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Prescribing antibiotics: Factors driving decision-making in general practice. A discrete choice experiment

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ABSTRACT

Background: Antimicrobial resistance is a threat to human health. We need to strive for a rational use of antibiotics to reduce the selection of resistant bacteria. Most antibiotics are prescribed in general practice, but little is known about factors influencing general practitioners' (GPs) decision-making when prescribing antibiotics.
Aim: To 1) assess the importance of factors that influence decisions by GPs to prescribe antibiotics for acute respiratory tract infections (RTIs) and 2) identify segments of GPs influenced differently when deciding to prescribe antibiotics.
Methods: A questionnaire survey including a discrete choice experiment was conducted. Danish GPs were asked to indicate whether they would prescribe antibiotics in six hypothetical choice sets with six variables: whether the GP is behind schedule, patient's temperature, patient's general condition, lung auscultation findings, C-reactive protein (CRP) level, and whether the patient expects antibiotics. Error component and latent class models were estimated and the probabilities of prescribing in different scenarios were calculated.
Results: The questionnaire was distributed to every Danish GP (n = 3,336); 1,152 (35%) responded. Results showed that GPs were influenced by (in prioritised order): CRP level (Relative importance (RI) 0.54), patient's general condition (RI 0.20), crackles at auscultation (RI 0.15), and fever (RI 0.10). Being behind schedule and patient expectations had no significant impact on antibiotic prescription at the aggregate level. The latent class analysis identified five classes of GPs: generalists, CRP-guided, general condition-guided, reluctant prescribers, and stethoscopy-guided. For all classes, CRP was the most important driver, while GPs were heterogeneously affected by other drivers.
Conclusion: The most important factor affecting Danish GPs' decision to prescribe antibiotics at the aggregate level, in subgroups of GPs, and across latent classes was the CRP value. Hence, the use of CRP testing is an important factor to consider in order to promote rational antibiotic use in the battle against antimicrobial resistance.

Credit author statement

Rikke Vognbjerg Sydenham: Conceptualisation, Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Visualization, Project administration. Dorte Ejg Jarbøl: Conceptualisation, Methodology, Investigation, Writing - Review & Editing. Malene Plejdrup Hansen: Conceptualisation, Methodology, Writing - Review & Editing. Ulrik Stenz Justesen: Conceptualisation, Methodology, Writing -

Abbreviations: GP, General practitioner; CRP, C-reactive protein; DCE, Discrete Choice Experiment; RTI, Respiratory tract infection; 95CI, 95% confidence interval; RI, Relative importance; RO, Rank order.

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1. Introduction

We are seeing a steady rise in resistant bacteria worldwide. One result is increased morbidity and mortality from otherwise harmless infections, making antimicrobial resistance the leading cause of diseases and death (Murray et al., 2022). New antibiotics are not being developed at the same pace as the march of antibiotic resistance (World Health Organization, 2015). The World Health Organisation stresses the threat that antimicrobial resistance poses to human health, and if we wish to preserve the effect of antibiotics, we will need to restrict their use to cases where they are absolutely essential (World Health Organization, 2014; World Health Organization, 2015). The use of antibiotics in humans and their use in agriculture are both drivers of antibiotic resistance and must be reduced. In our study we focus on improvements in general practice settings to reduce the use of antibiotics, since 75% of all antibiotic prescriptions to humans are issued by general practitioners (GPs) (Goossens et al., 2005; Aabenhus et al., 2016). Though antibiotic prescribing in Denmark is lower than in many other countries (World Health Organization, 2014), antimicrobial resistance is an increasing problem. A recent Danish study indicates that overuse takes place; this leaves room for improvement (Saust et al., 2018). Over the years several national campaigns have targeted healthcare professionals and the general public (Danish Patients and the Organisation of Danish Medical Societies, 2022; Statens Serum Institut). Furthermore, a National Action Plan addressing antibiotics in human healthcare was launched by the Danish Ministry of Health in 2017 (Danish Ministry of Health, 2017).

This paper explores the factors that influence decision-making in general practice when prescribing antibiotics and aims to identify ways to improve the quality of antibiotic prescribing. The decision-making process when GPs elect to prescribe antibiotics is complex and influenced by several factors (Buusman et al., 2007; Hansen C. R., 2016; Murshid and Mohaidin, 2017). Previous studies have identified the following factors: Time pressure, C-reactive protein (CRP), lung auscultation, certain physician characteristics, institutional environments, situations involving uncertainty regarding diagnosis, prognosis, continuity of care, patient expectations, and not knowing the patient (Brookes-Howell et al., 2012; Dempsey et al., 2014; Liu et al., 2019; McKay et al., 2016; McNulty et al., 2013; O'Connor et al., 2018; Poss-Doering et al., 2020; Sirota et al., 2017). CRP is a commonly used biomarker of inflammation and infection and can be quantified in a blood sample. The test can be performed as a point-of-care test in general practice with the result available within a few minutes. Multiple studies indicate that CRP testing influences antibiotic prescribing patterns among GPs and can reduce antibiotic use without compromising patient safety (Hunter, 2015; Little et al., 2013; Minnaard et al., 2017; Phillips et al., 2020; Aabenhus et al., 2014).

Little is known about the relative influence of different factors on antibiotic prescribing by GPs, least of all regarding the balance between clinical factors and patient expectations or time pressure. Research has primarily consisted of qualitative and observational studies. Qualitative data cannot reveal the relative importance of different factors when it comes to the decision to prescribe antibiotics. Observational studies are based on administrative data that does not routinely record all the factors that may influence the prescription decisions made by GPs. For this study we use a discrete choice experiment (DCE) to understand professionals decision-making in complex situations (Hifinger et al., 2017; Linley and Hughes, 2013; Lum et al., 2018). The base scenario describes a specific patient with an acute respiratory tract infection (RTI). The DCE varies several patient and appointment factors previously found to influence prescriptions for treating acute RTI. We asked GPs to state whether they would prescribe antibiotics in each case. Instead of being asked directly about potentially sensitive issues, GPs are presented with a scenario mimicking real life (Bateman et al., 2004).

Our study aimed to 1) assess the importance of factors that influence decisions by GPs to prescribe antibiotics for acute RTIs and 2) identify potential differences in factors influencing antibiotic prescribing for segments of GPs. We investigated how these factors influence GP prescription behaviour at the aggregate level and for subgroups of GPs based on both observable characteristics and unobservable characteristics, using a latent class approach. We compare groups of GPs using rank orders, relative importance scores, and the probabilities of prescribing in different case scenarios.

CRP proved to be the most important factor for antibiotic prescription both at the aggregate level and for subgroups and latent classes of GPs. We found that GPs do not differ markedly in their preferences for antibiotic prescribing based on observable characteristics such as age, gender, region, practice type, seniority, and whether they employ GPs in training. However, we identified five latent classes of GPs who differ in their prescribing behaviour. We found that one class of GPs was more reluctant to prescribe than the others, and that the class of CRP-guided GPs was almost as reluctant to prescribe as the class of reluctant prescribers. Previous studies have documented that CRP testing can reduce antibiotic prescribing (Andreeva and Melbye, 2014; Held et al., 2012; Lindström et al., 2015; Minnaard et al., 2017). Hence an important policy implication that may be derived from our study is that initiatives which promote CRP use may foster the even more rational use of antibiotics in general practice across all types of GPs. Our findings can be used by policy makers to design initiatives to promote rational prescription in general practice and hereby mitigate the problem of antimicrobial resistance.

