Article

JHP

Journal of Health Psychology
2023, Vol. 28(11) 1024–1037

DOI: 10.1177/13591053221149526
journals.sagepub.com/home/hpq
SAGE

Promoting prosociality toward future generations in antibiotic intake

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Abstract

Understanding individuals' preferences for antibiotics can help mitigate the acceleration of antibiotic resistance. Similar to the climate crisis, individuals "today" need to appropriately use antibiotics to reduce the negative consequences of antibiotic resistance for individuals "tomorrow." We use an established—yet novel in this research field—behavioral game approach to investigate individuals' preferences for antibiotics in the face of a between-generations conflict. In an online study, we investigated whether a between-generations (vs within-generations) conflict in antibiotic intake leads to larger overuse and how to promote appropriate use of antibiotics. Results indicate that overuse in the face of a between-generations (vs within-generations) conflict increased. Eliciting empathy toward future generations in the case of a between-generations conflict decreased overuse. Findings suggest that different representations of this social dilemma can influence people's preferences for antibiotics, and that empathy-based interventions might promote appropriate antibiotic use.

Keywords

antibiotics, decision-making, health behavior, health psychology, prosociality

Introduction

Antimicrobial resistance (AMR), that is, the process whereby pathogens such as viruses and bacteria no longer respond to medicines, is a growing concern, posing tremendous health and economic burdens worldwide. Each year, around 35,000 people die as a result of AMR in the United States alone (Centers for Disease Control and Prevention [CDC], 2019). If no further actions are taken to handle this threat, a cumulative loss of 100 trillion USD in global production is expected by 2050, as well as a steep global increase in annual deaths (O'Neill, 2016). This complex public health issue is influenced by many behaviors and calls for multifaceted interventions (World Health Organization [WHO], 2021).

Antibiotic resistance is the specific case of AMR when bacteria are involved, and one of

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the avenues for fighting it is through stewardship programs to educate and promote appropriate prescribing behavior in clinical settings (CDC, 2019). When it comes to the use of antibiotics in humans, decisions are often made in doctor–patient interactions (for a review, see Teixeira Rodrigues et al., 2013). Patients' preferences have been shown to play an important role in doctors' decisions to prescribe antibiotics (Kianmehr et al., 2019; Kohut et al., 2020; Kotwani et al., 2010). For instance, a vignette study with doctors found that they were more willing to prescribe antibiotics when patients showed higher expectations for the drugs (Sirota et al., 2017). Such preferences also matter after consultations when practices of self-medication and variables concerning compliance with the treatment may play a role (Ancillotti et al., 2018, 2020). Therefore, understanding patients' preferences can help mitigate the inappropriate use of antibiotics and, in turn, the negative societal effects thereof.

The social and temporal dilemma of antibiotic intake

From an individual perspective, people have different motivations to use antibiotics (Kianmehr et al., 2019). For instance, overuse of antibiotics can be driven by the urge to potentially achieve faster recovery while having little risk of side effects (Thorpe et al., 2020). However, antibiotics are not needed to treat some mild or self-limiting infections (CDC, 2019; National Institute for Health and Care Excellence [NICE], 2016), and excessive intake is damaging to society because overuse of antibiotics speeds up the process of antibiotic resistance. Qualitative evidence indeed suggests that one potential motivation driving appropriate use is the intent to preserve antibiotics' effectiveness (Ancillotti et al., 2018). The decision to take antibiotics can thus also be seen from a social perspective, as it not only affects the agent, but also poses negative externalities to society at large (Laxminarayan and Heymann, 2012). This tension between individual and social interests creates a social dilemma (Dawes, 1980) in the structural form of a commons dilemma (Hardin, 1968; Hollis and Maybarduk, 2015), where overuse of a restricted resource leads to collective suboptimal outcomes.

What further complicates this dilemma is that the societal consequences of antibiotic resistance due to antibiotic overuse are often temporally distant from the individual agent and its "effects are expected to significantly increase in gravity over the next decades" (Harring and Krockow, 2021:4). Similar to the climate crisis, in the social dilemma of antibiotic intake individuals "today" need to decide whether to appropriately take antibiotics only when necessary, in order to benefit other individuals "tomorrow" (Diamant et al., 2021; Krockow et al., 2021).

Some evidence suggest that the welfare of future patients indeed matters, at least for some doctors' prescribing decisions (Tarrant et al., 2020). Yet, the between-generations dynamic in antibiotic consumption has barely been addressed when it comes to patients' preferences. For instance, it is an open question what the behavioral consequences are when people represent antibiotic intake as a within- versus between-generations social dilemma, that is, when the antibiotic overuse has immediate consequences for the current generation or when such consequences are delayed to the future generation, respectively.

