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Review

Uncovering influential factors in human antibiotic prescribing: a meta-synthesis study informed by the Theoretical Domains Framework

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SUMMARY

This study aimed to identify modifiable determinants (facilitators and barriers) related to the choice of prescribing antibiotics in human medicine across clinical settings. Enhanced management of antibiotics can help slow the spread of resistant bacteria. A qualitative meta-synthesis approach was used, according to Sandelowski and Barroso's method. Included studies were evaluated using the Critical Appraisal Skills Programme. Findings were extracted and organized to form a qualitative meta-summary. The Theoretical Domains Framework, the Capabilities–Opportunities–Motivation (COM-B) model and the Behaviour Change Wheel were used as a coding matrix for data interpretation. The analysis of 63 included studies revealed barriers and facilitators in 12 of 14 domains specified by the Theoretical Domains Framework. Prescribers' capabilities, motivation and opportunities were found to be the main drivers of antibiotic prescribing behaviour. Knowledge, skills, beliefs, expectations, the influence of patients and colleagues, organizational culture and infrastructure characteristics have a significant impact on prescribing behaviours. A comprehensive inventory of factors related to antibiotic prescribing has been compiled. Interventions to promote appropriate antibiotic prescribing should take a systemic approach rather than focusing solely on individual-level variables. Furthermore, the adoption of co-design approaches for such interventions is desirable to ensure greater applicability and sustainability in the real-world context of organizations.

Introduction

Before the invention of antibiotics, infectious diseases were the primary cause of illness and death [1]. However, following the discovery of antibiotics, they have become the most commonly prescribed medications worldwide. Antibiotics are utilized to treat both severe and minor infections. Additionally, effective

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antimicrobials are essential for preventive and curative medicine. Unfortunately, the improper use of antimicrobials, such as excessive use, incorrect dosage, and prolonged duration, is a significant contributor to antibiotic resistance [2]. This has resulted in the emergence of antimicrobial resistance (AMR), which is linked to higher rates of illness, death and healthcare expenses [3,4].

AMR has emerged as a global health crisis, threatening the effectiveness of antibiotics, and posing significant challenges to healthcare systems worldwide [5]. In recent times, the improper utilization of antibiotics, encompassing their superfluous prescription for viral infections or lack of adherence to proper dosage and treatment duration, has been recognized as a significant factor in the emergence and dissemination of AMR. To illustrate, over half of all antibiotics are prescribed, sold, or dispensed in an inappropriate manner, and approximately 50% of patients fail to adhere to the correct usage of antibiotics [6]. Consequently, the comprehension of the factors influencing antibiotic prescribing behaviours has become imperative in the formulation of efficacious strategies aimed at addressing AMR.

Addressing this issue requires a comprehensive understanding of the modifiable determinants that influence healthcare professionals' prescribing decisions. These determinants encompass a wide range of factors, including individual characteristics, knowledge and attitudes, cultural norms, healthcare system factors and socioeconomic influences [7,8].

By studying these modifiable determinants, potential areas for intervention can be identified to develop targeted strategies to optimize antibiotic prescribing practices and fight against AMR. Such interventions can encompass educational initiatives aimed at improving healthcare professionals' knowledge of appropriate antibiotic use, implementing guidelines and protocols to standardize prescribing practices, and promoting antimicrobial stewardship programmes that facilitate rational prescription of antibiotics and inform evidence-based policy decisions [9,10]. However, despite the well-known role of human dynamics involved in antibiotic prescribing practices, current antimicrobial stewardship programmes continue to lack a human-centred approach and remain sporadic and fragmented [11,12]. Consequently, this aspect requires further investigation.

At present, qualitative review papers exist that assess modifiable determinants affecting antibiotic prescribing within specific healthcare settings or focusing on specific prescribers [13–17]. However, there has not yet been a comprehensive synthesis of these studies across various clinical areas. The synthesis of knowledge plays a crucial role in consolidating the outcomes of individual studies, thereby advancing our comprehension of a specific issue [18]. Qualitative meta-synthesis allows the integration and comparison of findings from different studies, allowing for the accumulation of knowledge that can potentially lead to the development of new frameworks, narratives, or interpretive explanations [19] through a theory-driven approach.

The Theoretical Domains Framework (TDF), the Capabilities–Opportunities–Motivation (COM-B) model and the Behaviour Change Wheel were used as theoretical underpinnings to guide this meta-synthesis.

The TDF and the COM-B model were adopted in this study to map the nature (facilitators and barriers) of the determinants of the antibiotic prescribing behaviour emerging from the qualitative literature. The TDF consists of 14 domains that capture key theoretical constructs relevant to behaviour change. These domains include knowledge, skills, beliefs about capabilities, beliefs about consequences, social influences, emotions, environmental context and resources, social/professional role and identity, beliefs about capabilities, goals, intentions, memory, attention, and decision processes [20]. TDF can be condensed into three core components: capability, opportunity and motivation (Figure 1) which are described by the COM-B model. This model demonstrates that human behaviour (B) results from the interaction between personal physical and psychological capabilities (C), to utilize social and environmental opportunities (O) via motivators (M) [21].

Complementarily, the Behaviour Change Wheel was adopted to identify behavioural change strategies that can be used to modify the target behaviour according to the facilitators and barriers mapped through the TDF and COM-B model. The Behaviour Change Wheel includes nine interventions functions (i.e., education, persuasion, incentivization, coercion, training, enablement, modelling, environmental restructuring and restrictions) to choose from based on the TDF and COM-B model assessment results [22]. According to these premises, the main objective of this study was to provide a meta-synthesis of prescribers' views on the modifiable determinants (barriers and facilitators) of human antibiotic prescribing using the TDF and the COM-B model as *a priori* coding frameworks. As a secondary objective, this study aimed to offer insights into possible behavioural change strategies to promote appropriate prescribing behaviours by applying the lenses of the Behaviour Change Wheel.

Materials and methods

This study employed a qualitative meta-synthesis approach, following the methodology outlined by Sandelowski and Barroso [23]. The purpose of meta-synthesis is to identify specific research questions and gather, select, evaluate, summarize and integrate qualitative evidence to address these questions. By engaging in qualitative meta-synthesis, researchers can provide new interpretations of the findings from primary studies.

In this meta-synthesis, the authors constructed their own interpretation of the data derived from the experiences shared by research participants. The themes or concepts that emerged in the final meta-synthesis were therefore distinct from the original lived or recounted experiences shared with the primary researchers. They represented 're-interpretations and integrated interpretations' of the original study result thus constituting a secondary-level analysis.

The study involved a strategic literature search after defining the research synthesis and determining the target. The included studies were evaluated using an accepted assessment tool, and the findings were extracted and analysed through a thematic inductive approach, forming a qualitative meta-summary as defined by Sandelowski and Barroso. Subsequently, comparison of the findings from the included studies was performed, leading to the creation of a meta-synthesis using the 'best-fit' framework synthesis method [24].

We employed the TDF [21] and the COM-B model [22] (Figure 1) as a coding matrix to interpret the findings of the included studies by providing a comprehensive understanding of the factors influencing antibiotic prescribing behaviours.

The study protocol was preregistered with the PROSPERO database (ID: CRD42023394430), and the meta-synthesis was

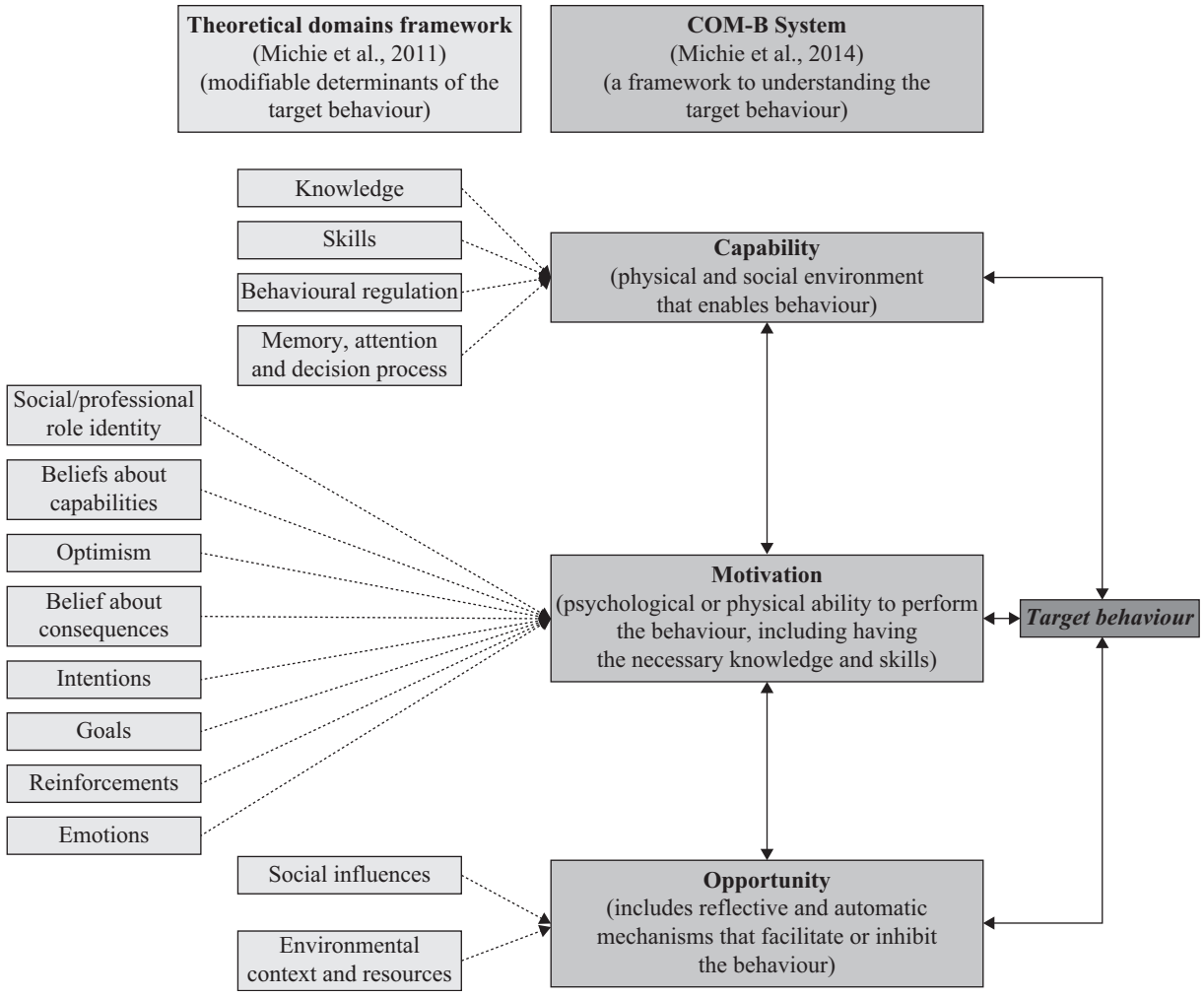

Figure 1. The Theoretical Domains Framework and the COM-B model.

reported in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA 2020 statement) [25].

Inclusion and exclusion criteria

We included qualitative research studies or mixed-methods studies that employed qualitative data collection and analysis methods. These studies were eligible if they reported the perspectives, opinions, or views of prescribers of any discipline, regarding at least one modifiable barrier or facilitator to antibiotic prescription for the treatment of any infectious disease. The target clinical population of the studies could encompass patients of any age.

