Influences on antibiotic prescribing by non-medical prescribers for respiratory tract infections: A systematic review using the Theoretical Domains Framework

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Synopsis

Background

The need to conserve antibiotic sensitivity through the management of respiratory tract infections (RTIs) without recourse to antibiotics, is a global priority. A key target for interventions is the antibiotic prescribing behaviour of healthcare professionals including non-medical prescribers (NMPs: nurses, pharmacists, paramedics, physiotherapists) who manage these infections.

Aim

To identify what evidence exists regarding the influences on NMPs antimicrobial prescribing behaviour and analyse the operationalisation of the identified drivers of behaviour using the Theoretical Domains Framework (TDF).

Methods

The search strategy was applied across 6 electronic bibliographic databases (eligibility criteria included original studies; written in English and published before July 2019; non-medical prescribers as participants; and looked at influences on prescribing patterns, of antibiotics for respiratory tract infections). Study characteristics, influences on appropriate antibiotic prescribing and intervention content to enhance appropriate antibiotic prescribing were independently extracted and mapped to the TDF.

Results

The search retrieved 490 original articles. Eight papers met the review criteria. Key issues centred around strategies for managing challenges experienced during consultations, managing patient concerns, peer support and wider public awareness of AMR. The two most common TDF domains highlighted as influences on prescribing behaviour, represented in all studies were; social influences and beliefs about consequences.

49

50 **Conclusions**

51 The core domains highlighted as influential to appropriate antibiotic prescribing should be
52 considered when developing future interventions. Focus should be given to overcoming social
53 influences (patients, other clinicians) and reassurance in relation to beliefs about negative
54 consequences (missing something that could lead to a negative outcome).

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56 **Word count:** 5502 (excluding abstract and references, including tables)

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Introduction

Multi-drug resistant infections represent one of the greatest threats to human health.[1] Each year in the EU alone, antimicrobial resistance (AMR) is responsible for an estimated 25,000 deaths and €1.5 billion in extra healthcare costs.[2] Loss of protection for patients undergoing operations and other medical procedures, prolonged stays in hospital, and longer illnesses are each direct consequences of infection with resistant micro-organisms.[1]

Respiratory tract infections (RTIs) are the most frequent acute problem for which patients consult within primary care, and about a quarter of the population present with an RTI each year.[3] Most of these infections are viral, self-limiting, and require only paracetamol, fluid and rest for recovery. [3] However, over 50% of patients who present with an RTI are prescribed an antibiotic.[4] Antibiotic exposure is significantly associated with resistance, and multiple courses of antibiotic treatment are associated with higher resistance rates in patients with RTIs.[5] Over-prescribing medicalises these self-limiting conditions, which reduces the likelihood that patients will adopt self-management strategies.[6] It also perpetuates the beliefs that antibiotics are effective for common infections and increases patient's intention to consult. [6] There are several adverse effects of antibiotics for RTIs that should be taken into account, such as vomiting, rashes, and diarrhoea, which are experienced by one in sixteen patients.[7] The need to conserve antibiotic sensitivity through the management of RTIs without recourse to antibiotics, is a global priority[5, 8-10] and a key target for interventions is the antibiotic prescribing behaviour of healthcare professionals who manage these infections.

Much research has focused upon trying to understand why general practitioners (GPs) prescribe antibiotics for RTIs, and it is evident that key influences include GPs' perception of patient expectations,[11] patient pressure,[12] diagnostic uncertainty and fear of complications,[13] factors imposed by healthcare systems and specific characteristics of clinician.[14] However, GPs are no longer solely responsible for treating and managing RTIs. In the United Kingdom (UK), around 46,000 nurses[15], 8000 pharmacists,[16] and over 1500 physiotherapists,

podiatrists and paramedics (i.e. allied health professionals (AHPs) [Health and Care Professions Council (HCPC)][17] have the same independent prescribing capability as doctors. The numbers of these 'non-medical prescribers' (NMPs) are steadily increasing[18] to fulfil the workforce needs of the National Health Service (NHS).[19,20] Nurse, pharmacists and AHPs frequently manage patients with RTIs, and data from 2015 identified they prescribe around 8% of all primary care antibiotics dispensed.[18] Given the numbers of these prescribers have risen from 29,000 in 2015[18] to currently 55,500 (see above), this figure is expected to be much higher.

It cannot be assumed that the factors that influence GP prescribing in RTI management are the same as those that influence NMP prescribing. Therefore, it follows that it cannot be certain that interventions to target the prescribing behaviour of GPs will be relevant and target all the drivers of behaviour amongst NMPs. Although interventions valued by GPs include those that involve learning from peers, are patient-centred (approaches adopted by NMPs), and benefit the practice as a whole,[11] there are currently no interventions that exist specifically to support appropriate antibiotic prescribing behaviour by NMPs. This, therefore, heightens the need to ensure that interventions are also informed by NMP experiences.

The first step in intervening to change practice must involve identifying the factors that influence NMPs antibiotic prescribing for RTIs and the context in which this occurs. Using behavioural science to analyse and understand these influences is critical to any intervention design as this helps decide what needs to change to achieve the desired behaviour. Application of behavioural science also facilitates later steps of intervention design, guiding the identification of the full range of behavioural change techniques that could be used to change the target behaviour.[21]

Aim

This research aimed to identify what evidence exists regarding the influences on NMPs antimicrobial prescribing behaviour and analyse the operationalisation of the identified drivers of behaviour using the TDF.

Method

Design

A systematic review to retrieve relevant, peer reviewed studies that focus on antibiotic prescribing behaviour for RTIs by NMPs. This systematic review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [22] (PRISMA).

Protocol and registration

The protocol for this review was submitted to PROSPERO[23] in July 2019 and approved in October 2019 (2019 CRD42019144826).

