*Running Title:* THE UNBEARABLE LIGHTNESS OF ANTIBIOTICS PRESCRIBING

*Expectations for antibiotics increase their prescribing: Causal evidence about localized impact*

Miroslav Sirota[1*], Thomas Round[2], Shyamalee Samaranayaka[3], Olga Kostopoulou[4]

[1]Department of Psychology, University of Essex, United Kingdom

[2]Primary Care & Public Health Sciences, King's College London, United Kingdom

[3]Department of Family Medicine, University of Sri Jayewardenepura, Sri Lanka

[4]Department of Surgery and Cancer, Imperial College London, United Kingdom

*Author Note*

Correspondence concerning this article should be addressed to Miroslav Sirota, Department of Psychology, University of Essex, Wivenhoe Park, Colchester, CO4 3SQ, United Kingdom (email: msirota@essex.ac.uk; phone: +44 (0)1206 874 229)

**Abstract**

*Objective:* Clinically irrelevant but psychologically important factors such as patients'
expectations for antibiotics encourage over-prescribing. We aimed to i) provide missing causal
evidence of this effect, ii) identify whether the expectations distort the perceived probability of a
bacterial infection either in a pre- or post-decisional distortions pathway and iii) detect possible
moderators of this effect. *Methods*: Family physicians expressed their willingness to prescribe
antibiotics (Experiment 1, $n_1$=305) or their decision to prescribe (Experiment 2, $n_2$=131) and
assessed the probability of a bacterial infection in hypothetical patients with infections either
with low or high expectations for antibiotics. Response order of prescribing/probability was
manipulated in Experiment 1. *Results*: Overall, the expectations for antibiotics increased
intention to prescribe (Experiment 1, $F(1,301)=25.32$, $p<.001$, $\eta_p^2=.08$, regardless of the
response order: probability first vs. prescribing first; Experiment 2, $OR = 2.31$, 95% CI[1.15,
4.70] and $OR = 0.75$, 95% CI[0.25, 2.11], vignettes 1 and 2, respectively). Expectations for
antibiotics did not change the perceived probability of a bacterial infection (Experiment 1,
$F(1,301)=1.86$, $p=.173$, $\eta_p^2=.01$, regardless of the response order; Experiment 2, $d$=-0.03, 95%
CI[-0.38, 0.31] and $d$=+0.25, 95% CI[-0.10, 0.59], vignettes 1 and 2, respectively). Physicians'
experience is positively associated with prescribing, but it did not moderate the expectations
effect on prescribing. *Conclusions*: Patients' and their parents' expectations increase antibiotics
prescribing, but their effect is localized – it does not leak into the perceived probability of a
bacterial infection. Interventions reducing the over-prescribing of antibiotics should target not
only clinical but psychological factors.

*Keywords: antibiotics prescribing, subjective probability, clinical decision-making, non-clinical
factors, probability distortion*

In the most comprehensive report to date on antimicrobial resistance, the World Health

Organization (WHO) has warned about increasing antibacterial resistance – resistance of a

microorganism to an antibacterial drug – as a real and present threat to public health (WHO,

2014). Without urgent action to mitigate the consequences of bacterial resistance we could be

heading toward a "post-antibiotic era", in which even minor injuries could become life-

threatening. The consequences are not only at a population level but also for individual patients

causing resistance to that antibiotic (Costelloe, Metcalfe, Lovering, Mant, & Hay, 2010). The

present paper aims to contribute toward the goal of mitigating the consequences of bacterial

resistance by providing causal evidence of clinically irrelevant but psychologically important

factors affecting the over-prescribing of antibiotics.

The inappropriate and excessive use of antibiotics remains one of the main causes of

antibacterial resistance (Hansen, Hoffmann, McCullough, Van Driel, & Del Mar, 2015;

Laxminarayan et al., 2013). In the United Kingdom, for example, the majority of antibiotics are

prescribed in primary care for respiratory tract infections such as acute otitis media, acute

sinusitis, and the common cold (Hansen et al., 2015; van den Broek d'Obrenan, Verheij,

Numans, & van der Velden, 2014). These infections are very common (more than 50% of adults

experience RTI symptoms during a six-month period, e.g., McNulty, Nichols, French, Joshi, &

Butler, 2013), but these are mostly viral in origin and self-limiting. Therefore, antibiotics are

seldom warranted (Cals et al., 2007).

Non-clinical factors – such as physicians' diagnostic uncertainty, patients' expectations

for antibiotics, and physicians' assumptions regarding these expectations – increase the over-

prescribing of antibiotics (Cals et al., 2007; Cockburn & Pit, 1997; Coenen, Michiels, Renard,

Denekens, & Van Royen, 2006). Many patients overestimate the effectiveness of antibiotics and,

in turn, "motivate" their physicians to prescribe them (Hansen et al., 2015; Hoffmann, Ristl, Heschl, Stelzer, & Maier, 2014). The majority of patients who expect antibiotics are prescribed them (McNulty et al., 2013). Patients are less satisfied in practices with a more frugal approach to antibiotic prescribing (Ashworth, White, Jongsma, Schofield, & Armstrong, 2015). In a survey of family physicians, 55% reported pressure to prescribe antibiotics, 45% had prescribed antibiotics for a viral infection knowing that they would be ineffective, and 44% admitted that they had prescribed antibiotics in order to get a patient to leave the consulting room (Cole, 2014).

The up-to-date evidence on the role of non-clinical factors in the over-prescribing of antibiotics features two limitations. First, the evidence is non-causal in nature. In a typical patient study, patients report their prior expectations after the consultation. Similarly, in a typical physicians' study, physicians retrospectively report their beliefs about the patients' expectations. Second, the evidence does not inform us about the scope of the impact. The effect of non-clinical factors might be restricted to the specific act of prescribing antibiotics (hereafter, localized impact) or it could also be generalized into the related domains such as the subjective probability of the related diagnostic category (hereafter, global impact). For instance, a physician prescribing antibiotics upon request for a patient with viral otitis media might rationalize her prescription by increasing the subjective perception of the bacterial cause of otitis media.

