financial situation could increase or decrease antimicrobial prescribing. In the private sector in Egypt, physicians were more likely to prescribe expensive broad-spectrum antimicrobials as they believed patients could afford them and preferred them.[41] Furthermore, surgeons in Australia were more likely to overprescribe surgical antimicrobial prophylaxis as they believed the patients' insurance would not cover hospital readmission for a postoperative infection.[49] In contrast, primary care physicians in Romania prescribed antimicrobials judiciously to impoverished patients to reduce their healthcare costs.[44] Patient education level was a more prevalent factor in the community when compared with the hospital setting. This affected how well the prescriber could communicate with the patient, including treatment plans and reasoning behind antimicrobial decisions. It was generally acknowledged that lower education levels resulted in increased demand for antimicrobials due to misconceptions and lack of knowledge regarding these medicines. These misconceptions were difficult to overcome and sometimes resulted in the prescription of antimicrobials when they were not necessary. Patients who lived in geographically remote areas were provided with antimicrobials more liberally due to difficulties in accessing healthcare and follow-up. This factor was only considered by prescribers in the community setting. A study from the United States highlighted that patients from a culture or background where there were fewer restrictions on the use and access of antimicrobials often had high expectation for antimicrobial treatment and this could influence prescribing decisions.[40] Finally, other complex social situations, such as a patient who was a recent immigrant or isolated older adult, may result in overprescribing of antimicrobials to prevent worse outcomes in these vulnerable patients.

Ceilings of care was mentioned by prescribers specializing in geriatric medicine in three studies (Appendix D). Advanced care plans may specify preferences for antimicrobial therapy. Furthermore, community physicians were more willing to prescribe antimicrobials to geriatric patients if their ceiling of care was community-based management.

3.5 | Medication- and condition-related factors

Medication-related factors that influenced antimicrobial prescribing were the availability, cost, potential adverse effects, antimicrobial spectrum, evidence for effectiveness, and medication characteristics including dosing regimen, dosage form, flavour and pharmacokinetics. Condition-related factors that influenced prescribing included the clinical presentation and symptoms, severity of illness, and suspected pathogen.

Availability (eight studies) and cost (four studies) of antimicrobials influenced prescribers' choices (Appendix D). The influence of availability (or unavailability) was much greater in rural areas and LMICs. Private-sector physicians in Egypt had a greater selection of antimicrobials available than those in the public sector.[41] The unavailability of antimicrobials appeared to impact narrow-spectrum antimicrobials more than broad-spectrum antimicrobials in both HICs and LMICs.[25,50,70] In rural China, antimicrobials could only be prescribed if they were included on essential medicines lists.[36] The cost of the antimicrobial itself was considered, as was the cost of complications if an antimicrobial was not prescribed (eg, hospital admission). Cost was more often considered by prescribers in private settings compared to the public sector. In LMICs, cost to the patient was an important consideration as it was believed to influence adherence.[68]

Nine studies in this review demonstrated that medication safety influenced prescribers' choices (Appendix D), including adverse effects of antimicrobials (eight studies), potential drug-drug interactions (two studies) and safety in pregnancy (one study). There was a preference for antimicrobials that caused fewer adverse drug reactions (ADRs) and treatment would be tailored if patients did experience ADRs. In geriatric patients, the decision not to prescribe antimicrobials could be justified by the desire to avoid ADRs in this vulnerable population.[75]

Prescribers would consider the suspected pathogen (eight studies) and antimicrobial spectrum (seven studies) when making treatment decisions (Appendix D). The first step in infection management was identifying the likely pathogen responsible, which generally started with determining if the infection was bacterial or viral in origin. When a suspected pathogen was determined, prescribers would then consider the spectrum of antimicrobial required. In general, narrow-

spectrum antimicrobials were preferred and restricted antimicrobials were avoided as empiric therapy and reserved for resistant infections. However, some prescribers would use broad-spectrum antimicrobials to avoid missing an unlikely or resistant pathogen,[54] or when the cause of infection was unclear and multiple sites were to be targeted simultaneously.[47]

