Psychological and Cultural Factors Influencing Antibiotic Prescription

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Abstract

Humans have been giving a selective advantage to antibiotic-resistant bacteria worldwide by inundating the environment with antimicrobials for about one century. As a result, the efficacy of antibiotics has been impaired. Antibiotic resistance is a public health problem, responsible for increases in mortality and extended stays at hospitals. Hospitals and other clinical settings have implemented stewardship measures to reduce antibiotic administration and prescription. However, these measures demand multifactorial approaches, including multidisciplinary teams in clinical settings and the education of professionals and patients. Individual and social psychology-based research should be considered, as social, cultural, and individual factors impact antibiotic prescription, as shown by recent studies indicating that mother-infant attachment and parenting styles play critical roles in antibiotic use.

Highlights:

1. Psychological and cultural factors affect antibiotic usage rate.
2. Antibiotic prescription for children with reactive and demanding behavior (ambivalent attachment pattern) is several times more frequent than for other children.
3. Infants to which antibiotics were prescribed tend to have overprotective, worried, or inconsistent mothers.
4. Among high-income countries, antibiotic prescription rates are higher in those that prize traditional values than in more secular-rational countries.
5. In conclusion, there is a relationship between cultural dimensions, individual psychological characteristics, and antibiotic prescription. These relationships must be further investigated, and the generated knowledge should be incorporated into antibiotic stewardship programs.

Keywords: Antibiotic resistance; Stewardship programs for antibiotic prescription; Mother-infant attachment; Inglehart-Welzel cultural maps; Psychology of antibiotic use; Sociology of antibiotic use.

The pandemics of antibiotic resistance

The use of antibiotics may have positive but also negative consequences (see Box 1). Already 50 years ago, some hospitals implemented "programs to control" antibiotic administration. At the time, the cause of these control programs were the toxic effects (ranging between severe diarrhea and death from anaphylaxis or aplastic anemia) and the high costs of these drugs to the hospital [1]. In those golden days of the antibiotic era, medical doctors and bacteriologists were well aware of antibiotic resistance, considered a problem for individual hospitalized patients, but not a public-health problem. Nowadays, antibiotic resistance is considered a serious world health challenge. A recent study by Murray and coworkers has shown that around 1.27 million people died in 2019 due to bacterial resistance to antibiotics worldwide [2]. As noted in a companion commentary paper, this number of deaths is close to the estimated number of deaths from malaria and AIDS together in the same year [3]. Not surprisingly, children are also victims of drug resistance. For example, about two hundred thousand neonatal sepsis deaths are attributable to resistant pathogens each year [4]. However, efforts should be done to increase the methodologic quality of the estimations of the correlation between mortality and antibiotic resistance [5].

Even when antibiotics target pathogenic bacteria, the antibiotic molecules affect trillions of bacterial cells comprising hundreds of commensal bacterial species forming the normal microbiota of human (or animal) bodies. Bactericidal antibiotics kill sensitive cells, and bacteriostatic antibiotics block bacterial replication. In both cases, sensitive cells leave unused resources, such as nutrients or colonizable space, so nearby antibiotic-resistant cells thrive even if resistance mechanisms are biologically costly. This counter-selection of sensitive cells is the basis of Darwinian natural selection occurring every day in patients, livestock, and the environment [6]. As a result, the human usage of these drugs is leaving an indelible antibiotic resistance footprint [7]. The impact of antibiotic usage on antibiotic resistance is such that there is a positive relationship between antibiotic use and resistance rate across countries [8–10]. However, we can learn from the social attitudes and antibiotic-policy measures taken in the countries with lower resistance rates and act on countries or regions where antibiotic usage is higher. Besides antibiotic resistance, the extensive use and release of industrial antibiotics might speed microbial evolution and could have deleterious consequences for the preservation of a healthy ecology of the planet [11].

Antibiotic stewardship programs: relevance and impact

Antibiotic stewardship programs (see **Glossary**) are institutional actions to improve antibiotic prescribing practices, mainly to reduce their use, thus avoiding the selection of antibiotic-resistant bacterial populations. Their objective is to mitigate the spread of antibiotic resistance by providing a more individualized (precision) therapy. In particular, they promote (i) the prescription of antibiotics only when necessary; (ii) a correct choice of antibiotics based on a precise bacteriological diagnosis (e.g., limiting the use of broad-spectrum antibiotics to specific cases); and (iii) appropriate doses, length, and route of treatment. These programs are complex, implying the involvement of medical doctors, nurses, epidemiologists, and pharmacists. This paper argues that antibiotic stewardship programs should involve other scientists: (i) sociologists, as controlling the "excess" of antibiotic's individual use should be considered together with controlling the "access"; and (ii) most importantly, psychologists and, in particular developmental psychologists [12], as it is discussed in depth in this work.