The psychological literature supports the possibility of such a "leakage": it offers indirect evidence and plausible psychological mechanisms. Indeed, physicians have overestimated a probability of streptococcal infection in patients presenting with clinical symptoms of a sore throat, and the physicians who treated with antibiotics prior to the throat culture results assigned a higher probability to streptococcus infection than those who did not (Poses, Cebul, Collins, &

Fager, 1985). This could indicate that the treatment decision affected the physicians' attribution of the probability of bacterial infection.

In terms of mechanisms, prior research has identified two pathways by which the non-clinical factors could affect the perceived probability: a direct and an indirect pathway. The direct, pre-decisional pathway postulates that the perceived probability is affected before the decision is made: the higher probability causes the decision. For example, prior research has found that the perceived severity of an outcome increased the perceived probability of the outcome (Harris, Corner, & Hahn, 2009; Juanchich, Sirota, & Butler, 2012; Vosgerau, 2010; Wallsten, 1981). Patients' expectations for antibiotics might be perceived as signals of clinical severity and, in turn, "leak into" the perceived probability of the bacterial infection. Aligned with the loss asymmetry account, the physicians might have elevated the probability of a bacterial infection which will cause the higher willingness to prescribe antibiotics – in other words, physicians might prefer to err on the side of caution and prescribe antibiotics to such patients (Weber, 1994). The indirect, post-decisional pathway postulates that the perceived probability is affected as a result of a post-decisional distortion: the higher probability is a consequence of the decision (e.g., Boiney, Kennedy, & Nye, 1997; Festinger, 1957; Levy & Hershey, 2006, 2008). Patients' expectations motivate physicians to increase the prescribing of antibiotics and, in turn, might affect the perceived probability of a bacterial infection via the process of rationalization of the prescribing behavior. Indeed, prior research has found that people have distorted medical probabilities to justify their decisions regarding the desired treatments (Levy & Hershey, 2006, 2008).

A better understanding of prescription behaviors and their scope would provide some insights into the underpinning mechanisms. It could also inform the theories of clinical decisions,

such as the threshold theory, by illuminating the non-clinical determinants of the decision

threshold (Elstein & Schwarz, 2002; Pauker & Kassirer, 1980). More importantly, it would

enable us to tailor cost-effective interventions for reducing the prescribing of antibiotics by

targeting the effect of non-clinical factors in physicians as well as in patients.

**The present research**

In the present experiments we set up three main aims to fill in the gaps outlined above.

First, to address the lack of causal evidence, we manipulated the effect of expectations of

antibiotics on family physicians' willingness to prescribe antibiotics (Exp. 1 & 2). We

hypothesized that the expectations would increase the physicians' willingness to prescribe

antibiotics. Second, to address missing evidence about the scope of the effect, we investigated

whether the expectations also affect – directly or indirectly – the subjective probability of a

bacterial infection (Exp. 1). To accomplish this, family physicians assessed the perceived

probability of a bacterial infection and their willingness to prescribe antibiotics on separate

screens and in different response orders. The localized-effect hypothesis predicts that the

expectations will only affect the willingness to prescribe antibiotics, whereas the global-effect

hypothesis predicts that the expectations will also affect the perceived probability of a bacterial

infection (whether directly or indirectly). Any interaction effect of the expectations and response

order on the perceived probability would indicate activation of either a direct or an indirect

pathway. If the expectations affect the probability in the "probability – prescription" order

condition then they affect the probability directly. If the expectations affect the probability in the

"prescription – probability" order condition then they affect the probability indirectly. Third, to

explore the role of moderators in the expectations effect, we focused on the moderating role of

the physicians' practicing experience and the subjective probability magnitude (Exp. 1 & 2).

## Experiment 1

**Method**

**Participants.** We powered the experiment to detect a small-to-medium effect size ($f = .17$ $\cong \eta_p^2 = 0.03$), the effect size assumed in other vignette-based studies of clinicians (e.g., Eva, Link, Lutfey, & McKinlay, 2010). Given $\alpha = .05$ and $\beta = .80$ for a $2 \times 2$ between-subjects ANOVA, such a power analysis resulted in a sample size of 274 participants (Cohen, 1988). The sample was adjusted by an additional 10% to account for a possible attrition rate.

Practicing family physicians were recruited via an email invitation to the physicians who took part in the previous studies carried out by the research team. In the email we encouraged potential participants to forward the invitation to their colleagues. We also received help with recruitment from local clinical research networks around the UK, who contacted primary care clinics on our behalf. Only certified and practicing family physicians were eligible to participate (i.e., participants had to provide a valid email address from the National Health Service in the UK to receive their reimbursement). Due to the various sources of the invitation emails and the implemented snowballing technique it would be misleading to estimate a response rate for the participants. We recorded 382 attempts to complete the questionnaire. A total of 305 family physicians (50.2% of whom were male; 18.4% practiced in an inner city, 46.9% in an urban area and 18.4% in a rural area) completed this task. The years of experience since the certification ranged from 0 to 40 years ($M = 10.5$, $SD = 9.2$ years). Upon completion of a 20-minute questionnaire administered online, comprising hypothetical patient vignettes – the vignette presented here and some other unrelated vignettes concerning cancer detection presented elsewhere (Sirota, Kostopoulou, Round, & Samaranayaka, 2016) – participants received a £20 Amazon voucher as a token of appreciation.