Representing the social dilemma of antibiotic intake as a between-generations (vs within-generations) conflict may even increase the exploitation of antibiotics by exacerbating individuals' proneness to overuse them. Specifically, the individual-level incentives for appropriate antibiotic intake could decrease because the consequences are delayed and therefore less tangible both for the decision maker and for members of the decision maker's generation. Research on the structurally similar climate-change dilemma indicates that people are less inclined to contribute to reduce the potentially negative consequences of climate change when these consequences are delayed and affect people in the future rather than when the consequences are (more) immediate (Jacquet et al., 2013). In this regard, research suggests that fostering empathetic concern and emotional engagement for future generations can promote pro-environmental behaviors (Brown et al., 2019). Evidence also shows that empathy can promote vaccination intentions in high-stakes scenarios such as pandemics (Pfattheicher et al., 2022). Thus, raising empathic concern may be a promising way to promote appropriate use of antibiotics to protect future generations' health.

Individual differences in antibiotic use

Considering the characteristics of this social dilemma, individual differences might also help understand antibiotic-related behaviors. First, prosocial concerns and higher valuation of the social welfare could be driving the documented motivation to appropriately use antibiotics, aiming to preserve their effectiveness (Ancillotti et al., 2018). Second, the temporal distance in the dilemma suggests that consideration for future consequences might influence antibiotic use, as this construct has been associated with other behaviors for which temporal discounting is relevant (e.g. eating behavior, van Beek et al., 2013).

Thus, we aim to investigate the social and temporal dynamics of health decisions in the context of antibiotic intake, as well as to explore the role of prosocial concerns and consideration for future consequences in this scenario. For this purpose, we use an interactive health game.

Interactive health behavior games

We model individual incentives to take antibiotics using an interactive behavioral game that allows us to vary the individual incentives in antibiotic intake—and, thus, model a within-versus between-generations social dilemma in antibiotic intake—while at the same time providing real consequences of individual decisions for both oneself and others. Behavioral games modeling social dilemmas (Freedman and Flanagan, 2017; Murnighan and Wang, 2016; Thielmann et al., 2021; Van Dijk and De Dreu, 2021) have been successfully applied in other health domains, (e.g. vaccination, Böhm et al., 2016; Chapman et al., 2012; Ibuka et al., 2014), and have several advantages. First, they allow us to isolate the effect of patients' individual preferences. This does not imply that doctors' prescriptions and recommendations do not matter; however, we are able to study the causal impact of individual preferences on behaviors without any confounding factors. Second, the approach is flexible regarding changing the underlying structure of behavioral incentives for different behaviors. This allows comparing antibiotic overuse when its consequences affect the current generation with when they affect the future generation instead, irrespective of the participants' actual knowledge and representation of the real-world situation. Third, because of such behavioral incentives, participants' decisions are truly consequential, both for themselves and for others. As such, random or socially desirable responding is likely to play less of a role as compared to, for instance, survey responses (Thielmann et al., 2021).

The present research

We conducted a pre-registered[1] experimental study using an adapted version of a behavioral game (Böhm et al., 2022) to investigate antibiotic overuse when the consequences of antibiotic resistance are borne by the current versus the future generation. Ethical approval was given by the Institutional Ethical Review Board from the Department of Psychology, University of Copenhagen (approval number: IP-IRB/19082021). All participants provided informed consent prior to participation and were not deceived.

Hypotheses

Evidence suggests that taking the perspective of future generations can affect how decision makers perceive the consequences of their own acts (e.g. climate change, Shahen et al., 2020). Concerning antibiotics, research suggests an association between physician's empathy and prescribing behavior (Sun et al., 2017). Furthermore, increasing empathy has been shown to increase prosocial concerns and promote different behaviors (e.g. vaccination intentions, Pfattheicher et al., 2022; pro-environmental behaviors, Brown et al., 2019). In the present study, we adapted this idea to test whether empathy toward the future generation can reduce overuse of antibiotics. Accordingly, we pre-registered the following three hypotheses. First, we expected that antibiotic intake in cases of mild disease is larger than zero (*overuse hypothesis*). Second, we expected that overuse is larger when the consequences affect future generations than when the consequences affect the current generation (*between-generations exploitation hypothesis).* Third, overuse in the between-generations setting should decrease when empathy toward the future generation is elicited versus not elicited (*empathy hypothesis).*

Materials and methods

Study design and participants. The study had a mixed design with one between-participant and one within-participant factor. The between-participant factor was treatment condition: *within-generations exploitation, between-generations exploitation*, and *between-generations exploitation + empathy.* Participants were randomly assigned to one of these three conditions. The within-participant factor was disease severity: *mild or severe* (see Procedures below).

