Psychological and Cultural Factors Influencing Antibiotic Prescription

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Abstract

Humans have inundated the environment worldwide with antimicrobials for about one century, giving selective advantage to antibiotic-resistant bacteria. Therefore, antibiotic resistance has become a public health problem responsible for increased mortality, and extended hospital stays because the efficacy of antibiotics has diminished. 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. Recent studies indicate that individual factors, such as mother-infant attachment and parenting styles, play a critical role in antibiotic use. Also, macro-contextual factors, such as economic, social, or cultural backgrounds, may impact antibiotic use rates. Therefore, research aiming to ameliorate stewardship measures must include psychological- and sociological-based research.

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

Antibiotics: benefits and disadvantages

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 [1,2]. In our days, the mass distribution of a broad-spectrum antibiotic agent to preschool children has reduced mortality in areas of sub-Saharan Africa [3]. Secondly, antibiotics have decreased infective morbidity and helped perform medical procedures like complicated surgeries, organ transplantation, intensive care, and anticancer chemotherapy [4]. Finally, a formerly unexpected benefit (in this case, an economic one): antimicrobials were suitable growth promoters in livestock [5]. The personal feeling about benefits is based on the prestige of antibiotics as the *only curing drugs*, preventing severe illnesses, blocking transmissible diseases, and mitigating the symptoms of the infection without significant toxicity risks.

On the other hand, antibiotics select resistant bacteria and may cause environmental damage to the microbiosphere. The risks-versus-benefits for the individual have been scarcely treated. They should include the cumulative effect of antibiotic exposure throughout life, increasing the risk of carrying multiresistant opportunistic bacteria, eventually lethal in elderly pathological events [6]. The consequences of multi-exposure to antibiotics could resemble chronic hypercholesterolemia, high blood pressure, or diabetes. Antibiotic abuse in children is frequent, critically involving social norms and mother-child behavioral cultures, but it might have negative consequences. A study involving a large children cohort from the U.S.A. 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 [7]. 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 [8–10]. Bile acid metabolism influenced by altered microbiota composition is likely associated with this body mass increase [10,11], recalling the effect of antibiotics on increasing weight in farm animals [12]. 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 [13–16].

The pandemics of antibiotic resistance

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 [17]. 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 regarded as a severe 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 [18]. 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 [19]. Not surprisingly, children are also victims of drug resistance. For example, about two hundred thousand neonatal sepsis deaths are attributable to resistant pathogens yearly [20]. However, efforts should be made to increase the methodologic quality of the estimations of the correlation between mortality and antibiotic resistance [21].

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 daily in patients, livestock, and the environment [22]. As a result, the human usage of these drugs is leaving an indelible antibiotic resistance footprint [23]. The total consumption of antibiotics across countries varies considerably [24,25] and the impact of antibiotic usage on antibiotic resistance is such that there is a positive relationship between antibiotic use and resistance rate across countries [26–28]. 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 up microbial evolution and have deleterious consequences for preserving a healthy ecology of the planet [29].

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. They aim to mitigate the spread of antibiotic resistance by providing a more individualized (precise) therapy.

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 [30]. 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 has increased more than a thousand-fold since then. For comparison, the Scopus database size only increased 3.3-fold in the same period.

The specific aims of antibiotic stewardship programs are to 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, particularly developmental psychologists [31], as we discuss in depth in this work.

The impact of culture on antibiotic use

Several researchers have proposed to include other areas of knowledge in these teams, including sociology, anthropology, economics, political sciences, and psychology [32–38]. In particular, behavioral sciences can help dealing with the antibiotic-resistance crisis with quantitative and qualitative methods [39].

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 [40]. We need all question types. Two recent papers by Borek et al. [41] and Wanat et al. [40] 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.