Clinical presentation, symptoms and their severity influenced antimicrobial prescribing decisions in 19 studies (Appendix D). In respiratory tract infections, the presence of a fever, productive cough, and chest signs increased the likelihood of an antimicrobial prescription.[38] In acute sinusitis, the presence of pain, fever, and fatigue increased the likelihood of an antimicrobial prescription.[73] The clinical presentation often impacted the prescribers' decision more than test results. In the management of urinary tract infection, for example, an antimicrobial may be prescribed if the urine dipstick was negative but the patient had symptoms suggestive of an infection,[42] and vice versa.[75] In general, the presence of a fever, inflammation, rapid onset of symptoms, or prolonged duration of illness all increased the likelihood of an antimicrobial prescription. In 11 studies, severity of infection was analysed (Appendix D) and determined if antimicrobials were to be prescribed, the spectrum of antimicrobial coverage, and whether IV or oral therapy would be used. Broad-spectrum IV antimicrobials were more likely to be prescribed in severe infections.

Other medication factors that were considered included the dosing regimen (four studies), pharmacokinetics (one study), dosage form (one study), flavour (one study), and evidence for effectiveness (three studies) (Appendix D). Antimicrobials with a convenient dosage regimen (daily or twice daily dosing) were preferred to maximize patient adherence, and this convenience may override guideline recommendations. Physicians from Pakistan expressed that the more expensive originator brand of antimicrobials was preferred as they believed these to be of a higher quality and more effective.[68] Furthermore, some prescribers chose an antimicrobial based on what they had found effective (or ineffective) for that indication in the past, despite guideline recommendations.

3.6 | External factors

External factors influencing prescribing were divided into organizational factors and other factors. Organizational factors included time pressures, collaboration with other healthcare professionals, institution-specific prescribing practices, feedback and oversight, private *vs* public sector, healthcare system pressures, antimicrobial funding restrictions, and infection control practices. Other factors influencing antimicrobial prescribing included evidence-based guidelines, diagnostic tests, ability to follow-up with the patient, antimicrobial resistance, pharmaceutical companies, and SARS-CoV-2 (COVID-19).

Time pressure was mentioned in 31 studies and was the most common factor identified influencing antimicrobial prescribing (Appendix D). It was found to be marginally more common in the community compared to the hospital setting, and much more frequently mentioned in HICs compared with LMICs. Prescribers in the ED and operating theatre felt more time pressure within the hospital setting. Antimicrobial prescribing decisions needed to fit within the existing contexts and pressures prescribers worked within. Physicians highlighted that providing an antimicrobial prescription when it was potentially not required was more time-efficient than educating patients or their carers on symptomatic relief and the reason an antimicrobial was not required. They favoured this saved time to catch up on other duties or to review other patients, particularly if they were running behind in their schedule or were working in a busy service. Lack of time also inhibited prescribers from reviewing patient charts in detail, accessing evidence-based guidelines, using diagnostics or consulting an antimicrobial stewardship (AMS) team or infectious diseases specialist to assist with prescribing decisions, often resulting in empiric prescribing based on previous clinical experience.

Evidence-based guidelines were used to guide antimicrobial prescribing decisions by physicians from both community and hospital settings in 25 studies (Appendix D). Guidelines were thought to be beneficial for making initial treatment decisions to reduce uncertainty in diagnosis and antimicrobial choice, and were also used as an authoritative source to support decisions not to prescribe. However, prescribers also highlighted issues with evidence-based guidelines. Some prescribers felt guidelines had large volumes of information that were difficult to read and comprehend, whereas others felt they were not comprehensive enough to guide treatment decisions in certain situations. Guidelines were underutilized in some community settings and LMICs due to limited availability. Patient resources were used by physicians in one study to support their decision not to prescribe antimicrobials by having patient-friendly information to explain this rationale.[72] Furthermore, some hospitals had institution-specific policies or practices (seven studies) that influenced prescribing (Appendix D), including informal practices, such as local behaviours or norms within a specific medical team, department or hospital, as well as more formal policies such as official institutional guidelines, AMS policies, an antibiogram and checklists. Physicians in India and Pakistan also stated that poor infection-control practices within their institution increased antimicrobial prescribing as prophylaxis against infection due to unhygienic environments.[50,68]

Diagnostic tests assisted with antimicrobial prescribing decisions in physicians from both community and hospital settings (25 studies) (Appendix D). These included C-reactive protein, X-rays, urine dipsticks, blood cultures and pathology. Similar to the use of guidelines, diagnostics could be used to facilitate rational prescribing and reduce uncertainty. In some instances they were used initially to aid diagnosis and empiric treatment options, whereas other physicians would only use diagnostics if initial treatment failed or there was no improvement in the patient's condition. Some major barriers to the uptake of diagnostic tests included the lengthy turnaround time (limiting the ability to use targeted antimicrobial therapy or de-escalate), lack of suitable tests in certain conditions (eg, cellulitis), and lack of availability in certain settings (particularly rural areas and LMICs).