Eligibility criteria

Articles were included if they: 1) reported results of original studies written in English; 2) included non-medical prescribers as participants; 3) looked at influences on prescribing patterns; of 4) antibiotics for respiratory tract infections. Specifically related to **PI(E)COS:** ***P-Participants/population:*** Pharmacists, nurses, physiotherapists, paramedics who are qualified to prescribe medicines independently i.e. NMPs. ***I(E)-Intervention (Exposure):*** Any studies that have investigated factors that influence antibiotic prescribing by NMPs for RTIs. ***C-Comparator(s):*** Not applicable; any healthcare context. ***O-Outcome(s):*** Antimicrobial prescribing behaviour. ***S-Study design:*** Any. **Target behaviour:** The target behaviour of interest was the adoption of a 'no antibiotic prescribing strategy' by NMPs for common, acute, uncomplicated self-limiting RTIs (including acute otitis media, acute sore throat/acute

143 pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis, acute cough/acute bronchitis).
144 This is based on National Institute for Health and Care Excellence[3] (NICE) guidance.
145
146 **Information sources and search strategy**
147 The search strategy for information sources was developed by MC, discussed with AC and
148 checked by an experienced librarian (EG). This strategy was applied across international
149 electronic databases Embase, Emcare, Scopus, Web of Science, Medline, CINAHL (via
150 EBSCO), by an experienced librarian (EG) and supplemented with hand searching of relevant
151 citations. Each database was searched using the Index Terms (i.e. MeSH/index terms) unique
152 to each database and a combination of Boolean (AND/OR) keywords in the title or abstract
153 (nurse* OR pharmacist* OR physiotherapist* OR "physical therapist*" OR paramedic.
154 Prescribing OR "prescriptive authority", antibiotic* OR antimicrobial* "respiratory tract
155 infection*"). No limits were placed on the searches other than inclusion of papers published in
156 English. All articles published up to July 2019 were included.
157
158 **Study selection**
159 Titles identified in the initial search were combined and duplicates removed. Article titles and
160 abstracts of all studies were initially screened by one reviewer (MC) using a screening
161 template that included pre-specified eligibility criteria. Two reviewers (MC/RL) independently
162 screened the remaining titles and abstracts to identify studies requiring full text review. Full
163 text reviews were independently screened by two reviewers (MC/RL) to select the final articles
164 included in this review.
165
166 **Data collection process and data items**
167 All data extraction and assessments were carried out by two reviewers (RL/MC). A data
168 extraction template was used to collect the following information: author, year, title, study aim,
169 design, setting, participants, sample size, sampling strategy, data collection, analytical
170 approach and main findings (see Table 1). Details related to influences on appropriate

antibiotic prescribing or intervention content to enhance appropriate antibiotic prescribing were independently extracted by two reviewers (AC/HF).

Risk of bias in individual studies

Two reviewers (MC/RL) independently assessed the methodological quality of included studies using the Mixed Methods Appraisal Tool[24] (MMAT) Version 2018. The MMAT allows the appraisal of mixed methods, qualitative and quantitative studies (the latter subdivided as randomised controlled trials, non-randomised studies and descriptive studies) [24]. See Table 2 for details of methodological quality criteria assessed within each category.

Synthesis of results

The results sections of papers were read and factors which influenced prescribing were deductively coded by two expert coders, AC/HF according to the 14 domains of the TDF as defined by Cane *et al*.[25] These are: 'Knowledge', 'Skills', 'Social/Professional Role and Identity', 'Beliefs about Capabilities', 'Optimism', 'Beliefs about Consequences', 'Reinforcement', 'Intentions', 'Goals', 'Memory, Attention and Decision Processes', 'Environmental Context and Resources', 'Social Influences', 'Emotions', and 'Behavioural Regulation'. The TDF is a widely used implementation framework in healthcare settings, originally designed to identify influences on health professional behaviour in relation to implementing evidence based practice. It is a synthesis of 128 constructs from 33 theories of behaviour change, which was developed from a collaboration between behavioural scientists and implementation researchers.[26] The TDF was chosen over other available frameworks (e.g. the Consolidated Framework for Implementation Research (CFIR))[27] because the TDF has been mapped to the Behaviour Change Technique Taxonomy version 1 (BCTTv1)[28] which then facilitates intervention design through the selection of evidence based behaviour change techniques (BCTs) . This type of analysis is still a relatively new way to use the TDF, but there

198 are previous systematic reviews of health interventions that have taken this approach (e.g.
199 post-fracture osteoporosis risk management[29] and pulmonary rehabilitation[30]). In some
200 instances, data was coded to more than one domain, but the rationale for this was discussed
201 between AC and HF and a code agreed that best represented the data. The same process
202 was followed for quantitative and qualitative data, and information from the method and
203 discussion sections were coded if they provided further context to data coded in the results.
204 Data was coded just to the first level of the TDF 14 domains, and not to the constructs within
205 each domain. After coding all papers the percentage agreement between the two reviewers
206 was calculated using the NVivo coding comparison feature. Overall agreement was high at
207 99.30%. After this, all excerpts where coding differed were discussed between the two
208 reviewers (AC and HF) and checked against the TDF domain definitions in order to reach
209 100% agreement. Thematic content analysis highlighted which of these domains was most
210 commonly cited to influence NMP antibiotic prescribing behaviour for RTIs (see Table 3).
211

212 **Results**

213 A total of 554 articles were initially identified, reduced to 490 once duplicates were removed.
214 Figure 1 shows the article selection process. Following quality assessment of studies (shown
215 in Table 2), a total of eight articles were included in the review (sample size; N=14,471).
216