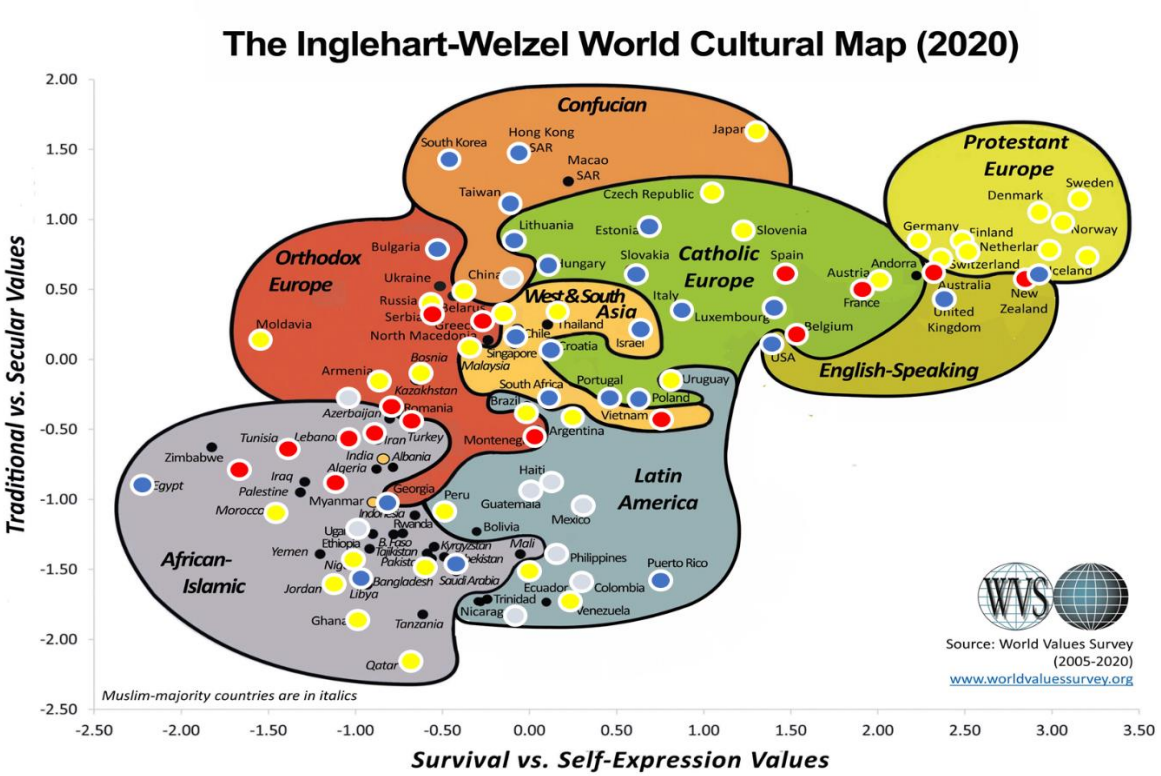

Figure 1. Antibiotic consumption per country versus human values in the different cultural-geographical regions of the world. Figure adapted from [44–46]. Dots refer to antibiotic consumption (D.D.D.s/1000 inhabitants/day) in 2015. Red dots refer to countries with ≥30 D.D.D.s; blue dots, with 20-30 D.D.D.s; light yellow dots, with 10-20 D.D.D.s, and light blue-white dots to countries with ≤10 D.D.D.s/1000 inhabitants/day. D.D.D. numbers were obtained from refs. [24,25,87,105]. 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 are closer to 2020 than 2022.

An interesting example is provided by the superimposition of antibiotic consumption by countries [24,25,42] and their cultural values, including religion [43] (Figure 1). The **Inglehart-Welzel cultural maps of the world** [44–46] 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.

Two subgroups of consumption values can be differentiated, corresponding to the highest secular and self-expression values in the historical European Protestant-German Empire (low consumption) and the historical European Catholic-Roman Empire, with lower self-expression values (high consumption). These differences have already been noticed in previous works, particularly focusing on Catholic-Flemish and Protestant-Flemish [43,47]. Countries that originated in the British Empire also have high antibiotic consumption. The highest consumption rates correspond to East-South European, Middle-East, and Northern-African countries, where traditional-survival values predominate. Low and very-low consumption countries predominate in areas of low income per capita, including several Latin-American and Central African countries, probably because people have lower accessibility to antibiotics, which precludes to consider cultural influences in antibiotic consumption. However, all of them correspond to countries with high survival-traditional values.