**Design.** A 2 (antibiotics expectations: low vs. high) × 2 (response order: probability first vs. prescribing first) factorial between-subjects design was employed with the probability of a bacterial infection of a hypothetical patient and a willingness to prescribe her antibiotics as dependent variables. The high expectation for antibiotics was induced by presenting the idea that the patient would soon be participating in an important sporting event, and this was accompanied by an indirect request for action from the patient's mother (see the full version in the Appendix). The aim of this manipulation was to create a belief that the patient was requesting antibiotics to resolve the action; our informal qualitative pre-test confirmed this assumption. The response order was manipulated by presenting either the bacterial probability question first, and then the question on antibiotics prescribing, or presenting them in a reversed order. The second question was always depicted unexpectedly on the next page. The allocation to one of the four conditions was randomized using a procedure of restricted blocked randomization, which leads to an equal number of participants in each group, also called the blocked randomization. (the blocked randomization was achieved using randomized.org, Urbaniak & Plous, 2013).

**Materials and procedure**. After providing informed consent, participants diagnosed and managed five hypothetical patients (see details in Sirota et al., 2016). One of them, a 15-year-old competitive swimmer called Sarah, presented with symptoms of acute otitis media (see the vignette in the Appendix). Sarah presented either with a finished swimming season (low antibiotics expectations) or with forthcoming swimming competitions that were felt to be important for her future career – information that was stressed by her mother who was requesting some action (high antibiotics expectations). Participants assessed the probability of a bacterial infection and expressed their willingness to prescribe antibiotics in a counterbalanced (and unexpected) response order. Participants assessed the probability of a bacterial infection ("How

likely is it that Sarah has a bacterial infection?") by positioning a cursor on a visual analog

probability scale (increments of 1) ranging from 0% (anchored as *bacterial is impossible, viral is*

*certain*) via 50% (anchored as *bacterial and viral are equally likely*) to 100% (anchored as *viral*

*is impossible, bacterial is certain*). Participants expressed their willingness to prescribe

antibiotics ("Would you prescribe antibiotics for Sarah to be taken from today?") by positioning

a cursor on a Likert scale ranging from 0 (anchored as *definitely would not*) to 10 (anchored as

*definitely would*). Participants then completed the other vignettes and answered a few socio-

demographic questions (namely: experience, gender, and area of practice). We conducted the

study in accordance with the ethical standards of the American Psychological Association.

**Statistical analyses**. To test the effect of antibiotics expectations and presentation order

on prescribing and perceived probability we planned to use two independent two-way analyses

of variance (ANOVAs). Since not rejecting the null hypothesis does not logically entail

accepting the null hypothesis, we quantified the evidence to support the null or alternative

hypothesis by computing a JZS Bayes factor ANOVA with default prior scales using

"BayesFactor" package in R (Morey & Rouder, 2015; Rouder, Morey, Speckman, & Province,

2012). This analysis was not planned, but carried out as a consequence of finding the null results.

In generic terms, a Bayes factor (BF) is the ratio of the probability of the data given model A

(e.g., $H_1$) to the probability of the data given model B (e.g., $H_0$). Thus, the Bayes factor expresses

the ratio of the marginal likelihood of the data under model A (e.g., $H_{1 \text{ expectation effect model}}$) and

model B (e.g., $H_{0 \text{ intercept-only model}}$) and allows us to quantify how many more times the data are

likely to occur under $H_1$ compared with $H_0$ or vice versa. For example, if the value of $BF_{10}$ is 5

then the data are five times more likely to occur under $H_1$. A Bayes factor of $BF_{10}$, with a value

lower than 1, indicates that $H_0$ is more likely and a value greater than 1 indicates that $H_1$ is more

likely. Furthermore, the Bayes factor values may also be interpreted as evidence categories, for example, $BF_{10}$ values between 1 and 3 indicate *anecdotal evidence* to support the alternative hypothesis, whereas values greater than 100 indicate *decisive evidence* to support the alternative hypothesis. The evidence categories are described in the Note of Table 1 (Jeffreys, 1961; Wetzels et al., 2011). Finally, to analyze the moderation effect of the experience and probability we planned to use a moderation analysis using PROCESS (Hayes, 2013).

**Results**

Overall, the physicians were slightly more willing to prescribe antibiotics than not, $M =$ 5.3 ($SD = 3.0$, scale 0 to 10). Manipulating the expectations for antibiotics clearly increased their willingness to prescribe antibiotics to the patient, whereas the different response order did not affect their willingness to prescribe (Figure 1, panel A). The physicians were more willing to prescribe antibiotics to the patient when they believed she expected antibiotics, $F(1, 301) =$ 25.32, $p < .001$, $\eta_p^2 = .08$; descriptively, they were slightly more willing to prescribe antibiotics if the prescription question was presented before the probability question. However, this difference did not reach statistical significance, $F(1, 301) = 3.35$, $p = .068$, $\eta_p^2 = .01$. The interaction effect was not significant, $F < 1$. The Bayes factor model comparisons (see Table 1) revealed that the expectations effect on prescribing model was substantially preferred to the intercept-only model by a factor of 7,750.4 ±0%. The expectations effect model was preferred to the full model, comprising both main effects and their interaction term, by a factor of 7.9 ±1.3%. On the other hand, the intercept-model was preferred to the response order model by a factor of 2.9 ±0% (since 1/0.341 = 2.9). This re-analysis showed that decisive evidence supports the effect of expectations on the willingness to prescribe antibiotics and anecdotal evidence supports the null effect of the response order (Table 1). Thus, we found decisive experimental evidence that

patients' expectations for antibiotics amplify physicians' willingness to prescribe antibiotics regardless of the response order of the probability and prescribing question. Such findings corroborate our first hypothesis of the causal effect of patients' expectations.