A patients' ability to follow-up influenced antimicrobial prescribing decisions in 15 studies (Appendix D) in physicians in the

community and ED primarily. If patient follow-up was not possible, there was a lower threshold for prescribing antimicrobials, including broader-spectrum antimicrobials, in the absence of a clear indication. This could occur when the physician reviewed the patient close to a weekend or an upcoming holiday, or if the physician was unable to follow-up with the patient due to their work schedule or the patients' lack of time or finances. Delayed antimicrobial prescribing was a method some physicians used to overcome lack of follow-up opportunity.

Collaboration with other healthcare professionals was an influential factor for antimicrobial decision-making in 19 studies (Appendix D), which involved discussions about diagnosis and the need for, and choice of, antimicrobial therapy. Physicians collaborated with medical colleagues (12 studies), the AMS team, including pharmacy and microbiology (seven studies), and, to a lesser extent, nursing staff (two studies). This was more influential in the hospital setting when compared with the community setting. Physicians valued the collaborative efforts of a medical team in complex cases, and the opinions of medical colleagues were often more effective at modifying prescription behaviour than guidelines. It was also highlighted in two studies of surgeons how poor communication could adversely impact the timing of pre-incision antimicrobials and the duration of postsurgery prophylaxis. This occurred due to lack of communication between the many members of the surgical team, including surgeons, anaesthetists, and junior physicians.[35,64] The collaboration between medical colleagues was strongly influenced by the medical hierarchy (11 studies) (Appendix D), and this was much more common in the hospital setting compared with the community. Junior physicians had very little autonomy and their prescribing decisions were strongly influenced by their senior colleagues, even if they did not agree with their recommendations. Prescribing in a manner that would satisfy senior colleagues was more important than following guidelines. An interspecialty hierarchy also existed where senior physicians were less likely to follow recommendations made by more junior members of the AMS team. In general, however, the AMS team was valued by physicians, and they were often consulted in uncertain cases. In Hong Kong, nursing staff would pressure physicians to prescribe antimicrobials for their patients, and the type and dose of antimicrobial was influenced by the ease of administration for nursing staff.[53] In residential aged-care facilities, physicians relied on information from nurses on the clinical condition of patients and their opinion on whether antimicrobials were required.[75] Moreover, physicians also adhered to prescribing etiquette principles as outlined in five studies (Appendix D). There was a desire not to contradict or undermine antimicrobial prescription decisions made by other physicians. This extended to GPs who succumbed to patients' demands for antimicrobials if their regular GP would usually give a prescription, and to intensive care unit physicians who would not override an antimicrobial decision made by the parent team.

AMR was an influential factor in antimicrobial decision making in 10 studies (Appendix D), where the evidence showed it could increase or decrease the likelihood of antimicrobial prescription and its spectrum. Some physicians stated that the concern for resistant infections forced them to prescribe broad-spectrum antimicrobials and use more aggressive antimicrobial treatment regimens to prevent the development of resistance. Alternatively, other physicians described how AMR resulted in more prudent antimicrobial prescribing and was used to justify not prescribing an antimicrobial or delayed prescribing. Some physicians stated that AMR was considered when reviewing new patients and resistance data was used to inform antimicrobial choice. In general, however, the main theme from the studies in this review is that there was good awareness of AMR and it was theoretically significant, but was not practically significant when treating an unwell patient.