Likewise, antibiotic prescription varies between practices inside a single country, e.g., the U.K. [48], or within even smaller regions [49–51]. There are some interesting patterns. For example, recent studies performed in Northern Ireland [51] or England [49,50] have shown that antibiotic prescription rates tend to be higher in rural practices. A possible explanation is that, in smaller communities, the networks are more tied based on interpersonal relationships [52]. Although the evidence is scarce to support this view, another study found that friends, colleagues, and neighbors' opinions affect dental patients' requests for antibiotics to avoid dental procedures [53].

Certainly, there is a complex mosaic of socio-cultural features in every region of the world influencing antibiotic consumption, including the availability of antibiotics, the robustness of local healthcare systems, and local politics on the use of antibiotics. However, advances in community psychology have revealed the close relationships between individual health, family relationships, and community functioning under different levels of social stress [54]. These trade-offs facilitate integrations between "first-order" (focused on the individual, as in the case of antibiotic stewardship) and "second-order interventions" (beyond the individual), leading to behavioral changes able to modify local social norms concerning the demand and use of antibiotics, as in the influence of mother's beliefs in antibiotic prescription [55,56]. Interventions based on community psychology should undoubtedly be adapted to the local socio-cultural differences, so that in any particular place, there should be an "appropriate demand for antibiotics" considering the local circumstances [43].

Antibiotic stewardship programs require a multidisciplinary approach

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 being risk-averse may impact the likelihood of antibiotic prescription by general practitioners (GPs) [57]. 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 valuable antimicrobials, something that has not occurred in anticancer therapy [58]. Similarly, fear of antibiotic resistance has, in some cases, improperly replaced fear of infection, either in individual patients or in massive drug administration (M.D.A.), to decrease children's morbidity and mortality in low-income countries.

Michel-Lepage et al. analyzed antibiotic prescriptions by G.P.s for tonsillitis in France. Both viruses and group A *Streptococcus* are causative agents of tonsillitis in children, and a "Rapid Antigen Diagnostic Test" (R.A.D.T.) distinguishes the two. G.P.s unwilling to accept uncertainty and risks (risk-averse G.P.s) used R.A.D.T.s more often; moreover, G.P.s would be more likely to prescribe antibiotics when R.A.D.T.s were not used [57]. Medical doctors may also be concerned about future complications [59]. Furthermore, older general practitioners prescribe antibiotics more often than younger ones [60]. Broad-spectrum antibiotics increase the risk of adverse consequences, including *Clostridium difficile* infections. However, although antibiotic

consumption is lower in less deprived areas in Northern Ireland, the proportion of broad-spectrum antibiotics is higher in those areas [50]. 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 [61].

As stated above, cultural background, as in the case of Catholic- and Protestant-Flemish, probably influences personal views about antibiotics; the former trusted and used more antibiotics and feared more complications if no medications were used than the Protestants. [47]. Such cultural values correlate with the frequency of antibiotic resistance. The respective Psychological attitudes can be 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) [43].

These attitudes have broader consequences as the probability of a patient receiving antibiotic treatment increases with the number of antibiotic prescriptions the patient received in the previous year or years [48,62]. Some studies indicate that medical doctors tend to overrate patients' expectations of antibiotic prescription [63,64]. 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., [65,66]. 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 [65,66].