The determination of the sample size was pre-registered and followed an a-priori power analysis using G*Power (Erdfelder et al., 2009) for a mixed-measures ANOVA with a within–between interaction. Based on background knowledge from the group's previous work with behavioral game experiments, a power of .95 was estimated to detect a small-to-medium effect size of $f = 0.15$, with two conditions being compared (*within-generations exploitation* vs *between-generations exploitation; between-generations exploitation* vs *between-generations exploitation + empathy*). Moreover, given a proper understanding of the game instructions, we assumed that intake between the two types of disease severity would be weakly correlated. Thus, a correlation between the repeated measures (i.e. intake in cases of mild vs severe diseases) of $r = 0.2$ was used. Alpha was set at .025 to adjust for multiple tests. This calculation returned a required sample size of $n = 272$ participants per condition, equaling $N = 816$ participants for all three between-participant treatments. Considering the complexity of the game, we expected potential exclusions due to failed attention checks (Hauser et al., 2018). Therefore, we pre-registered collecting data from $N = 1000$ participants. Data collection resulted in $n = 998$ participants with complete data. Considering data collection resulted in two conditions with an odd number of participants and that an even number was needed for pair matching (see below), we randomly excluded two participants (i.e. one from each of the two conditions with an odd number of participants). The resulting sample size was $n = 996$ (50.3% female, $M_{age} = 26.81$, $SD_{age} = 16.31$), with $n = 336$ in the *within-generations exploitation* condition, $n = 332$ in the *between-generations exploitation* condition, and $n = 328$ in the *between-generations exploitation + empathy* condition.[2]

Behavioral game of antibiotic intake. We applied and adapted a behavioral game recently devised by Böhm et al. (2022). The game models the intake of antibiotics as a dynamic commons dilemma (Hardin, 1968; Ostrom, 2000). Our adapted game version consists of x rounds played by two players. In each round, participants complete a real-effort task in which they are being paid based on the number of tasks completed.

In each round, a player is infected with a fictional mild or severe disease (each in $x/2$ of the rounds); the order of occurrence of mild and severe diseases across rounds is random. Hence, across all players and rounds, there are $2x$ infections (2 players $\times$ x rounds). The severity of the disease affects the number of tasks for which a player is paid, and, thus, the possibility to increase their utility. Specifically, players are paid for more tasks in cases of a mild disease than in cases of a severe disease, capturing the differential loss of utility due to infection with either disease.

There is a fixed number of x antibiotic units available jointly for both players to be used to cure at most half of the $2x$ overall infections. Specifically, taking the antibiotic in a specific round restores the maximum tasks for which the player can be paid in this round, irrespective of the severity of the disease. In other words, taking the antibiotic effectively cures the disease and increases a player's individual utility. Players make their decisions independently and without knowing the other player's decisions. Each intake decision by either player reduces the number of available units by one. Once all the x antibiotic units have been used, the antibiotic is no longer effective, and the remaining infections cannot be cured.

Each player maximizes their expected payoff by taking the antibiotic in every round, irrespective of whether the infection is mild or severe. However, if both players follow this selfish-rational strategy, their individual payoffs are lower than when they would both take the antibiotic only in cases of severe disease. In other words, antibiotic intake solely in cases of severe disease is socially optimal, whereas antibiotic intake in cases of both severe and mild diseases captures antibiotic overuse (for more details, see Böhm et al., 2022). Thus, in its standard form, the game models a conflict in antibiotic intake that leads to a social dilemma within generations, with decisions made within a two-player group being consequential for the respective players' payoffs, but not for others outside the group.

In a version representing the between-generations dilemma, generations are modeled by two players playing the first half ($x/2$ rounds: the first generation) and two other players subsequently playing the second half (another $x/2$ rounds: the second generation), with the overall number of rounds across generations being x as in the standard version described above. The occurrence of mild or severe diseases for each generation is also modeled as in the standard version, that is, each player in each generation faces exactly $x/4$ mild and $x/4$ severe diseases. There are only x effective antibiotic units available for all four players across the two generations; the situation thus generates $2x$ potential intake-situations by which to model scarcity of the resource. Thus, a crucial difference from the standard form of the game is that players of the first generation, due to their first-mover advantage, have enough antibiotic units available to cure both mild and severe diseases. If they do so, however, there will be an insufficient number of doses available for the second generation to treat severe infections.