The concept of antibiotic or antimicrobial stewardship to mitigate drug-resistance levels is relatively recent. In 1997, the Healthcare Epidemiology Society and the Infectious Diseases Society of America presented strategies for preventing antimicrobial resistance in hospitals [13]. According to the Scopus database (18/March /2022), no paper mentioned "antibiotic stewardship" or "antimicrobial stewardship" in the title or abstract in 1998, and just one refers to these words in 1999. However, the number of times these phrases appeared in scientific publications increased more than a thousand ~~times~~ fold since then. For comparison, the Scopus database size only increased 3.3 fold in the same period. Nowadays, there are scientific journals dedicated to stewardship programs, and the role of human educational behavior is increasingly considered in this field, as is the case of JAC-Antimicrobial Resistance from the British Society for Antimicrobial Chemotherapy, launched in 2019 and dedicated to "Education and research in antimicrobial stewardship and resistance".

Antibiotic stewardship programs require a multidisciplinary approach

Several studies have shown that the total consumption of antibiotics across countries varies considerably [14–16]. Even within a single country (UK), between and within practices, there is substantial variability in antibiotic prescription [17]. Epidemiological factors would not be able to explain these disparities. Other factors must play significant roles, including psychological, sociological, or cultural differences, and one can find differences among patients or prescribers. In this work's line, several researchers have proposed to include other areas of knowledge in these teams, including sociology, anthropology, economics, political sciences, and psychology [18–23]. In particular, behavioral sciences can help deal with the antibiotic-resistance crisis with quantitative and qualitative methods.

Qualitative studies focus on answers to "what, how, and why?" questions type, while quantitative studies focus on "how many, how much, and how often?" questions [24]. We need all question types. Two recent papers by Borek et al. [25] and Wanat et al. [24] highlighted the opportunities given by behavioral sciences (health psychology) and their qualitative methods to mitigate antibiotic resistance (hence, joining efforts to knowledge derived from quantitative methods). Some studies use both quantitative and qualitative methods. Moreover, hypothesis-driven strategies may prove highly helpful, and if successful, these hypotheses may end up fruitful beyond their original scope.

An interesting example is provided by the superimposition of antibiotic consumption by countries [14–16] and their cultural values, including religion [26] (Figure 1). The Inglehart-Welzel cultural maps of the world [27] consider two major dimensions of cross-cultural variation. First, "traditional versus secular-rational values". Traditional values emphasize the importance of religion (the Latin verb *religare* means "to bind"), and consequently child-parent submission ties, deference to authority, absolute standards, and traditional family values; secular-rational values have the opposite preferences to these traditional values. Second, "survival versus self-expression values". Survival values emphasize economic and physical (life-death) security; self-expression values prioritize subjective well-being, self-expression, and quality of life, and a shift in child-rearing values from an emphasis on hard work towards freedom, imagination and tolerance.