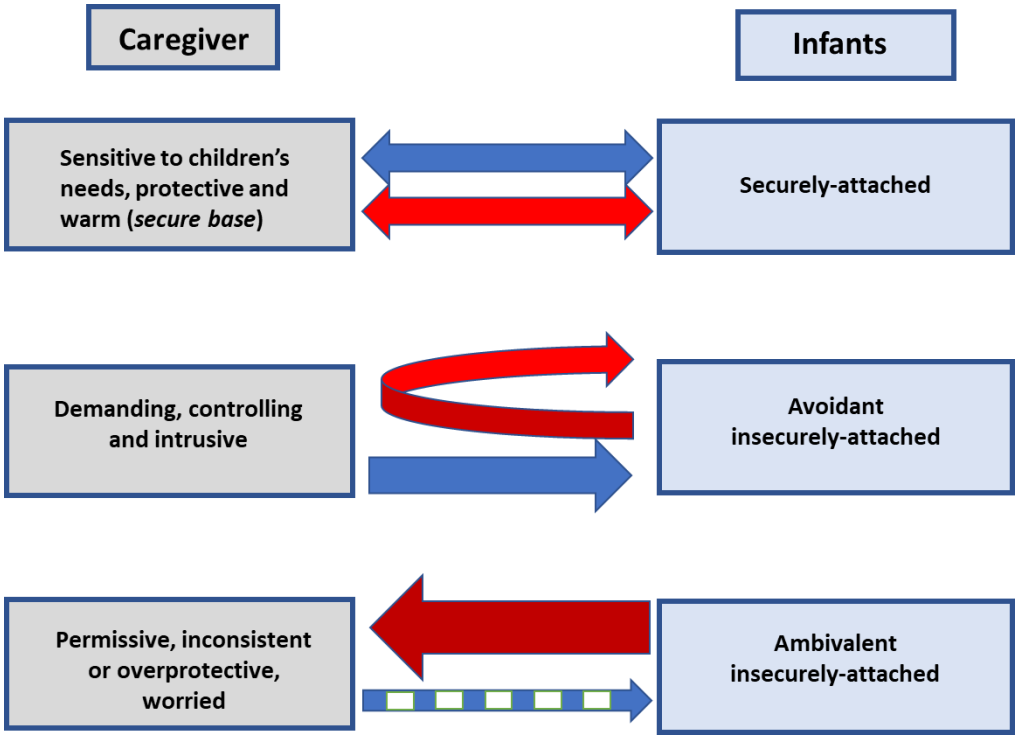

Figure 2. Caregiving and Mother-infant patterns of attachment. The grey boxes on the left correspond to different caregiving styles, and the blue boxes on the right illustrate the infant attachment patterns according to Bowlby [68] and Ainsworth [72]. Blue arrows represent the strength and direction 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.

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. [67] have shown that antibiotic prescriptions in the first nine months of life are 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 Box), 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 threats 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). 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 [67].

But how can parenting and **human attachment** (see Box and Figure 2) be associated with antibiotic uptake?

The experience of illness and pain triggers attachment behavior because, in these circumstances, individuals are under stress and threat and claim help from caregivers [68]. 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 [69,70]. 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 [71]. They oscillate with behaviors of proximity seeking, contact, and desire for comfort, aiming at getting responses and attention from caregivers [72].

Given the tendency of insecurely-ambivalent infants to inflate emotions near their caregivers and health professionals, Fuertes et al. [67] 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 **securely-attached** and **avoidant insecurely-attached infants** (Figure 3A) [67].

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 preterm) is three times more likely among ambivalent-attached infants (95% confidence interval, 1.02 - 8.99) than among the other infants [73]. 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%) [67,73]. 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 [74–76]. 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 [69,72,77,78]. Of course, many factors play a critical role in maternal sensitivity, namely family socioeconomic status (S.E.S.), 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 [67] (Figure 3B).