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Insert Figure 1 here

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Insert Table 1 here

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In terms of the perceived probability of a bacterial infection, physicians perceived the symptoms to be more likely caused by a viral rather than a bacterial infection ($M = 40.2\%$, $SD = 22.8\%$ of a bacterial infection). The antibiotics expectations and response order conditions did not affect the perceived probability of a bacterial infection (Figure 1, panel B). Descriptively, the physicians in the high expectations condition perceived the probability of a bacterial infection to be just slightly higher than the physicians in the low expectations condition, but this difference was not statistically significant, $F(1, 301) = 1.86$, $p = .173$, $\eta_p^2 = .01$. The physicians perceived approximately the same probability regardless of the main effect of the response order, $F < 1$ or the interaction effect, $F < 1$. Thus, such findings suggest that the probability was not affected, directly or indirectly, by the patient's high expectations for antibiotics. The Bayes factor model comparisons (see Table 1) revealed that the intercept-only model was preferred to the expectations effect model three times more ($BF_{01} = 3.4 \pm 0\%$), to the response order model almost seven times more ($BF_{01} = 6.7 \pm 0\%$), to the main effects model almost 22 times more ($BF_{01} = 22.2 \pm 1.1\%$), and to the full model 143 times more ($BF_{01} = 142.9 \pm 2.0\%$). Thus, the data

provide substantial to decisive evidence to support the intercept-only model against the models comprising different main and interaction effects (Table 1). Such evidence corroborates the hypothesis about the null effect of the patient's expectations. Taken together, our findings corroborate the localized-effect hypothesis, since we found the causal effect of expectations on willingness to prescribe antibiotics but this effect did not transfer to the perceived probability of a bacterial infection.

Two variables were considered to moderate the expectations effect on prescribing antibiotics: i) physicians' experience, and ii) the perceived probability. More experienced physicians were more willing to prescribe antibiotics, $r = .14$, $p = .012$, even when the probability perception of bacterial infection was controlled for, $r = .21$, $p < .001$. Further analysis, however, excluded the option that the more experienced physicians prescribed more easily because they were more sensitive to the expectations manipulation. In that case, experience would observe a moderation of the expectations effect on willingness to prescribe, which was not the case, $b = .02$, 95% $CI$ [-0.05, 0.09], $p = .555$, mean centered prior to the analysis (using PROCESS, Hayes, 2013). There was an independent source of the tendency to prescribe antibiotics by more experienced physicians. On the other hand, the perceived probability moderated the expectations effect on willingness to prescribe antibiotics ($b = -.02$, 95% $CI$ [-0.04, -0.002], $p = .034$). Probing conditional analysis, the effect of expectations has its peak at a minimal probability level, with increasing probability of a bacterial infection losing its strength and becoming insignificant at around 70%. This goes against an intuitive expectation that the patient's expectations would weigh more in a situation of diagnostic uncertainty (i.e., the middle point of the probability scale) rather than in a situation where a bacterial infection was unlikely (i.e., the low end of the probability scale) as was the case here.

**Experiment 2**

In Experiment 1, we found evidence of the effect of antibiotics expectations on willingness to prescribe antibiotics; the expectations did not influence the probability perception of bacterial disease. In Experiment 2, we addressed the three biggest limitations of the first experiment. First, we used a Likert scale to measure the willingness to prescribe instead of a more realistic choice question with two values (prescribe or not). It is possible that the antibiotics expectations effect would not translate into a more realistic prescribing decision. Furthermore, a real commitment to prescribing could also have a stronger distortion effect on the probability of a bacterial disease. Therefore, we used a dichotomous choice response question (prescribe or not) in Experiment 2.

Second, we presented the mother's and patient's expectations for antibiotics jointly. Evidence suggests that parents' expectations are an important factor in antibiotics prescribing (Mangione-Smith, McGlynn, Elliott, Krogstad, & Brook, 1999). Thus, it is possible that the expectations effect is limited to the parents' expectations. We separated the patient's expectations from the mother's expectations in Experiment 2 by presenting only the expectations of the patient.

Finally, in the original vignette we featured an external event (a swimming competition), but often the expectations are associated with "internal" events such as symptoms burden. The use of an external event was intentional to avoid confounding the patient's indication of expectations with the perceived probability of the disease. However, it is possible that an internal event might affect the perceived probability more strongly. In order to avoid the confounding variable whilst exploring this possibility we added a new vignette to address this question in Experiment 2.

**Method**

**Participants.** We powered the experiment to detect a medium effect size (Hedges' $g$ = 0.56 $\cong$ $OR$ = 2.75), found in Experiment 1. We required a minimum sample size of 127 participants for a logistic regression model with a binary predictor – to detect an odds ratio of 2.75, with 80% power at a 5% significance level. We estimated the probability of prescribing in the low expectation condition to be 0.42 based on the dichotomizing of the willingness to prescribe antibiotics as found in Experiment 1. Conservatively, we conducted this power analysis for a two-tailed test; the actual power for the achieved sample size and one-tailed test was 0.88.

Practicing family physicians were recruited via an online panel provided by a professional recruiting company (Qualtrics). Only certified and practicing UK family physicians were eligible to participate. According to the information from the recruiting company, 490 invitation emails were sent out overall. Of this number we recorded 246 accesses to the online questionnaire; 138 family physicians completed the online questionnaire (a 28.2% response rate). We excluded seven responses since they demonstrated a careless approach (Meade & Craig, 2012): they either did not pass the instructional manipulation check and/or they did not spend more than one third of the median response time on the questionnaire for the valid responses of the first five participants (i.e., > 240 sec). Both exclusion criteria were set up a-priori (before the data collection was completed). The instructional manipulation check consisted of a patient vignette mimicking the other vignettes (it described a 43-year-old architect presenting with a fever and a sore throat). Participants were asked to input the word "survey" in the text box below the vignette to indicate that they read the vignette. The text box was accompanied with the request: "Please enter your answer here".

A total of 131 family physicians (61.1% of whom were male; 18.3% practiced in an inner city, 57.3% in an urban area and 24.4% in a rural area) completed this task. The years of experience since the certification ranged from one to 35 years ($M = 14.1$, $SD = 9.4$ years). The participants were reimbursed with £7 for completing the 12-minute questionnaire administered online.