Search strategy

The search strategy combined terms for Sample (prescribers), Phenomenon of interest (antibiotic prescribing behaviour), Study design (qualitative data collection tools), Outcome (prescribers' attitudes) and Research design (qualitative approach) (see Supplementary Table S1 for details regarding the search string). The following databases were searched from their inception until February 2023: Embase, PubMed, Scopus, Web of Science, CINAHL, ProQuest. We searched the reference lists of relevant articles to screen for any relevant studies.

Study selection and data extraction

Results for each search were exported into reference manager software Zotero [26] and articles from non-English language journals and duplicates were removed.

Two researchers (M.A. and M.P.) independently and sequentially evaluated titles, abstracts and papers to determine their relevance to the research question. Any discrepancies between the reviewers were resolved through face-to-face discussions with a third author, S.B. The reasons for rejecting each paper were documented.

M.A. conducted the data extraction process using a pre-tested electronic form. This involved extracting data to facilitate quality assessment, provide study characteristics, and collate contents related to barriers and facilitators of antibiotic prescribing behaviours. Whenever available, verbatim quotes supporting the analysis of the primary authors were extracted to illustrate and reinforce their interpretations.

To ensure the accuracy of data extraction, a second researcher (S.B.) reviewed the data extraction for 10 papers without identifying any inaccuracies.

Quality appraisal

The quality of the papers was assessed using the Critical Appraisal Skills Programme (CASP) assessment tool for qualitative research [27]. The CASP checklist was adapted from a checklist form to a spreadsheet form that allowed for a more in-depth discussion of potential methodological challenges in the primary studies. The modified forms included the following domains: research aims, methodology, research design, recruitment strategy, data collection, data analysis, reflexivity, ethical considerations, findings, and value of research. The overall quality assessment of 'high', 'medium' or 'low' was based on the evaluation by two reviewers and active discussion until consensus was reached in the case of rating discrepancies. No studies were excluded as a result of the quality assessment; rather, the methodological rigour of each contributing study contributed to the confidence assessments of each review finding.

Evidence synthesis

The process of data synthesis in this study followed the 'best-fit' framework synthesis method, which is based on the framework method for analysing qualitative data [24]. The a priori coding framework used for this synthesis was the TDF. This approach offers a structured and transparent way to synthesize large amounts of data and simplifies the creation of coding frameworks or 'matrices' outlining the key stages of the evidence synthesis.

Initially, one author (M.P.) coded each data extract into the relevant 14 domains of the TDF. The categorization was independently verified by two researchers, S.B. and M.A., who had extensive experience with the TDF. Any disagreements among the researchers were resolved through discussion until a consensus was reached. At this stage, the data extracts were also classified as barriers or facilitators to antibiotic prescribing behaviour.

S.B. reviewed the coded data extracts to explore relationships, and clusters were formed when concepts within each domain showed commonalities. These clusters were further condensed into higher-level concepts related to prescribers' behaviours, leading to the synthesis of a set of barriers and facilitators.

M.A., M.P. and S.B. collectively reviewed the TDF-coded matrix along with the final set of barriers and facilitators to ensure agreement. Subsequently, the identified barriers and facilitators were mapped to the relevant domains of the TDF by two researchers (M.A. and S.B.). Once the domains were determined, all potentially effective behaviour change techniques (BCTs) for those domains were identified using the mapping table by Cane and colleagues [28], which links BCTs to TDF domains.

Results

Figure 2 shows a PRISMA 2020 flow diagram summarizing the identification, screening and inclusion of studies. The search in electronic databases yielded 6683 records, from which 2909 remained after deduplication. The screening of the title and abstract excluded 2709 records as not relevant for the current meta-synthesis, leaving 200 articles for full-text assessment. Of these, 137 were excluded as not fulfilling inclusion and exclusion criteria, yielding a final set of 63 articles for inclusion in the study.

Quality appraisal

Supplementary Figure S2 displays the quality assessment results for the included qualitative studies. Based on the CASP criteria, the majority of the studies (60; 95%) [16,29–87] were determined to have a low risk of bias. In contrast, three studies (5%) [88–90] were classified as having a moderate risk of bias. The main criteria poorly addressed was the researcher's reflexivity.

Description of included studies (meta-summary)

Table I shows the characteristics of the 63 studies included in the meta-synthesis.

Geographical location of studies

The majority of studies were conducted in Europe (31; 49%) [16,29,31–37,39–44,47,49,54,56,57,65–70,80,82–85,89], with only a limited amount of research conducted in Africa [77] (1; 2%). A more detailed distribution of studies by country is represented in Figure 3.

Prescriber characteristics

The subjects participating in the included studies predominantly consisted of solely physicians (42; 67%) [29–35,37,38,40–43,46,47,49,51–53,56,58–60,62,63,65–67,69–71,74,75,77,79–82,84,85,87,90]. In seven studies (11%) [48,50,54,55,57,83,86], both physicians and nurses were involved as prescribers and in eight articles (13%) [16,39,44,45,64,72,88,89], pharmacists were also included. Other professionals involved as prescribers, although to a lesser extent, included veterinarians [45], medical interns [61], informal health providers [64], paediatricians [89] and advanced practice providers [78]. The prescriber type was not specified in three studies [36,73,76].

Regarding the specialty of the prescribers, the majority were general practitioners (GPs) (36; 57%) [29,30,32–35,37,41–44,46,51,53,57,60,63–65,67–75,78,80,84–87,89,90]. Other specialties mentioned, although to a lesser extent, include urologists and surgeons [31]; infection specialists, oncologists, anaesthesiologists, gastroenterologists, respiratory specialists, haematologists [40]; periodontologists, oral surgeons, implantologists and endodontists [49]; geriatricians [16,54]; palliative care physicians [54]; internists [31,54,55]; family physicians [55], paediatricians [55,59,61], emergency physicians [55], nursing home physicians [56], orthopaedists [61], and dentists [66,77,81,82]. Other professions of the subjects included in the studies were nurses [16,45,56,83], nurse assistants [56], nurse practitioners [59], microbiologists [16] and primary care providers [52]. The specialty of the prescribers was not specified in six studies [36,38,39,48,50,88].

Practice areas and clinical settings

Most of the studies included in the analysis were conducted in both urban and rural areas (28; 44%) [29,32–36,38,43,44,46,48,50,51,57,64–67,69,75,77,79–81,83,85,88,90]. Eleven studies [30,41,42,45,49,52,62,70,78,84,86] specifically focused on urban areas, while three studies [54,55,87] focused on

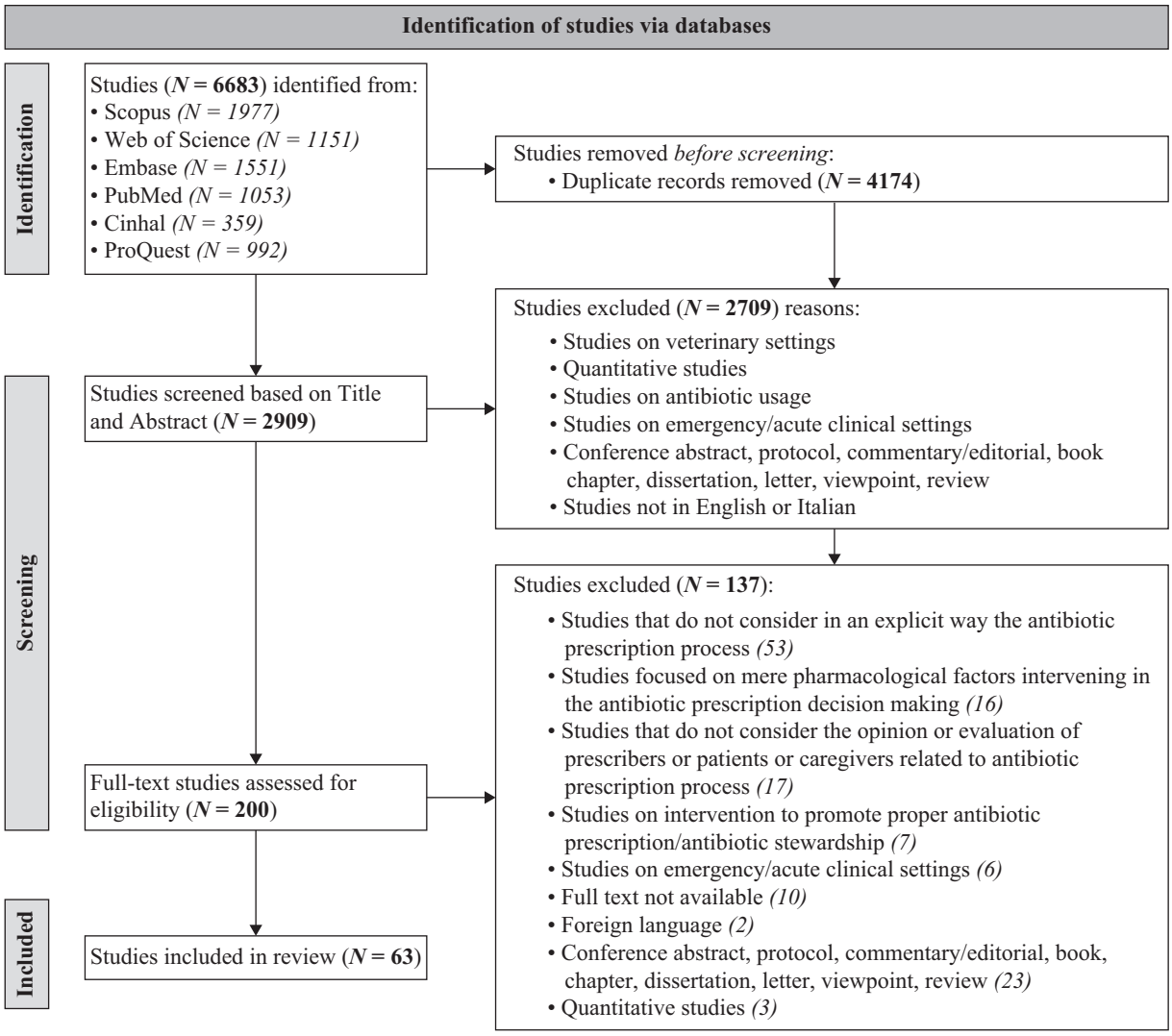

Figure 2. PRISMA 2020 flow diagram for new systematic reviews that included searches of databases only.

rural areas. Twenty-one studies (33%) [16,31,37,39,40,47,53,56,58–61,63,68,71–74,76,82,89] did not provide specific information regarding the practice area.

Regarding clinical conditions of interest, the following were identified: respiratory tract infections (23; 37%) [30,35–37,41,44,46,48,51,54,55,57,63,65,71,79,80,83–85,87,88,90], urinary tract infections (6; 9%) [35,36,52,54,56,84], and dermatologic infections (2; 3%) [35,36,83]. Three studies (4%) [43,49,77] focused on dental infections, while two studies focused on otitis/middle-ear infection [35,68] and one study (2%) focused on acute infectious conjunctivitis [69]. Finally, one study involved patients with influenza-like illnesses [29].

Thirty-two studies (51%) did not specify a specific clinical area [16,31–34,38–40,42,45,47,50,53,58–62,64,66,67,70,72–76,78,81,82,86,89].

The primary work setting for the included studies was predominantly in primary care (42; 67%) [29,30,32–36,41–45,50,53,55,56,60,63–75,78,80–82,84–87,89,90]. Twelve studies (19%) were conducted in a hospital setting [31,39,40,47,61,62,76,77,79]. Other work settings mentioned included community health centres [48,49], rural health units [88], private clinics [52,58,59,88], long-term care facilities [16], nursing homes [54,83] and municipal acute care units [54]. Only three included studies (5%) did not provide information about the specific work setting [37,46,51].