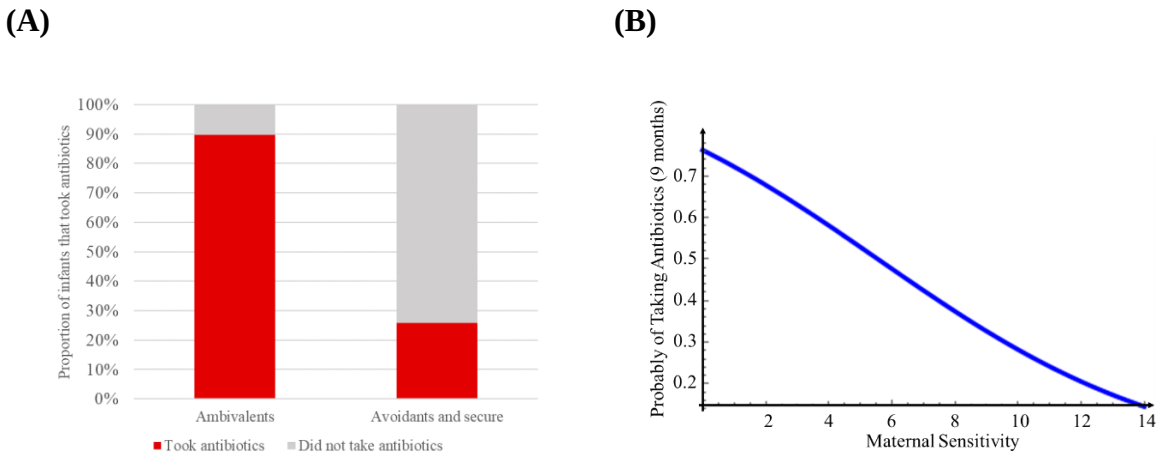

Figure 3. The likelihood of taking antibiotics depends on the mother-infant relationship. (a) In the first nine months of life, the odds of consuming antibiotics among insecurely-ambivalent attached infants were 25 times higher (95% confidence interval, 7.01–89.40) than among infants with the other two attachment patterns combined (secure and insecure-avoidant). See the text for definitions. Data from Fuertes et al. [67]. (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 [67].

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 [79]. 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 [69], whereas the odds for antibiotic use are higher only for ambivalent infants [67]. 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 [67,79]. The antibiotic prescription rate in the Netherlands has been one of the lowest in the European region, with 12 defined daily doses (D.D.D.s) per 1000 inhabitants per day [24]. In contrast, Portugal consumed more than the double, 26 D.D.D.s per 1000 inhabitants per day [24] (Figure 1). With a lower number of prescriptions in the Netherlands, the impact of maternal sensitivity on antibiotic prescription may fade away.

In a qualitative nursing study performed in a large U.K. city in the south of England [80], mothers reported that they had overrated their trust in antibiotics, and their anxiety reduced when their children used antibiotics. Although some were aware of antibiotics misuse or disadvantages, they would not hesitate to administrate an antibiotic if they felt over concerned with their children's health. Thus, informing and supporting families during children's health crises is necessary. A relevant asset in Portugal is the National Early Interventional Service (S.N.I.P.I. – Sistema Nacional de Intervenção Precoce), which aims to support children under six and their families. Multidisciplinary teams (composed of health, educational and social professionals) visit families at their homes and children at schools to implement collaborative practices to support children's development, education, health, and well-being [81]. These practices are life-context and family-centered based, organized to promote positive parenting and strengthen children's life contexts. Future stewardship programs can be implemented with the collaboration of these teams, targeting three major areas: (i) promoting information availability and sharing among health, educational and social services regarding children's health and medications; (ii) reinforcing family support when children are ill or in health emerging situations; and (iii) promote the awareness and training of early Interventional professionals on the antimicrobial use.

Fighting the causes

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 [67,82–84]. 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 (both with low antibiotic consumption, 13 and 18 D.D.D.s/1000 inhabitants/day, respectively) also indicated low proportions of ambivalent-attached infants, 3.9% (two ambivalent-attached out of 51 infants) and 9.8% (7/71), respectively [85,86]. In contrast, ambivalent attachment in Israel (with average antibiotic consumption of about 22 D.D.D.s/1000 inhabitants/day [87]) is overrated in both Arabic (13%) and Jewish (26%) samples [84,88]. Yet, the effect of religion is not clear-cut; family socioeconomic status and parents' educations have large contributions to attachment patterns prevalence [88]. 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 [84,88,89]. Studies comprising large and representative samples in each country could unveil the relationship between cultural, social, economical, regional, 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 societies occupy the central part of the Inglehart-Wenzel World Cultural Map (figure 1), and are associated with a consistent over-use of antibiotics.