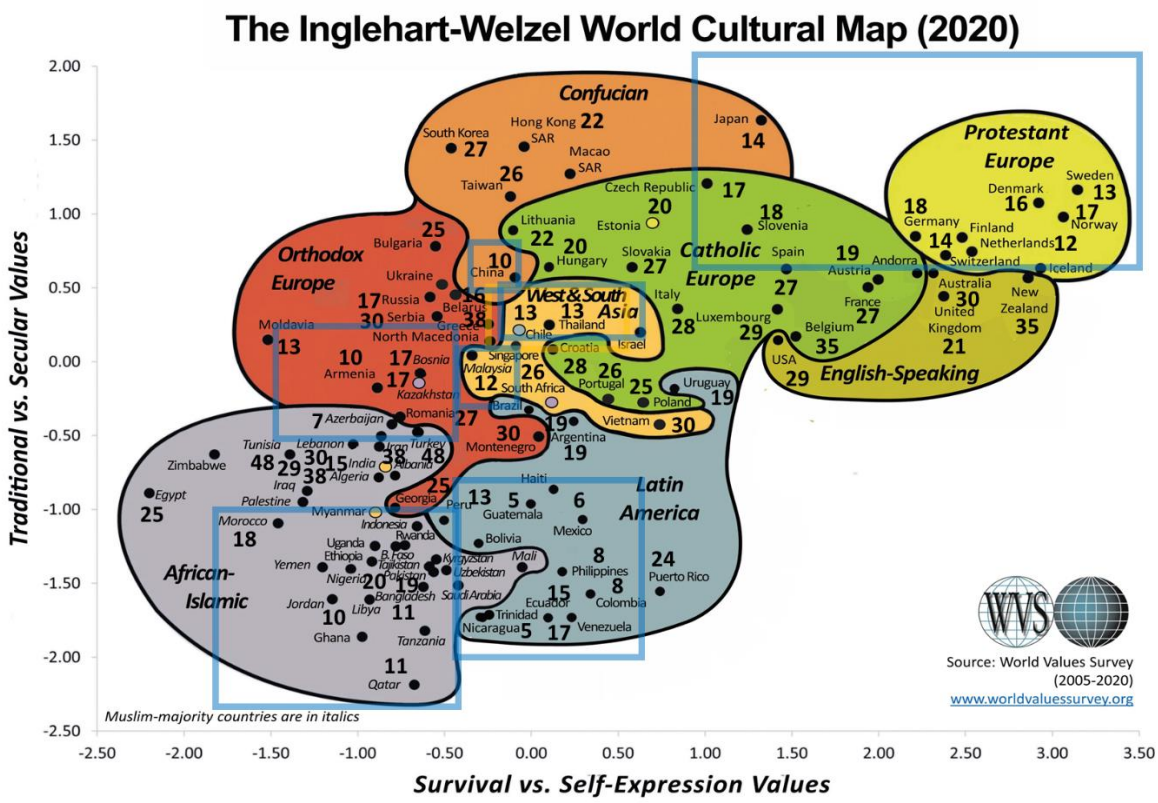

Figure 1. Antibiotic consumption (DDDs/1000 inhabitants/day) per country (numbers in black) during the last 10-15 years versus human values in the different cultural-geographical regions of the world. Figure adapted from [27], where blue boxes indicate the ensembles of countries with consistently lower values of antibiotic consumption. Most numbers were obtained from Klein et al. [15], and, because of the changing rates over the last decade (to less consumption, particularly in Europe), some of them might somewhat differ in some cases from other sources, but the differences between countries (more or less consumption) are essentially maintained

among culturally separated countries. Note that the 2022-version of the Inglehart-Welzel World Cultural Map has already been released. However, here we present the 2020 version because the data about antibiotic consumption in different countries Klein et al (2018) (ref. [15]) are closer to 2020 than 2022.

Certainly, such a comparison of values and antibiotic consumption indicates that, besides the access to antibiotics provided by the national health services, antibiotic policies, including antibiotic stewardship programs, should be specifically designed accordingly to socio-cultural differences among countries, in a sense, with social psychology. Antibiotic consumption is highly dependent on local social norms [28].

With few exceptions, Psychology has been outside the scope of antibiotic stewardship programs. When they do, they often focus on the psychological characteristics of professionals who prescribe or develop antibiotics. For example, fear of failure or risk-averse may impact the likelihood of antibiotic prescription by general practitioners (GPs) [29]. Fear of antibiotic toxicity might, in some cases, inappropriately overcome the fear of death by severe infection, which has negatively influenced the development of potentially useful antimicrobials, something that has not occurred in anticancer therapy [30]. Similarly, fear of antibiotic resistance has, in some cases, improperly replaced fear of infection, either in individual patients or in massive drug administration (MDA), to decrease children's morbidity and mortality in low-income countries (see Box 1).

Michel-Lepage et al. analyzed antibiotic prescriptions by GPs for tonsillitis in France. Both viruses and group A *Streptococcus* are causative agents of tonsillitis in children, and a "Rapid Antigen Diagnostic Test" (RADT) distinguishes the two. GPs unwilling to accept uncertainty and risks (risk-averse GPs) used RADTs more often; moreover, GPs would be more likely to prescribe antibiotics when RADTs were not used [29]. Medical doctors may also be concerned about future complications [31]. Moreover, older general practitioners prescribe antibiotics more often than younger ones [32]. In a review discussing the missing links of antimicrobial stewardship programs, Charani et al. remind us that already in the 1970s, antibiotics were characterized as 'drugs of fear' because frequently, doctors may choose to prescribe broad-spectrum antibiotics and more prolonged than the necessary duration of treatment [33].

Studies with control groups to learn if there are psychological differences between patients who leave health appointments with an antibiotic prescription and those who do not are scarce. For example, a study found that participants with a Catholic background (Catholic Flemish) trusted and used more antibiotics than those with a Protestant background (Protestant Flemish) and that the former feared more complications than Protestants if no medications were used. This difference resulted in higher use of antibiotics by the Catholics than by Protestant participants [34]. Such religious values correlate with the frequency of antibiotic resistance, and consumption differences were interpreted as "my health and my children's health should be assured by others, and I should loudly claim for help" (Catholics) or "I am personally responsible for decisions concerning my health and the health of my family, and my emotions should be repressed, as I am the responsible for the action" (Protestants) [26]. Therefore, individual cultural differences impact the likelihood of antibiotic use [34]. Moreover, the probability of a patient receiving antibiotic treatment increases with the number of antibiotic prescriptions the patient received in the previous year or years [17,35]. Some studies indicate that medical doctors tend to overrate patients' expectations of antibiotic prescription [36,37]. In this last factor, we have psychological factors of both the patient and the medical doctor. Furthermore, the odds of patients receiving inappropriate antibiotic prescriptions (e.g., for acute respiratory tract infection caused by viruses) is higher when the patient is of working age (e.g., [38–40]. Therefore, time pressure, perhaps linked to uncertainty, also increases the probability of antibiotic usage.