**Design.** A simple (antibiotics expectations: low vs. high) between-subjects design was implemented in two different patients' vignettes. In the first vignette (ear infection), we induced the high expectations for antibiotics by an indirect request for antibiotics coming directly from the patient participating in an important sporting event (i.e., an external event). This was similar to the vignette used in Experiment 1 but did not feature the mother. In the second vignette (cold), we induced the high expectations for antibiotics by a direct request for antibiotics expressed by a patient complaining about his symptoms of a cold (i.e., an internal event: *"He insists that you help him today to recover quickly as his symptoms are really bothering him. He is keen to get back to work soon, and hopes you can prescribe him antibiotics today"*).

In contrast with the previous experiment, the response order was fixed: the participants always saw the question on antibiotics prescribing first and the probability question second (this was depicted unexpectedly on the next page). The allocation to one of the two expectations conditions was randomized for each participant and vignette independently. The randomization was automated using an algorithm implemented in Qualtrics (randomization per block). The presentation order of the vignettes was fixed (the ear infection vignette starting always first).

**Materials and procedure**. After providing informed consent, participants answered three socio-demographic questions (namely: experience, gender, and area of practice). Then they diagnosed and/or managed several hypothetical patients. The first of them, an 18-year-old

competitive swimmer called Sarah, presented with symptoms of acute otitis media (see the "ear infection" vignette in the Appendix). This hypothetical patient was virtually the same as the one described in Experiment 1, but was older, attending university, and presenting alone (not with her mother as in Experiment 1). Physicians were first asked whether they would prescribe antibiotics ("Would you prescribe antibiotics for Sarah to be taken from today?") by selecting a "Yes" or "No" answer to the question. The presentation of the choices was randomized. Then, they assessed the probability of a bacterial infection ("How likely is it that Sarah has a bacterial infection?") by positioning a cursor on a visual analog probability scale (increments of 1) ranging from 0% (anchored as *bacterial is impossible, viral is certain*) via 50% (anchored as *bacterial and viral are equally likely*) to 100% (anchored as *viral is impossible, bacterial is certain*). Afterwards, participants diagnosed and managed four other hypothetical patients (cases not relevant to antibiotics prescribing), which were used as filler items. Then they saw the second vignette: a 38-year-old financial advisor called David, who presented with a cough and symptoms of a cold (see the vignette "cold" in the Appendix). Participants decided whether to prescribe antibiotics and subsequently assessed the probability of bacterial disease using the same questions as in the first vignette. Finally, they were presented with the vignette serving as an instructional manipulation check (see above). We conducted the study in accordance with the ethical standards of the American Psychological Association.

**Statistical analyses.** We planned to analyze the effect of antibiotics expectations on prescribing using a simple logistic regression and a complementary Bayes factor analysis using a contingency table with fixed margin columns, assuming independent binomial sampling within rows (Morey & Rouder, 2015). We planned to analyze the effect of antibiotics expectations on the perceived probability using an independent samples *t*-test and a complementary default

Bayesian *t*-test (using a Cauchy prior distribution and the prior scale $r = 0.707$; all Bayes factor analysis were conducted using "BayesFactor" package in R, Morey and Rouder (2015)). The logic behind Bayes factors and their interpretation is described in the method section of Experiment 1. Finally, to analyze the moderation effect of the experience and probability we planned to use a moderation analysis using PROCESS (Hayes, 2013).

**Results**

Overall, 51.9% of the physicians prescribed antibiotics in the first vignette, whereas only 12.2% prescribed them in the second vignette. As indicated in Figure 2, we replicated the effect of antibiotics expectations increasing the prescribing of antibiotics in the first vignette, $OR = 2.31$, 95% CI[1.15, 4.70], $z = 2.34$, $p = .019$; we also replicated the null effect on the perceived probability, $t(129) = -0.20$, $p = .842$, Cohen's $d = -0.03$, 95% CI[-0.38, 0.31]. The Bayes factor model comparison suggested that the non-independence model of antibiotics expectations and prescribing was around three times more likely than the independence model (no association between the expectations and prescribing), $BF_{10} = 3.4 \pm 0\%$. Furthermore, a Bayesian default *t*-test favored the null hypothesis around five times more than the alternative hypothesis, $BF_{01} = 5.3 \pm 0\%$. We found, however, no effect of antibiotics expectations on prescribing in the second vignette, $OR = 0.75$, 95% CI[0.25, 2.11], $z = -0.57$, $p = .572$ and, consistently with that, no effect on the perceived probability, $t(129) = 1.40$, $p = .164$, Cohen's $d = +0.25$, 95% CI[-0.10, 0.59] (see Figure 2). Indeed, the Bayes factor analysis suggested that the independence model (no association between the expectations and prescribing) was six times more likely than the non-independence model of antibiotics expectations and prescribing, $BF_{01} = 6.0 \pm 0\%$. Furthermore, a Bayesian default *t*-test favored the null hypothesis two times more than the alternative hypothesis, $BF_{01} = 2.2 \pm 0\%$.

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Insert Figure 2 here

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The moderation analysis showed similar, although not significant, data patterns to the first experiment. First, experience was positively correlated with prescribing in both scenarios although these correlations were not significant (respectively, $r_{pb} = .10$, $p = .237$ and $r_{pb} = .10$, $p = .242$). Furthermore, similarly to Experiment 1, experience did not moderate the expectations effect on prescribing in the first scenario ($b = 0.03$, 95% CI[-0.05, 0.11], $z = 0.78$, $p = .438$) nor in the second scenario ($b = 0.03$, 95% CI[-0.09, 0.14], $z = 0.44$, $p = .658$). Second, the perceived probability was correlated with prescribing in the first scenario, $r_{pb} = .50$, $p < .001$ and in the second scenario, $r_{pb} = .45$, $p < .001$. In contrast with the first experiment, the perceived probability did not moderate the expectations effect on prescribing in the first ($b = 0.05$, 95% CI[-0.01, 0.10], $z = 1.77$, $p = .078$) nor in the second scenario ($b = 0.02$, 95% CI[-0.03, 0.08], $z = 0.88$, $p = .381$).