The dilemma thus shifts from a within-generations to a between-generations conflict. Consequently, the first generation's higher (lower) uptake of antibiotics in cases of the between-generations compared to the within-generations conflict would indicate a lower (higher) valuation for the future generation's health compared to valuing the present generation's health. In other words, comparing the between-generations with the within-generations version of the game allows for drawing causal inferences about the potential impact of intergenerational discounting on antibiotic intake.

Experimental manipulations

Within-/between-generations exploitation manipulation. Participants in the *within-generations exploitation* condition played the game in its standard form (Böhm et al., 2022), whereas participants in the two other conditions used the between-generations version of the game. Note that all conditions had a game with 20 rounds, but in the *between-generations exploitation* and the *between-generations exploitation + empathy* conditions a different generation of participants played the second half of the game in another study—which is not part of the present manuscript. To make conditions comparable, the last 10 rounds played in the *within-generations exploitation* condition were excluded from the analyses. Instructions were the same for all conditions, except for nuances concerning the within-versus between-generations manipulation. Participants in the within-generations setting were informed that they would play with another participant for 20 rounds and that both had 20 doses of effective antibiotics to be shared by them. Participants in the between-generations settings were informed that they would play with another person for 10 rounds, and that there were also 20 doses for the group. Participants in the between-generations conditions were informed that the number of doses left by them would be available for two other participants to play the remaining 10 rounds in the future.

Empathy manipulation. Participants in the *between-generations exploitation + empathy* condition were additionally presented with an intervention before playing the game. The intervention was designed to induce empathy for the subsequent generation and consisted of two parts linking a real-world case of antibiotic resistance to the experimental context of this study (see Supplemental Materials). The first part was an audio recording 2 minutes and 10 seconds in length, which was also available as text and was adapted from a public health campaign (Chaintarli et al., 2016). This consisted of a mother's narrative about the negative consequences of antibiotic resistance experienced by her baby. In the second part, participants were asked to write how they would feel if they were in the position of the future generation and there were no effective doses of antibiotics left for them to treat the hypothetical disease. The empathy manipulation proved successful in a pre-test (see Supplemental Materials).

Measures

Dependent variable. The main dependent variable was antibiotic intake in cases of mild and severe disease in the game, where intake of antibiotics in cases of mild disease is defined as overuse as it is only selfish rational but creates negative externalities for others (whereas intake in cases of severe disease is both selfishly rational and collectively optimal). This was at the group level, with intake across both players being summed by disease severity. The dependent variable thus ranged on a scale from zero to 10 for both intake decisions in mild and severe cases of the disease, resulting in two observations per group.

Individual differences. Prosocial concern was assessed with the Honesty-Humility (HH) subscale from the HEXACO personality model (10 items, Cronbach's $\alpha = 0.69$), using the HEXACO-60 questionnaire (HEXACO-60; Ashton and Lee, 2009), for example, "I wouldn't pretend to like someone just to get that person to do favors for me" (range 1–5, "strongly disagree" to "strongly agree"). Consideration of Future Consequences (CFC) was assessed with 12 items (Cronbach's $\alpha = 0.83$) proposed by Strathman et al. (1994) for example, "I consider how things might be in the future and try to influence those things with my day-to-day behavior" (range 1–5, "extremely uncharacteristic" to "extremely characteristic").

Antibiotic-related behaviors were measured with four items adapted from Scaioli et al. (2015), for example, "Do you use leftover antibiotics when you have a cold, a sore throat, or the flu, without consulting your doctor?" (categorical, "yes" vs "no").

Finally, we also assessed demographic variables such as age, gender, and whether participants had children (see Supplemental Table S1).

Procedures. Participants from the United States and the United Kingdom were recruited via Prolific (www.prolific.co; Palan and Schitter, 2018), and were compensated £3.13 on average for their participation. Participants were also entitled to participate in a lottery that randomly selected approximately 30% of the sample to receive a bonus payment based on the behavior-contingent incentives in the game as described below. The whole experiment took place online and the platform Qualtrics (Qualtrics, Provo, UT) was used to program and present the experiment to participants. Average participation time was 36 minutes (SD = 67); treatments did not differ regarding participation time (see Supplemental Table S2).