The impact of patients' psychology in drug prescription: the special case of pediatric populations

Pediatric appointments can be even more complex because at least a third person is involved, the patient's caregiver. An infant, the respective caregiver, and the doctor interact to solve the infant's complaints. It is reasonable to assume that the psychological characteristics of all of them may have a role in the likelihood of antibiotic prescription. Infants are under stress because they are ill and in a strange place (the medical office) and close to a stranger (the doctor). The respective caregiver (usually the mother or the father) may also be under stress, worried about the child, and perhaps feeling the obligation to go to work [38–40].

Recent studies involving infants and their mothers demonstrated how promising Developmental Psychology could be for understanding the overprescription of antibiotics and for antibiotic stewardship programs. For example, Fuertes et al. [41] have shown that antibiotic prescriptions in the first nine months of life tend to be more likely in a particular group of infants than the other infants. The odds are impressive: for these children (ambivalent insecurely-attached infants to their mothers – see below and Boxes 2 and 3), the odds of antibiotic consumption were 25 times higher (95% confidence interval, 7.01 - 89.40) than in other children. These infants tend to over-externalize their emotions in the presence of threat or under stress (e.g., when ill, scared, or frustrated). In this inconsistent behavior, they alternate between a seeking proximity posture and rejecting their caregiver's affection (Box 2). Also, mothers' behavior may help us anticipate whether their infants are likely to take (or have taken) antibiotics in the first nine months of life [41].

But how can parenting and human attachment (Boxes 2 and 3, and Figure 2) be associated with antibiotic uptake?