217 **[INSERT FIGURE 1 AROUND HERE]**

218

219 The key characteristics and main findings from included studies can be found in Table 1.
220 Four of the studies aimed to explore prescribers (nurse practitioners, non-medical prescribers,
221 general practitioners) experiences of RTI consultations. [31, 32- 33, 34] Key issues centred around
222 challenges experienced during consultations (e.g. managing patients'/parents' expectations,
223 diagnostic uncertainty, confidence in the quality of evidence relating to numerous clinical
224 guidelines, roles and perception of prescribers' (NMPs) roles) and strategies for managing
225 consultations (e.g. reinforcing no-prescribing decisions, delayed prescribing, education (self-

management of symptoms and negative consequences of antibiotics), managing patient concerns (reassurance, empathy, clinical examination), peer discussion and wider public awareness of AMR). Courtenay *et al*. (2017)[35] explored both patient and NMP expectations of consultations and identified alignment between expectations in these two groups. Regardless of patient expectations or the management strategy used during consultations, high levels of patient satisfaction for all aspects of the consultation were identified. Reported factors influencing patient satisfaction were patient-centred strategies that included understanding patients' concerns, communicating and explaining treatment decisions.[35] Using the TDF and COM-B, Courtenay *et al*. (2019)[31] identified twelve domains and forty naturally occurring BCTs[28] that facilitated prescribers' behaviour. For example, in the TDF domain *knowledge*, corresponding BCTs identified included 'instruction on how to perform the behaviour', 'information about health consequences' and 'social comparison'.

The design of the studies included two quasi-experimental,[36-37] four qualitative,[31, 32, 33, 34,] one mixed-methods,[35] and one cross-sectional quantitative. [38] In the two quasi-experimental studies, Davis and Whyte (2008)[36] introduced and evaluated a nurse-led quality-assurance based programme involving physicians (n=6), nurse practitioners (n=4) and physician assistants (n=2) and Brown (2018), an antibiotic stewardship programme involving nurse practitioners (n=5) and medical doctors (n=3). Although Davis and Whyte (2008)[36] found a decrease in the use of broad-spectrum antibiotics post-intervention, there was no decrease in prescribing rates overall and an increase rate of delayed prescriptions post-intervention. In Brown (2018)'s study[37], antibiotic prescribing rate decreased by 10% with 87% of participants believing that antibiotics were overused, and 99% that antibiotic resistance is a problem.

Most of the studies were conducted in primary care (n=5).[31-35] The rest of the studies were conducted in a hospital-owned urgent care centre (n=1),[37] a network of community health centres (n=1)[3036] and one study utilised a national databases of survey data.[38] The sample in included studies consisted of nurse practitioners and doctors, [32, 37-38] patients, nurse and

pharmacist prescribers,[31,35] physicians, nurse practitioners and physician assistants,[36] and nurse practitioners/prescribers.[33-34] All studies were carried out in developed countries: five in the UK,[31-35] and three in the United States.[36-38]

[INSERT TABLE 1 AND TABLE 2 AROUND HERE]

TDF analysis

Table 3 highlights that across the quantitative and qualitative data, the two most common influences on NMPs prescribing behaviour highlighted from the TDF were; beliefs about consequences (featured in 8/8 studies) and social influences (8/8), which were represented in all studies reviewed. Knowledge (7/8), social/professional role and identity (7/8), memory, attention and decision processes (7/8) and environmental contexts and resources (7/8) were the next most common domains to be reported in studies, featuring in 85.7% of the reviewed literature. Skills was mentioned as an influencer in five of the studies. Beliefs about capabilities and emotion featured less, in only three of the eight studies. Goals were mentioned in two studies and behavioural regulation in one study. The domains of Optimism and Intentions were not mentioned at all as influencers of NMPs antibiotic prescribing behaviour for RTIs. Examples of the excerpts of text from all study designs (qualitative, quantitative and mixed methods) used to code for these domains is presented in Table 4. Excerpts are presented in quotation marks, with qualitative quotations presented in italics.

[INSERT TABLE 3 AND 4 AROUND HERE]

Discussion

This review aimed to identify what evidence exists regarding the influences on NMPs antimicrobial prescribing behaviour. The TDF[25] was used in an attempt to gain a more detailed understanding of the operationalisation of the identified drivers of behaviour. This is the most recent synthesis of theories and models, that takes into account not only psychological, but also social and environmental factors. Using this framework, the most common influences on antibiotic prescribing behaviour in this review were social influences

and beliefs about consequences, each identified in all studies. Other influences in the majority of studies were knowledge, social professional role and identity, memory, attention and decision processes, environmental context and resources and skills. For comparison, we are unaware of any research that has used the TDF to explore GPs antibiotic prescribing behaviour, however, our findings do support previous research that has used the TDF to explore antibiotic prescribing by healthcare professionals in long-term care facilities.[39]Although social professional role and identity was not identified by these researchers, knowledge, environmental context and resources, social influences, beliefs about consequences and memory, attention and decision processes were reported to be the main influences. Previous research has identified domains unique to NMPs,[31] such as emotion, goals, and skills, however, evidence here shows there is also overlap with influencers of other health professional antibiotic prescribing behaviour.

The identity as an NMP was highlighted as an important influence, and the importance of doing the right thing by way of the patient and the health care system has been found as a strong influence, both in this review and elsewhere[31, 40]. In the UK at least, this, in part, can be linked to the national antibiotic guardianship initiative.[41] However, there is an acknowledgement that the current knowledge and skills needed for the behaviour to occur, may require additional education and training.[42] These intervention functions should be considered, alongside other components such as environmental restructuring, modelling and enablement in future intervention development.

Environmental context and resources were commonly cited as influencing factors, in that when working within a short clinic timeframe or in an out of hours service, an antibiotic prescription is more likely.[32] Future work needs to consider how best to manage time on limited resources, while also having protocols in place for behaviours such as providing delayed prescriptions and ways to monitor and gain feedback on usage of these.