In each round, participants completed four typing tasks, and the number of tasks for which they could get paid depended on their behavioral strategy in the game, resembling a real-life situation where individuals' health status may impact their productivity in their work life (Figure S1, Supplemental Materials). If untreated in a given round (i.e. deciding against antibiotics, or deciding in favor of antibiotics when they are ineffective), paid tasks were reduced to one in cases of mild disease, and to zero in cases of severe disease. If treated (i.e. deciding in favor of antibiotics given that they are still effective), participants recovered, regardless of disease severity, and got paid for all four tasks in the respective round. Participants did not have information regarding others' decisions or when the antibiotic had already become ineffective. Demographics were assessed before the game and the remaining measures of individual differences and antibiotic-related behavior were assessed at the end of the study.

Participants were pair-matched within 2 weeks after completing the study. Then, we cross-checked the decisions within each group to identify when antibiotic units became ineffective and calculated behavior-contingent bonuses. The payment per completed task was £0.02 pounds. In total, $n = 318$ participants were randomly selected to receive the bonus payment ($M = £0.63$, SD = £0.18). Bonuses were paid via Prolific.

Results

Confirmatory analyses. On average, participants took the antibiotic in cases of a mild disease 1.52 times (out of 5; SD = 1.84) and 4.51 times (out of 5; SD = 0.93) in cases of severe disease (for descriptive statistics per condition and severity, see Supplemental Table S3). To test the *overuse hypothesis*, that is, intake of antibiotic in cases of mild disease, we conducted one-sided *t*-tests for independent samples against zero (pooled across treatments) on the average intake decisions on the group level (i.e. aggregated intake across both players; see Figure 1). Supporting our hypothesis, antibiotic intake in cases of mild disease was larger than zero, $t(497) = 26.27$, $p < 0.001$, $d = 2.36$. This result was replicated when conducting the analysis for each condition separately (Supplemental Table S4).

Next, we conducted mixed-measures ANOVAs aggregated at the group level to test whether conditions differed in antibiotic intake decisions, with two observations per group (i.e. intake for each symptom severity: mild or severe). Importantly, antibiotic intake differed across conditions, $F(2, 495) = 8.40$, $p < 0.001$, $\eta^2 = 0.03$. The ANOVA testing the *between-generations exploitation hypothesis* (i.e. *within-generations exploitation* vs *between-generations exploitation*) revealed that intake in the *between-generations exploitation* condition ($M = 12.71$, SD = 3.01) was higher than that in the *within-generations exploitation* condition ($M = 12.08$, SD = 2.64), $F(1, 332) = 4.09$, $p = 0.043$, $\eta^2_p = 0.01$. Furthermore, intake decisions differed based on the severity of symptoms $F(1, 332) = 1387.50$, $p < 0.001$, $\eta^2_p = 0.80$, and the interaction effect between condition and severity was also significant, $F(1, 332) = 11.50$, $p < 0.001$, $\eta^2_p = 0.03$. These findings show that people were more willing to decide in favor of antibiotics when the consequences of overuse would affect the future generation, and this effect was moderated by disease severity.

Moreover, the ANOVA testing the *empathy hypothesis* (i.e. *between-generations exploitation* vs *between-generations exploitation + empathy*) showed that overall intake decreased in the *empathy* condition ($M = 11.4$, SD = 3.06), $F(1, 328) = 15.41$, $p < 0.001$, $\eta^2_p = 0.04$, compared to the *between-generations exploitation* condition. Again, there was also an effect of severity $F(1, 328) = 1447.03$, $p < 0.001$, $\eta^2_p = 0.81$, and an interaction effect between condition and severity, $F(1, 328) = 9.24$, $p = 0.002$, $\eta^2_p = 0.02$. This indicates that inducing empathy for the future generations decreased antibiotic intake, with this effect being again moderated by disease severity.

Exploratory analyses. To ascertain which levels of severity drove the observed differences and