2. Method

2.1. Institutional setting

Danish general practice is a tax-funded institution where most services are free of charge for users. GPs are self-employed and financed by a mixed capitation and fee-for-service system. Medical expenditures are partly subsidised. GPs work in single-handed practices (42% of all practices) or in partnership practices (58%) with typically two to six GPs sharing management and financial responsibility. Practices have an average of 1737 listed patients per GP (The Danish Organisation of General Practitioners, 2020). Most practices employ practice nurses, health care assistants and secretaries, and in a few cases pharmacologists, but only medical doctors can prescribe antibiotics. Point-of-care CRP testing has been available in Danish general practice since the 1990s and is used daily in most practices. GPs receive a governmental reimbursement for providing CRP tests (Haldrup et al., 2017).

2.2. Study population and data collection

The study population was made up of all GPs in Denmark with an identifiable practice provider number. Every provider number listed in the Danish Health Authorities' Organisation Register is linked to one or more GPs, and each GP is identified with a unique authorisation ID. This register is of high validity, since it is used by health authorities to administer settlements of accounts to the GPs for health services performed. Contact information, age, and seniority for each GP were retrieved from publicly available registers.

The questionnaire was distributed to all GPs in Denmark (N = 3336). Questionnaire data was collected from May to September 2019. Invitation was distributed by postal mail containing an information letter with a hyperlink to the online survey. Data were analysed anonymously.

Information on the survey was disseminated through regional newsletters. Two reminder letters were sent out. The GPs received a small fee for their time.

2.3. The discrete choice experiment

The DCE is a validated quantitative research method. Respondents are presented with a series of carefully constructed scenarios arranged into choice tasks with several characteristics (attributes) varying systematically at different levels (Hauber et al., 2016; Soekhai et al., 2019). The characteristics and scenarios are developed based on theory, empirical evidence, and qualitative research (Coast et al., 2012). The respondents' choices across choice tasks allow the research team to estimate and rank the influence of each attribute being studied (Johnson et al., 2013; Train, 2002).

In our study the scenarios described several patient and appointment factors (attributes) that may influence GPs when they decide whether to prescribe antibiotics to a specified patient with symptoms of acute RTI. The base scenario included some fixed patient characteristics and the varying attribute levels are described in Online Appendix 1. This method is in line with best practice for studies of professionals' decision-making in this area (Arellano et al., 2015; Gonzalez et al., 2017; Hifinger et al., 2017; Offerhaus et al., 2015).

2.3.1. Identification of attributes and levels

Following best practice guidelines, a six-stage process was used to create the base scenario and identify the attributes and levels to be included in the DCE (Bridges et al., 2011; Johnson et al., 2013): 1) Literature was searched focusing on factors influencing GPs prescribing behaviour when handling patients with infections. 2) Two focus group interviews were held with three GPs in each and consultation observations followed by interviews were performed with three GPs (a total of nine participants) (Malterud et al., 2016). All interviews were semi-structured and moderated by a member of the research team. The interviews used open-ended questions to identify factors that influence GPs' decisions to prescribe antibiotics. For the focus group interviews participants were asked to recall recent cases, while in the individual interviews the questions were based on the patients the GP had just seen. Interviews were audio-recorded, transcribed, and analysed using an inductive thematic approach. 3) An expert panel discussion was conducted with two medical doctors with clinical microbiology as their speciality, two researchers from the field of infectious diseases in general practice (both medical doctors), one GP with broad research experience, and one health economist. The expert panel discussion aimed to select and validate attributes and levels. 4) A workshop with the research team was held to select the final set of six attributes and levels. 5) The questionnaire was tested in think-aloud interviews with nine medical doctors working in general practice. The aim was to test the relevance, acceptability, and comprehensiveness of the DCE instrument. Adjustments were made to the attributes and levels and questionnaire phrasing. 6) A pilot test of the DCE and questionnaire was distributed to 100 randomly chosen GPs to test survey administration and face validity of pilot results in terms of structure and variation in data. Respondents were asked to provide feedback on the relevance, acceptability, and feasibility of the questionnaire.

The process of creating the base scenario and identifying attributes and levels is described in detail in Online Appendix 1. When creating the base scenario our emphasis was on presenting a clear case that resembles a patient often seen in general practice without a high risk of severe illness in itself: a 65-year-old male with a six-day history of a cold and sore throat. The attributes included in the final DCE are shown in Table 1. The patient's current general condition remained an important topic for GPs throughout the qualitative work and was included as an attribute in the final design. In the qualitative work the GPs described the current general condition as the first appearance of the patient presenting in the consultation, including skin colour, movements, contact, and breathing; these gave the GP important information as to whether the patient was critically affected by the disease. The four CRP levels used for the DCE were based on national and international guidelines for CRP cut-off values (BjerrumHansen et al., 2014; National Institute for Health and Care Excellence Uk, 2019). Guidelines do not state a threshold for deciding to prescribe antibiotics but instead provide indications of limits where the cause of illness is likely to be of bacterial origin. As no strict cut-off values exist it was decided to include both a very low CRP value (5 mg/L) as well as a relatively high CRP value (120 mg/L) to indicate that immediate antibiotic treatment was probably not indicated or indicated, respectively. The values in between (35 mg/L and 80 mg/L) were chosen to illustrate cases in which it can be difficult to decide on antibiotic treatment based on the result of the CRP test alone.

Table 1
Attributes and levels in the DCE.

Attribute	Explanation	Levels
Programme for the day	Whether you are on schedule or behind with today's appointments.	(0) You are on time (1) You are 30 min behind
Temperature	Patient temperature measured rectally prior to the consultation.	(0) 37.8 °C (1) 38.8 °C
Patient's current general condition	Describe your overall assessment of the general appearance of the patient, as shown by his/her hue, skin, breathing, and responsiveness.	(0) Current general condition not affected (1) Current general condition affected
Lung auscultation	Your stethoscopy findings.	(0) Normal stethoscopy (1) Crackles
CRP	C-reactive protein measured in mg/l immediately before your consultation with the patient.	(0) CRP 5 (1) CRP 35 (2) CRP 80 (3) CRP 120
The patient's expressed expectations of antibiotics	The patient indicates during the consultation whether he expects an antibiotic prescription.	(0) Does not express expectations of antibiotics. (1) Expresses expectations of antibiotics.

2.3.2. Experimental DCE design

We used a Bayesian D-efficient experimental design. The advantage of efficient designs, as opposed to orthogonal designs, is that they typically require fewer choice sets and smaller sample sizes to ensure sufficient statistical power (ChoiceMetrics, 2018). The required sample size is a function of the initial belief about the parameter values (referred to as priors), and the DCE design (de Bekker-Grob et al., 2015; Rose and Bliemer, 2013). In an efficient design, the parameter priors are assumed to be known and fixed. A Bayesian efficient design allows for uncertainty about the parameter priors by making use of random priors described by random distributions (ChoiceMetrics, 2018). In our case, we assumed that all parameters followed a normal distribution with mean and standard deviation as estimated from the quantitative pilot test.

In total, 128 possible scenarios can be constructed based on the attributes and levels in Table 1. These were reduced to a subset of choice tasks for inclusion in our DCE. To ensure sufficient degrees of freedom to estimate all main effects, 12 choice tasks were specified, and these were selected by using NGENE software. The 12 choice tasks were created to ensure that the attribute levels were as balanced as possible and with minimal correlation between the attribute levels. They were split into two blocks of six choice sets each to reduce the burden on each respondent. Blocking was performed using the minimum correlation principle, where the average correlation between the blocking column and the design columns in the experimental design are minimised (ChoiceMetrics, 2018). For the pilot test best-guess priors were used and the results from the pilot were used to determine the priors in the final design. The required sample size was calculated by Ngene software using the S-estimate from the final experimental design (ChoiceMetrics, 2018). This is based on significance level, statistical power level, statistical model used in the DCE analysis, initial belief about the parameter values, and the DCE design (Rose and Bliemer, 2013). A sample size of 282 respondents was needed to ensure sufficient statistical power to estimate main effects in our study.