309

310 ***Limitations***

311 In many of the studies, the sample sizes were small, or the measurements narrowly focused,
312 therefore, generalisability is limited. It is also of note that the studies included were only from
313 the UK and USA, overlooking NMP roles in other western countries, and in other parts of the
314 world. It was also notable that in the main, the NMPs included in this review were nurse
315 prescribers, despite many other health professional groups being involved in prescribing.
316 However, this review provides a broad picture of the current literature and areas for
317 improvement in this area. The theoretical domains identified as important for future
318 intervention must also be taken with some caution. The team could only code for what was
319 contained within the studies included in the review, and some of these had a specific focus on
320 one or more of the domains (e.g. Courtenay *et al*., 2017[35] had a specific focus on patient
321 expectations, which links to the social influences domain of the TDF). Only the qualitative
322 study by Courtenay *et al*., 2019,[31] explicitly explored all 14 domains. By virtue, the omission
323 of other domains (optimism, intention) as influencers in the other papers included in the review
324 may be due to the fact that they were not measured or the focus of research, or that they were
325 implicitly assumed and not explicitly stated, rather than the fact that they do not influence the
326 behaviour. As the science of behaviour change evolves, and more studies use better reporting
327 and the full domains for research (such as Courtenay *et al*., 2019[31]), these limitations will
328 lessen.

329

330 ***Conclusion***

331 Interventions should be systematically developed, evidence-based and theoretically driven.
332 There are a broad range of influences on antibiotic prescribing behaviour and interventions
333 are unlikely to target all of them with clear evidence of effect. This review has conceptualised,
334 using a behavioural lens, a wide range of influences that require changing, which may serve
335 as possible targets for behaviour change techniques to support appropriate antibiotic
336 prescribing in the future. Influences include overcoming social influences (patients and other

clinicians) and reassurance in relation to beliefs about possible negative consequences (missing something that could lead to a negative outcome). The next steps for intervention design are (1) to ensure all domains are examined for their influence on NMP's antibiotic prescribing behaviour (2) to set goals and objectives for the intervention (3) agree the influences to target in an intervention (using APEASE criteria)[21] (4) develop the intervention, this can be done with reference to the behaviour change taxonomy[28]. The evidence base to date suggests that the intervention is likely to involve education and training in interpersonal communication. This review also highlights the need to ensure knowledge is up-to-date and that the environment in terms of clinical appointment time and setting is conducive to appropriate prescribing behaviour (e.g. appropriate clinic time and a protocol for out of hours working). Professional role and identity needs to be upheld, and the use of antibiotic guardian prompts can support this, serving as both a reminder of identity and the need to avoid inappropriate antibiotic prescriptions. These are all areas for future intervention.

Acknowledgement

We would like to thank Elizabeth Gillen for her contribution to this review.

Funding

The study was carried out as part of our routine work through allocated research hours.

Transparency declarations

None to declare

Author contributions

MC and AC made a substantial contribution to the conception and design of the work. MC made a substantial contribution to the review process, and identification of relevant studies, with the final inclusions approved by all authors. RM and MC made a substantial contribution to the data extraction from the studies. AC and HF made a substantial contribution to the

365 theoretical domains data extraction and analysis from the studies. All authors contributed to
366 the interpretation of findings. AC drafted the manuscript and all authors contributed to and
367 approved the final version to be published. All authors agree to be accountable for all aspects
368 of the work in ensuring that questions related to the accuracy or integrity of any part of the
369 work are appropriately investigated and resolved.
370

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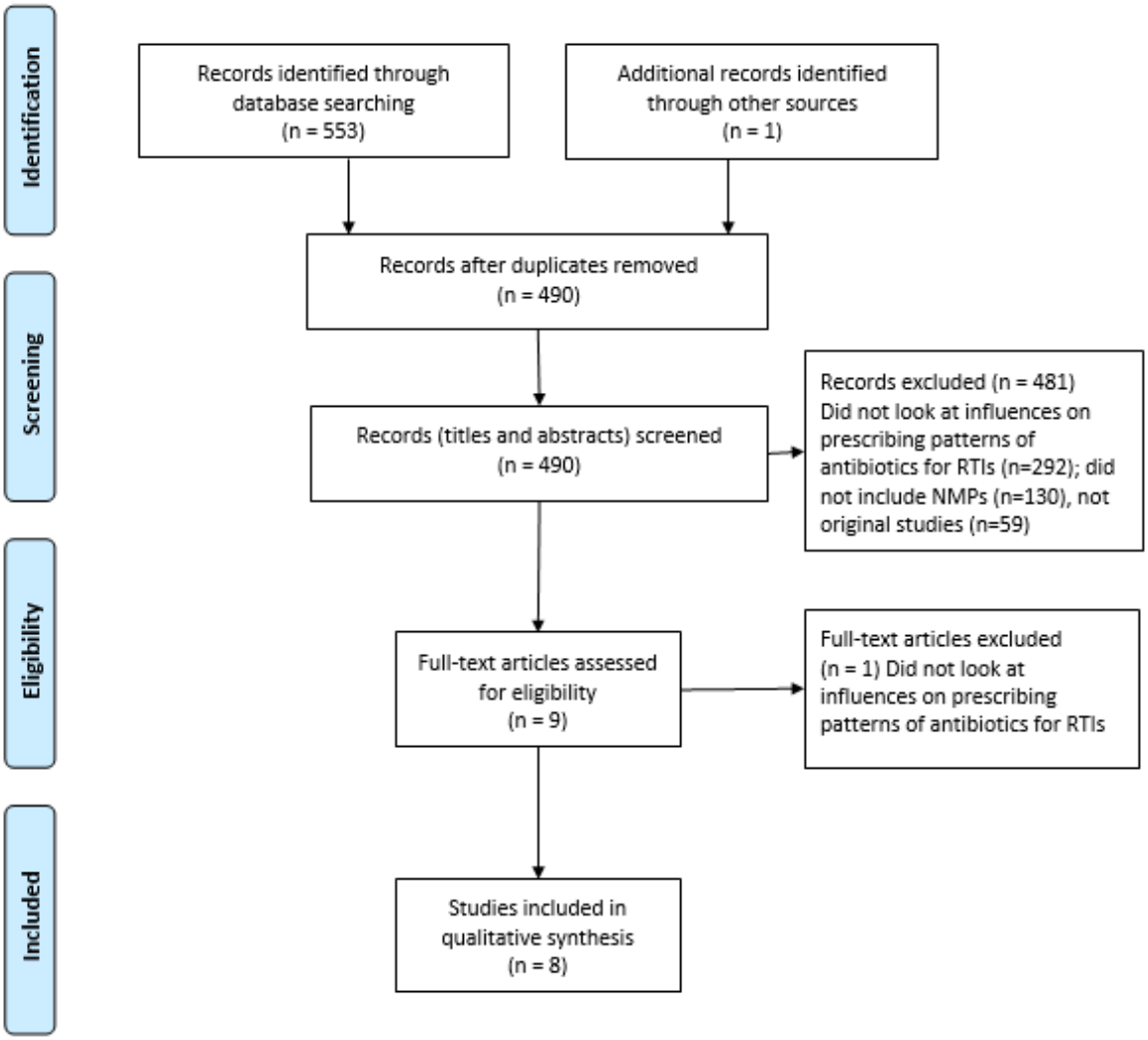