Study designs

Considering the nature of the research approach, the majority of the studies employed a qualitative research design (55; 87%) [16,29,31–48,50,52–54,56–60,62,64–68,70,72–89]. A smaller portion of the studies adopted a mixed-methods approach (8; 13%) [30,49,51,61,63,69,71,90]. The predominant methods employed for data collection were interviews (39; 62%) [16,29,31,36,37,39,40,43,44,47–50,52,53,55–59,62–68,70,73–75,77,78,81,83,84,86,88,90], focus groups (7; 11%) [38,41,60,61,85,87,89], and observations (2; 3%) [42,71]. Several studies utilized a combination of two or more data collection methods (14; 22%) [30,32–35,45,46,54,69,72,76,79,80,82]. Data analysis was carried out using various techniques, including thematic analysis (36; 57%)

Table I
Study characteristics

First author, year of study	Country of study	Aim(s) of the study	Prescriber sample (*N*; age range min—max or mean age, years; % women)	Type of prescriber(s)	Prescriber(s) specialty	Practice area	Clinical condition	Target patient age	Work setting	Research design	Method of data collection	Method of data analysis	Theoretical perspective
Ashdown, 2016	UK	To investigate which factors influence GPs' antibiotic prescribing decision in the management of at risk children with ILI	41; 0—30; 58.5%	Physician	GP	Urban, rural	ILI	Paediatric	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Biezen, 2019	Australia	To compare GPs' and parents' views on antibiotics for RTI in young children	20; 31—70; 30%	Physician	GP	Urban	RTI	Paediatric	Primary care	Mixed-method	Interviews, focus groups	Thematic analysis	Not specified
Björkman, 2010	Sweden	To explore and describe perceptions of antibiotic prescribing among Swedish hospital physicians	20; 31—70; 5%	Physician	Internists, urologists, urgeons	Not specified	Not specified	Adult	Hospital	Qualitative	Interviews	Thematic analysis	Phenomenology
Bjornsdottir, 2001	Iceland	To explore GPs' reasons for prescribing antibiotics by telephone	10; 32—66; 20%	Physician	GP	Urban, rural	Not specified	Adult	Primary care	Qualitative	Observations, interviews	Open coding, axial coding, and selective coding	Grounded Theory
Bjornsdottir, 2002	Iceland	To explore GPs' views on their obligations with respect to diagnosing infections and prescribing antibiotics	10; 48; 20%	Physician	GP	Urban, rural	Not specified	Paediatric, Adult	Primary care	Qualitative	Observations, interviews	Open coding, axial coding, and selective coding	Grounded Theory
Bjornsdottir, 2002	Iceland	To explore physicians' perceived reasons for deciding to prescribe antibiotics	10; 48; 20%	Physician	GP	Urban, rural	Not specified	Adult	Primary care	Qualitative	Observations, interviews	Open coding, axial coding, and selective coding	Grounded Theory
Bjornsdottir, 2010	Iceland	To understand the use of evidence by GPs in the diagnostic process preceding antibiotic prescribing, and to explore changes over time in this diagnostic process	10; 48; 20%	Physician	GP	Urban, rural	Dermatological infection, acute bronchitis, pneumonia, UTI, tonsillitis, sinusitis, middle-ear-infection	Adult	Primary care	Qualitative	Observations, interviews	Open coding, axial coding, and selective coding	Grounded Theory

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Table I (*continued*)

First author, year of study	Country of study	Aim(s) of the study	Prescriber sample (*N*; age range min–max or mean age, years; % women)	Type of prescriber(s)	Prescriber(s) specialty	Practice area	Clinical condition	Target patient age	Work setting	Research design	Method of data collection	Method of data analysis	Theoretical perspective
Boiko, 2020	UK	To investigate contemporary patient expectations and experiences of antibiotic prescribing in England	31; 62; 77,4%	Not specified	Not specified	Urban, rural	UTI, RTI, dermatological infection	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Butler, 1998	UK	To better understand reasons for antibiotics being prescribed for sore throats	38; N/A; N/A	Physician	GP	Not specified	URTI; sore throat	General population	Not specified	Qualitative	Interviews	Content analysis	Not specified
Chandy, 2013	India	To explore perceptions of major stakeholders on antibiotic prescribing behaviours	53; 19–66; N/A	Physician	Not specified	Urban, rural	Not specified	General population	Primary care, hospital, pharmacy	Qualitative	Focus group	Content analysis	Not specified
Charani, 2013	UK	To identify: (1) attitudes and perspectives of healthcare professionals on antimicrobial prescribing; (2) barriers to and facilitators of adherence to quality improvement interventions in antimicrobial prescribing; and (3) determinants of antimicrobial prescribing behaviours including contextual, environmental and social factors	39; N/A; N/A	Physician, nurse, pharmacist	Not specified	Not specified	Not specified	General population	Hospital	Qualitative	Interviews	Content analysis	Not specified
Christensen, 2022	Norway	To explore factors affecting hospital physicians' antibiotic prescribing practices to identify potential targets for improvement of future ASPs	14; 29–66; 64%	Physician	Infectivologists, oncologists, anesthesiologists, surgeons, gastroenterologists, pneumologists, haematologists	Not specified	Not specified	General population	Hospital	Qualitative	Interviews	Thematic analysis	Not specified

Coenen, 2000	Belgium	To explicate GPs' diagnostic (and therapeutic) decisions regarding adult patients who consult them with complaints about coughing, and to investigate what determines decision making	24; 35; 54%	Physician	GP	Urban	RTI	Adult	Primary care	Qualitative	Focus groups	Content analysis	Not specified
Colliers, 2021	Belgium	To describe how patients present their problem and how GPs interact with this and elicit the ICE of patients, and in what possible ways this doctor—patient communication relates to antibiotic prescribing for RTIs in out-of-hours care	19; 26—64; 63%	Physician	GP	Urban	Not specified	Adult, paediatric	Primary care	Qualitative	Observation (analysis of video recordings)	Descriptive inductive and deductive analysis	Not specified
Cope, 2015	UK	To produce an account of the attitudes of general practitioners towards the management of dental conditions in general practice, and to explore how GPs use antibiotics in the treatment of dental problems	17, N/A; 53%	Physician	GP	Urban, rural	dental infection	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Courtenay, 2019	UK	To identify the factors that influence nurse and pharmacist prescriber management of RTIs	21; N/A; N/A	Pharmacist; nurse	GP	Urban, rural	RTI	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Theoretical Domains Framework
da Silva-Brandao, 2023	Brazil	To explore how in-locus and multi-level social factors influence antibiotic prescriptions and dispensing practices in the context of human and animal health in primary care in Brazil	26; 22—52; 72%	Physician, pharmacist, nurse, veterinarian	GP, pharmacist, nurse, veterinarian	Urban	Not specified	Adult	Primary care	Qualitative	Interviews, observations	Thematic analysis	One Health approach

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Table I (*continued*)

First author, year of study	Country of study	Aim(s) of the study	Prescriber sample (*N*; age range min–max or mean age, years; % women)	Type of prescriber(s)	Prescriber(s) specialty	Practice area	Clinical condition	Target patient age	Work setting	Research design	Method of data collection	Method of data analysis	Theoretical perspective
Dallas, 2014	Australia	To explore the attitudes of trainees in general practice towards antibiotic use and resistance, and the perceived influences on their prescribing	17; N/A; 82%	Physician	GP	Urban, rural	URTI, acute bronchitis	General population	Not specified	Qualitative	Interviews, focus group	Iterative Thematic Analysis and Constant Comparison	Not specified
De Souza, 2006	Ireland	To determine the factors that influence non-consultant hospital doctors in their decision to prescribe antimicrobial agents	22; N/A; 36%	Physician	Non-consultant hospital doctors	Not specified	Not specified	General population	Hospital	Qualitative	Interviews	Thematic analysis	Framework method
Dempsey, 2014	USA	To identify and understand primary care clinician perceptions about antibiotic prescribing for acute bronchitis	26; N/A; N/A	Physician; nurse	Not specified	Urban, rural	Bronchitis	Adult	Hospital, community health center	Qualitative	Interviews	Structural and thematic analysis	Not specified
Dooling, 2014	Egypt	To understand the reasons for prescribing antibiotics for ARI	40; N/A; N/A	Physician and pharmacists	Not specified	Urban, rural	ARI	Adult	Hospital, rural health units, private clinics	Qualitative	Interviews	Thematic analysis	Not specified
Dormoy, 2021	France	To explore dentists' perceptions of antibiotic resistance	17; 44,7; 35%	Physician	GP, periodontology; oral surgery; implantology; endodontics	Urban	Dental infection	Adult	Community health center	Mixed-method	Interviews	Thematic analysis	Not specified
Emgard, 2021	Tanzania	To describe primary healthcare workers' experiences of antibiotic prescription for children under 5 years of age and their conceptions of antibiotic resistance	20; 31–65; 50%	Physician, nurse	Not specified	Urban, rural	Not specified	Paediatric	Primary care	Qualitative	Interviews	Content analysis	Phenomenology
Fleming, 2014	Ireland	To explore healthcare professionals' views of antibiotic prescribing in long-term care facilities	37; N/A; 65%	Physician, nurse, pharmacist	GP, geriatricians, microbiologists, nurses, pharmacists	Not specified	Not specified	Elderly	Long-term care facilities	Qualitative	Interviews	Content analysis	Theoretical Domains Framework

Fletcher-Lartey, 2016	Australia	To describe the role patient expectations play in GPs' antibiotic prescribing in URTIs	32; N/A; N/A	Physician	GP	Urban, rural	URTI	General population	Not specified	Mixed-method	Interviews	Thematic analysis, typologies and explanatory analysis	Not specified
Grigoryan *et al.*, 2019	USA	To understand why primary care providers choose certain antibiotics or durations of treatment and the sources of information they rely upon to guide antibiotic-prescribing decisions	18; N/A; 50%	Physician	Primary care providers	Urban	UTI	General population	Clinic	Qualitative	Interviews	Thematic analysis	Not specified
Guo, 2021	Singapore	To explore processes underpinning decision-making for antibiotic prescribing	30; 27—69; 60%	Physician	GP	Not specified	Not specified	General population	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Harbin, 2022	Norway	To explore in-depth both physicians' and nurses' perceptions of persisting barriers and facilitators of appropriate antibiotic use after the implementation of a structured antibiotic improvement programme	25; 43; 20%	Physician, nurse	GP, geriatricians, palliative doctors, internists	Rural	RTI, UTI	Elderly	Nursing homes, municipal acute care units	Qualitative	Interviews, focus group	Thematic analysis	Not specified
Hart, 2006	USA	To examine social processes — to provide insight into the antibiotic prescribing process	21; 32—58; 43%	Physician, nurse	Family physicians, internists; paediatricians, emergency doctors	Rural	ARI	General population	Primary care	Qualitative	Interviews	Open coding, axial coding, and selective coding	Grounded Theory
Hartman, 2022	Poland, Netherlands, Norway; Sweden	To identify relevant factors that contribute to antibiotic prescribing for UTIs in frail older adults	61; 27—69; N/A	Physician	GP, nursing home doctors, nurses, nurse assistant	Not specified	UTI	Elderly	Primary care	Qualitative	Interviews	Thematic analysis	Framework method
Horwood, 2016	UK	To investigate healthcare professional diagnostic and antibiotic prescribing decisions	28; N/A; N/A	Physician, nurse	GP	Urban, rural	RTI	Paediatric	Primary care	Qualitative	Interviews	Thematic analysis	Not specified