Each choice task consisted of two hypothetical scenarios. The respondent was given the opportunity to prescribe antibiotics either to the patient presented in scenario A, the patient in scenario B, to both patients, or to neither of the patients (unforced choice). If both were chosen, the respondents were subsequently asked to state which of the two patients they would be most inclined to prescribe antibiotics to (forced choice). We generated one choice variable. If respondents selected one response *A, B or None* in the unforced choice then this is the value of the choice variable, and if respondents chose *Both* then the choice variable used responses *A or B* from the forced choice. The Online appendix 2 shows the structure of the DCE choice set.

2.3.3. Statistical analysis

To assess the importance of factors that influence decisions by GPs to prescribe antibiotics for acute RTIs, we used a dummy-coded mixed logit error component model in which the decision on antibiotic prescribing for all responding GPs was the outcome and the attributes were the explanatory variables. Since patient benefit is included, together with profit, in the standard utility function of health care professionals (Ellis and McGuire, 1986), we considered it reasonable to assume that GPs maximise utility to act as the best possible agent for the patient when deciding in which consultations to prescribe antibiotics. We therefore used random utility theory to explain the utility of a GP n for prescribing antibiotics in alternative i. Where n refers to the specific GP (respondent) and i refers to the specific alternative (scenario).

The true utility is:

$$U_{in} = V_{in} + \varepsilon_{in} \tag{1}$$

The observable systematic component of utility, V_{in}, constitutes the observable component of the variance in choice of alternative i. The non-observable component, ε_{in}, is treated as random. If we assume that the utility function is additive linear, the observable component for individual n for alternative i becomes $V_{in} = \beta \cdot X_{in}$, where $X_{in} = (X_1, X_2, \dots X_r)$ is a vector of attributes. The linear predictor, V, of the applied models can be written as:

$$\begin{aligned} V_{in} = {} & \alpha_i + \beta_1 \cdot Xdelayed_{in} + \beta_2 \cdot Xfever_{in} + \beta_3 \cdot Xaffectedcondition_{in} \\ & + \beta_4 \cdot Xstethoscopy_{in} + \beta_5 \cdot XCRP35_{in} + \beta_6 \cdot XCRP80_{in} + \beta_7 \cdot XCRP120_{in} \\ & + \beta_8 \cdot Xexpect_{in} \end{aligned} \tag{2}$$

A logit model can be applied, assuming that the error terms are independent, and the extreme value random variables are identically distributed. The alternative specific constant, α, is specified as random by decomposing it into the mean, θ, and standard deviation, η_n, such that

$$\alpha_{in} = \theta \cdot z_{in} + \eta_n \cdot z_{in} \tag{3}$$

z refers to observed variables relating to alternative i. The alternative specific constant refers to opting out, that is not prescribing antibiotics in any of the two consultations.

Assuming that the coefficients vary over respondents with density $f(\beta)$, we defined a mixed logit error component model, which also relaxes the independent of irrelevant alternatives (IIA) assumption and allows for the panel structure in the data (due to the answering of six choice sets each). The probability for respondent n of choosing alternative i is:

$$P_{in} = \int \left(\frac{e^{\mu X_{in} \beta}}{\sum_{j=1}^{J} e^{\mu X_{ij} \beta}} \right) f(\beta) d\beta \tag{4}$$

where μ is the scale parameter (which is inversely related to the error variance) (Train, 2002).

We conducted several robustness checks. Firstly, we weighted the observations in our data by the inverse of their probability of being sampled. We weighted on GP gender, age, region, seniority, and practice type. Secondly, we estimated a nested logit model. In the study design, the alternatives have a nested structure in which the alternatives for prescribing antibiotics may have correlated error terms, while the alternative not to prescribe may be independent from the decision to prescribe. Thirdly, we estimated a mixed logit error component model on a restricted sample of observations by excluding the “both” answers from the analysis. Fourthly we estimated a random regret minimization model as GPs may have used a regret minimization strategy rather than a utility maximization strategy in their prescription decision (Chorus, 2010).

To identify segments of GPs influenced differently in their decision to prescribe antibiotics, subgroup analyses were first estimated for observable characteristics (gender, age, seniority, practice type, having GP trainees, and geographical region). We performed likelihood-ratio (LR) tests to test the null-hypothesis that all coefficients were the same between subgroups.

We also performed a latent class analysis in order to determine whether heterogeneity among respondents is present without being related to the identified observable characteristics. This analysis assumes that respondents can be grouped according to their stated prescribing behaviour and can take account of unobserved prescribing heterogeneity. Class membership is latent and thus not based on a-priori decided characteristics, but rather on respondents’ stated prescription decisions. This implies that GPs do not belong to a specific class, but that the probability of belonging to a class can be estimated. The choice probability for the latent class model can be described by:

$$P_{in} = \sum_{m=1}^{M} S_m \left(\frac{\beta_m x_{in}}{\sum_j \beta_m x_{jn}} \right) \tag{5}$$

M defines the number of segments or classes in the population. S_m is the share of the population in segment m. The model is useful when heterogeneity among the population is present but cannot be explained by observable factors. The analyses were performed with two to seven classes, and best model fit based on Akaike information criterion (AIC) and Bayesian information criterion (BIC) determined the number of classes (Greene and Hensher, 2003; Zhou et al., 2018).

In all regression models, a significant coefficient for an attribute indicates that the specific attribute has significant impact on a GP's decision to prescribe antibiotics. A positive (negative) sign on the coefficient indicates that the attribute increases (decreases) the probability that a GP will prescribe antibiotics. The parameter estimates in the different models are not directly comparable due to the scale parameter, μ, Therefore, we calculated the relative importance of each attribute for all models by dividing the difference between the coefficient for the level with highest utility and level with the lowest utility by the sum of differences for all attributes and determined rank orders (Malhotra and Birks, 2007). Since parameter estimates are not directly comparable across subgroups and latent classes, we calculated the probabilities of prescribing antibiotics for five scenarios defined by differences in attribute levels to further illustrate the variance between GPs and classes. The five scenarios, described in Table 5, were chosen to illustrate differences in likelihood of prescribing for each subgroup of GPs and each class with increasing case severity.

Table 2
Characteristics of respondents and the GP population.

Characteristic	Respondents (n = 1152) n (%)	Total GP population (n = 3336) n (%)
Gender		
Male	526 (45.7)	1500 (45.0)
Female	626 (54.3)	1836 (55.0)
Age		
<45 years	338 (29.3)[a]	836 (25.1)
45–54 years	401 (34.8)	1.108 (33.2)
55–64 years	316 (27.4)	949 (28.4)
≥65 years	91 (7.9)[a]	392 (11.8)
Missing	6 (0.5)[a]	51 (1.5)
Region		
Capital Region	284 (24.7)[a]	1055 (31.6)
Region of Zealand	141 (12.2)	457 (13.7)
Region of Southern Denmark	302 (26.2)	786 (23.6)
Central Denmark Region	349 (30.3)[a]	807 (24.2)
North Denmark Region	76 (6.6)	231 (6.9)
Seniority		
<5 years	230 (20.0)	626 (18.8)
5–14 years	441 (38.3)	1.190 (35.7)
≥15 years	474 (41.1)	1.462 (43.8)
Missing	7 (0.6)[a]	58 (1.7)
Practice organisation		
Solo	252 (21.9)	821 (24.6)
Partnership	900 (78.1)	2515 (75.4)

[a] Statistically significant difference ($p < 0.05$) detected in a *t*-test for differences in proportions among respondents versus total population.