Feedback and oversight influenced antimicrobial prescription decisions in six studies (Appendix D). Physicians were generally unwilling to provide feedback to their colleagues on their prescribing habits because maintaining an amicable working relationship was considered more important than optimizing prescribing and counteracting AMR. Furthermore, direct feedback from government or other authoritative bodies was also limited but was more common in the public sector when compared with the private sector. Studies from Canada and China have shown that feedback does change prescribing behaviour and can reduce the overall rate of antimicrobial prescribing.[72,76]

Employment within a public or private setting influenced antimicrobial prescribing decisions in five studies (Appendix D). This had more influence on physicians from the community when compared with those from the hospital setting. Physicians expressed the difficulty of not prescribing antimicrobials to private patients who pay for a consultation,[42,59,61] and this often resulted in the prescription of antimicrobials when they were not necessarily required to satisfy paying patients. In the public sector, there may be funding restrictions on consultations and on which antimicrobials were subsidized, resulting in physicians prescribing shorter antimicrobial courses or only prescribing antimicrobials that are nationally funded. In contrast, physicians in the private sector were more likely to prescribe the more expensive originator brand of an antimicrobial.[45,56]

Representatives from pharmaceutical companies had an influence on antimicrobial prescribing in five studies (Appendix D), which appeared to be more common in the community setting and in the private sector. Information provided by pharmaceutical companies made it difficult for physicians to distinguish between promotional material and scientific evidence, and could make physicians more likely to prescribe the antimicrobial being promoted.

Healthcare system pressures, including hospital admission, length of hospital stay, bed pressures, and healthcare costs, influenced antimicrobial decision making in five studies (Appendix D). Physicians in the community or emergency department may prescribe antimicrobials to reduce the likelihood of hospital admission. This was more likely if the patient had presented multiple times with the same complaint or had spent a prolonged period in emergency. Managing a patient with antimicrobials in the community was considered more economical overall than managing them in the hospital. Likewise, for patients already admitted to hospital, physicians may decide to prescribe antimicrobials if they believe it could reduce hospital stay. Furthermore, due to bed pressure in the hospital, physicians may be

pressured to discharge patients without waiting for results to confirm diagnosis of an infection, which could result in unnecessary antimicrobial prescriptions to ensure any potential infection is covered.

Three studies discussed the influence of the COVID-19 pandemic on antibiotic prescribing (Appendix D). COVID-19 resulted in increases and decreases in antibiotic prescribing during different stages of the pandemic. Antibiotic prescribing increased early in the pandemic due to recommendations to use azithromycin to manage COVID-19 and the difficulties distinguishing between COVID-19 and a bacterial infection on a chest X-ray. Antibiotics were also prescribed to patients with confirmed COVID-19 to treat or prevent superimposed bacterial infections. In the height of the pandemic, there were fewer patients with bacterial respiratory tract infections, resulting in fewer antibiotic prescriptions. Furthermore, ED physicians recounted that many patients who presented to the ED with respiratory symptoms were seeking COVID-19 testing rather than antibiotics.

4 | DISCUSSION

This systematic review of qualitative studies provides an overview of factors influencing antimicrobial prescribing decisions by physicians. Forty factors influencing antimicrobial prescribing by physicians were identified, including novel factors that have not been published in previous systematic reviews. These include the physician-patient relationship, benevolence, prescribing habits, the physician's specialty, risk factors for infection, ceilings of care, patient preferences, medication characteristics, patient access to follow-up, antimicrobial resistance, prescribing etiquette, and influences of COVID-19 on antimicrobial prescribing (as the first review on this topic published since the beginning of the pandemic). The most common factors mentioned were time pressure, patient/carer demand for antimicrobials, diagnostic uncertainty, clinical experience, and the use of evidence-based guidelines and diagnostic tests, highlighting that the physicians themselves and factors external to the patient, physician or medication were most influential. Understanding these factors is vital for the creation of targeted antimicrobial stewardship interventions to minimize the burden of AMR.[78]