Figure 1: PRISMA flow diagram of systematic review of studies that investigate the influences on non-medical prescribers antibiotic prescribing behaviour for respiratory tract infections.

516 **Table 1: Characteristics of studies included in the systematic review investigating the influences on non-medical prescribers antibiotic**
517 **prescribing behaviour for respiratory tract infections.**
518

Author (year)	Study location	Study aim	Design	Setting	Sample	Analytical approach
[37]Brown (2018)	USA	To evaluate the outcome of an antibiotic stewardship program on provider antibiotic prescribing for ARIs	A quasi-experimental study Intervention and questionnaires	Hospital-owned urgent care centers located within different urban and suburban regions across the St. Louis, Missouri metropolitan area.	5 nurse practitioners and 3 medical doctors	Wilcoxon sign-rank tests and McNemar tests to detect differences between baseline and post- intervention antibiotic prescribing rates. Chi-square tests for association between provider type/ antibiotic prescription. Pre/post questionnaire survey. Median/ Mann-Whitney U tests.
[35]Courtenay *et al*. (2017)	UK	To i) explore patients' expectations and experiences of nurse and pharmacist non-medical prescriber-led management of RTIs, ii) examine whether patient expectations for antibiotics affect the likelihood of receiving them and iii) understand factors influencing patient satisfaction with RTI consultations.	Mixed methods: questionnaires with patients and semi-structured interviews with patients and NMPs	Primary care	Questionnaires from 120 patients Interviews with 22 patients and 16 nurse and pharmacist NMPs	Questionnaires: descriptive statistics and Fisher's exact test to explore associations. Semi-structured interviews: inductive thematic analysis
[31]Courtenay *et al*., 2019 UK	UK	To i) use a theoretical framework to identify the factors that influence management of RTIs by nurse and pharmacist prescribers and	A qualitative approach, utilising semi-structured interviews	Primary care	17 nurses and 4 pharmacists	An initial inductive approach and thematic analysis, followed by a deductive approach, whereby codes were mapped to the appropriate 'domains' within the TDF. Interview quotes were then coded for the BCTs described by the population when

		ii) identify BCTs that can be used as the basis for the development of a theoretically informed intervention to support appropriate prescribing behavior by these groups				discussing what influenced their behaviour.
[36]Davis and Whyte (2008)	USA	To examine the effect of a nurse-led quality-assurance-based program designed to decrease inappropriate antibiotic prescribing rates in patients suffering from viral upper respiratory tract infections.	A quasi-experimental design based upon pre- and post-intervention measurement via chart reviews.	A network of community health centers in the Southeastern United States.	6 physicians, 4 nurse practitioners and 2 physicians assistants	Demographic data was summarized through descriptive statistics. The raw rates of antibiotic prescribing were calculated and compared using ANOVA.
[38]Ladd (2005)	USA	To determine antibiotic prescribing rates for nurse practitioners (NP) and factors associated with NP and physician (MD) antibiotic prescribing.	Cross-sectional retrospective analysis of datasets	National Hospital Ambulance Medical Care Survey (NHAMCS) and National Ambulatory Medical Care Survey (NAMCS); both annual surveys conducted by the National Center for Health Statistics (NCHS)	National probability sample of 506 NP and 13692 MD patient visits from 1997-2001	Bivariate analyses with uncorrected Pearson's correlations and logistic regression
[34]Philp and Winfield (2010)	UK	To understand why nurse practitioners in primary care prescribe antibiotics for some cases of otitis media.	An interpretative qualitative research approach using semi structured interviews	Primary care	8 primary care nurse practitioners	Thematic analysis
[33]Rowbotham *et al*. (2012)	UK	To explore how nurse prescribers (NPs) and other non-medical prescribers (NMPs) experience RTI consultations, and challenges of a no-prescribing strategy	Semi-structured interviews, focus groups	Primary care	Interviews: 15 NPs Focus groups (n=3): 21 NPs and NMPs	Grounded theory

[32]Williams *et al*. (2018)	UK	To explore general practitioner (GP) and NP views on and experiences of prescribing in primary care out-of-hours (OOH) services.	Semi-structured interviews	Primary care OOH	15 GPs and 15 NPs	Inductive thematic analysis

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520 **Table 2: Quality assessment of included studies for the systematic review investigating the influences on non-medical prescribers**
521 **antibiotic prescribing behaviour for respiratory tract infections using the MMAT.**
522

Study	Screening questions		Qualitative					Quantitative descriptive					Mixed methods				
	S1	S2	1.1	1.2	1.3	1.4	1.5	4.1	4.2	4.3	4.4	4.5	5.1	5.2	5.3	5.4	5.5
Brown (2018)	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	Y	Y	N	Y	N/A	N/A	N/A	N/A	N/A
Courtenay *et al*. (2017)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Can't tell	Y	Y	Y	Y	Y	Y
Courtenay *et al* (2019)	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Davis and Whyte (2008)	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	Y	Y	Can't tell	Y	N/A	N/A	N/A	N/A	N/A
Ladd (2005)	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A
Philp and Winfield (2010)	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Rowbotham *et al*. (2012)	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Williams *et al*. (2018)	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