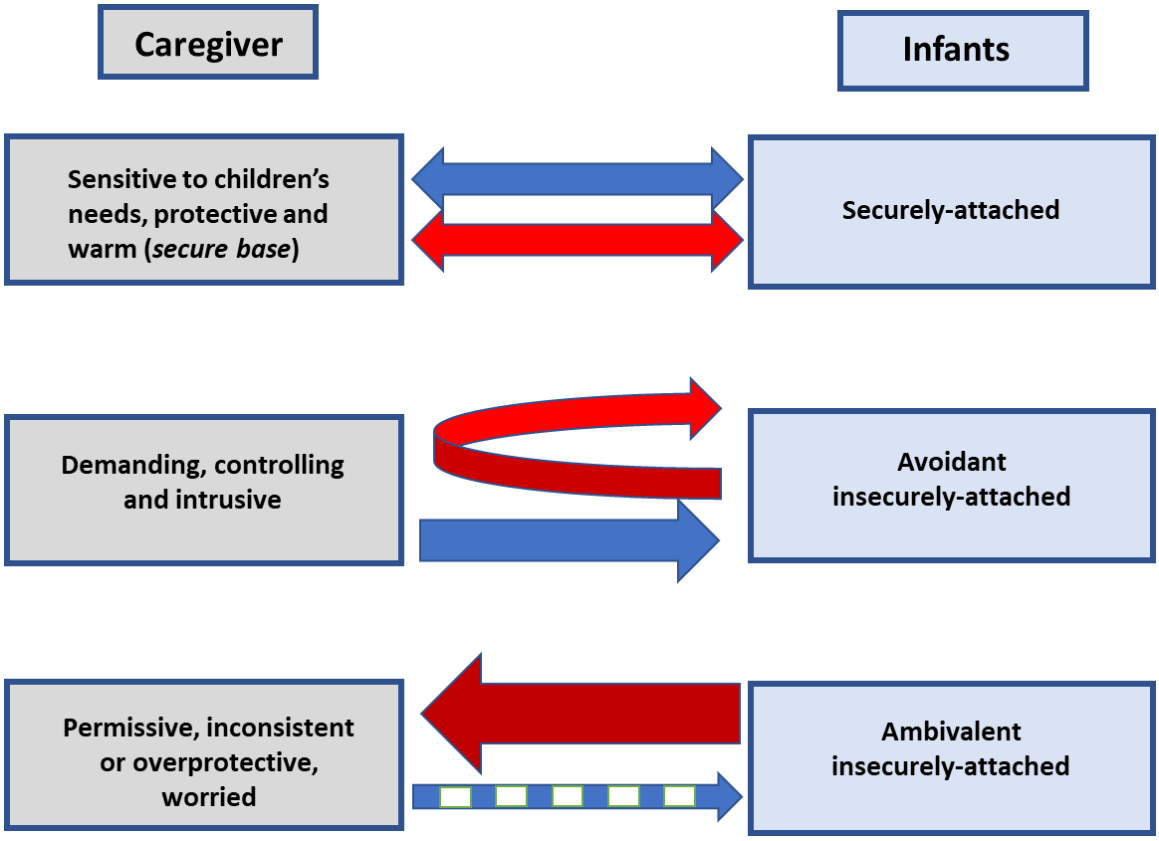

Figure 2. Caregiving and Mother-infant patterns of attachment. The grey boxes on the left correspond to different caregiving styles, and the blue boxes on the right illustrate the infant attachment patterns according to Bowlby [42] and Ainsworth [43]. Blue arrows represent the strength and direction of caregiving. In the case of secure attachment, the arrow is bidirectional because relationships are reciprocal and mutually engaged. The intermittent arrow of ambivalent attachment represents the caregiver's inconsistent response. Red arrows represent the infant attachment behavior, a behavioral strategy to cope with adults' caregiving. Infants with an ambivalent attachment communicate their needs intensively when facing the inconsistent response from their caregivers – this is represented with a robust red arrow. Avoidants turn to themselves to find means to solve their needs.

Given the tendency of insecurely-ambivalent infants to inflate emotions near their caregivers and health professionals (see Box 3), Fuertes et al. [41] hypothesized that that behavior pattern could lead to antibiotic use in the first nine months. Indeed, 89.7% (26 out of 29) of ambivalent

insecurely-attached infants, contrasting with 25.7% (27 out of 105) of the other infants, i.e., of insecurely-attached avoidant and securely-attached infants (Figure 3A) [41].

Another study, this time with infants with low gestational weight (lower than 1599 g) ranging between 23 to 34 gestational weeks, also shows that antibiotic prescription in the first nine months of corrected age (because some infants of this study were preterms) is three times more likely among ambivalent-attached infants (95% confidence interval, 1.02 - 8.99) than among the other infants [44]. This proportion is impressive given that we know that children with low birth weight have more comorbidities and are more likely to take antibiotics than others (60.0% against 39.6%) [41,44]. In fact, many very low-birth children are prone to infections, which could weaken the impact of attachment patterns on antibiotic prescription.

The attachment relationship between infants and their caregivers starts as soon as birth. Therefore, an insecure-ambivalent mother-infant attachment originates early and results from daily interactions with caregivers. For example, mothers of insecure-ambivalent infants are more unresponsive in free play than other mothers, and mothers of securely attached infants are more sensitive to their infants during free play [45–47]. Developmental psychologists define maternal sensitivity as the mother's ability to read and interpret an infant's solicitations and stressful signals and her ability to comfort the infant [43,48–50]. Of course, many factors play a critical role in maternal sensitivity, namely family socioeconomic status (SES), maternal education, parents' mental health, number of family risk factors, or parental stress. A binary logistic regression analysis has shown that maternal sensitivity predicts antibiotic uptake in the first nine months of the infant's life [41] (Figure 3B).

(A) (B)