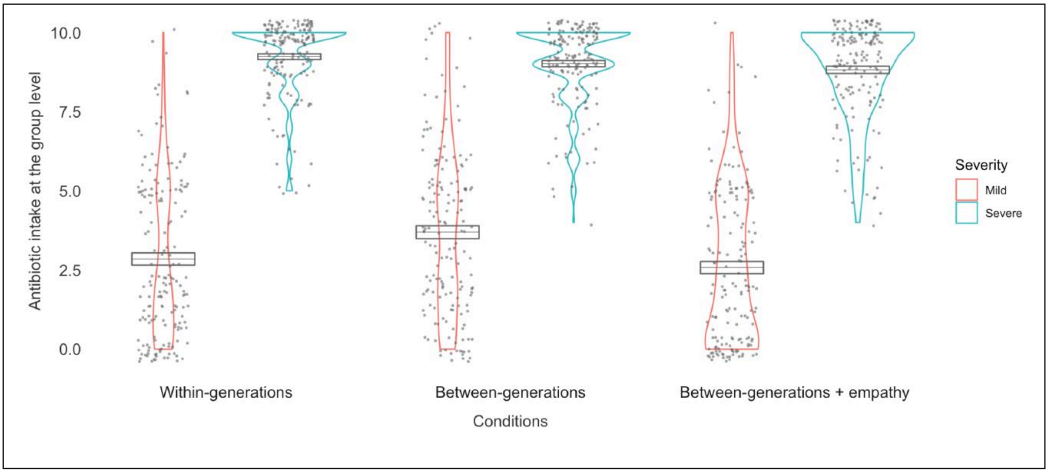

Figure 1. Antibiotic intake in the I-Resist game at the group level per experimental condition and level of severity.
N = 996; *n*1 = 168 (Within-generations exploitation), *n*2 = 166 (Between-generations exploitation), and *n*3 = 164 (Between-generations exploitation + empathy) with two participants per group. Dots indicate single data points, gray lines represent means and quartiles. Colored lines around the dots create areas representing the probability that observations occur in the respective area, with narrower (wider) areas indicating lower (higher) probability.

whether antibiotic overuse (i.e. intake in cases of mild disease) was indeed different between conditions as predicted by the *between-generations exploitation* and *overuse hypotheses*, we conducted exploratory post-hoc pairwise comparisons using Tukey's correction. The first comparison revealed that the intake in the *within-generations exploitation* and *between-generations exploitation* conditions differed in cases of mild disease, $t(664) = -3.83$, SE = 0.22, $p < 0.001$, $d = -0.07$, but not in cases of severe disease, $t(664) = 0.99$, SE = 0.22, $p = 0.751$, $d = 0.02$. Likewise, the intake in the *between-generations exploitation* and the *between-generations exploitation + empathy* conditions differed in cases of mild disease, $t(650) = 4.95$, SE = 0.22, $p < 0.001$, $d = 0.09$, but not for severe cases, $t(650) = 0.86$, SE = 0.22, $p = 0.824$, $d = 0.02$, indicating that overuse was lower when empathy was elicited. These results thus provide further support for the *between-generations exploitation hypothesis* and the *empathy hypothesis*.

Next, we explored whether the *within-generations exploitation* and *between-generations + empathy* conditions differed in antibiotic intake. A two-way ANOVA with these conditions and severity as predictors indicated that intake in the *within-generations exploitation* condition ($M = 12.08$, SD = 2.64) was higher than in the *between-generations exploitation + empathy* condition ($M = 11.40$, SD = 3.06), $F(1, 330) = 4.78$, $p = 0.029$, $\eta^2 = 0.01$. There was also a main effect of severity, with intake in cases of severe disease ($M = 9.03$, SD = 1.36) being higher than in cases of mild disease ($M = 2.71$, SD = 2.49), $F(1, 330) = 1702.12$, $p < 0.001$, $\eta^2 = 0.83$. The interaction effect was not significant.

We also tested the two last hypotheses in structurally equivalent mixed effects logistic regressions on the individual level (Supplemental Tables S5 and S6). To explore the role of individual differences on general antibiotic intake decisions, we conducted a mixed effects logistic regression with condition, severity, Honesty-Humility (HH), Consideration of Future Consequences (CFC), antibiotic-related behavioral items, and round as independent variables. The dependent variable was the individual decision to take antibiotics (irrespective of the severity of the disease);

participants were treated as a random effect (Bates et al., 2021; see Supplemental Table S7). We first tested for main effects and found that HH, OR = 0.75, 95% CI [0.62, 0.91], $p = 0.003$, and CFC, OR = 0.60, 95% CI [0.49, 0.74], $p < 0.001$, were negatively associated with the decision to take antibiotics in the game. Specifically, people with higher prosocial concern and those who tend to weigh the future consequences of their actions more heavily were less likely to decide in favor of antibiotics. From the items assessing antibiotic-related behaviors, only having used antibiotics in the previous 6 months was associated with more decisions in favor of antibiotics in the game, OR = 1.43, 95% CI [1.10, 1.86], $p = 0.008$.