## General Discussion

In two experimental studies of family physicians, we identified three important pieces of evidence. First, we found evidence of the effect of a non-clinical factor – in this case, patients' and parents' expectations for antibiotics – on the willingness of physicians to prescribe antibiotics. This evidence had a causal nature and occurred regardless of the response order. Second, we observed only a localized effect of this manipulation. It only affected the willingness to prescribe antibiotics (or prescribing decisions) but not the perceived probability of a bacterial infection; the effect was absent in both response order conditions. Third, the more experienced physicians tended to be more willing to prescribe antibiotics, but not because they were more

sensitive to the patient's expectations manipulation: experience did not moderate the expectation effect. In fact, some limited evidence of Experiment 1 indicates that what did moderate the expectations effect was the perceived probability of a bacterial infection – the expectations effect declined with the increasing probability of a bacterial infection.

Our findings corroborate the previous non-experimental findings identifying the non-clinical factors as important components in the physicians' antibiotics prescribing behavior (Cals et al., 2007; Cockburn & Pit, 1997; Coenen et al., 2006; Cole, 2014). Although our manipulation cannot capture the variability of the non-clinical factors reported in the prior studies (e.g., Coenen et al., 2013), it does provide a unique value in providing a causal link between the expectations and the physicians' prescribing. We did not observe the effect in the cold vignette (Experiment 2). This lack of the effect perhaps occurred because the presented clinical picture of a cold was incompatible with antibiotics prescribing – as shown by the very low prescribing rate or perhaps due to the experimental manipulation or procedure (e.g., the direct request of the antibiotics might have caused a psychological reactance in the physicians). We hope that our methodological approach could inspire future studies that would be required to identify causal effects of other non-clinical factors. An ecologically valid vignette approach would also enable a systematic factorial design of the various non-clinical factors, which could help us to disentangle the relative contributions of the non-clinical factors.

Our findings, however, did not support the pathways postulated in prior research according to which the non-clinical factors might affect the perceived probability, either directly (e.g., pre-decision distortion, Wallsten, 1981) or indirectly (e.g., post-decision distortion, Levy & Hershey, 2006). None of the two systematic distortions – which could escalate the over-prescribing of antibiotics – have been observed in our study. It is still possible that the physicians

perceived the patient's expectations as a cue of clinical severity, but this was not severe enough to activate the loss asymmetry mechanism. Alternatively, the loss asymmetry function was activated but it was not big enough to be measurable in the changed perceived probability. In this respect, a vignette where the absence of antibiotics might lead to more severe consequences would be more revealing. Physicians also avoided rationalizing their prescription decisions by increasing the probability of a bacterial infection. This might have occurred, perhaps, because the inconsistency was externalized – attributed to the patient's intentions ("Antibiotics are not needed, but if you want them, I can prescribe them") – and, therefore, the physicians did not need to strive for consistency.

Along with the theoretical importance of these pathways, our research also has important clinical implications. From a clinical point of view, non-clinical factors and, specifically, social influences might contribute to the over-prescribing of antibiotics and, in turn, to the increased antibiotic resistance (Costelloe et al., 2010). This is particularly important in situations in which most of the interventions designed to reduce antibiotic over-prescribing are focused on clinical guidelines (NICE, 2015). To reduce over-prescribing of antibiotics, potential interventions should target patients' expectations, physicians' beliefs about these expectations, and physicians' skills in managing these expectations. Consistently with such a conclusion, prior complex intervention studies have found the most effective interventions to be those that target both patients and clinicians during consultations, facilitating shared decision-making (Coxeter, Del Mar, McGregor, Beller, & Hoffmann, 2015; Ranji, Steinman, Shojania, & Gonzales, 2008; Vodicka et al., 2013).

Despite the evidence for the expectations effect found here, overcoming three limitations could increase our confidence in the theoretical and clinical conclusions drawn here. First,

researchers should focus on providing causal evidence using more ecological approaches than vignettes, such as using simulated patients and measuring actual prescribing behavior. In light of the recent evidence on the high predictive validity of vignettes, this should not be perceived as a substantial limitation (Evans et al., 2015). Second, future research should study a more complex network of variables than studied here, which will enable us to disentangle their mutual contributions, since non-clinical factors may well represent a network of different concepts. Finally, future research should investigate the effects of non-clinical factors across different diagnostic situations, since the identified behavior can be context-specific. The endeavor to overcome these limitations will be crucial for tailoring the most effective interventions.

**Conclusion**

In two experiments with practicing physicians, we found evidence that patients' expectations increase physicians' willingness to prescribe antibiotics. Such an effect has a local nature: it does not distort, directly or indirectly, the physicians' perceived probability of a bacterial infection. Physicians' experience is positively associated with prescribing, but it did not moderate the expectations effect on prescribing. We encourage further experimental research into the impact of non-clinical factors on the prescribing of antibiotics, and the development of interventions which take the socio-cognitive context of prescribing into account.

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**Table 1: Quantified evidence for models (Bayes factors)**

| BF denominator | BF nominator | | | |
| --- | --- | --- | --- | --- |
| | Model 1<br>$BF_{E/}$ | Model 2<br>$BF_{RO/}$ | Model 3<br>$BF_{E+RO/}$ | Model 4<br>$BF_{E+RO+E*RO/}$ |
| *Willingness to prescribe* | | | | |
| Intercept-only model | 7750.4 | 0.341 | 4511.4 | 975.0 |
| Full model $_{E+RO+E*RO}$ | 7.9 | 0.0003 | 4.6 | 1 |
| *Probability* | | | | |
| Intercept-only model | 0.290 | 0.149 | 0.045 | 0.007 |
| Full model $_{E+RO+E*RO}$ | 39.6 | 20.3 | 6.2 | 1 |

*Note*. BF: Bayes factor, E: expectations (factor 1), RO: response order (factor 2), E*RO: interaction term of the expectations and the response order;
Evidence category for $BF_{01}$ (as suggested by Jeffreys, 1961): evidence to support $H_0$: *decisive* evidence (> 100), *very strong* evidence (100 – 30), *strong* evidence (30 – 10), *substantial* evidence (10 – 3), *anecdotal* evidence (3 – 1); evidence to support $H_1$: *decisive* evidence (< 1/100), *very strong* evidence (1/100 – 1/30), *strong* evidence (1/30 – 1/10), *substantial* evidence (1/10 – 1/3), *anecdotal* evidence (1/3 – 1); $BF_{10} = 1/BF_{01}$.