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Hosoglu, 2021	Turkey	To understand the relevant factors involved in antibiotic prescription in primary care settings and the barriers obstructing appropriate antibiotic use	14; N/A; N/A	Physician	Family physicians	Not specified	Not specified	Adult	Primary care; private clinic	Qualitative	Interviews	Thematic analysis	Not specified
Kohut, 2020	US	To identify the factors that make perceived patient demand so powerful in shaping antibiotic prescribing decisions	25; N/A; 64%	Physician	Family physicians, internists, paediatricians, nurse practitioners	Not specified	Not specified	General population	Private clinic	Qualitative	Interviews	Content analysis	Not specified
Kotwani, 2010	India	To find out the various factors involved in antibiotic prescribing	36; N/A; N/A	Physician	GP	Not specified	Not specified	Adult	Primary care	Qualitative	Focus groups	Open coding, axial coding, and selective coding	Not specified
Lam, 2021	Hong Kong	To explore the antibiotic prescribing behaviours of the medical interns in Hong Kong and their barriers to appropriate antibiotic prescription	7; N/A; N/A	Medical intern	Internal medicine, surgery, paediatrics, orthopaedics	Not specified	Not specified	General population	Hospital	Mixed-method	Focus groups	Content analysis	Not specified
Livorsi, 2015	Indiana	To understand the context in which physicians practice and the professional and psychosocial factors that influence physicians' antibiotic-prescribing decisions	30; 30–50; 33%	Physician	Hospitalist medicine, pulmonary/critical care	Urban	Not specified	General population	Hospital	Qualitative	Interviews	Thematic analysis	Not specified
Lum, 2018	Australia	To establish the dominant factors influencing GP decision-making in antibiotic prescribing	10; 4–24; 50%	Physician	GP	Not specified	RTI	General population	Primary care	Mixed-method	Interviews	Content analysis	Not specified
Nair, 2019	India	To understand the drivers for various antibiotic prescription choices	21; N/A; N/A	Physician, pharmacists, informal health providers, nurses	GP	Urban, rural	Not specified	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Framework method

O'Doherty, 2019	Ireland	To investigate why GPs in Ireland continue to prescribe antibiotics for acute respiratory tract infection, despite widely publicized guidelines and evidence of their ineffectiveness	13; N/A; 31%	Physician	GP	Urban, rural	ARI	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Oliveira, 2017	Portugal	To explore issues influencing antibiotic prescribing by Portuguese dentists.	14; N/A; 29%	Physician	Dentists	Urban, rural	Not specified	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Framework method
Petursson, 2005	Iceland	To explore the reasons given by Icelandic general practitioners for their non-pharmacological prescribing of antibiotics	16; N/A; N/A	Physician	GP	Urban, rural	Not specified	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Phenomenology
Philp, 2010	UK	To understand why nurse practitioners in primary care prescribe antibiotics for some cases of otitis media	8; N/A; N/A	Nurse	GP	Not specified	Otitis	Paediatric	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Raspopovic, 2016	Montenegro	To identify factors that affect improper prescribing of antibiotics, which will further facilitate the implementation of specific interventions to improve the use of antibiotics and the emergence of antibiotic resistance in our conditions	8; N/A; N/A	Physician, pharmacists, paediatrician	GP	Not specified	Not specified	Adult, paediatric	Primary care	Qualitative	Focus group	Thematic analysis	Not specified
Rose, 2006	UK	To investigate the non-clinical determinants of the management of acute infective conjunctivitis in children	39; N/A; N/A	Physician	GP	Urban, rural	Acute infective conjunctivitis	Paediatric	Primary care	Mixed-method	Interviews, survey	Thematic analysis	Not specified
Saliba-Gustafsson, 2021	Malta	To explore GPs' understanding of antibiotic use and resistance, and	20; 52; N/A	Physician	GP	Urban	Not specified	Adult	Primary care	Qualitative	Interviews	Content analysis	Not specified

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Table I (*continued*)

First author, year of study	Country of study	Aim(s) of the study	Prescriber sample (*N*; age range min—max or mean age, years; % women)	Type of prescriber(s)	Prescriber(s) specialty	Practice area	Clinical condition	Target patient age	Work setting	Research design	Method of data collection	Method of data analysis	Theoretical perspective
		describe their perceived barriers and facilitators to prudent antibiotic prescribing for acute RTIs in Malta											
Scott, 2001	USA	To identify those aspects of physician-patient communication that influence physicians to prescribe antibiotics for respiratory infections	298; N/A; N/A	Physician	GP	Not specified	ARI	Adult, paediatric	Primary care	Mixed-method	Observations	Content analysis	Not specified
Sharaf, 2021	Qatar	To optimize appropriate antibiotic prescription and use, which would support the implementation of an ASP	50; N/A; N/A	Physician; pharmacists	GP	Not specified	Not specified	Adult	Primary care	Qualitative	Interviews, focus groups	Open coding, axial coding, and selective coding	Not specified
Sharara, 2021	USA	To understand the intertwined work systems of discharge antibiotic decision-making and antibiotic medication management to identify barriers to and strategies for discharge Antibiotic Stewardship	37; N/A; 81%	Not specified	GP	Not specified	Not specified	Adult	Primary care	Qualitative	Interviews	Content analysis	Not specified
Shokouhi, 2017	Iran	To explain family physicians' beliefs about antibiotic prescription in Ahvaz	8; 37,8; N/A	Physician	GP	Not specified	Not specified	Adult	Primary care	Qualitative	Interviews	Content analysis	Not specified
Simeoni, 2022	Canada	To identify potentially modifiable determinants of antibiotic prescribing for patients presenting to primary care with URTI symptoms	20; N/A; 35%	Physician	GP	Urban, rural	Not specified	Adult	Primary care	Qualitative	Interviews	Content analysis	Theoretical Domains Framework
Singh, 2021	South Africa, India	To investigate the drivers for infection management and antimicrobial	61; N/A; N/A	Not specified	Surgeons	Not specified	Not specified	Adult	Hospital	Qualitative	Observation, interviews	Open coding, axial coding, and selective coding	Grounded Theory

		stewardship across high-infection-risk surgical pathways											
Sneddon, 2022	Ghana	To explore the antibiotic prescribing behaviour and knowledge of teams treating dental patients in two Ghanaian hospitals	15; N/A; N/A	Physician	Dentist team	Urban, rural	dental infection	Adult	Hospital	Qualitative	Interviews	Thematic analysis	Not specified
Spencer, 2022	Nashville, USA	To identify social, behavioural, and environmental drivers of outpatient antibiotic prescribing for paediatric patients	55; N/A; 78%	Physician, advanced practice provider	GP	Urban	Not specified	Paediatric	Primary care	Qualitative	Interviews	Thematic analysis	Grounded Theory
Stefan, 2022	Massachusetts, USA	To identify factors that influence providers' decisions to prescribe antibiotics in patients presenting to the hospital with an asthma exacerbation	16; N/A; 38%	Physician	Pneumologists, emergency doctors	Urban, rural	Asthma	Adult	Hospital	Qualitative	Interviews, focus groups	Content analysis	Theoretical Domains Framework
Strandberg, 2013	Sweden	To explore GPs' perceptions and experiences regarding antibiotic prescribing for RTIs in Swedish primary care	13; N/A; 77%	Physician	GP	Urban, rural	RTI	Adult	Primary care	Qualitative	Interviews, focus groups	Thematic analysis	Not specified
Teoh, 2019	Australia	To obtain a greater understanding of the perceptions, attitudes and factors that influence dental prescribing for all major relevant drug classes	15; N/A; N/A	Physician	Dentists	Urban, rural	Not specified	Adult	Primary care	Qualitative	Interviews	Thematic analysis	Not specified
Thompson, 2020	UK	To identify clinician and patient factors influencing urgent dental care for adults during actual appointments; and to identify elements sensitive to context	102; N/A; N/A	Physician	Dentists	Not specified	Not specified	Adult	Primary care	Qualitative	Observations, interviews	Thematic analysis	Ethnography
van Buul,2014	Netherlands	To examine factors that influence antibiotic prescribing in long-term care facilities,	26; 26–61; 81%	Physician, nurse	GP, geriatricians, nurses	Urban, rural	URTI, RTI, dermatological infection	Elderly	Nursing home	Qualitative	Interviews	Iterative thematic analysis and constant comparison	Not specified

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Table I (*continued*)

First author, year of study	Country of study	Aim(s) of the study	Prescriber sample (*N*; age range min–max or mean age, years; % women)	Type of prescriber(s)	Prescriber(s) specialty	Practice area	Clinical condition	Target patient age	Work setting	Research design	Method of data collection	Method of data analysis	Theoretical perspective
		and present a conceptual model that integrates these factors											
van der Zande, 2019	UK	To understand contextual factors related to GPs' antibiotic prescribing behaviours in low, high and medium prescribing primary care practices	41; N/A; 54.8%	Physician	GP	Urban	UTI, URTI, RTI	Adult	Primary care	Qualitative	Interviews	Thematic Analysis	Not specified
Vazquez-Lago, 2011	Spain	To ascertain GPs' opinions on and attitudes to antibiotics and resistance and discuss whether these differed from those found in other countries with lower consumption and resistance rates	33; N/A; 42.4%	Physician	GP	Urban, rural	URTI	Adult, paediatric	Primary care	Qualitative	Focus groups	Thematic analysis	Not specified
Yates, 2018	USA	To explore factors in influencing provider decisions to prescribe antibiotics	17; N/A; 70.6%	Physician, nurse	GP	Urban	Not specified	Adult, paediatric	Primary care	Qualitative	Interviews	Thematic analysis	Phenomenology
Yin, 2019	China	To present patterns of antibiotic prescribing by doctors in village clinics and to assess factors related to antibiotic prescribing	16; 37–68; 12.5%	Physician	GP	Urban, rural	URTI	Adult	Primary care	Mixed-method	Interviews	Content analysis	Not specified
Zhang, 2016	China	To explore the knowledge, attitudes and practices of village doctors regarding the prescribing of antibiotics for children under 15 years with URTIs	65; 40–51; 38.5%	Physician	GP	Rural	URTI	Paediatric	Primary care	Qualitative	Focus groups	Thematic analysis	Grounded Theory

ARI, acute respiratory infection; ASP, antimicrobial stewardship programme; GP, general practitioner; ICE, Ideas, Concerns and Expectations; ILI, influenza-like illness; RTI, respiratory tract infection; URTI, upper respiratory tract infection.