Next, we explored whether the effects of HH and CFC were moderated by the severity of the disease and condition while controlling for demographic variables. This model indicated that the effect of condition was moderated by HH. In detail, HH was associated with lower antibiotic intake only in the *between-generations exploitation + empathy* condition, OR = 0.58, 95% CI [0.37, 0.92], $p = 0.021$. The results also showed that people with higher levels of considerations of future consequences were more likely to decide in favor of antibiotics in cases of severe disease, and the opposite occurred for cases of mild disease, OR = 2.14, 95% CI [1.68, 2.74], $p < 0.001$. This suggests that holding higher consideration for consequences resulting from one's actions promotes optimal antibiotic intake in the behavioral game of antibiotic intake. Furthermore, males were more likely to decide in favor of antibiotics, OR = 1.83, 95% CI [1.44, 2.33], $p < 0.001$, whereas not having children had the opposite effect, OR = 0.57, 95% CI [0.44, 0.75], $p < 0.001$. There was also a negative effect of round on intake decision, indicating that people decided less frequently in favor of antibiotics in later rounds, OR = 0.96, 95% CI [0.94, 0.98], $p < 0.001$.

Discussion

Antimicrobial resistance is on the rise. The problem is at least partly rooted in individual preferences for antibiotic intake (Thorpe et al., 2021) in situations where an antibiotic treatment is not necessary (e.g. common colds). Previous research investigated how people decide whether to use antibiotics when the negative consequences of antibiotic resistance are immediate (Böhm et al., 2022). Considering that the negative consequences of AMR are usually delayed and pose an even greater threat to future generations than to the current one (e.g. Harring and Krockow, 2021), we extended this line of research by examining the impact of representing antibiotic intake as a between-generations (vs within-generations) social dilemma.

We utilized the power of behavioral games to modify the behavioral incentives in the social dilemma underlying antibiotic intake. Results showed that—despite equal individual-level incentives—participants were more likely to overuse antibiotics when the negative consequences were imposed on the future generation (vs participants' own generation), where the consequences of antibiotic resistance can be perceived as temporally and personally more distant. As such, the findings suggest that the way people perceive the temporal aspects in the consequences of antibiotic resistance can be a potential source for the accelerating problem of antibiotic resistance. This aligns with research comparing the threats of AMR and climate change, which suggests that people can feel less inclined to change their behaviors when they perceive the negative consequences of these problems to happen far in the future (Roope et al., 2019).

Our findings also provide a positive outlook. We aimed to induce empathy toward the future generation by adapting a real-world intervention promoting awareness of antibiotic resistance. The intervention reduced antibiotic overuse in the game context, which aligns with previous studies showing that such narratives can be useful for changing attitudes and behaviors related to health (for a meta-analysis, see Shen et al., 2015). In addition to its practical value, this finding contributes to the increasing evidence that promoting perspective-taking and empathy in interactive health decisions can be a way to facilitate health behavior, not only to benefit oneself but also to benefit others, such as in the case of (prosocial) vaccination (e.g. Vandeweerdt et al., 2022; for a review, see Böhm and Betsch, 2022).

Interestingly, antibiotic intake in the *between-generations exploitation* + *empathy* condition was also significantly different from the intake observed in the *within-generations exploitation* condition. Given that the between-generations setting might be a more accurate representation of the real-world social dilemma of antibiotic intake (Harring and Krockow, 2021; although it may not necessarily be represented as such by individual decision makers), this result suggests that—despite the delayed consequences of antibiotic overuse for future generations rather than the current one—inducing empathy provides a promising tool to avoid excessive overuse.

Individual differences

Regarding the role of individual differences in antibiotic-intake decisions, we found that participants with higher concerns for future consequences were less likely to overuse antibiotics. This supports evidence linking perception of future consequences to health decisions (Murphy and Dockray, 2018). One implication is that communicating the potential future harm of one's behaviors might help to reduce antibiotic overuse, at least among those individuals who care about future consequences. Prosocial concern, measured via Honesty-Humility from the HEXACO personality model (Ashton and Lee, 2009), was also linked to participants' antibiotic intake decisions. Similar findings regarding the role of rather stable individual-level differences in prosocial concern have been shown in the context of prosocial vaccination (Böhm and Betsch, 2022), but have, to the best of our knowledge, not been tested in the context of antibiotic intake yet. However, one of our exploratory analyses suggested that prosocial concern was associated with less use of antibiotics only when empathy is induced. One likely explanation could be that prosocial tendencies in this specific setting unfold behaviorally particularly when empathy toward others is elicited. Future work should investigate further possibilities to behaviorally activate traits such HH in the context of antibiotic intake, harnessing prosocial concerns to promote appropriate use of antibiotics. Relatedly, replicating and extending these findings could enable the development of tailored interventions promoting appropriate antibiotic intake for individuals with different personality characteristics.