3. Results

Of the 3336 GPs receiving an invitation to the survey, 1152 responded (34.5%). Table 2 presents characteristics of the participating GPs and the Danish GP population showing that the participants were representative with respect to gender and practice organisation, while they were slightly younger and not completely evenly distributed geographically.

3.1. Factors influencing GPs' decision to prescribe antibiotics for acute RTIs

Table 3 demonstrates the main effects of the attributes on antibiotic prescribing. The results indicate that the CRP level (Relative Importance (RI) = 0.54) is the most influential factor in GP prescribing decisions. Other influential factors are the patient's current general condition (RI = 0.20), lung auscultation (RI = 0.15), and the patient's temperature (RI = 0.10). We found no significant effect on antibiotic prescribing when GPs were delayed in their programme for the day or when patients expressed expectations of antibiotics.

The sensitivity analyses show that the results are robust to the inclusion of sampling weights in the estimation (Online appendix 3), taking the nested data structure into account (Online appendix 4), and removing the "both" option from the analysis, except that lung auscultation becomes equally important as patient's current condition (Online appendix 5), and estimating a random regret minimization model (Online appendix 6).

3.2. Segments of GPs influenced differently in their decision to prescribe antibiotics

Subgroup analyses related to GP characteristics showed only minor differences between gender, age groups, seniority, practice organisation, and location (region in Denmark) (Online appendix 7). For all subgroups, the CRP level was the most influential factor for prescription behaviour. Probabilities for prescribing in the five defined scenarios show minor differences across gender, age, seniority, and practice location (Online appendix 8). Female GPs, younger GPs, GPs with less seniority, and GPs in the region of Northern Denmark seem to be less inclined to prescribe than their colleagues.

In the latent class analysis, a comparison of model fit revealed that a model with five classes of GPs fit the data best. These classes all have CRP as the most important attribute and are distinguished by differences in the relative importance of other attributes (Table 4). The GP classes are: 1) generalists influenced by CRP, general condition, lung auscultation and temperature (comprising 31.7% of all responses), 2) CRP-guided influenced by CRP to a higher degree than the other classes (22.4%), 3) general condition-guided primarily influenced by CRP and general condition (19.7%), 4) reluctant prescribers who are least inclined to prescribe antibiotics, and influenced by CRP, followed by general condition, lung auscultation and temperature (15.9%), and 5) stethoscopy-guided who are primarily influenced by CRP and lung auscultation and not significantly by the patients' general condition (10.4%). Running late in their daily programme impacted on prescribing for two classes; the stethoscopy-guided GP, who would be *less* inclined to prescribe when delayed, and the CRP-guided GP, who would be *more* inclined to prescribe when delayed. The CRP-guided GPs and the reluctant prescribers were less likely to prescribe antibiotics if the patient expressed an expectation. The stethoscopy-guided GP, on the other hand, would be more inclined to do so.

Table 3
Mixed logit error component model.

Attribute name	Attribute level	Utility coef. [95CI]	Relative influence (Rank order)
Programme for the day	30 min behind schedule	−0.049 [-0.114; 0.016]	0.00 (5)
Temperature	38.8 °C	1.256 [1.169; 1.344]	0.10 (4)
Patient's current condition	Current condition affected	2.629 [2.477; 2.780]	0.20 (2)
Lung auscultation	Crackles at stethoscopy	1.965 [1.837; 2.094]	0.15 (3)
C-Reactive Protein	CRP 35	1.894 [1.742; 2.045]	0.54 (1)
	CRP 80	5.497 [5.213; 5.782]	
	CRP 120	7.023 [6.676; 7.369]	
The patient's expressed expectations of antibiotics	Expresses expectations of antibiotics	−0.018 [-0.085; 0.049]	0.00 (6)
Opt out		6.146 [5.810; 6.481]	
SD Opt out [95CI]		1.393 [1.268; 1.518]	
Observations	20,736		
Log likelihood	−5880.28		
Chi 2	447.88		
Prob > chi2	0.0000		

Mixlogit command performed in Stata with 1000 Halton draws (Hole, 2007). A positive (negative) sign of the utility coefficient indicates that the attribute makes the GP more (less) inclined to prescribe. Opt out should be interpreted as the preference for not prescribing. RI: Relative importance. RO: Rank order.Reference levels: Programme for the day: On time. Temperature: 37.8 °C. Patient's current general condition: not affected. Lung auscultation: no abnormalities. C-Reactive Protein: 5. Expressed expectations: Does not express expectations of antibiotics.

The probability of prescribing for each class in each of the five defined scenarios is shown in Table 5. In a scenario with crackles on auscultation, general condition affected, and CRP level at 35 mg/L, for example, we found that the reluctant prescribers have a 15.4% probability of prescribing, whereas the CRP-guided GPs and generalists have a 24.0% and 35.6% probability of prescribing antibiotics, respectively. At the other end of the scale, we found the stethoscopy-guided and the general condition-guided GPs having an 88.4% and an 89.9% probability of prescribing antibiotics. Across the five defined cases, the CRP-guided GPs, together with the reluctant prescribers, have relatively low probabilities of prescribing antibiotics compared to the other classes.

4. Discussion

The CRP value proved to be the most important factor affecting Danish GPs' decisions to prescribe antibiotics at the aggregate level, in subgroups of GPs based on observable characteristics, and across latent classes. Affected general condition, crackles at lung auscultation, and fever were also important influences on the decision to prescribe, although less influential than CRP values. Being behind schedule and patient expectations had no significant impact on prescribing at the aggregate level. However, both factors were significant in some segments of the GP population, although not to the same extent as the clinical factors. This indicates that GPs generally act rationally when handling patients with symptoms of an acute infection.

We only found minor differences in preferences based on observable GP characteristics. However, the latent class analysis revealed marked preference heterogeneity among GPs, and five classes were identified. One class of GPs was more reluctant to prescribe than the others. Interestingly, the class of CRP guided GPs were almost as reluctant to prescribe as the class of reluctant prescribers. Previous studies support the argument that CRP testing can reduce antibiotic prescribing and that a CRP test interpreted along with clinical symptoms can safely be used to rule out bacterial infections of clinical importance (Andreeva and Melbye, 2014; Held et al., 2012; Lindström et al., 2015; Minnaard et al., 2017). This is also reflected in national guidelines (BjerrumHansen et al., 2014).

The patient's current general condition was the second-most important factor identified, meaning that the classic virtues of general practice represented by the GPs clinical assessment are of high importance. To our knowledge, the importance of GPs' assessment of their patients general condition on antibiotic prescribing has not previously been explored and very little research has been conducted in exploring the concept of general condition (Dale et al., 2019; Ebell et al., 2020). Studies have considered GPs intuition or clinical gestalt which may reflect the same thing, i.e., the interpretation of the overall impression of the patient (Brookes-Howell et al., 2012; Dale et al., 2019). We found that the general-condition-guided GPs were more likely to prescribe antibiotics than the CRP-guided GPs. There may be variation in the cues used by GPs to assess the general condition. Further research is needed to determine the nature of cues that GPs use to assess a patient's current general condition, whether cues are used consistently by a given GP and across GPs, and the validity of these cues for prescribing. This knowledge may help foster rational antibiotics use.