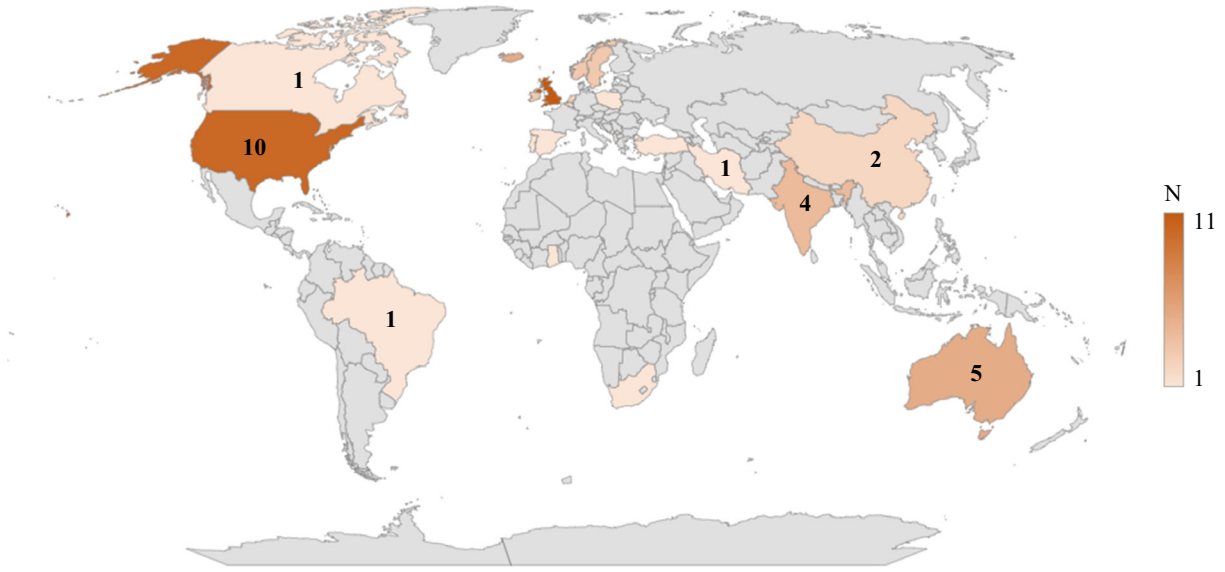

Figure 3. The geographical location of studies.

[29—31,36,40,43—49,51—54,56—58,62,64—69,77,78,80—89], content analysis (16; 25%) [16,37—39,41,50,59,61,63,70,71,73—75,79,90], open, axial and selective coding (8; 13%) [32—35,55,60,72,76] as well as descriptive and deductive analysis (1; 2%) [42]. In most instances, the studies did not explicitly mention a specific theoretical framework employed for designing the qualitative studies (41; 65%) [29,30,36—43,46,48,49,51—54,57—63,65,68—74,77,80,81,83,84,88—90]. However, among those studies that did provide details on theoretical frameworks, the following were mentioned: Grounded Theory (8; 13%) [32—35,55,76,78,87], Phenomenology (4; 6%) [31,50,67,86], TDF (4; 6%) [16,44,75,79], Framework method (4; 6%) [47,56,64,66], One Health approach (1; 2%) [45] and Ethnography (1; 2%) [82].

Modifiable determinants (barriers and facilitators) of antibiotic prescribing behaviours (meta-synthesis)

Following consensus discussions, extracts were coded into 12 of the 14 domains of the TDF between five and 12 explanatory themes extracted per domain (Table II, Figure 4). The domains related to 'Intentions' and 'Optimism' have not been identified.

Further clustering of similar concepts within domains produced 45 facilitators and 36 barriers influencing antibiotic prescribing behaviour (see Supplementary data S3 for further details).

The key themes regarding the final barriers and facilitators to antibiotic prescribing behaviour within relevant domains of the TDF and COM-B are described below and summarized in Table II. These are grouped into three themes comprising 'capabilities', 'motivations' and 'opportunities'. We have also illustrated the process of selecting and characterizing BCTs by providing hypothetical examples prepared by the research team.

Key theme one: capability

Capability refers to the combination of mental and physical abilities that affect how healthcare professionals prescribe antibiotics. This includes factors that either support or hinder their ability to make appropriate prescribing decisions. These factors are linked to professionals' knowledge, skills, memory, attention, decision-making processes, and strategies for regulating their behaviour.

The study findings indicate that several capability factors influence antibiotic prescribing behaviours. These factors include professionals' understanding and awareness of AMR and their capacity to influence patients' behaviour through negotiation and interpersonal skills. Additionally, their ability to adhere to pharmacological guidelines plays a role in determining the appropriateness of their antibiotic prescription practices.

In more detail, the facilitators of prescribing behaviours associated with capability can be attributed to professionals' experience of significant clinical uncertainty regarding the necessity of antibiotics and regarding the progression of the patient's disease [16,29,31,33—35,40,44,45,48—51,54,55,57,58,60,62,67,72,73,79,81,83].

Other facilitating factors stem from professionals' positive attitudes towards antibiotic prescribing practices [32,34,37], which may be influenced by established work habits and a lack of personalized feedback regarding their own antibiotic prescribing rates [48,75,84]. The lack of competencies in adopting delayed prescribing strategies and inadequate patient education skills also serve as significant facilitators [29,42,44]. In contrast, there are potential factors that prevent inappropriate antibiotic prescription. These barriers can be attributed to negative experiences resulting from the adverse consequences of antibiotic use in the past. In particular, prescribers may display a conservative inclination when it comes to following treatment approaches employed with previous patients [16,29,30,46,49,50,56,57,71,75,78,81,83,90]: clinicians' deep knowledge of the patients' history may orient a wiser antibiotic prescription. Moreover, highly proficient clinical and diagnostic skills [29,37,41,44,50,56,57,67,68,70,75,81,85,90] along with the absence of continuous training on updated evidence regarding antibiotics [31,58,74,87], constitute additional relevant obstacles to

Table II
Qualitative synthesis: facilitators and barriers of (inappropriate) antibiotic prescribing behaviours in the included papers

Key theme	Domain in the TDF and number of studies coded within domain (and references)	Facilitators (F) and Barriers (B)	Illustrative excerpts supporting the themes
Capability	Memory, attention and decision processes (*N*=32) [14,27–32,36–38,40,41,44–47,49–51,53,53,56,58,59,63,64,68,69,75,77,79,80]	Clinical uncertainty about whether antibiotics are indicated (F)	I think that we, because of uncertainty, may be somewhat more active. And for the same reason that we sometimes give more broad-spectrum antibiotics than they do for example at the department of infectious diseases, it will be. When you do not know, you use something stronger. [27]
		Clinical uncertainty about diagnosis and illness progression (F)	Sometimes, I feel it is difficult to choose the correct dose and interval of antibiotics. And I am not sure whether I should prescribe antibiotics if the child had fever alone or when there is uncertainty in the diagnosis … [83]
		Patterns of overprescribing practice (F)	The same antibiotics are used in treatment as in the prophylaxis, as I told you about. This is not so good, I know, but this is the way it is. The theory is theory but this is practice. That's why it is rather common that fluoroquinolones are also used in uncomplicated UTI. Yes, I have seen resistant bacteria sometimes, with for example *Lexinor*. But this is nothing I have been thinking about. [27]
		Shared decision-making (B)	It is always important in family medicine that we establish a very close and long relationship with your patient. And a correct relationship is always a partnership. So, when you have established a partnership, that means there is a great degree of trust and communication channels are naturally opened. So once that happens, it is very easy to be able to come up with a management plan that both agree on. And usually, the patients would listen to the doctor. [49]
		Trial and error approach (B)	… if a young woman … says she has a terrible burning sensation due to cystitis … symptoms … I mean, she is unable to bring the urine and these drugs have to get to the countryside … it is no good making a fuss about it, but then you just prescribe some medication and … then wait and see. [28]
		Antibiotic cost-benefit trade-off (B)	I may treat someone who is very frail, but I wouldn't treat someone who is well … simply because the consequences of not treating would be more serious, with the risk of hospitalisation. So I am talking about a threshold prescribing, and I think I do adjust that threshold according to the individual … based on their risk. [40]
	Knowledge (*N*=33) [14,26–29,31–34,36,40,41,44–48,50–52,56,60,63,68,71,74–76,78,81–84]	Prescriber unaware of antimicrobial resistance (F)	Antibiotic resistance is not a problem when you look at community prescription patterns. For us GPs, it's not a big issue. [47]
			… writing a prescription for an antibiotic is seen as an action or a response, a quick action or a quick response to some problem … I would doubt that resistance is at the forefront of that decision at that time. [14]
		Prescriber knowledge about antibiotics side effects (B)	I know antibiotics are not good. It kills the good bacteria as well as the bad bacteria … [26]
		Prescriber lack of clinical knowledge (F)	I think we use them [antibiotics] without even knowing why, out of fear [41]
		Prescriber knowledge of procedural guidelines to manage patient care (F)	I believe in the importance of using research and empiric evidence to support clinical practice. I also don't have a lot of confidence in my own memory of my education or of the longevity of the lessons I received 10, 15, 20 years ago in medical school. Knowledge changes. Available medications change. Antibiograms change. People change. And even for things I treat regularly, the knowledge around them does change. And so, I think it serves our patients better to provide treatments that are more aligned with the best available evidence. [74]
		Familiarity with specific drugs (B)	I think a lot of it has to do with familiarity and comfort. [48]
		Familiarity with the treatment of serious infectious (B)	Yes, this [infectious diseases] is a major part of our work … If you have an infection unit [at the hospital] it may look different than here, but for us infections are a very large part of our activities, I would say. [27]
		Prescriber lack of knowledge about antibiotics dosage (F)	Sometimes, I feel it is difficult to choose the correct dose and interval of antibiotics. And I am not sure whether I should prescribe antibiotics if the child had fever alone or when there is uncertainty in the diagnosis … [83]
		Prescriber lack of knowledge about patients' previous treatment pathway (F)	I would look to see do they have a temperature, not all the elderly will develop a temperature, some of them are immuno-compromised for various reasons so they don't always necessarily have a temperature. So looking at sats, looking at clinical findings, looking at have they gone off food, are they obviously unwell in themselves. I think that is one thing that sometimes guidelines don't capture. They don't capture that sort of, they will have criteria set down but they don't cover that sort of knowing the patient bit. [14]
	Skills (*N*=36) [14,25–29,33,33,37,38,40–42,45,46,48,52–54,63–67,69–72,74,76–79,81,83,86]	Lack of skills and material to dialogue about antibiotics (F)	Some GPs will just write a prescription for 7 days with 250 mg of amoxicillin, three times a day. And it's a homeopathic dose it's a pat on the head and a piece of green paper, and the patient comes away from that consultation happy, they have got their antibiotics, they won't get better because of the antibiotics, they will get better because it is self-limiting, viral RTI. But what that health care professional is doing, is perpetuating the expectation of I am unwell, I will get antibiotics I will get better. The hard thing you have to do as a prescriber is to turn around and say you don't need antibiotics at this time. [40]