**Figure Captions**

*Figure 1.* (A) Effect of expectations (low vs. high) on willingness to prescribe antibiotics in two different response orders (probability first vs. prescribing first). (B) Effect of expectations (low vs. high) on the probability of a bacterial infection in two different response orders (probability first vs. prescribing first).

*Note.* Error bars represent 95% *CI*s.

*Figure 2.* (A) Effect of expectations for antibiotics (low vs. high) on prescribing antibiotics (in %) in two different vignettes (sample estimates). (B) Effect of expectations for antibiotics (low vs. high) on the probability of a bacterial infection in two different vignettes.

*Note*. The error bars in panel A represent 95% Agresti-Coull confidence intervals for a binomial proportion. The error bars in panel B represent 95% confidence intervals for mean.
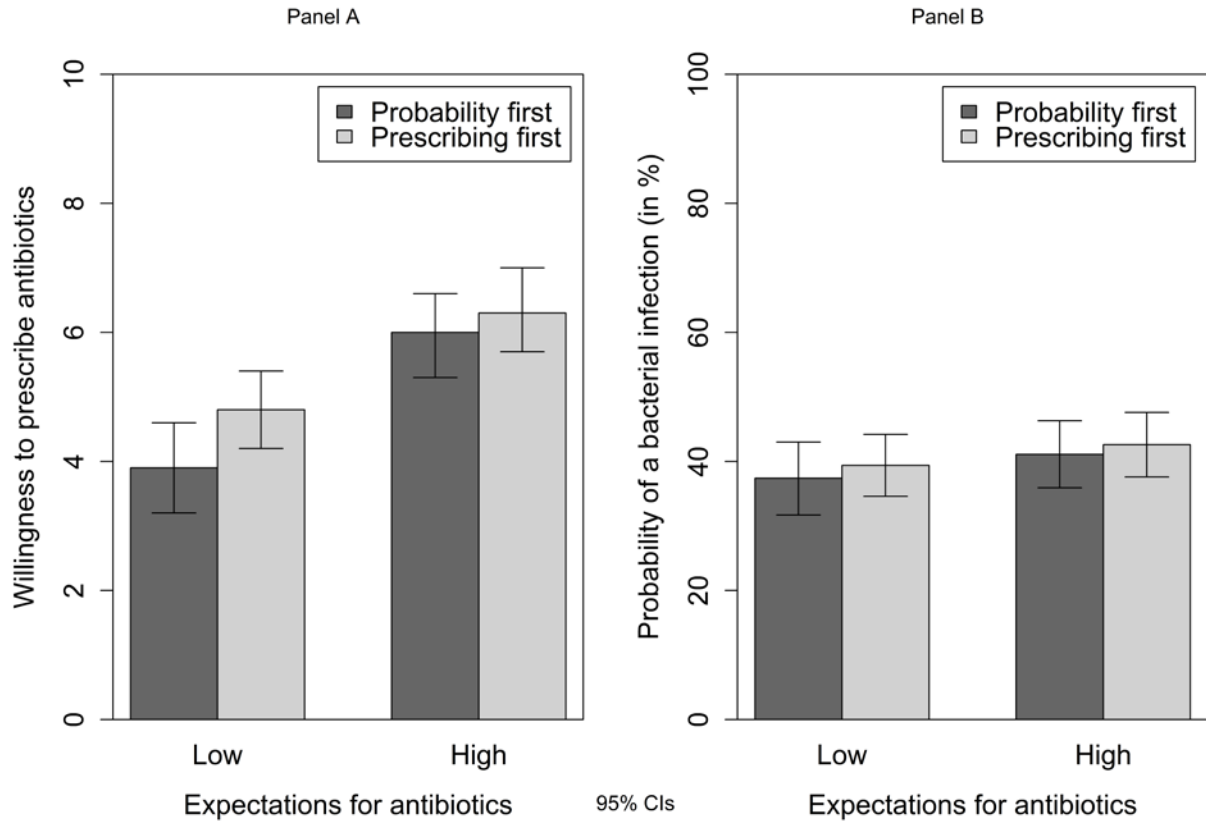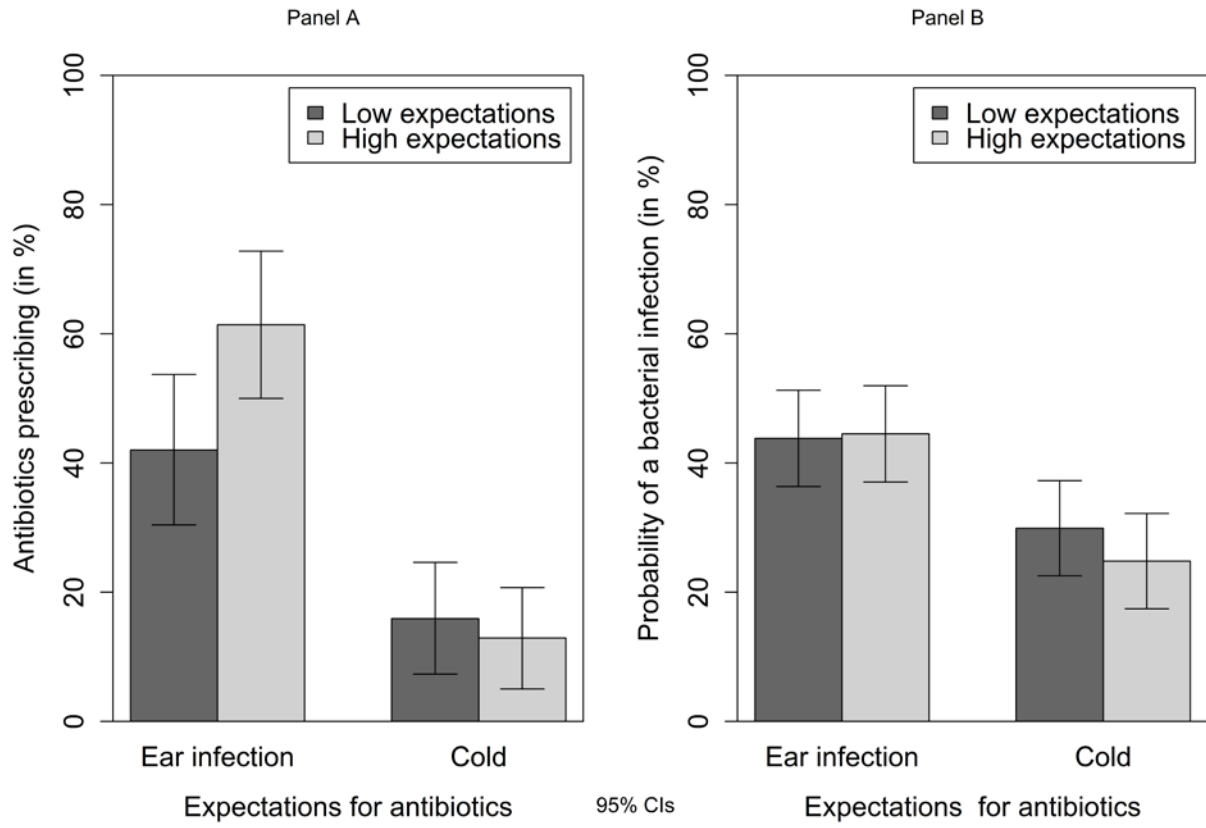
Figure 1