Studies have found that time pressure and patient requests are associated with higher levels of antibiotic prescribing (Dempsey et al., 2014; Liu et al., 2019; McNulty et al., 2013; Poss-Doering et al., 2020; Sirota et al., 2017). We found that time constraints and patient expectations only influenced certain groups of GPs, and this influence was ambiguous because some GPs were more inclined to prescribe antibiotics due to time constraints and patient expectations while others were less inclined. Our finding of no overall effect of patient expectations and time constraints on antibiotic prescribing may be explained by 1) the inclusion of clinical factors that have a larger influence, and 2) patient expectations and time constraints influence different segments of GPs in different directions. This heterogeneity in behaviour may result in an insignificant effect at the aggregate level.

The study has important policy implications. We found heterogeneity as to the factors driving antibiotic prescribing decisions among GPs and that these differences are not well captured by observable GP characteristics. A latent class model, as used in this study, can help us

Table 4
Latent class model.

	Generalist	RI (RO)	CRP-guided	RI (RO)	General condition-guided	RI (RO)	Reluctant prescriber	RI (RA)	Stethoscopy-guided	RI (RA)
	Coef. [CI95]		Coef. [CI95]		Coef. [CI95]		Coef. [CI95]		Coef. [CI95]	
30 min behind schedule	−1.345 [-1.727;-0.964]	0.070 (5)	1.593 [0.898; 2.288]	0.092 (3)	0.292 [0.104; 0.481]	0.026 (5)	−0.036 [-0.429; 0.358]	0.002 (6)	−1.135 [-1.762;-0.508]	0.096 (3)
38.8 °C	2.142 [1.796; 2.488]	0.111 (4)	0.221 [-0.546; 0.989]	0.013 (6)	1.000 [0.772; 1.229]	0.088 (4)	1.366 [0.957; 1.776]	0.092 (4)	0.015 [-0.486; 0.517]	0.001 (6)
Current condition affected	2.848 [2.391; 3.306]	0.148 (2)	2.146 [1.426; 2.866]	0.124 (2)	3.142 [2.729; 3.555]	0.278 (2)	3.585 [2.935; 4.235]	0.242 (2)	0.384 [-0.235; 1.002]	0.033 (4)
Crackles at auscultation	2.723 [2.193; 3.254]	0.141 (3)	0.562 [-0.313; 1.438]	0.032 (5)	1.526 [1.240; 1.811]	0.135 (3)	2.343 [1.699; 2.987]	0.158 (3)	4.725 [3.108; 6.342]	0.401 (2)
CRP 35	2.131 [1.526; 2.736]	0.507 (1)	5.219 [3.131; 7.306]	0.693 (1)	1.918 [1.550; 2.285]	0.469 (1)	1.429 [0.652; 2.207]	0.478 (1)	0.274 [-0.273; 0.821]	0.439 (1)
CRP 80	8.129 [7.155; 9.103]		9.904 [7.605; 12.203]		4.363 [3.661; 5.066]		5.544 [4.511; 6.577]		2.897 [1.664; 4.131]	
CRP 120	9.764 [8.651; 10.876]		12.017 [9.606; 14.428]		5.309 [4.527; 6.091]		7.070 [5.790; 8.350]		5.180 [3.321; 7.040]	
Expresses expectations of antibiotics	0.429 [0.111; 0.747]	0.022 (6)	−0.810 [-1.281;-0.340]	0.047 (4)	−0.039 [-0.223; 0.144]	0.003 (6)	−0.391 [-0.720;-0.062]	0.026 (5)	0.358 [0.048; 0.668]	0.030 (5)
Opt out	8.296 [7.239; 9.354]		9.078 [6.673; 11.484]		4.399 [3.648; 5.151]		9.058 [7.498; 10.619]		3.352 [1.864; 4.841]	
Class share	0.317		0.224		0.197		0.159		0.104	
Model fit										
Observations	20,736									
Log likelihood	−5443.88									
AIC	11,233.17									
BIC	10,985.75									
Pseudo-R2	0.273									

Lclogit command performed in Stata with 150 iterations. A positive (negative) sign of the utility coefficient indicates that the attribute makes the GP more (less) inclined to prescribe. Opt out should be interpreted as the preference for not prescribing. RI: Relative importance. RO: Rank order.Reference levels: Programme for the day: On time. Temperature: 37.8 °C. Patient´s current general condition: not affected. Lung auscultation: no abnormalities. C-Reactive Protein: 5. Expressed expectations: Does not express expectations of antibiotics.

uncover latent groups of GPs who may differ on unobservable variables. We identified five segments of GPs who are influenced differently. The variation in prescribing behaviour between the segments is not tied to observable characteristics, but the existence of different segments illustrates that all GPs cannot be targeted by one intervention. Awareness of this can be used by policy makers in the design of new policy schemes aimed at reducing antibiotic use in general practice in the sense that multi-faceted interventions should be offered. This knowledge may also be of relevance for individual GPs to reflect on and increase awareness of their own profile in order to focus on rational prescribing behaviour. This could also be implemented in medical education initiatives. Importantly, the study identified CRP level as the most important determinant for all GPs when deciding to prescribe antibiotics. Hence an important policy implication from our study is that initiatives which promote CRP use may foster an even more rational use of antibiotics in general practice across all types of GPs. This study finding can be used by policy makers to design initiatives and guidelines to promote rational prescription in general practice and hereby mitigate problems with antimicrobial resistance.

Danish GPs are experienced users of the CRP test to support decision-making, and it is used daily in most practices. If CRP testing was implemented in countries that do not routinely use it at present this could promote more rational antibiotic use. However, more studies are needed to scrutinise when the test is appropriate to use. A recent DCE study found that patients prioritise tests with high confidence, which is more likely to be present in a specific test (e.g. polymerase chain reaction test for a specific pathogen) than with the non-specific CRP test (Mott et al., 2020).

More than one third of all Danish GPs participated in the study. This corresponds with the response rates of other previous surveys among GPs (Riisgaard et al., 2020; Andersen et al., 2019). The study participants were representative of the Danish GP population with respect to gender and practice organisation but were slightly younger and not completely evenly geographically distributed. As our results are robust to sample weighting, it is likely that they can be generalised to the Danish GP population. We further found that our results are robust to different model specifications. We are therefore confident in the robustness of our findings.

Our DCE was carefully designed to capture important parameters in the decision-making process that leads to clinical decisions. The results are based on hypothetical scenarios, and patient pressure and being behind schedule may not be experienced as strongly as in real life. We found a significant influence of both attributes for some of the latent classes. This indicates that GPs are to some extent influenced by these factors. In support of this, in our qualitative work we found that GPs were willing to talk openly about being influenced by time pressure or patient expectations. The DCE has the advantage of not asking directly about potentially taboo topics but rather presenting a realistic scenario (Bateman et al., 2004). Furthermore, the DCE is anonymous and not face-to-face. Though issues with 'social desirability bias' were carefully considered throughout the study design process, it may still influence the results to some extent. Studies so far have shown reasonable external validity for DCEs in some contexts, but relatively little research has been conducted in this area (Krucien et al., 2015; Quaife et al., 2018).

One patient case is used as the basis for the DCE in this study. This may affect the generalisability of our findings to other patient types. However, this study design ensures that all GPs answer the DCE with the same patient in mind which minimises uncontrolled variability and ensures that results are not driven by unobserved differences in perceived patient needs. Several studies have asked healthcare professionals to state treatment intentions for a defined patient using a DCE type task (Arellano et al., 2015; Hifinger et al., 2017; Offerhaus et al., 2015). Nevertheless, a more comprehensive impression of the importance of the different factors for decision making could be investigated further by exploring other patient cases of RTIs. As with all DCE studies we can assess the importance of included attributes only. Thus, we

Table 5
Probability of prescribing for each class in 5 selected scenarios.