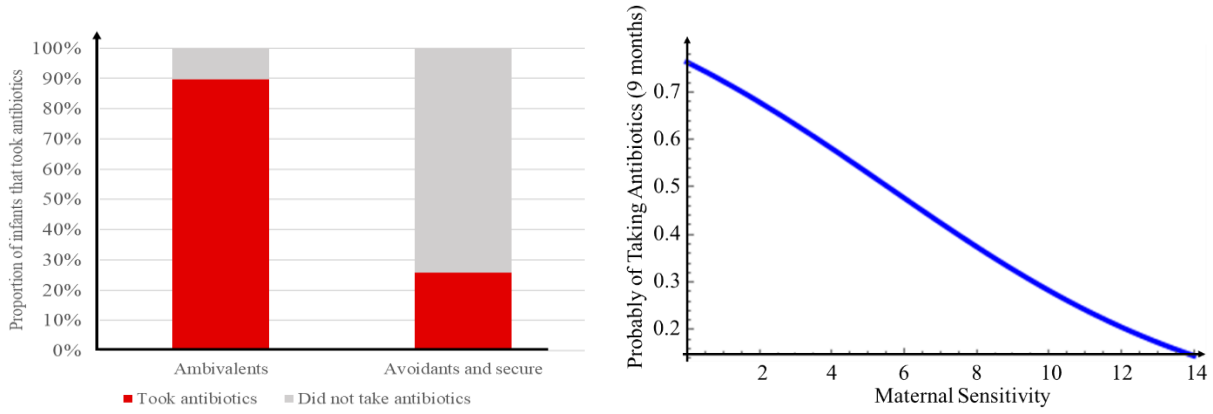

Figure 3. The likelihood of taking antibiotics depends on the mother-infant relationship. (A) In the first nine months of life, the odds of consuming antibiotics among insecurely-ambivalent attached infants were 25 times higher (95% confidence interval, 7.01–89.40) than among infants with the other two attachment patterns combined (secure and insecure-avoidant). See the text for definitions. Data from Fuertes et al. [41]. (B) Relationship between maternal sensitivity and antibiotic consumption in the first nine months of the infant. Fuertes et al. (2020) performed a binary logistic regression analysis showing that maternal sensitivity (scored between 0 and 14) predicts antibiotic uptake in the nine months of the baby's life with β = - 0.21 and the constant C = 1.167. The line represents $\frac{1}{1+e^{-(C+\beta.m)}}$, which is the probability that the infant takes antibiotics in the first nine months of life, and m is maternal sensitivity [41].

In another study, Stern et al. (2020) found that the odds of antibiotic use in the first 12 months of the infant's life also decrease with maternal sensitivity, defined as the extent to which the mother promptly and appropriately responds to the infant's signals and needs [51]. The size effect of this relation was low, and there are at least two explanations for that. The proportion of the three attachment patterns among infants in this study is unknown. However, maternal sensitivity is higher for both insecurely-attached infants (avoidants and ambivalents) patterns [49], whereas the odds for antibiotic use are higher only for ambivalent infants [41]. Therefore, if the proportion in the sample of insecure-avoidant infants is high or the proportion of insecure-ambivalent infants is low, the impact of maternal sensitivity on antibiotic use should become less clear. An alternative

explanation is related to the fact that Stern et al. (2020) performed their study in the Netherlands and Fuertes et al. (2020) in Portugal [41,51]. The antibiotic prescription rate in the Netherlands has been one of the lowest in the European region, with 12 defined daily doses (DDDs) per 1000 inhabitants per day [15]. In contrast, Portugal consumed more than the double, 26 DDDs per 1000 inhabitants per day [15] (Figure 1). With a lower number of prescriptions in the Netherlands, the impact of maternal sensitivity on antibiotic prescription may fade away.

The formerly presented (Figure 1) Inglehart-Wenzel World Cultural Map reflects such differences. Indeed, four studies in the Netherlands found that only 3.7% to 10.8% of infants were ambivalent-attached, against 19.5% (25/108), 19.5% (16/82), or 21.6% (29/134) in three recent Portuguese studies performed with independent samples [41,52–54]. These results suggest that ambivalent attachment behavior should be more frequent in countries with more antibiotic consumption, mainly when antimicrobials are easily available by public health services. Although many factors affect attachment organization (since the reasons for children's stress are multiple, not only being sick), it would be interesting to study the association between antibiotic consumption and the prevalence of attachment patterns across cultures. For example, studies performed in Sweden and Germany ("European Protestant" countries that stand together in Figure 1) with low antibiotic consumption (Figure 1) also indicated low proportions of ambivalent-attached infants, 3.9% (2 ambivalent-attached out of 51 infants) and 9.8% (7/71), respectively [55,56]. In contrast, ambivalent attachment in Israel is overrated in both Arabic (13%) and Jewish (26%) samples [54,57]. Yet, the effect of religion is not clear-cut; family socioeconomic status and parents' educations have large contributions to the attachment patterns prevalence [57]. Moreover, unfortunately, most studies indicating the proportion of attachment patterns across countries were published many years ago, show a high heterogeneity between samples within countries, and/or were performed with small samples that may not mirror the whole country [54,57,58]. Studies comprising large and representative samples in each country could unveil the relationship between cultural factors, religion and traditional factors, parenting, and health practices. However, the "ambivalent-attached" behavior of children might reflect the "ambivalent" cultural attitudes of the societies, particularly those where the secular-rational values of "modernity" and self-expression coexist with the traditional, secular values that assure survival under extreme circumstances. These ambivalent societies occupy the central part of the Inglehart-Wenzel World Cultural Map (figure

1), and are associated with a consistent over-use of antibiotics. Children are crying for an antibiotic, but society is responsive to this demand.

Concluding remarks

Antibiotics are the most frequent medications prescribed in the pediatric population [59–63], which is unfortunate because antibiotic usage contributes to drug resistance and may have individual adverse effects (Box 1). On the other hand, pediatric antimicrobial stewardship programs have successfully decreased antibiotic use, healthcare costs, and antibacterial resistance in both inpatient and outpatient settings.