Figure 2

**Appendix**

**Ear infection vignette (as used in Experiment 1)**

Sarah Robinson is 15 years old. She has been registered with your practice since birth. Her immunisations are up to date, and she does not have any major past medical history. She attends the local secondary school and is a competitive swimmer, training regularly at a nearby swimming club.

Today, she comes in with her mother complaining of fever for 3 days and pain in her right ear since yesterday. The fever responds to both paracetamol and ibuprofen but rises again after a few hours. The earache is getting worse. Her right ear feels blocked and she complains of reduced hearing. There is no discharge from the ear. She has no cough and no difficulty breathing. Further history taking reveals nothing significant.

On examination, her temperature is 38.5 °C, her throat looks red and her tonsils are slightly enlarged with no exudate. She is slightly congested. Examination of the right ear reveals a normal ear canal, red eardrum, diminished light reflex, no fluid levels and no perforation.

*Her mother insists you to help her to recover quickly as Sarah is due to take a part in the final round of the National Youth Championship swimming competition in 4 days time. This competition is extremely important for her, as she could lose her chance to gain a sport's scholarship.*

*Note.* The text represents the vignette presented in the condition with high expectations. Italics (not in the original text) indicate the text that was removed from the vignette presented in the condition with low expectations (in which an additional sentence appeared at the end of the first paragraph, *"Her last swimming competition of the season was two weeks ago."*).

**Ear infection vignette (as used in Experiment 2)**

Sarah Robinson is 18 years old. She has been registered with your practice since birth. Her immunisations are up to date, and she does not have any major past medical history. She attends the local university and is a competitive swimmer, training regularly at a nearby swimming club.

Today, she comes in complaining of fever for 3 days and pain in her right ear since yesterday. The fever responds to both paracetamol and ibuprofen but rises again after a few hours. The earache is getting worse. Her right ear feels blocked and she complains of reduced hearing. There is no discharge from the ear. She has no cough and no difficulty breathing. Further history taking reveals nothing significant.

On examination, her temperature is 38.5 °C, her throat looks red and her tonsils are slightly enlarged with no exudate. She is slightly congested. Examination of the right ear reveals a normal ear canal, red eardrum, diminished light reflex, no fluid levels and no perforation.

*Sarah insists you to help her to recover quickly as she is due to take a part in the classification round of the National Championship swimming competition in 4 days time. This competition is extremely important for her, as she could lose her chance to gain a sport's scholarship.*

*Note.* The text represents the vignette presented in the condition with high expectations. Italics (not in the original text) indicate the text that was removed from the vignette presented in the condition with low expectations (in which an additional sentence appeared at the end of the first paragraph, "*Her last swimming competition of the season was two weeks ago.*").

**Cold-like symptoms vignette (as used in Experiment 2)**

David Taylor is a 38-year-old financial advisor. He is newly registered to your practice, has no major past medical history and is not on any regular medications. He does not smoke and drinks alcohol only occasionally.

Today, he comes in complaining of a cough that he has had for one week. The cough started with a runny nose, sore throat and cold-like symptoms, with a self-reported fever. The fever responds to both paracetamol and ibuprofen but rises again after a few hours. He reports that he is coughing up green/yellow sputum, without any blood. He also denies any shortness of breath, though he does feel tired. He took a few days off work.

On examination he looks coryzal and congested. His temperature is 37.8°C. Pulse, blood pressure and respiratory rate are all normal. His chest is clear with no crepitations or wheezing heard. His throat is slightly red with no exudates. He has a few swollen cervical lymph nodes.

*He insists that you help him today to recover quickly as his symptoms are really bothering him. He is keen to get back to work soon, and hopes you can prescribe him antibiotics today.*

*Note.* The text represents the vignette presented in the condition with high expectations. Italics (not in the original text) indicate the text that was removed from the vignette presented in the condition with low expectations (in which an additional sentence appeared at the end of the first paragraph, "*Her last swimming competition of the season was two weeks ago.*").