Considering our experimental results, it is noteworthy that the effect sizes obtained were small. Further research is needed to draw reliable conclusions on the practical relevance of different representations of the conflict (i.e. within- vs between-generations), and to clarify the effectiveness of using patients' stories and empathy-based interventions in the field. Although there is some evidence documenting the effectiveness of the public campaign which inspired our empathy manipulation (Chaintarli et al., 2016), it is less clear what the specific contributions of the patients' stories are. If the effects prove to be valid in a field setting, even small effects could be important given the relevance of antibiotic resistance for individual and public health.

The present study has some limitations. We assessed intake decisions in a behavioral game scenario, so we cannot assume that the findings would translate to real behavior. Thus, there are several factors limiting the generalizability of our results. For instance, in the game, participants were informed about the consequences of their antibiotic-decisions for themselves and others. However, in the real world, people are often unaware of the mechanisms of antibiotic resistance and the role of their antibiotic-decisions on the problem is less tangible. Moreover, in the real world, people do not experience multiple sequential infections and antibiotic resistance is not defined in terms of number of doses available for a small group of people. AMR is a complex issue, and the consequences of real overuse are clearly more serious.

Furthermore, considering the demographic characteristics of our sample, our findings cannot be generalized to other populations with specific ethnicities, educational and income backgrounds, limited access to internet, and that do not have English as a primary language.

Other limitations concern the empathy manipulation used. Besides telling a story, the manipulation also informed about the consequences of AMR and, therefore, its effect could have been partly driven by increased knowledge and not by empathy alone. By using and adapting intervention materials from the real world, we must accept this limitation and cannot disentangle these effects here. Limitations concerning ethics and unintended effects could also affect the implementation of such interventions. Ethical aspects regarding the use of sensitive health data should be considered when using patients' stories. Moreover, unintended effects of the intervention — such as the possibility of empathy decreasing the use of antibiotics even when they are needed (i.e. misuse), should be carefully considered. In summary, implementation of empathy-based interventions to promote appropriate use of antibiotics should consider and address barriers that could hinder their effectiveness (Waltz et al., 2019).

Conclusion

We provide evidence that antibiotic overuse in behavioral games modeling the social dilemma of antibiotic intake is at least partly driven by the fact that the negative consequences of antibiotic resistance are delayed and largely posed on future generations. As a remedy to this behavioral problem, we find that inducing empathy for future generations can promote appropriate antibiotic intake. Over and above these specific findings, our research shows the potential of using behavioral games to study antibiotic intake, not only as a tool to understand the driving factors of human preferences and behavior, but also as a method to test novel interventions before rolling them out in large-scale and potentially costly randomized controlled trials. We call for future research contributing to a better understanding and to the development and testing of behavioral interventions to promote appropriate use of antibiotics.

Author contributions

All authors contributed to the study's conceptualization, investigation, and methodology. APS was also responsible for data collection, formal analysis, and writing the original draft.

CB and RB also contributed with funding acquisition. All authors revised, edited, and approved the final version of the manuscript.

Data sharing statement

The current article is accompanied by the relevant raw data generated during and/or analysed during the study, including files detailing the analyses and either the complete database or other relevant raw data. These files are available in the Figshare repository and accessible as Supplemental Material via the Sage Journals platform. Ethics approval, participant permissions, and all other relevant approvals were granted for this data sharing. The data files from the current study are also available in the OSF repository at https://osf.io/tmxbn/?view_only=8e011ae6e5984d98916aab45e368e7e.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the German Research Foundation [grant numbers BO 4466/2-2 and BE 3970/8-2]. The funding institution had no influence on the research design nor on the interpretation of its results.

Ethics approval

Ethical approval was given by the Institutional Ethical Review Board from the Department of Psychology, University of Copenhagen (approval number: IP-IRB/19082021).

Pre-registration

The present study was pre-registered (https://aspredicted.org/a54n2.pdf).

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Notes

1. Link to the pre-registration form: https://aspredicted.org/a54n2.pdf.
2. As pre-registered, this study used comprehension checks (e.g. "In total, how many doses of the antibiotics are there for you and the other participant to use together?") as an exclusion criterion (see Supplemental Materials). Participants would be excluded if they failed both attempts in at least two items (out of four). No participants had to be excluded based on these terms.

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