523 Note: Y = quality criteria meet; N = quality criteria not met; N/A = quality criteria did not apply due to the study design. None of the include studies used a
524 quantitative randomised controlled trials or quantitative non-randomised method hence criteria 2.1-2.5 and 3.1-3.5 were not included in the table. See Appendix
525 1 for the full list of criteria used.
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Table 3: Data extraction of studies from the systematic review investigating the influences on non-medical prescribers antibiotic prescribing behaviour for respiratory tract infections coding to the Theoretical Domains Framework

Papers **TDF Domains**	**Brown (2018)**	**Courtenay *et al*. (2017)**	**Courtenay *et al*. (2019)**	**Davies & Whyte (2008)**	**Ladd, *et al*. (2005)**	**Philip & Winfield (2010)**	**Rowbotham *et al*. (2012)**	**Williams, *et al*. (2018)**	**Included in papers % (of 8)**
Knowledge	■	■	■	■		■	■	■	87.5% (7/8)
Skills		■	■			■	■	■	62.5% (5/8)
Social/Professional Role and Identity	■	■	■		■	■	■	■	87.5% (7/8)
Beliefs about Capabilities			■			■	■		37.5% (3/8)
Optimism									0% (0/8)
Beliefs about consequences	■	■	■	■	■	■	■	■	100% (8/8)
Reinforcement			■						12.5% (1/8)
Intentions									0% (0/8)
Goals			■				■		25% (2/8)
Memory, attention & decision processes	■	■	■		■	■	■	■	87.5% (7/8)
Environmental context and resources	■	■	■		■	■	■	■	87.5% (7/8)
Social influences	■	■	■	■	■	■	■	■	100% (8/8)
Emotion			■				■	■	37.5% (3/8)
Behavioural regulation			■						12.5% (1/8)

Key: grey cells indicate the TDF domain was present in the data, white (no colour) cells indicate the TDF domain was not present in the data

531 **Table 4: Data extraction of excerpts from studies within the systematic review investigating the influences on non-medical prescribers**
532 **antibiotic prescribing behaviour for respiratory tract infections coding to the Theoretical Domains Framework**
533

TDF Domains	Narrative description of findings within each domain	Example excerpts from studies
Knowledge	The knowledge of the following were described as helping to overcome challenging situations in consultations and facilitating appropriate prescribing decisions by NMPs: knowledge that people are often seeking reassurance that it isn't something worse (e.g. chest infection) rather than a prescription when they have an RTI, knowledge of guidelines and local formularies, knowledge about treatments, the side effects of antibiotics and in particular management of RTIs without antibiotics (including self-management strategies patients could try at home), knowledge of how to support patients in understanding their prescribing decisions (information leaflets, treatment explanations etc), lack of feedback on how patients used a delayed prescription, and how to manage treatment expectations. NMPs reported lack of knowledge of patient histories and variable quality of medical records, knowledge of the patient and their family, as influences on appropriate antibiotic prescribing. However, some described these as a barrier to and others as facilitators of prescribing decisions in RTI being made according to guidelines. NMPs reported having less knowledge and training than medical prescribers. The overlap in viral and bacterial infection symptoms presented a challenge and they also related their knowledge gap to difficulties in knowing how to manage complex cases (adults or children with serious comorbidities). A transient NMP workforce was a barrier to training and education around appropriate antibiotic prescribing. Audit, supervision and feedback on their own prescribing practices, and knowledge of local and national antibiotic prescribing rates were seen as helpful in reducing antibiotic prescribing rates. Knowledge of the consequences of antibiotic prescribing was important, but did not change practice as NMPs had not seen or had any direct experience of the consequences of antibiotic overuse.	"Lack of feedback on what patients do with a delayed antibiotic prescription was described as a barrier to using the delayed strategy, owing to a perceived likelihood of the prescription being 'cashed in' against medical advice. *"...we can't follow the patients up, we don't follow them through, we have no idea whether they actually follow the instructions for delaying the prescription or whether they actually go and cash in their prescription and start the antibiotics straightaway"*. (NP 18/1000, NHS OOH)" (Williams *et al*., 2018, p799) *"The factors determined most to influence all providers' antibiotic prescribing included the following:…thinking there is a need to wait for microbiology results before treating an infectious disease" (Brown, 2018, p.11)*

Skills	Empathy and the ability to manage patient's emotions in consultations were key skills reported across studies that facilitated NMPs prescribing decisions through helping patients and NMPs align in their treatment decisions. More specifically these included: skills in quickly developing rapport with patients /their caregivers, actively exploring and managing patient treatment expectations, communicating no prescribing decisions in language they can understand, managing patient's concerns, reassuring them they are doing the right things, good physical examination skills and ability to relate these to the patient's experience and the treatment plan, validating their symptoms and experiences (rather than dismissing them as a simple virus). These skills were discussed as facilitators, but not universally, for example, knowing the patient and having a rapport that developed over time, was in some cases seen as a barrier to appropriate antibiotic prescribing. NMPs also described using delayed prescriptions to 'keep the peace' and to help people 'feel in control of things.' Other NMPs used safety-netting, sign-posting and educating patients about red flag symptoms to support patients with their no-treatment decisions.	*"… "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." (I15N)" (Courtenay et al., 2019, p5)*
Social/Professional Role and Identity	Prescribing by doctors was described by NMPs as an established role, and NMPs felt that patients often did not trust a no-prescribing decision by an NMP assuming they would have got a prescription if they had seen a doctor. In these instances NMPs would seek support from a peer to endorse their decision making to patients, or suggest to the patient they sought a second opinion. However, examples were given of doctors undermining NMPs no-treatment decisions and their antibiotic guardianship, and prescribing antibiotics for a patient. Quantitative data showed differences in antibiotic prescribing for RTI between doctors and NMPs. This had an effect on professional identity as specific practices were linked to each profession – NMPs prescribing by guidelines, and doctors basing their decisions on 'gut feeling.' Both doctors and NMPs felt that more complex patients should be dealt with by doctors. NMPs felt more accountable for their decision making, and more open to criticism compared to doctors. NMPs felt that empowering patients with self-management strategies and	*"...I find it tricky because sometimes I feel the patients think I'm not giving them antibiotics because I'm a nurse and that if they saw a doctor they would get them instead [...] Sometimes, unfortunately, if they have not been happy with not getting them, and they've re-booked to see a doctor, sometimes they are then given them. So the next time I see them, it just makes it that much harder all over again to try and convince them"* NP 20/1001, Private OOH Organization" (Williams *et al.*, 2018 p798) "Pre-intervention patients had a 3.3