Probability of prescribing % (CI95)	Generalist	CRP-guided	General condition-guided	Reluctant prescriber	Stethoscopy-guided
Crackles and CRP 5	0.4 [0.1; 0.6]	0.0 [0.0; 0.1]	5.3 [2.1; 8.6]	0.1 [0.0; 0.2]	79.8 [59.8; 99.7]
Crackles, general condition affected and CRP 5	6.2 [3.7; 8.6]	0.2 [-0.2; 0.5]	56.7 [46.0; 67.3]	4.2 [1.5; 6.9]	85.3 [74.6; 96.0]
Crackles, general condition affected and CRP 35	35.6 [22.4; 48.8]	24.0 [9.3; 38.7]	89.9 [86.2; 93.6]	15.4 [6.7; 24.1]	88.4 [81.6; 95.2]
Crackles, general condition affected, CRP 35 and patient expecting antibiotics	45.9 [33.5; 58.3]	12.3 [-0.5; 25.2]	89.5 [85.6; 93.5]	11.0. [4.4; 17.6]	91.6 [86.3; 96.9]
Crackles, general condition affected, CRP 80 and patient expecting antibiotics	99.7 [99.4; 100.0]	93.8 [88.4; 99.3]	99.0 [98.4; 99.6]	88.3 [81.1; 95.5]	93.8 [88.4; 98.4]

Base case: A 65-year-old male with a six-day history of a cold and sore throat. In addition, he now presents with a productive cough. No chronical conditions. He does not smoke. Blood pressure is 125/75 mmHg. Base scenario: The GP is on time with the programme for the day. The patient has a temperature of 37.8 °C. Patient's current general condition is not affected. Lung auscultation is with no abnormalities. C-Reactive Protein 5. The patient does not express expectations of antibiotics. Changes from this are stated in the left column. Corresponding changes in probabilities of prescribing is shown for each class of GPs.

cannot evaluate the importance of other factors (e.g., comorbidity or age) that have been shown to influence antibiotic prescribing in other studies (Liu et al., 2019; Poss-Doering et al., 2020) but have not been included as attributes in this study.

5. Conclusion

The most important factor affecting Danish GPs' decision to prescribe antibiotics at both the aggregate level, in subgroups of GPs based on observable characteristics, and across latent classes was the CRP value. Hence, CRP is a crucial factor to consider in the endeavour to promote rational antibiotic use in the battle against antimicrobial resistance.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2022.115033.

References

Danish Patients and the Organization of Danish Medical Societies, 2022. Vælg Klogt (Choosing Wisely). Available from: https://vaelgklogt.dk/.

Aabenhus, R., Jensen, J.U., Jorgensen, K.J., Hrobjartsson, A., Bjerrum, L., 2014. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Database Syst. Rev. 11, Cd010130. https://doi.org/10.1002/14651858.CD010130.pub2. Epub 2014/11/07 PubMed PMID: 25374293.

Aabenhus, R., Siersma, V., Hansen, M.P., Bjerrum, L., 2016. Antibiotic prescribing in Danish general practice 2004-13. J. Antimicrob. Chemother. 71 (8), 2286–2294. https://doi.org/10.1093/jac/dkw117. Epub 2016/04/24 PubMed PMID: 27107098.

Andersen, C., Jensen, M.B.B., Toftegaard, B.S., Vedsted, P., Harris, M., Research Group, Ö., 2019. Primary care physicians' access to in-house ultrasound examinations across Europe: a questionnaire study. BMJ Open 9 (9), e030958. https://doi.org/10.1136/bmjopen-2019-030958. Epub 2019/10/03 PubMed PMID: 31575576; PubMed Central PMCID: PMCPMC6773286.

Andreeva, E., Melbye, H., 2014. Usefulness of C-reactive protein testing in acute cough/respiratory tract infection: an open cluster-randomized clinical trial with C-reactive protein testing in the intervention group. BMC Fam. Pract. 15, 80. https://doi.org/10.1186/1471-2296-15-80. Epub 2014/06/03 PubMed PMID: 24886066; PubMed Central PMCID: PMCPMC4016668.

Arellano, J., González, J.M., Qian, Y., Habib, M., Mohamed, A.F., Gatta, F., et al., 2015. Physician preferences for bone metastasis drug therapy in Canada. Curr. Oncol. 22 (5), e342–e348. https://doi.org/10.3747/co.22.2380. Epub 2015/12/03 PubMed PMID: 26628874; PubMed Central PMCID: PMCPMC4608407.

Bateman, I., Carson, R., Day, B., Hanemann, M., Hanleys, N., Hett, T., et al., 2004. Economic valuation with stated preference techniques: a manual. Ecol. Econ. https://doi.org/10.4337/9781781009727.

Bjerrum, L.G.-H., Hansen, B.M.P., et al., 2014. Luftvejsinfektioner - Diagnose Og Behandling. The Danish College of General Practitioners. https://vejledninger.dsam.dk/media/files/13/luftvejsinfektioner-samlet-udgave-3-.pdf.

Bridges, J.F., Hauber, A.B., Marshall, D., Lloyd, A., Prosser, L.A., Regier, D.A., et al., 2011. Conjoint analysis applications in health–a checklist: a report of the ISPOR good research practices for conjoint analysis task force. Value Health 14 (4), 403–413. https://doi.org/10.1016/j.jval.2010.11.013. Epub 2011/06/15 PubMed PMID: 21669364.

Brookes-Howell, L., Hood, K., Cooper, L., Coenen, S., Little, P., Verheij, T., et al., 2012. Clinical influences on antibiotic prescribing decisions for lower respiratory tract infection: a nine country qualitative study of variation in care. BMJ Open 2 (3). https://doi.org/10.1136/bmjopen-2011-000795. Epub 2012/05/24 PubMed PMID: 22619265; PubMed Central PMCID: PMCPMC3364454.

Buusman, A., Andersen, M., Merrild, C., Elverdam, B., 2007. Factors influencing GPs' choice between drugs in a therapeutic drug group. A qualitative study. Scand. J. Prim. Health Care 25 (4), 208–213. https://doi.org/10.1080/02813430701652036. Epub 2007/11/29 PubMed PMID: 18041657; PubMed Central PMCID: PMCPMC3379761.

Chorus, C., 2010. A new model of random regret minimization. Eur. J. Transport Infrastruct. Res. 10 https://doi.org/10.18757/ejtir.2010.10.2.2881.

Coast, J., Al-Janabi, H., Sutton, E.J., Horrocks, S.A., Vosper, A.J., Swancutt, D.R., et al., 2012. Using qualitative methods for attribute development for discrete choice experiments: issues and recommendations. Health Econ. 21 (6), 730–741. https://doi.org/10.1002/hec.1739. Epub 2011/05/11 PubMed PMID: 21557381.

Dale, A.P., Marchello, C., Ebell, M.H., 2019. Clinical gestalt to diagnose pneumonia, sinusitis, and pharyngitis: a meta-analysis. Br. J. Gen. Pract. : J. Roy. Coll. Gen. Pract. 69 (684), e444–e453. https://doi.org/10.3399/bjgp19X704297. Epub 2019/06/19 PubMed PMID: 31208974; PubMed Central PMCID: PMCPMC6582453.