		Promote patient engagement in decision-making (B)	"It is always important in family medicine that we establish a very close and long relationship with your patient. And a correct relationship is always a partnership. So when you have established a partnership, that means there is a great degree of trust and communication channels are naturally opened. So once that happens, it is very easy to be able to come up with a management plan that both agree on. And usually the patients would listen to the doctor." [49]
		Patient education skills (B)	Generally speaking, you know I'm not impressed by the scoring systems, I've done quite a lot of paediatrics, I'm pretty confident about spotting sick children. I'm confident about guiding parents about what to do in case I've actually got it wrong and given false reassurance. So, I'm pretty confident with all that sort of stuff. [25] So you educate your patient in terms of: this is why we're not too certain on giving you antibiotics; you might have a resistance when it's over, and when you do need it, and it's more serious, it might not work as well. And a lot of the time they do tend to understand that; it's just making them aware of what's going on. [80]
		Clinical and diagnostic skills (B)	… You have to be competent, not only with your history taking … But, examination skills; you have to be able to examine … The patient; you have to be able to relate those findings … to the patient in a language that they can understand. [40]
		Continuous training about antibiotics (B)	"Training of doctors after graduation is required. Postgraduate education is required. Doctors should receive serious training in antibiotic use." [54]
		Negotiation skills (B)	"Definitely. If you're seeing patients in 10–15 min intervals, it's very hard. It's easier to write the prescription for an antibiotic than it is to have the discussion about why they may not need that." [82]
		Skills to inquire about patient's agenda (B)	''if you're seeing patients … without any continuity, then … then you can't waste it … time, so you can't observe the child in a day or two, so you're responding to some insecurity factor.'' [63]
		Skill to build trusted relationships with patients (B)	It is always important in family medicine that we establish a very close and long relationship with your patient. And a correct relationship is always a partnership. So when you have established a partnership, that means there is a great degree of trust and communication channels are naturally opened. So once that happens, it is very easy to be able to come up with a management plan that both agree on. And usually the patients would listen to the doctor. [49]
		Skill to assess patient self-care attitudes (B)	A patient often does not take the medicine when you prescribe it or it is wrongly taken. [85]
		Skill to comply with guidelines (B)	… There is one drug that you used to prescribe for chest infections and it was always for 7 days and the guidelines now are actually for 5 days, and now I always check my guide … and now I am more confident to say no actually it should only be five but when I very first started prescribing I found that really difficult … because I felt maybe I should be prescribing longer than it says on the guide, because more experienced people are telling me that, so I think when you are a newly qualified prescriber, the more experienced people can have a strong influence over you and it is not always right. [40]
	Behavioural regulation (*N*=15) [25,31,38,40,44,50,52,62,63,66,71,75,76,78,80]	Delayed prescribing (B)	… there are times when I will weaken against my better judgment but I will recommend a delayed prescription then it is up to the parents what they choose to do. [64]
		Lack of continuity of care and in-progress patient monitoring (F)	Previously they were kept in the hospital to rest the intestine, today they are sent home with two antibiotics. I think, that when we are not able to bring the patients back for a second visit, it makes us incautious and makes us use more [antibiotics] than we used before. [27] Lack of continuity, when you don't see somebody … all the time, that trust isn't built. So I think that helps, if you have continuity that helps improve judicious use of antibiotics. [82]
		Lack of comparative antibiotic prescribing rates (F)	I am happy about that, because that is all about auditing your own practice and doing things like that yes. I mean I do go through periods where I audit people that I see, what's happened, did they come back, did they get better, did they get worse, and that also kind of reassures you as well that you are either doing the right or the wrong thing … [40]
		Lack of feedback on antibiotic prescribing rate (F)	… In choosing to make a conscious decision to not give in [to a patient demanding antibiotics] I would have to deal with any possible strong negative reviews during that timeframe because I've received some strong negative reviews […] The internet is forever, and Google will find all things that my name is related to. [55]
Motivation	Social/professional role and identity (*N*=27) [14,25,26,28,29,31–35,39,41–43,49,53,57,62–64,66–68,71,76,81,84]	Valuing professional autonomy (B)	I'm a clinician and have some degree of independent practice; protocols are quite constrictive and restrictive for individual patient use. [35]
		Multidisciplinary approach (B)	I would be the one dealing with the GPs all the time on their rounds … so even though I think so and so might need an antibiotic or whatever, it is the doctors call in the end. [14] And it's something about us just increasing the understanding. We also had … internal education now in … spring where all of us doctors were given prepared … lectures, really, that we were supposed to give for everyone in the staff. Interdisciplinary, too, right down to … yes … yes I don't know, I wouldn't exactly say the cleaning[staff] …. but it was almost, so it was almost the whole … it was the whole group, and it was terrific because we … so, so we kind of get such a collective call to mobilize about the importance of … eh … reducing antibiotic use. […] it keeps us on our toes a bit more. I think the people working here also find it more interesting when there is that responsibility. […] I never get called now about … about problems with the room smelling [52]

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Table II (*continued*)

Key theme	Domain in the TDF and number of studies coded within domain (and references)	Facilitators (F) and Barriers (B)	Illustrative excerpts supporting the themes
		Unclear role responsibility (F)	… So I've got that responsibility to the health service and to society, and that partly comes with the privilege of being a prescriber … I think this is definitely part of my role. [40]
		Conceive the patient as an active player in the treatment process (B)	I think it's really hard when [GPs] say, no, no look, you know, you've got to come back and see me … if it's right on the cusp, and you're dealing with adults, I do think that you can respect the adult and say [that], because the other thing is people have had to take time off work to come in and see you [59]
			My feeling about prophylactic antibiotics for UTIs and stuff is I ask the family and the patient 'do you feel it is helping or making a difference' and if it isn't I stop it [14]
		Value patients' beneficence (F)	I think at the end of the day, you have to do the best for the patient, and that will do the best for the population. Sometimes, doing the best for the patient is not giving them antibiotics unless they need it, and that will ultimately help with antibiotic resistance. [71]
		Valuing professional authority (B)	… and some patients […] then demand treatment. […] When I am convinced that 'this is pointless, this is medically completely pointless'. Then I don't do it [prescribe antibiotics]. [79]
			Well, especially the frail older adults today, they see the doctor a bit like God. Well, that is a bit exaggerated, but you know what I mean, they do what the doctor says, they find it very important what the doctor says. [52]
		Rigid professional boundaries (F)	… So I've got that responsibility to the health service and to society, and that partly comes with the privilege of being a prescriber … I think this is definitely part of my role. [40]
	Belief about capabilities (*N*=12) [23,30,33,40,41,55,60,69,75,76,80,82]	Lack of empowerment on antimicrobial stewardship (F)	In terms of antibiotics I don't know necessarily if there is a huge role there, there are roles in other medicines management issues but not particularly antibiotics. [14]
		Confidence in diagnosis and not-antibiotic treatment (B)	You shouldn't lose your self-confidence now that there are so many different ways of testing. You should feel that you actually can make a clinical assessment, so that it's kind of going back to that. [76]
		Self-belief in decision making (B)	So I frame it in terms of 'I've looked at you very carefully. And it's really clear to me that this is an infection that is not going to benefit from antibiotics.' In fact I would be running pretty much all the risks and the harms of antibiotics, and none of the benefits, you know 'the harms of antibiotics being diarrhoea and vomiting and rash, I wouldn't want to give you any of those [side effects].'. and the other thing I say to them is, 'if I thought I could help you with antibiotics, I would give them to you in a second. [59]
		Comfort with prescribing practices (B)	You can't say I would do this every time if it was this, or I would do that every time if it was that, and if you looked at the evidence and if you looked at the huge amount of GPs you would never get anyone do the same. That's the thing because we are all different, aren't we? Our health-care beliefs are different and our experiences are different. [64]
		Overvalued perception of antibiotics benefit (F)	[…] prescribing antibiotics, is that one is concerned about, that every single prescription that is beneficial to the individual, that it is at the same time also a step towards breeding. [30]
		Self-efficacy in managing symptomatic patients (B)	More observation, yes, observation of this patient. Because if the temperature is not high, the patient may be […], a little dehydrated, or drinks little … […] Because, in general, some hematuria, or color … and … blood of urine does not mean to immediately give an antibiotic, maybe that's where irritation happened, yes, ordinary. [52]
		Self-efficacy in planning treatment and gaining patient's consent (B)	If I really don't think they need it, I try my hardest not to prescribe. If I feel it's going to end up in a huge battle, er and um then I may say, "Well I'll give you a prescription to keep. I would strongly recommend that you don't go and get this at the moment, because I honestly don't
			Think your child needs it, and it may actually make things worse rather than better. But the prescription is there, and you've got it should you need it. [53]
	Belief about consequences (*N*=20) [26,32,35,39,44,45,51,55,56, 65,66,69–71,73,75,77–79,83]	Perception of harming the professional-patient relationship (F)	I've had maybe one or two that have been really difficult and won't accept what I'm saying. But again, usually with a standby script, they're quite happy with that because they feel they've got what they want. And you've kind of not given them quite what they want. So it's a little bit of a compromise, but without completely destroying sort of your relationship, you know, your doctor/patient relationship. [53]
		Perceived lack of patient engagement (F)	We have discussed this with the partners in our call group. That you are much quicker to give antibiotics in the weekends. Just because these patients, these families are strangers. You don't know them very well. [79]
		Concern that patient will (need to) reconsult (F)	Previously they were kept in the hospital to rest the intestine, today they are sent home with two antibiotics … I think, that when we are not able to bring the patients back for a second visit, it makes us incautious and makes us use more [antibiotics] than we used before. [27]

	Concern about maintaining patient satisfaction when not giving something tangible (F)	So something else I've been saying to people recently as well is "you can feel just as poorly with a viral infection as you can with a bacterial infection". And that seems to help people, because they feel like if you don't send them away with antibiotics they haven't gone out with a licence to be ill, you know, their doctor said it's just a virus. So, saying to them, you, you will feel really poorly with this, the only difference is I can't give you something to make you better. [80]
		They're showing up in the office. They're paying for something, and they expect something in return. And my advice isn't enough. [82]
	Risk of complaints and litigation (F)	When you are working in polyclinic[s], you have [the] government on your back … but in the private sector, the issue is when … medical legal [issues arise] … or patient come after you with a lawyer letter … when things happen, their backs are not covered. [49]
		But I'm gonna play defensive and give a prescription to avoid a complaint, because complaints are so time consuming, stressful, and, at the end of the day, one is … I'm in doubt that I'm gonna get support." [80]
	Perceived risk of clinical worsening (F)	You probably do end up prescribing more for the elderly than you would for you or me who are younger, in the fact that you are always slightly worried that if you don't prescribe then they will get worse. [14]
	Expectancies of antibiotic benefit (F)	No drugs have been produced without any side effects. However, physicians should weigh up different options and see whether benefits of the drug outweigh its side effects. [70]
	Expectancies of antibiotic side-effects (B)	If we see that, when antibiotics have been used previously, the patient has had, for example, major side effects, ailments, and the urinary tract infection which they have now is not bothering them[…]. Eh … and there are no signs that the infection is spreading, like that kind of stuff. So, so then it's like to stay cool and think that "No, then we'll let it be", eh … because there's no point in exposing the patient to that again. If what we see is a recurring problem, that side effects, for example, become a major ailment for them, then we can refrain and wait. [52]
Emotions (*N*=29) [14,23,27,32, 33,36–41,45,49,50,53,54,58, 63,64,66,68,75,76,78,80–83,85]	Fear of doctor shopping (F)	… if they are absolutely insistent and I know they are pretty much going to walk out of the door and request for another doctor, I'd give them a script … [26]
		You have to use your clinical acumen. You feel if I don't give antibiotics and patient goes to another physician or to chemist who prescribes antibiotic and he gets cured. You lose a patient … [56]
	Fear of clinical consequences (F)	You probably do end up prescribing more for the elderly than you would for you or me who are younger, in the fact that you are always slightly worried that if you don't prescribe, then they will get worse. [14]
	Empathy for unwell patients (F)	I just happened to have had some patients recently of whom I thought in retrospect I just shouldn't have done it [prescribed antibiotics]. But sometimes you do it for the family. […] In the past I used to be more principled about this, I would say look, you shouldn't do this, and now I think well, it's a process for them too and I do tell them [that there is not much point], but if they can't go along with that yet then I don't push harder. [79]
	Stress/burnout (F)	… Towards the end of the day, I am a little bit more lenient, because you are tired and a bit stressed and you want to go home, and sometimes it can be an easy fix. I try not to, but sometimes, whether at the beginning of the day you weren't quite sure, you would rationalise it a bit more and explain it a bit more, whereas you might at the end of the day, you might sort of lean to like well I am not quite sure, ok just take them. [40]
	Fear of harming professional reputation (F)	"But I'm gonna play defensive and give a prescription to avoid a complaint, because complaints are so time consuming, stressful and, at the end of the day, one is … I'm in doubt that I'm gonna get support …." [42]
	Patient/family anxiety (F)	So if someone presents repeatedly to different GPs and there's actually nothing, no change on each occasion, by the third time someone's going to do something because they think," Gosh, there must be something really bad here, this person has come in three times in a fortnight, they're obviously worried, we need to do something." If you come often enough, something will be done because people's anxiety goes up. [53]
	Prescriber anxiety (F)	I know that there are instances when I have erred on the side of caution and given an antibiotic. If I was real anxious about it and thinking that if I give the antibiotic, I am playing it safe and covering just in case. In those instances, it is probably driven by fear [58]
Goals (*N*=24) [25,26,31,33,36,40,45,46,49, 51,53,55,60,62,63,71,73,74,76–78,80–82]	Sake of patient well-being (B)	… if the gentleman is going to die anyway then any antibiotic resistance is not relevant. So in my mind that is something of a mitigating thing. [79]
		At least here in long-term care … eh … here we're very concerned with finding a soothing treatment. […] there is nothing to be cured here. They should feel good; it should be about quality of life. So … if we believe that an antibiotic treatment can provide a better quality of life for the patient, yes, then that's very nice. Do we think that it can't do that, that it doesn't matter, then it's better to let it be and instead relieve any minor ailments the patient may have. There is, there is always reflection about what … the patient in focus [52]
	Sake of patient safety (F)	I tend to probably cover things a bit more because … if something goes wrong I want to make sure that the patients going to be safe [42]