Many studies have shown that several factors impact the likelihood of antibiotic prescription, rather than only health factors or medical indicators. For example, the quality of attachment to the caregivers in the first year of life correlates with antibiotics prescription. The mechanisms involved in these associations are still unclear, but perhaps there is a complex interaction between children's strategies to obtain care and relief when ill and the parents' ability (or difficulty) to meet their needs and support children in self-regulating during sickness. Such behaviors may trigger infants' and parents' distress and children's overreactions, leading to miscommunication of symptoms to health professionals. These processes are far from being understood, creating the need for new longitudinal research lines that include new dimensions, namely infants' and caregivers' psychology.

Antibiotic stewardship programs already involve multidisciplinary teams, mainly composed of medical doctors, nurses, and pharmacists, but the battle against the pandemics of antibiotic resistance could improve significantly by including other areas of knowledge, as several previous studies have already demonstrated [21,64–67]. The works discussed here indicate that, beyond physical factors, individual psychological differences between patients or between patients' caregivers impact antibiotic prescription. We suggest that these "attachment psychological dynamics" reflect the societies' cultural attitudes, and those countries where rational-modernity behaviors coexist with traditional values are expected to have an ambivalent behavior leading to higher antibiotic consumption (see Outstanding Questions box).

Box 1: Individual benefits and disadvantages of antibiotic use

Benefits

Antibiotics have transformed modern medical and veterinary sciences since the second half of the 20th century. Firstly, antibiotics have been precious in treating bacterial infections. For example, in early times, with penicillin only, the mortality rate associated with pneumococcal pneumonia decreased by about four to eightfold **[68,69]**. In our days, the mass distribution of a broad-spectrum antibiotic agent to preschool children has reduced mortality in areas of sub-Saharan Africa **[70]**. Secondly, antibiotics have not only decreased the infective morbidity, but helped perform medical procedures like complicated surgeries, organ transplantation, intensive care, and anticancer chemotherapy **[71]**. Finally, a formerly unexpected benefit (in this case for human nutrition) beyond these two health-related: antimicrobials are suitable growth promoters in livestock **[72]**. The individual feeling about benefits is based on the prestige of antibiotics as the *only* curing agents, preventing severe illnesses, blocking transmissible diseases and mitigating the symptoms of the infection without major risks of toxicity.

Disadvantages

The negative consequences of overuse of antibiotics on human health of human communities have been extensively published, being mostly focused on toxicity and the selection of antibiotic-resistant bacteria, but environmental damage of the microbiosphere cannot be discarded. The risks-versus-benefits for the individual have been scarcely treated and should include the cumulative effect of antibiotic exposure throughout life, increasing the risk of carrying multiresistant opportunistic bacteria, eventually lethal in elderly pathological events **[73]**. The consequences of multi-exposure to antibiotics could resemble chronic hypercholesterolemia, high blood pressure, or diabetes. Antibiotic abuse in children is particularly frequent, critically involving social norms and mother-child behavioral cultures, but might have negative consequences. A study involving a large children cohort from the USA has revealed a positive association between antibiotic prescription in the first six months of infants' life and the development of asthma and allergy when they are six years old **[74]**. Another study involving several thousands of dyads of infants with their mothers found a positive association between antibiotic prescription in the first six months of life and an increased probability of being overweight at seven years old among children whose mothers had an average healthy weight, indicating the role of early damage of individual microbiota **[75] [76] [77]**. Bile acid metabolism influenced by altered microbiota composition is likely associated with this body mass increase **[77,78]**, recalling the effect of antibiotics on increasing weight in farm animals **[79]**. Moreover, antibiotic uptake increases pathogens' susceptibility and is related to several health conditions such as inflammatory bowel disease, rheumatoid

arthritis, type 1 diabetes, and atopy **[80–82]**. At the individual level, negative beliefs about antibiotics include fear of toxicity, frailty, and general weakness.

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Box 2 – Patterns of infant attachment to caregivers

Human beings are prone to become attached to caregivers (primarily mothers/fathers) during their first year of life [42]. Across human cultures, the quality of attachment affects all areas of individual development, from socialization and close relationships to language or cognitive development. A body of research has shown that infants' quality of early care becomes internalized, forming maps of representation of their own self, others' behavior, and relationships, and shaping infants' social functioning from early ages to adulthood [42,83]. Children can function in the world with confidence if they can develop trust in the accessibility and reliability of their attachment figures. This confidence results from secure relationships between the infant and their main caregivers [42].