Danish Ministry of Health, 2017. National Action Plan on Antibiotics in Human Healthcare. Danish Ministry of Health. https://sum.dk/Media/6/2/National-handlingsplan-for-antibiotika-til-mennesker-UK%20version.pdf.

de Bekker-Grob, E.W., Donkers, B., Jonker, M.F., Stolk, E.A., 2015. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. Patient - Patient-Cent. Outcome. Res. 8 (5), 373–384. https://doi.org/10.1007/s40271-015-0118-z.

Dempsey, P.P., Businger, A.C., Whaley, L.E., Gagne, J.J., Linder, J.A., 2014. Primary care clinicians' perceptions about antibiotic prescribing for acute bronchitis: a qualitative study. BMC Fam. Pract. 15, 194. https://doi.org/10.1186/s12875-014-0194-5. Epub 2014/12/17 PubMed PMID: 25495918; PubMed Central PMCID: PMCPMC4275949.

Ebell, M.H., Chupp, H., Cai, X., Bentivegna, M., Kearney, M., 2020. Accuracy of signs and symptoms for the diagnosis of community-acquired pneumonia: a meta-analysis. Acad. Emerg. Med. 27 (7), 541–553. https://doi.org/10.1111/acem.13965. Epub 2020/04/25 PubMed PMID: 32329557.

Ellis, R.P., McGuire, T.G., 1986. Provider behavior under prospective reimbursement. Cost sharing and supply. J. Health Econ. 5 (2), 129–151. https://doi.org/10.1016/0167-6296(86)90002-0. Epub 1986/05/10 PubMed PMID: 10287223.

Gonzalez, J.M., Johnson, F.R., McAteer, H., Posner, J., Mughal, F., 2017. Comparing preferences for outcomes of psoriasis treatments among patients and dermatologists in the U.K.: results from a discrete-choice experiment. Br. J. Dermatol. 176 (3), 777–785. https://doi.org/10.1111/bjd.14798. Epub 2016/06/14 PubMed PMID: 27292093.

Goossens, H., Ferech, M., Vander Stichele, R., Elseviers, M., 2005. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet 365 (9459), 579–587. https://doi.org/10.1016/s0140-6736(05)17907-0. Epub 2005/02/15 PubMed PMID: 15708101.

Greene, W.H., Hensher, D.A., 2003. A latent class model for discrete choice analysis: contrasts with mixed logit. Transp. Res. Part B Methodol. 37 (8), 681–698. https://doi.org/10.1016/S0191-2615(02)00046-2.

Haldrup, S., Thomsen, R.W., Bro, F., Skov, R., Bjerrum, L., Søgaard, M., 2017. Microbiological point of care testing before antibiotic prescribing in primary care: considerable variations between practices. BMC Fam. Pract. 18 (1), 9. https://doi.org/10.1186/s12875-016-0576-y. PubMed PMID: 28125965.

Hansen, C.R.B.C.P., Sahm, L.J., 2016. Factors influencing successful prescribing by intern doctors: a qualitative systematic review. Pharmacy 4 (3). https://doi.org/10.3390/pharmacy4030024. Epub 2016/08/24 PubMed PMID: 28970397; PubMed Central PMCID: PMCPMC5419364.

Hauber, A.B., González, J.M., Groothuis-Oudshoorn, C.G., Prior, T., Marshall, D.A., Cunningham, C., et al., 2016. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR conjoint analysis good research practices task force. Value Health 19 (4), 300–315. https://doi.org/10.1016/j.jval.2016.04.004. Epub 2016/06/22 PubMed PMID: 27325321.

Held, U., Steurer-Stey, C., Huber, F., Dallafior, S., Steurer, J., 2012. Diagnostic aid to rule out pneumonia in adults with cough and feeling of fever. A validation study in the primary care setting. BMC Infect. Dis. 12, 355. https://doi.org/10.1186/1471-2334-12-355. Epub 2012/12/19 PubMed PMID: 23245504; PubMed Central PMCID: PMCPMC3560221.

Hifinger, M., Hiligsmann, M., Ramiro, S., Watson, V., Berghea, F., Péntek, M., et al., 2017. Influence of disease activity on RA treatment choices in countries with restricted access to expensive, innovative drugs: a discrete choice experiment among rheumatologists. RMD Open 3 (2), e000453. https://doi.org/10.1136/rmdopen-2017-000453. PubMed PMID: 28912960.

Hole, A.R., 2007. Fitting mixed logit models by using maximum simulated likelihood. STATA J. 7 (3), 388–401. https://doi.org/10.1177/1536867X0700700306.

Hunter, R., 2015. Cost-effectiveness of point-of-care C-reactive protein tests for respiratory tract infection in primary care in England. Adv. Ther. 32 (1), 69–85. https://doi.org/10.1007/s12325-015-0180-x. Epub 2015/01/27 PubMed PMID: 25620538; PubMed Central PMCID: PMCPMC4311066.

Johnson, F.R., Lancsar, E., Marshall, D., Kilambi, V., Muhlbacher, A., Regier, D.A., et al., 2013. Constructing experimental designs for discrete-choice experiments: report of the ISPOR conjoint analysis experimental design good research practices task force. Value Health 16 (1), 3–13. https://doi.org/10.1016/j.jval.2012.08.2223. Epub 2013/01/23 PubMed PMID: 23337210.

Krucien, N., Gafni, A., Pelletier-Fleury, N., 2015. Empirical testing of the external validity of a discrete choice experiment to determine preferred treatment option: the case of sleep apnea. Health Econ. 24 (8), 951–965. https://doi.org/10.1002/hec.3076. Epub 2014/07/06 PubMed PMID: 24986760.

Lindström, J., Nordeman, L., Hagström, B., 2015. What a difference a CRP makes. A prospective observational study on how point-of-care C-reactive protein testing influences antibiotic prescription for respiratory tract infections in Swedish primary health care. Scand. J. Prim. Health Care 33 (4), 275–282. https://doi.org/10.3109/02813432.2015.1114348. Epub 2015/12/09 PubMed PMID: 26643196; PubMed Central PMCID: PMCPMC4750737.

Linley, W.G., Hughes, D.A., 2013. Decision-makers' preferences for approving new medicines in wales: a discrete-choice experiment with assessment of external validity. Pharmacoeconomics 31 (4), 345–355. https://doi.org/10.1007/s40273-013-0030-0.

Little, P., Stuart, B., Francis, N., Douglas, E., Tonkin-Crine, S., Anthierens, S., et al., 2013. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. Lancet 382 (9899), 1175–1182. https://doi.org/10.1016/s0140-6736(13)60994-0. Epub 2013/08/07 PubMed PMID: 23915885; PubMed Central PMCID: PMCPMC3807804.

Liu, C., Liu, C., Wang, D., Zhang, X., 2019. Intrinsic and external determinants of antibiotic prescribing: a multi-level path analysis of primary care prescriptions in Hubei, China. Antimicrob. Resist. Infect. Control 8, 132. https://doi.org/10.1186/s13756-019-0592-5. PubMed PMID: 31406571.

Lum, E.P.M., Page, K., Whitty, J.A., Doust, J., Graves, N., 2018. Antibiotic prescribing in primary healthcare: dominant factors and trade-offs in decision-making. Infect. Dis. Health 23 (2), 74–86. https://doi.org/10.1016/j.idh.2017.12.002.

Malhotra, N.K., Birks, D.F., 2007. Marketing Research: an Applied Approach. Prentice Hall/Financial Times.

Malterud, K., Siersma, V.D., Guassora, A.D., 2016. Sample size in qualitative interview studies: guided by information power. Qual. Health Res. 26 (13), 1753–1760. https://doi.org/10.1177/1049732315617444. Epub 2015/11/29 PubMed PMID: 26613970.