	educating them about antibiotics and antibiotic resistance was part of their role, especially those who had pledged to be antibiotic guardians. This was seen as a responsibility they had not just for their patients, but for society and to the healthcare system. Physical examination skills were not seen as central to NMPs roles, but described as helping to reassure patients about their symptoms and accepting of NMPs decision not to prescribe antibiotics.	times (p = .001) and post-intervention patients had a 4.2 times (p ≤ .0005) greater likelihood of being prescribed an antibiotic if they were seen by a MD [medical doctor] versus a NP. With NPs [nurse prescribers], the proportion of antibiotics prescribed decreased from a pre-intervention value of 20% to 12% after intervention, p = .210. With MDs, the proportion of antibiotics prescribed decreased from a pre-intervention value of 45% to 34% after intervention." (Brown, 2018, p11)
Beliefs about Capabilities	Lack of confidence in their knowledge and decisions meant advice from senior colleagues reduced appropriate prescribing decisions. NMPs felt less confident in their prescribing decisions because they had less training than medical prescribers. They also felt more exposed to criticism, and described a lack of legal protection for NMPs. However, this was linked to more careful and considered prescribing practices. Prescribing guidelines were felt to be clear, but implementing them in reality was challenging, particularly when managing a parent's anxieties about a child who was not ill. As NMPs gained experience, they gained confidence in managing these experiences and 'not giving in to parents.'	*"… 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."* (I10N)" (Courtenay *et al*., 2019, p5)
Optimism	No data extracted and coded to this domain.	

Beliefs about consequences	NMPs were concerned about overuse of antibiotics locally and nationally and the consequences of antibiotic resistance. They also believed that most patients would be satisfied with a no-prescribing decision if they felt listened to, had a physical examinations and their concerns discussed and reassurance provided. However there were a range of other consequences that NMPs took into account when making their prescribing decisions. For example, where follow-up wasn't possible, if the weekend, or the patient was unlikely to follow-up if symptoms deteriorated (linked to socio-economic status / availability of services for some minority ethnic groups) a delayed or prophylactic prescription was typically offered. NMPs also noted that people who attended out of hours clinics were generally more unwell and so more likely to receive a prescription. For patients with comorbidities, NMPs would err on the side of caution and offer a prescription because of concerns about the consequences if they were wrong.	*"*If patients are compromised immunologically, so they have got sort of an underlying immune disorder then I would probably error (sic) on the side of caution. Even if I wasn't necessarily totally convinced, I would be worried not to treat." (NP5)" (Rowbotham *et al*., 2012, p. 2625). "NPs believe antibiotics are overused locally (89%) and nationally (99%)." (Brown, 2018, p 12)
Reinforcement	Appropriate prescribing was reinforced through audits of prescriptions and individualised feedback showing NMPs how their prescribing rates related to those of their peers was viewed as a 'scary' but necessary process. NMPs who showed the highest prescribing rates were invited for further training, whilst those who performed best according to practice guidelines received rewards for them / their practice.	*"This year we have looked at the use of quinolones, ketasporines and Co-amoxiclav… influenced by the national agenda but also our local medicines management team at the CCG, they push that agenda as one of their priorities for the year and resource it through the prescribing incentive scheme. So inevitably there were rewards available to practices and practitioners, so that will influence my prescribing for sure".* (I21P)" (Courtenay *et al*., 2019, p6)
Intentions	No data extracted and coded to this domain.	
Goals	NMPs had or set goals for their prescribing rates, they were motivated to keep their prescribing low, to maintain their credibility amongst their colleagues. An example of an implementation intention was also found, where NMPs stated that they would only prescribe antibiotics if the diagnosis was a bacterial rather than viral infection. They further stated they would not prescribe in response to patient pressure.	*"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." (I16N)"* (Courtenay *et al*., 2019, p6)