In sum, considering the multiinfluence of psychological, social, educational, economic, and cultural factors on antibiotic use, we propose multidisciplinary, local, and family-based interventions to prevent antibiotic misuse. Calvo-Villamañán et al. advocate a global and systemic

response rather than decisions made by country [38]. Rather than specific problems of the countries as a whole, the causes seem to be: i) the lack of literacy on antibiotics use, ii) the presence of false conceptions about the ill effects of the antibiotics, and iii) the anxiety and overwhelming feelings facing illness (generated, for example, by attachment disorders). Consequently, it is essential to focus interventions on the causes.

Concluding remarks

Antibiotics are the most frequent medications prescribed in the pediatric population [90–94], which is unfortunate because antibiotic usage contributes to drug resistance and may have individual adverse effects. 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. For another example, Patients' insecurity and anxiety impact patient-doctor interaction. A study involving infants aged between 6 and 32 months found no differences between the prevalence of otitis in securely and insecurely attached infants [95]. Nevertheless, mothers of insecurely-attached infants become more anxious and have more negative perceptions of their infants' health conditions [95,96]. Furthermore, insecure-ambivalent teenagers and adults have higher symptom-reporting and request more health visits [97–99]. However, this can be mitigated by alternative supporting attitudes of caregivers and doctors.

Antibiotic stewardship programs already involve multidisciplinary teams, mainly composed of medical doctors, nurses, and pharmacists, but the battle against the pandemics of antibiotic

360 resistance could improve significantly by including other areas of knowledge, as several previous
361 studies have already demonstrated [35,39,100–103]. The works discussed here indicate that,
362 beyond physical factors, individual psychological differences between patients or between
363 patients' caregivers impact antibiotic prescription. Further research may investigate if "attachment
364 psychological dynamics" reflect the societies' cultural attitudes, and if those countries where
365 rational-modernity behaviors coexist with traditional values are expected to have an ambivalent
366 behavior leading to higher antibiotic consumption (see Outstanding Questions box).

Box – Patterns of infant attachment to caregivers

Human beings are prone to become attached to caregivers (primarily mothers/fathers) during their first year of life [68]. 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 [68,70]. 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 [68].

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 [68]. 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 [104].

In the late sixties and seventies, Mary Ainsworth developed an experimental protocol denominated Strange Situation to study attachment behavior [72]. 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 [70,72].

Using this experimental paradigm, Ainsworth found two main patterns among insecurely attached infants, which are somewhat opposite [72]. 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 [75,76]. For a review, see Cassidy and Shaver [70].

Glossary

Ambivalent insecurely-attached infants: one of the two main attachment patterns among insecurely attached infants. These 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. Moreover, these infants communicate their needs intensively when facing inconsistent responses from their caregivers and tend to exacerbate emotions.

Antibiotic stewardship programs: these institutional actions aim to improve antibiotic prescribing practices, mainly diminish their use by prescribing to specific individuals that should benefit from antimicrobial use.

Avoidant insecurely-attached infants: these infants turn to themselves to find means to solve their needs. One of the two patterns of insecurely attached infants.

Human Attachment: during their first year of life, human beings are prone to become attached to caregivers (primarily mothers and fathers). Infants adopt a behavioral strategy to maintain proximity with caregivers and to obtain care and comfort from them.

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.

Secular-rational values: have the opposite preferences to traditional values (see below).

Securely-attached infants: these infants are reciprocal and mutually bound 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.

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.

Survival values: these values emphasize economic and physical (life-death) security. These values frequently oppose to self-expression values.