McKay, R., Mah, A., Law, M.R., McGrail, K., Patrick, D.M., 2016. Systematic review of factors associated with antibiotic prescribing for respiratory tract infections. Antimicrob. Agents Chemother. 60 (7), 4106–4118. https://doi.org/10.1128/AAC.00209-16. PubMed PMID: 27139474.

McNulty, C.A., Nichols, T., French, D.P., Joshi, P., Butler, C.C., 2013. Expectations for consultations and antibiotics for respiratory tract infection in primary care: the RTI clinical iceberg. Br. J. Gen. Pract. : J. Roy. Coll. Gen. Pract. 63 (612), e429–e436. https://doi.org/10.3399/bjgp13X669149. Epub 2013/07/10 PubMed PMID: 23834879; PubMed Central PMCID: PMCPmc3693799.

Minnaard, M.C., de Groot, J.A.H., Hopstaken, R.M., Schierenberg, A., de Wit, N.J., Reitsma, J.B., Broekhuizen, B.D.L., van Vugt, S.F., Neven, A.K., Graffelman, A.W., Melbye, H., Rainer, T.H., Steurer, J., Holm, A., Gonzales, R., Dinant, G.J., van de Pol, A.C., Verheij, T.J.M., 2017. The added value of C-reactive protein measurement in diagnosing pneumonia in primary care: a meta-analysis of individual patient data. CMAJ (Can. Med. Assoc. J.) 189 (2), E56–e63. https://doi.org/10.1503/cmaj.151163. Epub 2016/09/21 PubMed PMID: 27647618; PubMed Central PMCID: PMCPMC5235926.

Mott, D.J., Hampson, G., Llewelyn, M.J., Mestre-Ferrandiz, J., Hopkins, M.M., 2020. A multinational European study of patient preferences for novel diagnostics to manage antimicrobial resistance. Appl. Health Econ. Health Pol. 18 (1), 69–79. https://doi.org/10.1007/s40258-019-00516-0.

Murray, C.J.L., Ikuta, K.S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., et al., 2022. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. https://doi.org/10.1016/S0140-6736(21)02724-0.

Murshid, M.A., Mohaidin, Z., 2017. Models and theories of prescribing decisions: a review and suggested a new model. Pharm. Pract. 15 (2), 990. https://doi.org/10.18549/PharmPract.2017.02.990. Epub 2017/06/30 PubMed PMID: 28690701.

ChoiceMetrics Ngene 1.2 User Manual & Reference Guide, 2018. http://www.choice-metrics.com/NgeneManual120.pdf.

National Institute for Health and Care Excellence (Uk), 2019 Sep. Pneumonia in Adults: Diagnosis and Management. National Institute for Health and Care Excellence (Uk), London.

O'Connor, R., O'Doherty, J., O'Regan, A., Dunne, C., 2018. Antibiotic use for acute respiratory tract infections (ARTI) in primary care; what factors affect prescribing and why is it important? A narrative review. Ir. J. Med. Sci. 187 (4), 969–986. https://doi.org/10.1007/s11845-018-1774-5. Epub 2018/03/14 PubMed PMID: 29532292; PubMed Central PMCID: PMCPMC6209023.

Offerhaus, P.M., Otten, W., Boxem-Tiemessen, J.C., de Jonge, A., van der Pal-de Bruin, K. M., Scheepers, P.L., et al., 2015. Variation in intrapartum referral rates in primary midwifery care in The Netherlands: a discrete choice experiment. Midwifery 31 (4), e69–78. https://doi.org/10.1016/j.midw.2015.01.005. Epub 2015/02/11 PubMed PMID: 25660846.

Phillips, R., Stanton, H., Singh-Mehta, A., Gillespie, D., Bates, J., Gal, M., et al., 2020. C-reactive protein-guided antibiotic prescribing for COPD exacerbations: a qualitative evaluation. Br. J. Gen. Pract. : J. Roy. Coll. Gen. Pract. 70 (696), e505–e513. https://doi.org/10.3399/bjgp20X709865. Epub 2020/05/20 PubMed PMID: 32424045; PubMed Central PMCID: PMCPMC7239040.

Poss-Doering, R., Kamradt, M., Stuermlinger, A., Glassen, K., Kaufmann-Kolle, P., Andres, E., et al., 2020. The complex phenomenon of dysrational antibiotics prescribing decisions in German primary healthcare: a qualitative interview study using dual process theory. Antimicrob. Resist. Infect. Control 9, 6. https://doi.org/10.1186/s13756-019-0664-6. PubMed PMID: 31921412.

Quaife, M., Terris-Prestholt, F., Di Tanna, G.L., Vickerman, P., 2018. How well do discrete choice experiments predict health choices? A systematic review and meta-analysis of external validity. Eur. J. Health Econ. : HEPAC : Health Econ. Prevent. Care. https://doi.org/10.1007/s10198-018-0954-6. Epub 2018/01/31 PubMed PMID: 29380229.

Riisgaard, H., Waldorff, F.B., Kirstine Andersen, M., Pedersen, L.B., 2020. Does accreditation of general practice promote patient-reported quality of care? A natural cluster randomised experiment. BMJ Open 10 (6), e034465. https://doi.org/10.1136/bmjopen-2019-034465. Epub 2020/06/14 PubMed PMID: 32532767; PubMed Central PMCID: PMCPMC7295420.

Rose, J.M., Bliemer, M.C.J., 2013. Sample size requirements for stated choice experiments. Transportation 40 (5), 1021–1041. https://doi.org/10.1007/s11116-013-9451-z.

Saust, L.T., Bjerrum, L., Siersma, V., Arpi, M., Hansen, M.P., 2018. Quality assessment in general practice: diagnosis and antibiotic treatment of acute respiratory tract infections. Scand. J. Prim. Health Care 36 (4), 372–379. https://doi.org/10.1080/02813432.2018.1523996.

Sirota, M., Round, T., Samaranayaka, S., Kostopoulou, O., 2017. Expectations for antibiotics increase their prescribing: causal evidence about localized impact. Health Psychol. 36 (4), 402–409. https://doi.org/10.1037/hea0000456. Epub 2017/02/17 PubMed PMID: 28206788.

Soekhai, V., de Bekker-Grob, E.W., Ellis, A.R., Vass, C.M., 2019. Discrete choice experiments in health economics: past, present and future. Pharmacoeconomics 37 (2), 201–226. https://doi.org/10.1007/s40273-018-0734-2. Epub 2018/11/06 PubMed PMID: 30392040; PubMed Central PMCID: PMCPMC6386055 The full detailed dataset generated during the current study will not be publicly available due to ongoing analysis, but more details regarding the simplified dataset are available from: the corresponding author on reasonable request.

Statens Serum Institut. Antibiotika eller ej (Antibiotics or not). Available from: https://www.antibiotikaellerej.dk/.

The Danish Organisation of General Practitioners, 2020. PLO Faktaark (Fact Sheet from the Danish Organisation of General Practitioners). The Danish Organisation of General Practitioners.

Train, K., 2002. Discrete Choice Methods with Simulation. Cambridge University Press.

World Health Organization, 2014WHO (Ed.), Antimicrobial Resistance Global Report on Surveillance, vol. 92. World Health Organization.

World Health Organization, 2015. Global Action Plan on Antimicrobial Resistance. World Health Organization, Geneva, p. 2015.

Zhou, M., Thayer, W.M., Bridges, J.F.P., 2018. Using latent class Analysis to model preference heterogeneity in health: a systematic review. Pharmacoeconomics 36 (2), 175–187. https://doi.org/10.1007/s40273-017-0575-4.