Time pressures on physicians' consultation increased inappropriate antimicrobial prescribing and has previously been mentioned in systematic reviews.[17,18] Physicians typically have very demanding workloads and can only dedicate a small amount of time for each patient. Time constraints limit a physician from completing a thorough assessment of a patient, reading guidelines for antimicrobial prescription advice, and performing and reviewing diagnostic tests and results. Previous studies have demonstrated that under time pressure, physicians asked fewer questions about the symptoms of the presenting illness, conducted less thorough clinical examinations and wrote a higher volume of prescriptions.[79,80] Physicians mentioned that they would favour prescribing an antimicrobial when it was potentially not necessary over proper clinical assessment and patient education as it was more time efficient. This is of particular concern given that half the world's population have access to primary care where the average consultation time is less than 5min.[81] Time pressures had a greater influence on prescribing in physicians from the community and in HICs. A systematic review on factors affecting inappropriate antibiotic use in LMICs also did not report time pressures as an influential factor; however, it is assumed that this is due to either under-representation of LMICs in this review or under-reporting of the issue rather than the absence of time pressures given that primary care physicians in China, Pakistan and Bangladesh have all reported reviewing more than 90 patients in one day.[81]

Patient and carer demand for antimicrobials increased prescribing and has been reported as an influential factor in antimicrobial prescribing in previous reviews.[16,18] Some physicians also took patient preferences into account when considering the type of antimicrobial to prescribe, its dosage form, and route of administration. Patient preference was frequently reported to influence antimicrobial prescribing in the management of respiratory tract infections. This is likely a consequence of extensive patient misconceptions about the utility of antibiotics in the management of viral respiratory tract infections.[82,83] Patient and carer demand was more commonly reported by physicians in the community setting compared to the hospital setting. Guo et al suggest this may be a result of patients perceiving physicians in primary care as providing a transactional service rather than a health service. In these instances, physicians are more likely to succumb to the demands for antimicrobials.[45] There has also been a movement within healthcare to have patients more involved in decision-making, which has been shown to improve health outcomes and patient and physician satisfaction.[84] There appears to be difficulty balancing patients advocating for their health interests and their lower clinical knowledge when compared to physicians, resulting in increased antimicrobial prescriptions. Further to this, physicians perceived demand for antimicrobials to be higher in patients with lower education levels. Delayed antimicrobial prescribing was often a strategy used by physicians to meet patient demand for antimicrobials where it was felt they were not necessary in order to provide a desirable outcome for both parties. Parent demand for antimicrobials for their child was mentioned as an influential factor in all four studies investigating prescribing in paediatrics. Biezen et al's study on the views of parents and GPs in managing respiratory tract infections found only 8% of interviewed parents expected antibiotics for their child.[28] It is evident that physicians may be misinterpreting what patients are seeking from a consultation and overestimating demand for antimicrobials.

Diagnostic uncertainty increased inappropriate antimicrobial prescribing due to fears of consequences to the patient and physician if antimicrobials were underprescribed when they were required. This has been reported in prior systematic reviews.[16,17] Diagnostic uncertainty was a more common factor in community and rural settings. It is expected that this is a result of reduced access to guidelines and diagnostic testing that facilitate rational prescribing. Diagnostic uncertainty was reported to be a more influential factor in HICs compared with LMICs. Again, this is likely due to under-representation of LMICs in this review. A prior systematic review highlighted that LMICs have limited laboratory facilities, which results in diagnostic uncertainty,

poor clinical decision making and inappropriate antimicrobial use.[85] Diagnostic uncertainty was common in physicians managing paediatric and geriatric patients, likely due to a reduced ability for these patients to provide an accurate medical history and describe their infective symptoms. Furthermore, the utility of some diagnostic tests, such as culturing, are limited by their prolonged turnaround time, reducing their ability to guide empiric therapy and narrow antimicrobial spectrum. The development of novel, rapid, low-cost diagnostics is a priority for addressing AMR globally.[15,86,87]

Clinical experience was generally more valued by physicians than the results of diagnostic tests and recommendations in evidence-based guidelines when making decisions about antimicrobials. The importance of clinical experience in antimicrobial prescribing has been reported in previous systematic reviews.[17,18] Physicians often rely on their clinical knowledge, previous experience, and prescribing habits developed over years of practising to choose antimicrobials. Clinical experience is linked to confidence in decision-making. Physicians with more experience stated this increased their confidence in stopping or de-escalating antimicrobial therapy, made it easier to refuse patient demand for antimicrobials or to make antimicrobial choices in the context of a specific patient, and made them more willing to take on risk. Physicians with less experience stated they had less knowledge and confidence in their antimicrobial decision-making, particularly the decision to prescribe narrow-spectrum antimicrobials. Importantly, increased confidence with increased experience does not necessarily equate to more appropriate prescribing. A previous study showed no correlation between a physician's age and their knowledge of antimicrobials.[88]