However, infants must use different behavioral strategies to maintain a close proximity with caregivers. Children learn to adapt their behavior according to their caregivers' responses during infancy. Accordingly, Bowlby found that some infants are securely attached to their caregivers, while others are insecurely attached [42]. Securely attached infants tend to exhibit their emotions and intentions openly by spontaneous communication of their needs or seeking closer contact with caregivers. By using their caregiver as a secure base for exploration, securely attached infants are easily comforted. In contrast, insecurely-attached stressed infants do not rely on a secure base. Securely-attached children and adolescents have better academic outcomes, more friends at school, and positive relationships with their loved ones [84].

In the late sixties and seventies, Mary Ainsworth developed an experimental protocol denominated Strange Situation to study attachment behavior [43]. The Strange Situation paradigm consists of an experimental protocol that takes 21 minutes and is composed of eight episodes where the central idea is to observe the reaction under mild but increasing levels of stress on the infant. In this protocol, the infant is introduced to a strange playroom, interacts with

an unfamiliar adult (the stranger), and is submitted to brief separations from and reunions with the parent [43,83].

Using this experimental paradigm, Ainsworth found two main patterns among insecurely attached infants, and they are somewhat opposite to each other [43]. Insecurely-attached avoidant (or simply avoidant) infants likely avoid proximity with their attachment figures by over-activating the exploratory system (e.g., playing with toys). In contrast, ambivalent insecurely-attached infants (or simply ambivalent infants) tend to show contradictory behaviors, trying to attract the attention of their caregivers, but simultaneously showing their angriness for presumed lack of response, including some resistance to physical contact [46,47]. For a review, see Cassidy and Shaver [83].

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Box 3: Ambivalent insecurely-attached infants: crying for antibiotics!

The experience of illness and pain trigger attachment behavior because, in these circumstances, individuals are under stress and threat and claim help from caregivers [42]. Caregivers frequently respond by providing means to lessen infants' pain. However, some caregivers respond to infants' needs with the conviction of children's potential for endurance and self-healing, and inconsistency, anxiety, or simply no interaction [49,83]. In response to this caregiver's behavior, these infants tend to amplify emotional displays, a typical behavior pattern of ambivalent insecurely-attached infants, expressing anxiety responses with heavy crying, inability to self-soothe, or strong motor reactions [85]. They oscillate with behaviors of proximity seeking, contact, and desire for comfort, aiming at getting responses and attention from caregivers [43].

Patients' insecurity and anxiety impact patient-doctor interaction. A study involving infants aging between 6 and 32-months found no differences between the prevalence of otitis in securely and insecurely attached infants [86]. However, mothers of insecurely-attached infants become more anxious and have more negative perceptions of their infants' health conditions [86]. Furthermore, insecure-ambivalent teenagers and adults have higher symptom-reporting and

request more health visits [87–89]. However, this can be mitigated by alternative supporting attitudes of caregivers and doctors.

One possible explanation is that medical consultations are often stressful situations. In the case of pediatric appointments, infants are ill, their parents are often stressed, and someone unknown to the infant (health professional(s)) provides intrusive care. Unfortunately, this stress might impact pediatric consultations and infant evaluation, mainly in the case of insecurely-attached infants. To prevent this effect, pediatric teams often adopt personal and friendly postures when in contact with children [90].

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Glossary

Antibiotic Stewardship Programs: these institutional actions aim to improve antibiotic prescribing practices, mainly to diminish their use.

Inglehart-Welzel cultural maps of the world: according to the political scientists Ronald Inglehart and Christian Welzel, there are two major dimensions (created by running factor analysis over a set of ten indicators) of cross-cultural variation in the world. The two dimensions are traditional values versus secular-rational values and survival values versus self-expression values.

Traditional values: these values emphasize the importance of religion and, consequently, child-parent submission ties, deference to authority, absolute standards, and traditional family values. The opposite of secular-rational values.

Secular-rational values: have the opposite preferences to these traditional values.

Survival values: these values emphasize economic and physical (life-death) security. The opposite of self-expression values.

Self-expression values: these values prioritize subjective well-being, self-expression, and quality of life, and a shift in child-rearing values from an emphasis on hard work towards freedom, imagination, and tolerance. The opposite of survival values.

Infant Attachment behavior: infant behavioral strategy to maintain the proximity with caregivers and to obtain care and comfort from them.

Ambivalent attachment pattern: one of the two patterns of insecure attachment. These infants communicate their needs intensively when facing inconsistent responses from their caregivers and tend to exacerbate emotions.

Avoidant pattern: one of the two patterns of insecurely attached infants. These infants turn to themselves to find means to solve their needs.

Secure pattern: securely attached infants are reciprocal and mutually with caregivers (mostly mothers and fathers). These infants display their emotions and intentions openly by spontaneous communication of their needs or seeking closer contact with caregivers.

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