(*continued on next page*)

Table II (*continued*)

Key theme	Domain in the TDF and number of studies coded within domain (and references)	Facilitators (F) and Barriers (B)	Illustrative excerpts supporting the themes
		Not losing patients (F)	I think initially I was probably a lot less confident to say to patients no, and I think now it's become a lot easier because I'm not afraid that they're going to hate me and never come back. [42] If I am not completely sure and I simply don't trust the situation, then I will [prescribe antibiotics]. In that case I think well, better safe than sorry. [79] I train junior doctors as well and sometimes, you know, I explain that it's a case of you might either lose a relationship with a patient, you know, and lose the benefit you could have had in the long term, over an antibiotic prescription. So it's a difficult balancing act. [80]
		Sake of patient satisfaction (F)	Well the concerns are patient satisfaction is not necessarily quality of care. You're being judged on what someone's expectations were when they came in and if they don't get what they think they should have got, they're not happy. And that's gonna affect your patient satisfaction scores. … It's counter-productive to the whole theory about antibiotic stewardship but that's part of the thing providers are getting judged on. It's not quality of care; that's patient satisfaction. [42]
	Reinforcement (*N*=6) [34,40,44,63,71,85]	Maintaining a good relationship with the patient (F)	I have to admit you would occasionally cave in because you don't want to make the situation worse. You don't want make their health worse but you don't want to make the doctor patient relationship worse either [47]
		Trust building (F)	Trust doesn't come ready-packaged; somewhere you have to start building that trust. [76]
		Prescribing at an appropriate rate (B)	So I know we have our weekly meeting here, where anything that — even if it's just a small thing — it will be brought up informally. I think having that constant or regular communication, I think, will help things massively. [80] It's very important for me. Because I try to prescribe the least possible antibiotics. [52]
		Align with current reporting practices (B)	Comparing to other centres, yes but so what? What you are going to do is compare your errors really to their errors. What you need to do is to compare to what you should be doing and see if that can be implemented, if you can do that. [14]
Opportunity	Social influences (*N*=54) [14,26–45,47,49–51,53,54,56–75,77,79,80,82–84,86]	Patient/family expectation and pressure for antibiotic (F)	I admit there's been times I've prescribed antibiotics that I actually don't think is appropriate. Um, but the person is so: adamant about it or difficult to deal with or just completely insistent about it, that. sometimes it's exhausting actually trying to convince them that they don't need them [antibiotics], so the path of least resistance is just to write a script, and liked There! Get out of my room. [47]
		Prescribing practices guided by hierarchical relationships (F)	I do know one supervisor in particular will give his patients antibiotics even for something that sounds very viral, and therefore when I see his patients, I feel I'm expected to do that as well, because his patients have been seeing him for many years. So they expect it too, so I'm definitely more likely to give his patients antibiotics even when I don't think it's justified. [42]
		Peer pressure toward prescribing (F)	So over in Bath and Somerset, that is what they (medicines management team) has been doing, so if you are over prescribing, against your peers, you are identified and you are invited to come down for a training day. It is a little bit heavy handed, but we are heading towards a very scary place and I think we need to be quite bold with our interventions. [40]
		Drug promotion (F)	The company representative gives only the good points of the products. He forces doctors to write the latest antibiotic. [56]
	Environmental context and resources (*N*=56) [14,25,28–31,34–54,56,57,60,61,63–67,71–86]	High workload/time pressure (F)	Yeah, that … does play a factor. So let's say if there [are] time constraints, sometimes I don't have the luxury of time to explain in detail … So definitely … it will lead to more antibiotic prescription[s] … because we don't have the time to explain in detail … so we end[ed] up giving more to those who insist[ed]. [49]
		Lack of in-house guidelines (B)	I have met many children with upper respiratory infection and I give antibiotics based on the guidelines, and I have never met a child coming back to me with the same problem. I have experience of not giving antibiotics to neonates for a long time. Most of the time neonates suffer dehydration fever and I encourage the mothers to breastfeed and they recover. [46]
		Lack of point of care testing (B)	We do not have these tests [urine sticks] in a nursing home, we are thinking about introducing them … and I think it would give me the possibility of more targeted antibiotic therapy, in the sense, well, confirmation of infection urinary tract anyway […] it is about money, […] but if you do not have it, well, I have to decide, especially since I do not do visits to nursing home every day, […] but if I do not have it, well, I just order empirical treatment, right. [52]

Lack of decision support system (B)	I use UpToDate. That's simple. I can click from Epic, so it's right there on my chart. [I'm] talking to the patient, and I just click and pop it up. [48]
	I am a big proponent of decision support because I don't think any of us can keep it all in our brains anymore … Maybe input a couple of criteria regarding your patient's situation and then it could give you some choices that are all evidence-based but then you would select with your patient the most appropriate option for them. [82]
Timing-dependent prescription decision-making (i.e., end of the working day, around the weekend) (F)	I think the problem with this is obviously 'cos it's a Friday evening. A Friday morning and you can still say well see how she goes over the next couple of hours and if there's any problem then bring her back, but a Friday evening if you're not in on the Saturday makes it, that judgment a little bit harder. [25]
Lack of benchmarking and local antibiotic target/audit (B)	… We have a training session, like an audit with the local CCG [clinical commissioning group] team, in relation to our practices antibiotic prescribing and comparing it to the area in the northwest … so that kind of helped influence and perhaps reduced my antibiotic prescribing. [40]
Lack of participation in antibiotic stewardship initiatives (B)	Well now this is a hot topic. We have a National Antibiotic Protection Program and we had several courses on this subject, that we should actually give antibiotics cautiously so as not to lose their beneficial effects, because this resistance is growing at an alarming rate and each of us should think twice before giving antibiotic prescription. [52]
Lack of environmental prompts about over prescription risks (B)	"Yeah, and then it backs up your decision a little bit more. […] So, if [a tool could show] if a 30 year old comes with a chest infection, and their observations are normal, most of them will clear the infection without needing antibiotics, then that would massively change my practice, 'cause I'd be much more confident." [80]
Patient geographical remoteness (F)	… but if they are … for example in the countryside or on a farm and … need to travel 40 km or more … then, … actually I just try to … use the history to decide on such things. [28]
Hygiene concern about the patient's living place (F)	I made a suture on a patient's hand; we could see that the hands were very dirty, with dirty nails, it may not have any infection in there, but if I do not give an AB …, it evolves to an infection that I do not know [what it would be], so sometimes at this point I would rather go on with the AB prescription than waiting to see what happens … It takes a while for them to come again, then something worse happens. [41]
Patient's financial and professional status (F)	"(…) when a low-income family comes to the health facility (hospital) there are charges like consultation fee, laboratory investigations fee. So, they skip that and go to the pharmacies and explain what is their problem and they buy [antibiotics]." [46]
Prescriber's short employment period (F)	I am someone with lower antibiotic prescribing rates however, I only work part time. I wouldn't want my data to be high as this would look really bad amongst colleagues. [40]
Public awareness campaign (B)	I do think a big barrier is patient education. Um, public education. And even just the damage of antibiotics, what we have been doing with antibiotics … I shouldn't give you an antibiotic because of XYZ but every time I give you an antibiotic and you don't need one, we're on tributing to this bigger problem. Um, and that's the thing, that you know when someone is not feeling well, they don't care about the bigger problem." [82]

GP, general practitioner; TDF, Theoretical Domains Framework.

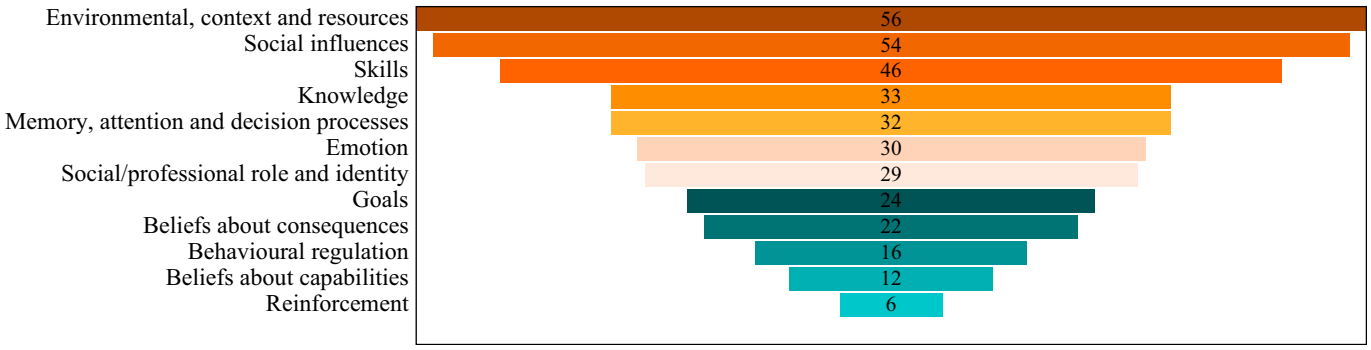

Figure 4. Modifiable determinants (barriers and facilitators) of antibiotic prescribing behaviour in the light of the Theoretical Domains Framework, as identified in the included studies, sorted by frequency (*N*).

appropriate prescribing behaviours. Lastly, organizational care models that promote continuity of care and ongoing monitoring of patients can help reduce inappropriate antibiotic prescriptions [56,60,70,73,75,86].

Key theme two: motivation

Motivational factors in prescribers encompass the brain processes that drive and guide antibiotic prescribing choices and behaviours. Motivation can be either automatic, driven by emotions or impulses, or reflective, arising from evaluations and plans. Several studies have found that healthcare professionals' concerns about losing patients or caregivers, their beliefs regarding the negative consequences of AMR, and their acceptance of their professional role in reducing AMR significantly influence their motivation to engage in responsible antibiotic prescribing practices.