Access to evidence-based guidelines and diagnostic testing is an essential component of AMS to guide prudent antimicrobial use.[15,89] Policies, guidelines, and diagnostic testing have been shown to be influential factors in antimicrobial prescribing in previous reviews.[16,18] Whilst guidelines are used to direct treatment decisions by many physicians, many others favoured prescribing in a manner to reduce risk and uphold their professional reputation with their patients and colleagues. In particular, however, physicians mentioned guidelines as an authoritative source to support their decision not to prescribe antimicrobials, particularly when explaining their recommendation to patients. Guidelines appeared to be used more frequently by junior physicians to reduce uncertainty and increase confidence in their choices. Resource limitations restrict the use of evidence-based guidelines to assist prescribing in LMICs. Whilst evidence has shown that optimal prescribing of antimicrobials in accordance with evidence-based guidelines minimizes the development of resistance,[11] it is clear that many physicians still value their clinical experience and autonomy more than recommendations in guidelines. Diagnostic stewardship is a relatively new concept that involves interventions to improve the appropriate use of microbiological testing and diagnostics to guide clinical decisions. Underutilisation of diagnostic tests can have negative effects on patient outcomes.[89] Improving access to evidence-based prescribing guidelines and diagnostic testing is necessary in LMICs and other resource-limited settings. The Infectious Diseases Society of America recommends the development of facility-specific antimicrobial prescribing guidelines based on local resistance patterns and epidemiology for successful AMS programs and increased guideline adherence.[90]

Medication- and condition- related factors were infrequently mentioned by physicians as influencing antimicrobial prescribing compared to other types of factors. Previous systematic reviews demonstrated clinical signs and symptoms of infection,[16,17] and the severity of illness influenced antimicrobial prescribing.[16] Interestingly, no prior systematic reviews discussed how properties of the antimicrobial itself can influence prescription decisions. It is to be expected that this is a consideration made by physicians in every encounter, but it has not been previously reported in a systematic review. Physicians may deviate from optimal therapeutic choices recommended in guidelines due to the characteristics of the antimicrobial, such as its dosing form or schedule, in an effort to improve patient adherence. Additionally, physicians in only nine studies mentioned the potential harms of antimicrobial therapy as influencing their decision making. Rarely did physicians cite potential adverse effects as a reason not to prescribe antimicrobial therapy. There was an overall theme that antimicrobials are perceived as harmless and their potential immediate consequences, such as adverse effects or long-term consequences of AMR, are not often considered when making decisions about if, and which, antimicrobial is to be prescribed.

The data from this systematic review can be used to create a model of physicians' antimicrobial prescribing process, starting from reviewing the patient to selecting an antimicrobial, which includes the factors that physicians consider and how each step in the process is influenced by the physician themselves, the patient, the patient's condition, the antimicrobial, and organizational and external factors (Figure 3). Physicians initially review the patient by assessing their medical history, age and risk factors, and examining for clinical signs, symptoms and severity of infection. The way they interpret the patient's presentation is influenced by their clinical experience, knowledge, their pre-existing relationship with the patient and time pressures. Then, physicians attempt to make a diagnosis and identify a suspected causative pathogen based on the information they have gathered with potential assistance from diagnostic tests. Formation of a diagnosis is influenced by their clinical experience and knowledge, the degree of diagnostic uncertainty and collaboration with other healthcare professionals. Once a provisional diagnosis has been made, physicians decide if an antimicrobial is required based on their own clinical knowledge, evidence-based guidelines or local policies. This is influenced by the physician's previous clinical experience, fear of consequences (to the patient and themselves), benevolence, antimicrobial resistance, the effect on their income, collaboration with other healthcare professionals, patient demand and preferences, and whether the physician is working within the private or public sector. Finally, if an antimicrobial is required, physicians need to select an agent considering the antimicrobial spectrum, cost, availability, dosing regimen, and potential for drug-drug interactions and adverse effects. This selection is influenced by the prescriber's knowledge and clinical experience, antimicrobial resistance, pharmaceutical companies, patient preferences and sociodemographic factors, and whether the physician is