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

References

1. Tomasz, A. (1997) Antibiotic Resistance in Streptococcus pneumoniae. *Clinical Infectious Diseases* 24, S85–S88
2. Singer, M. *et al.* (2008) Historical and Regulatory Perspectives on the Treatment Effect of Antibacterial Drugs for Community-Acquired Pneumonia. *CLIN INFECT DIS* 47, S216–S224
3. Keenan, J.D. *et al.* (2018) Azithromycin to Reduce Childhood Mortality in Sub-Saharan Africa. *New England Journal of Medicine* 378, 1583–1592
4. Laxminarayan, R. *et al.* (2013) Antibiotic resistance—the need for global solutions. *The Lancet Infectious Diseases* 13, 1057–1098
5. Rushton, J. (2015) Anti-microbial Use in Animals: How to Assess the Trade-offs. *Zoonoses and Public Health* 62, 10–21
6. Baquero, F. (2007) Evaluation of risks and benefits of consumption of antibiotics: from individual to public health. In *Encyclopedia of Infectious Diseases: Modern Methodologies* (Tibayrenc, M., ed), John Wiley and Sons, Hoboken, New Jersey.
7. Risnes, K.R. *et al.* (2011) Antibiotic exposure by 6 months and asthma and allergy at 6 years: Findings in a cohort of 1,401 US children. *American journal of epidemiology* 173, 310–8
8. Ajslev, T.A. *et al.* (2011) Childhood overweight after establishment of the gut microbiota: the role of delivery mode, pre-pregnancy weight and early administration of antibiotics. *International journal of obesity* 35, 522–9
9. Saari, A. *et al.* (2015) Antibiotic Exposure in Infancy and Risk of Being Overweight in the First 24 Months of Life. *Pediatrics* 135, 617–626
10. Korpela, K. *et al.* (2016) Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children. *Nat Commun* 7, 10410
11. Vrieze, A. *et al.* (2014) Impact of oral vancomycin on gut microbiota, bile acid metabolism, and insulin sensitivity. *Journal of Hepatology* 60, 824–831
12. Cox, L.M. (2016) Antibiotics shape microbiota and weight gain across the animal kingdom. *Animal Frontiers* 6, 8–14

13. Francino, M.P. (2016) Antibiotics and the Human Gut Microbiome: Dysbiose sand Accumulation of Resistances. *Front Microbiol* 6
14. Gensollen, T. *et al.* (2016) How colonization by microbiota in early life shapes the immune system. *Science* 352, 539–544
15. Livanos, A.E. *et al.* (2016) Antibiotic-mediated gut microbiome perturbation accelerates development of type 1 diabetes in mice. *Nat Microbiol* 1, 1–13
16. Jian, C. *et al.* (2021) Early-life gut microbiota and its connection to metabolic health in children: Perspective on ecological drivers and need for quantitative approach. *eBioMedicine* 69
17. Kunin, C.M. *et al.* (1973) Use of Antibiotics. *Ann Intern Med* 79, 555–560
18. Murray, C.J. *et al.* (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet* 399, 629–655
19. Laxminarayan, R. (2022) The overlooked pandemic of antimicrobial resistance. *The Lancet* 399, 606–607
20. Laxminarayan, R. *et al.* (2016) Access to effective antimicrobials: a worldwide challenge. *The Lancet* 387, 168–175
21. Pezzani, M.D. *et al.* (2021) Methodological quality of studies evaluating the burden of drug-resistant infections in humans due to the WHO Global Antimicrobial Resistance Surveillance System target bacteria. *Clinical Microbiology and Infection* 27, 687–696
22. Andersson, D.I. and Hughes, D. (2017) Selection and Transmission of Antibiotic-Resistant Bacteria. *Microbiol Spectr* 5
23. Patrick, D.M. and Hutchinson, J. (2009) Antibiotic use and population ecology: How you can reduce your "resistance footprint." *CMAJ* 180, 416–421
24. Klein, E.Y. *et al.* (2018) Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences* 115, E3463–E3470
25. Browne, A.J. *et al.* (2021) Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study. *The Lancet Planetary Health* 5, e893–e904
26. Goossens, H. *et al.* (2005) Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *The Lancet* 365, 579–587
27. Davies, J. and Davies, D. (2010) Origins and Evolution of Antibiotic Resistance. *Microbiol Mol Biol Rev* 74, 417–433