Memory, attention & decision processes	Data extracted in this theme related to decision processes and highlighted that guidelines and protocols aided prescribing decisions. However, NMPs' decision making was also driven by beliefs about consequences as discussed above (worry about patient access to other services if they deteriorated), the environmental context and resources (e.g. time) discussed below and patient's knowledge of antibiotic resistance. Delayed prescriptions were seen as a compromise to manage patient expectations for treatment, concerns about deterioration and lack of time to explain a no-treatment decision.	*"I think they quite like that option, it's all about patient information, and if as a clinician, you don't feel the need for antibiotics, but you know maybe it's a long weekend or something,…so that they have a plan. So you know if things deteriorate and spitting turns green, they have the antibiotics."* (NMP 5)" (Courtenay *et al*., 2017. p5)
Environmental context and resources	Time to educate patients about treatment decisions (NMPs often had around 10-15 minutes), and time and resources to follow-up patients supported NMPs to make prescribing decisions in line with guidelines were highlighted. Having tailored and local patient information sheets, leaflets, guidelines, point of care testing, and decision support tools were also resources that supported NMPs to prescribe in line with guidance. These were important resources as they were tangible materials that could be shared with patients, particularly patient leaflets and information sheets that particularly helped support patients in accepting a no-prescribing decision. Patient related factors, including language barriers between patient and NMP (due to patient's hearing issues, different languages or learning difficulties) was an issue for prescribing according to guidance as it hindered communication and NMPs described how this could interfere with correct diagnosis and appropriate prescribing decisions. Studies included in this research did not report that NMPs had access to resources such as patient information in a range of languages, levels of reading ability or a translator. Access to medical records in out of hours services was variable, and was only present when general practices had provided access, this lack of access to medical records was a barrier to prescribing in line with guidelines. The local context and region also affected prescribing rates with variation seen across regions.	*"We're really, really fortunate here...our appointment times, if you're booked into the nurse clinic, they're half-hour appointments, so we can really spend time providing the education and explaining why we're not giving antibiotics."* NP 13/1000, NHS OOH" (Williams *et al*., 2018, p800). "NPs prescribed significantly fewer antibiotics for viral infections to Medicaid patients than their MD counterparts." [later in the results] "Medicaid insurance status was negatively predictive of antibiotic prescribing. Medicaid patients were almost 75% less likely to receive an antibiotic for a viral upper respiratory infection as compared to the referent category of private insurance." (Ladd *et al*., 2005, p418-19)

	Prescribing also varied according to the health insurance status of patient in the USA, however this was not found in a UK study where prescribing in NHS was compared to private clinics.	
Social influences	Trust between the NMP and their patients influenced prescribing decisions, for some this enhanced prescribing in line with guidelines, whereas others prescribed against guidelines to maintain patient trust. NMPs deployed a range of skills (discussed above) to manage the social influences, particularly where they perceived pressure to prescribe, or that patients required reassurance. Positive social influences made the prescribing decisions easier. Pressure from patients to prescribe was understood in two different ways, (1) the transactional nature of consultations - patients come to the clinic, wait to be seen which all requires effort, and in turn the NMP feels they need to give something (a prescription) to the patient for that effort.(2) NMPs understood the disruption illness caused to people's day to day lives or the anxiety it caused for them if they or their child was unwell and a prescription was seen by patients as a quick fix for this. Raising public awareness about antibiotic resistance supported conversations about no-treatment decisions in consultations. Collaborative working with other prescribers also enabled consistent messaging about antibiotics use to be given to patients, although there were examples of inconsistent prescribing within practices or medical prescribers undermining NMP's no treatment decisions. NMPs felt their own level of confidence was also key social influence on whether or not a patient would accept a no-prescribing decision.	*"The factors determined most to influence all providers' antibiotic prescribing included the following:…providing an antibiotic to maintain patient trust, p = .571"* (Brown, 2018, p.11) *"I have been in this surgery many years so I know lots of parents now that I knew as babies and they know me, and over time they trust and accept what you are saying and try things out. Because they know you they will say that they will ring back and that sort of thing, whereas while you haven't got that opportunity in out of hours and you don't know people and that makes it a bit more difficult."* (NP6)" (Philip & Winfield, 2010, p18)
Emotion	Emotions experienced by NMPs influenced prescribing decisions. These included anxieties about making the wrong decision, particularly in out of hours settings, and so deciding to treat just in case. Feeling tired and stressed, were also barriers to appropriate prescribing as offering a treatment over no treatment was seen as an easy fix. NMPs energy levels varied during the day and across the week. NMPs also reported frustration when medical prescribers undermined their decision making and gave a patient a prescription after they had decided not to prescribe for that patient.	*"Amongst parents particularly that concern that they need to do something for their child and they have that anxiety that their child won't get better or will become very unwell. They bring that to the consultation saying, 'Here's my child. They're sick. I'm really worried*

		about them. Do something for them please.' That fear perhaps that if you don't do something this might be the one child who got worse." NP 11/ 1000, Private Non-Profit OOH" (Williams *et al*., 2018, p800)
Behavioural regulation	NMPs awareness of their own antibiotic prescribing rate supported them to self-regulate their prescribing practice. Above we described that audits and feedback were undertaken and NMPs were shown their prescribing rates against local and national prescribing rates. However, NMPs also described self-auditing and reviewing their own practice on a regular basis.	*"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…(I3N)"* (Courtenay *et al*., 2019, p 5).

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Appendix 1: MMAT version 2018 – methodological quality criteria used in the review, as taken from Hong *et al*. 2018[30]

Screening questions (for all types)
S1. Are there clear research questions?
S2. Do the collected data allow to address the research questions?

Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.

1. Qualitative
1.1. Is the qualitative approach appropriate to answer the research question?
1.2. Are the qualitative data collection methods adequate to address the research question?
1.3. Are the findings adequately derived from the data?
1.4. Is the interpretation of results sufficiently substantiated by data?
1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?

2. Quantitative randomized controlled trials
2.1. Is randomization appropriately performed?
2.2. Are the groups comparable at baseline?
2.3. Are there complete outcome data?
2.4. Are outcome assessors blinded to the intervention provided?
2.5 Did the participants adhere to the assigned intervention?

3. Quantitative nonrandomized
3.1. Are the participants representative of the target population?
3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?
3.3. Are there complete outcome data?
3.4. Are the confounders accounted for in the design and analysis?
3.5. During the study period, is the intervention administered (or exposure occurred) as intended?

4. Quantitative descriptive
4.1. Is the sampling strategy relevant to address the research question?
4.2. Is the sample representative of the target population?
4.3. Are the measurements appropriate?
4.4. Is the risk of nonresponse bias low?
4.5. Is the statistical analysis appropriate to answer the research question?

5. Mixed methods
5.1. Is there an adequate rationale for using a mixed methods design to address the research question?
5.2. Are the different components of the study effectively integrated to answer the research question?
5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?
5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?

604 5.5. Do the different components of the study adhere to the quality criteria of each tradition
605 of the methods involved?
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