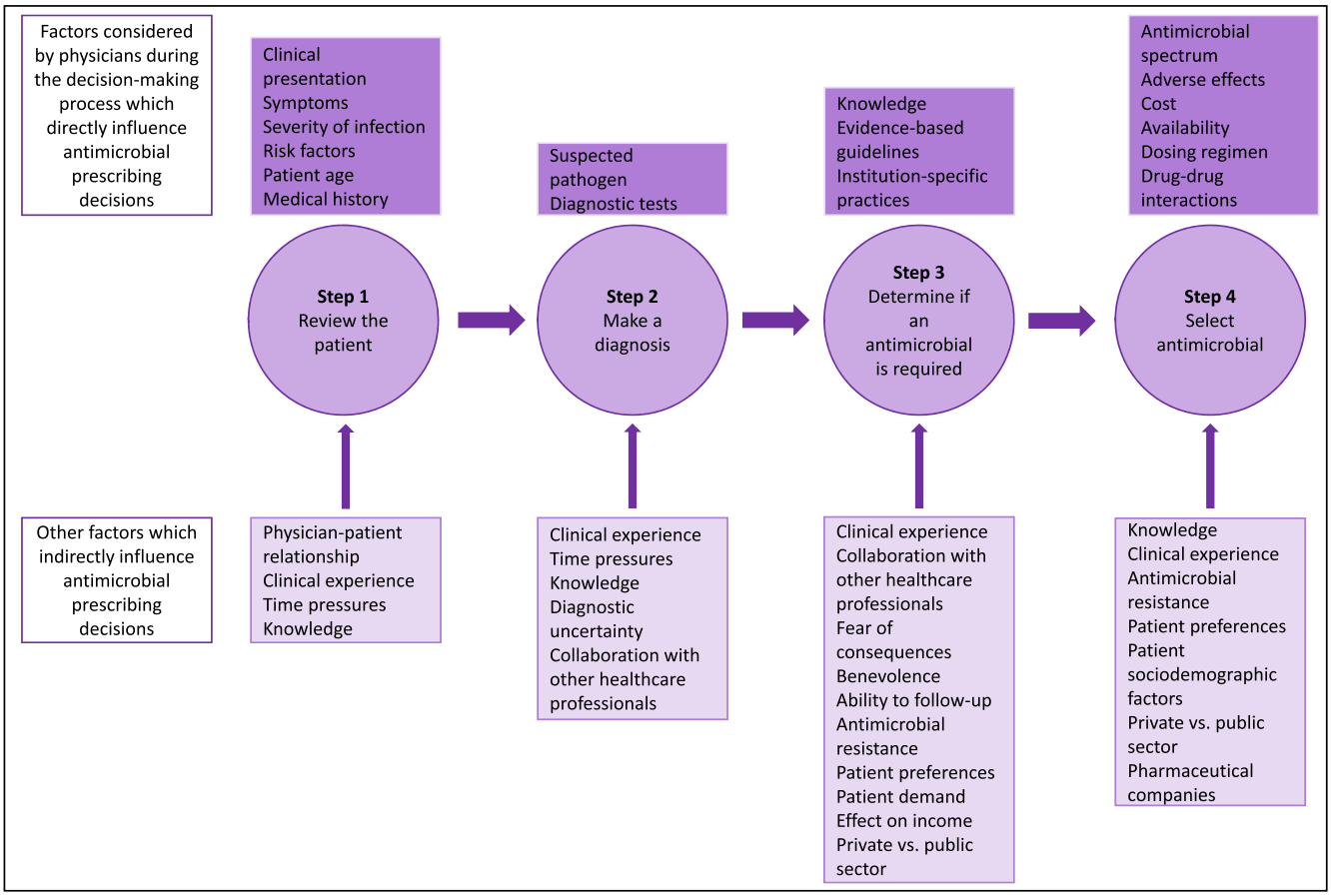

FIGURE 3 A proposed four-step model of physicians' antimicrobial prescribing process and the factors impacting each step. Factors can be either deliberate considerations that directly influence prescribing (factors above the circles) or more subtle that indirectly influence prescribing (factors below the circles). In the four-step proposed model, physicians firstly review the patient and their infective symptoms, then diagnose the infection and likely causative pathogen, determine if an antimicrobial is required for management, and finally choose an antimicrobial agent.