Among the factors that restrict inappropriate antibiotic prescribing behaviours, professionals' confidence in their ability to diagnose and manage non-antibiotic treatments [31,73], their comfort with prescribing practices [36,44,52,67,69], and their expectations regarding potential antibiotic side effects play a significant role [36,49,73,90]. Furthermore, a multi-disciplinary approach characterized by clear role boundaries and responsibilities among healthcare professionals, along with perceiving patients as active participants in their health management, appears to facilitate more appropriate antimicrobial prescriptions [16,32,33,73,76,85,88].

Moreover, the included studies suggest that other potential facilitating factors of antibiotic prescription related to motivational processes may involve healthcare professionals' perception of low patient adherence and engagement in treatment [33,65,85], expectations of patients seeking multiple doctors' opinions (doctor shopping) [60,75], and concerns about patient complaints in the absence of an antibiotic prescription [55,69]. In addition, emotional factors can also play a role in prescription decisions. The fear of adverse clinical outcomes for the patient [16,36,55,57,68,70,79,82,84,85,87], heightened empathy towards patients who are unwell [42,43] and anxious family caregivers [30,57,68] can all influence healthcare professionals' likelihood of prescribing antibiotics. Experiencing high levels of stress, anxiety, and burnout [31,37,40,43—45,53,54,57,72,86], as well as the fear of damaging their professional reputation [49,67], can further contribute to the decision to prescribe antibiotics. Lastly, professionals' goals and reinforcement strategies can also impact prescription choices in various ways. The desire to prioritize patients' safety [50,79,82] and satisfaction [55,59,86], as well as the willingness to maintain a strong therapeutic alliance [57,59] and build trust with patients and their families [53,68,75], may increase the rates of appropriate prescribing behaviours. Conversely, receiving material or immaterial incentives [38,44,67,89] and having access to decision support systems may decrease inappropriate prescribing practices [44,48,52,86].

Key theme three: opportunity

A third cluster of factors influencing prescriber behaviours consists of environmental opportunities or constraints related to the availability of resources that facilitate responsible antimicrobial prescribing, as well as social influences on their prescribing practices. Heavy workloads and time pressures [29—35,37,40,43—45,49,51,53,57,63,67,68,72,79,81,86], as well as the need to treat remote and vulnerable populations with limited access to services [43,46,77,82], have been reported to increase antibiotic prescription rates. Additionally, the timing of prescription decision-making can influence healthcare professionals' behaviour. Making antibiotic prescription decisions outside of regular working hours, such as during out-of-hours periods, may pose challenges to engaging in appropriate antibiotic prescribing practices [29,44,49,68].

Conversely, the presence of public awareness campaigns promoting prudent antibiotic use [44], participation in antimicrobial stewardship initiatives [56,73], and the use of environmental prompts and decision support systems may reduce antibiotic overprescribing [44,48,52,73,86].

Furthermore, the findings across multiple studies suggest that antimicrobial prescribing decisions are heavily influenced by hierarchies and 'prescribing etiquette' — a set of unwritten social rules that healthcare professionals recognize and follow, which sometimes override policy and guidelines [39,63]. Patients'/families' behaviour and demands for antibiotics also have an impact on prescribing decisions [30,32,34—36,41—44,48,49,51,53,54,57,58,60,63—75,78,79,81,84,86—88,90].

Potential intervention functions and BCTs to promote appropriate antibiotic prescribing behaviours

Based on the Behaviour Change Wheel [22], the results of this meta-synthesis suggest that targeted and tailored

interventions to promote more appropriate antibiotic prescription should focus on education, training, persuasion, modelling, and environmental restructuring. These types of interventions are deemed appropriate for the following purposes clustered into the three COM-B components.

Interventions to address determinants at the 'capability' level

Education: Increasing knowledge and understanding of AMR and guidelines to promote more appropriate antibiotic prescriptions. This can be achieved by informing, explaining, showing and providing feedback to prescribers and clinicians involved in the prescription process.

Training: Enhancing the skills required for undertaking appropriate prescribing behaviours through simulated practice and feedback.

Interventions to address determinants at the 'motivation' level

Persuasion: promote a cultural shift through antibiotic stewardship initiatives to establish a positive and distinctive professional identity for antimicrobial stewardship. This approach helps health professionals define themselves in terms of that professional identity.

Modelling: Presenting individuals with examples of appropriate prescribing behaviours to serve as role models, encouraging them to imitate these behaviours. This approach can also involve incentivizing peer-to-peer comparisons, where individuals are motivated to compare their own prescribing practices with those of their peers.

Interventions to address determinants at the 'opportunity' level

Environmental restructuring: Creating a supportive organizational environment that facilitates more appropriate prescribing behaviours. This can involve activities such as organizational audits, nudges, availability of decision aids support systems, and counteracting improper antibiotic demands from patients by raising awareness among consumers about the risks of AMR.

By employing these intervention functions, efforts can be made to address the multi-faceted issues surrounding antimicrobial prescribing and stewardship effectively.

Discussion

This study represents the first meta-synthesis of qualitative evidence on modifiable determinants (barriers and facilitators) of antibiotic prescribing behaviour in human medicine across clinical contexts, guided by a behaviour-change framework. The thematic analysis of the included studies revealed highly comparable themes across clinical domains and type of prescribers, strengthening the validity of the findings in this study.

Consistent with previous studies [15,91], the results highlighted the complexity of factors involved in the prescriber's decision-making process, providing valuable insights for the development of antibiotic stewardship programmes and behavioural change initiatives.

Notably, the study underscored that antibiotic prescribing behaviour is influenced by factors beyond the guidance provided by antimicrobial guidelines and evidence-based clinical practice. Instead, it revealed that prescribing behaviour is influenced by a systemic interplay of factors related to the characteristics and resources of the prescribing environment, as well as intrinsic and extrinsic variables related to the prescriber, thus confirming previous studies on this aspect [92]. This finding aligns with previous research [75] and emphasizes the intricate and multi-faceted nature of healthcare professionals' behaviour when it comes to responsible antimicrobial prescribing in human medicine. Several factors were identified as playing a role in influencing healthcare professionals' capability, opportunity and motivation to prescribe antimicrobials responsibly.

In terms of capability, factors such as knowledge about AMR and access to training were found to be influential. These factors contribute to healthcare professionals' understanding and competence in prescribing practices. The meta-synthesis also identified the importance of opportunity factors, including the availability of resources that facilitate AMR stewardship and the influence of social factors such as peers, patients and hospital managers. These factors shape the opportunities healthcare professionals have to engage in responsible prescribing practices.

Motivation was found to be a key factor in the antibiotic prescribing process. Healthcare professionals' concerns for patient safety and well-being, the fear of losing patients, and the need to maintain a strong therapeutic alliance with families were identified as motivational factors. Beliefs about the consequences of AMR and the recognition of professionals' role in reducing AMR further contribute to their motivation to prescribe antimicrobials responsibly.

The interaction of these multiple factors contributes to the complex decision-making process surrounding responsible antimicrobial prescribing. Understanding these factors can inform the design of interventions aimed at improving rational antibiotic prescribing practices.

Furthermore, comprehending the modifiable determinants of antibiotic prescribing behaviours also presents an opportunity to involve patients in the battle against AMR. Patients and caregivers' expectations and demands for antibiotics, their knowledge of appropriate antibiotic use, and their understanding of the implications of AMR can significantly impact healthcare professionals' prescribing decisions, as suggested by previous studies [51,93,94]. Therefore, educating and empowering patients to make informed choices regarding antibiotic usage can contribute to reducing inappropriate prescriptions and improving patient outcomes.

Moreover, studying the modifiable determinants of antibiotic prescribing behaviours can inform the development and implementation of effective policy interventions at national and international levels. Policy initiatives aimed at promoting responsible antibiotic use, such as regulations on antibiotic sales, establishment of surveillance systems, and incentives for research and development of new antibiotics, can benefit from a comprehensive understanding of the factors that shape prescribing behaviours.

Qualitative methodology is increasingly being employed in medical research to explore complex topics and offer novel insights in the field [95]. In the context of antibiotic prescribing, this methodology has proven valuable in understanding the subjective perspectives of key stakeholders, particularly physicians and policymakers. This paper provides a comprehensive understanding of the factors perceived by prescribers (physicians and non-medical prescribers) to influence

antibiotic prescribing practices and contribute to antibiotic misuse. The findings of this study complement previous quantitative research [96,97] and enhance our existing knowledge regarding the relationship between these identified factors and prescribers' perceptions and experiences. The in-depth understanding of both physicians' and non-medical prescribers' perspectives provided here could be essential in effectively addressing the global concern surrounding antibiotic misuse.

Regarding the study limitations, it is important to note that this study has certain constraints. Firstly, it only includes peer-reviewed studies and excludes grey literature, potentially leading to the omission of relevant information. To address this, future research should consider incorporating a broader range of sources. Additionally, the study focuses on studies published in English and Italian, which may introduce language and geographic biases. It is advisable to include studies from other languages and regions in order to obtain a more comprehensive understanding.

Furthermore, the quality of the included studies varied after applying the CASP appraisal tool. While researcher reflexivity was not explicitly addressed in any of the studies, we acknowledge that this aspect was inadvertently overlooked. However, the consistency of the themes identified across all the studies in this meta-synthesis helps mitigate this limitation. It is important for future research to be mindful of researcher reflexivity and incorporate it into the study design and analysis.

These acknowledgements highlight the limitations of the current study and suggest areas for improvement in future research to address these limitations and enhance the validity and generalizability of the findings.

In conclusion, this meta-synthesis has highlighted the key influences on antibiotic prescribing across various clinical settings and populations. Relational and environmental variables have emerged as crucial drivers of prescribers' decisions to administer antibiotics. It is of paramount relevance to implement multi-disciplinary collaborative antimicrobial stewardship strategies that promote shared decision-making practices with patients and caregivers. This approach addresses practice and knowledge variability and increases awareness of AMR. The synthesis of existing studies can provide useful information for the development of evidence-based and theory-driven antibiotic stewardship interventions, specifically targeting antibiotic (over)prescribing in the future.

Considering the implications of this meta-synthesis, it is crucial for subsequent interventions aimed at improving rational antibiotic prescribing in human settings to adopt a systemic approach that goes beyond focusing solely on individual variables. This means recognizing the complexity of the prescribing process and considering the broader organizational, contextual and clinical factors that influence antibiotic use. Further evidence should be collected to better understand the weight of each TDF's domain intervening in specific organizational, clinical and cultural contexts.

In addition, it is desirable to incorporate co-design approaches when developing these interventions. By involving relevant stakeholders, including healthcare providers, patients, and caregivers, in the design process, interventions can be better tailored to the specific needs and challenges of real-world organizational contexts. This participatory approach can enhance the applicability and sustainability of interventions, increasing their chances of success [12,98].

Further research is needed to delve into the most effective behavioural change strategies for ensuring appropriate antibiotic prescribing. Understanding the specific strategies that are most impactful in influencing prescriber behaviour can inform the development of more targeted interventions. This research should explore the relationships between various individual factors (both intrinsic and extrinsic to the prescriber), contextual factors, and environmental variables. By investigating these relationships, we can gain more precise insights into the determinants of antibiotic prescribing and design interventions that are better suited to specific clinical settings [99].

By considering these implications and conducting further research in these areas, we can advance the development of evidence-based interventions that effectively address the challenges of rational antibiotic prescribing, contributing to the fight against AMR.

Conflicts of interest statement

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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