working within the private or public sector. Interventions aimed at changing antimicrobial prescribing practices should consider these four stages in the decision-making process. This process is complex with many competing demands, but considering these factors during all four stages simultaneously may increase the success of such interventions. Having factors influencing prescribing linked to different stages of the prescribing process is useful for mapping results to existing frameworks when designing future interventions, for example the COM-B model.[91]

Prescribers are aware of AMR as a significant global health issue, but there is little ownership of this issue personally and there is little recognition of it impacting their individual practice. Prescribers view the immediate harm to the patient by underprescribing antimicrobials as outweighing the potential long-term population harm of AMR by overprescribing antimicrobials. The interests of the individual patient and the global health system are mutually exclusive and prioritizing short-term defined harms over future potential harms is innate human behaviour.[18] This is driven by diagnostic uncertainty, fear of adverse outcomes, diagnostics and guideline limitations, time pressures, and the minimal awareness for adverse effects and consequences of antimicrobial overuse. Addressing factors that amplify harm to the patient and the physician is essential for counterbalancing the population harm of AMR. Furthermore, the lack of repercussions for antimicrobial overuse when compared with underuse tilt the scales in favour of overprescribing. Policymakers have already begun considering changes in subsidy and payments, prescriber training and regulation to reduce overuse and rebalance the scales between underprescribing and overprescribing antimicrobials.[92]

Interventions to enhance prescribing practices should firstly focus on the most common factors influencing antimicrobial choices. Incorporating antimicrobial decision support tools into prescribing programs can streamline the antimicrobial decision-making and prescribing process given physicians' time constraints. Balancing a physician's clinical experience, autonomy, and adherence to prescribing guidelines is difficult. Education and empowerment of physicians around antimicrobial stewardship may be useful. Increased patient education efforts on antimicrobial use and safety, particularly around the role of antibiotics in viral infections, should assist in improving patient knowledge and reducing unnecessary antimicrobial demand. Finally, improving access to and the usefulness of guidelines and diagnostic testing, particularly in low-resource settings, will be vital to reduce diagnostic uncertainty and improve prescribing.

The strength of this review is the inclusion of the views of physicians from all settings and countries, and comparing factors between them. Including only qualitative studies gave more depth and context to the factors influencing prescribing. However, it is important to note the heterogeneity of these studies and the variability in their quality and relevance of information. Whilst no studies were excluded based on quality or bias, they contributed variable findings to the data synthesis, and this did not influence data analysis and interpretation. The exclusion of non-physician prescribers limits the application of the findings to pharmacist and nurse-practitioner prescribers, whose numbers are growing.[93–95] Likewise, excluding studies that did not separate the views of physician and non-physician prescribers and those that were not published in the English language may have resulted in missing data. Whilst it is well established that AMR disproportionately affects LMICs, most studies included in this review were from HICs, and the unique factors influencing prescribing in LMICs may not be fully represented.

5 | CONCLUSIONS

This systematic review presents a detailed synthesis of the prescriber, patient, medication, condition, and external factors influencing antimicrobial prescribing decisions. It identified that the immediate harm to the patient and prescriber due to underprescribing antimicrobials outweighed the future harm to the population due to overprescribing. This is largely driven by diagnostic uncertainty, fears of negative outcomes for the patient and prescriber, the desire to satisfy patient demand for antimicrobials, and the lack of access and utility of evidence-based guidelines and diagnostic tests. Global evidence demonstrates antimicrobial use is widely suboptimal, despite many attempts at improving it. Understanding the factors influencing prescribing decisions and targeting the prescriber, patient, medication, condition and external factors influencing decision-making is vital for the success of interventions aimed at optimizing prescribing. Furthermore, increased feedback and oversight on physicians' antimicrobial prescribing behaviour, including penalties for overprescription, are also necessary to balance the scales between the consequences of underprescribing and overprescribing. Future interventions should aim to consider how to appropriately balance the immediate patient risk and the future population risk of antimicrobial prescribing decisions in the context of the growing threat of AMR.

AUTHOR CONTRIBUTIONS

All authors contributed to this review. Conception and analysis design were performed by S.R., J.-G.C., P.A. and J.-W.A. Data collection was performed by S.R. and Y.C.K. The first draft of the manuscript was written by S.R. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

None to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

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