28. Megraud, F. *et al.* (2021) Helicobacter pylori resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community. *Gut* 70, 1815–1822
29. Baquero, F. (2021) Threats of antibiotic resistance: an obliged reappraisal. *Int Microbiol* 24, 499–506
30. Shlaes, D.M. *et al.* (1997) Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis* 25, 584–599
31. Goff, D. (2022) BSAC Vanguard Series: The future of antibiotic stewardship-managing access and excess. *J Antimicrob Chemother* 77, 863–864
32. Furuya, E.Y. and Lowy, F.D. (2006) Antimicrobial-resistant bacteria in the community setting. *Nat Rev Microbiol* 4, 36–45
33. Charani, E. *et al.* (2014) The Role of Behavior Change in Antimicrobial Stewardship. *Infectious Disease Clinics* 28, 169–175
34. Tonkin-Crine, S. *et al.* (2015) Contribution of behavioural science to antibiotic stewardship. *BMJ* 350, h3413
35. Lorencatto, F. *et al.* (2018) Driving sustainable change in antimicrobial prescribing practice: how can social and behavioural sciences help? *J Antimicrob Chemother* 73, 2613–2624
36. Bassetti, M. *et al.* (2019) Challenges and research priorities to progress the impact of antimicrobial stewardship. *Drugs Context* 8, 212600
37. Cuevas, C. *et al.* (2021) Improving antibiotic use through behaviour change: a systematic review of interventions evaluated in low- and middle-income countries. *Health Policy and Planning* 36, 754–773
38. Calvo-Villamañán, A. *et al.* (2022) Tackling AMR from a multidisciplinary perspective: a primer from education and psychology. *Int Microbiol* DOI: 10.1007/s10123-022-00278-1
39. Böhm, R. *et al.* (2022) Behavioral determinants of antibiotic resistance: The role of social information. *Appl Psychol Health Well Being* DOI: 10.1111/aphw.12345
40. Wanat, M. *et al.* (2022) The value, challenges and practical considerations of conducting qualitative research on antimicrobial stewardship in primary care. *JAC-Antimicrobial Resistance* 4, dlac026
41. Borek, A.J. *et al.* (2022) How can behavioural science contribute to qualitative research on antimicrobial stewardship in primary care? *JAC-Antimicrobial Resistance* 4, dlac007

42. WHO (2018) *WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation.*
43. Baquero, F. *et al.* (2002) Antibiotic consumption and resistance selection in Streptococcus pneumoniae. *J Antimicrob Chemother* 50 Suppl S2, 27–37
44. (2022) The Inglehart-Welzel World Cultural Map - World Values Survey 7 .[Online]. Available: http://www.worldvaluessurvey.org/
45. Inglehart, R. *et al.*, eds. (2022) World Values Survey: All Rounds - Country-Pooled Datafile. *Madrid, Spain & Vienna, Austria: JD Systems Institute & WVSA Secretariat. Dataset Version 3.0.0.* DOI: doi:10.14281/18241.22
46. Haerpfer, C. *et al.* (2022) World Values Survey Wave 7 (2017-2022) Cross-National Data-Set. Version: 5.0.0. *World Values Survey Association.* DOI: doi.org/10.14281/18241.20
47. Deschepper, R. *et al.* (2002) Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city. *Patient Educ Couns* 48, 161–169
48. Palin, V. *et al.* (2019) Antibiotic prescribing for common infections in UK general practice: variability and drivers. *J Antimicrob Chemother* 74, 2440–2450
49. Curtis, H.J. *et al.* (2019) Time trends and geographical variation in prescribing of antibiotics in England 1998–2017. *Journal of Antimicrobial Chemotherapy* 74, 242–250
50. Thomson, K. *et al.* (2020) An examination of trends in antibiotic prescribing in primary care and the association with area-level deprivation in England. *BMC Public Health* 20, 1148
51. Devine, P. *et al.* (2022) Trends, Variation, and Factors Influencing Antibiotic Prescribing: A Longitudinal Study in Primary Care Using a Multilevel Modelling Approach. *Antibiotics* 11, 17
52. Rockenbauch, T. and Sakdapolrak, P. (2017) Social networks and the resilience of rural communities in the Global South: a critical review and conceptual reflections. *Ecology and Society* 22
53. Thompson, W. *et al.* (2020) Clinician and Patient Factors Influencing Treatment Decisions: Ethnographic Study of Antibiotic Prescribing and Operative Procedures in Out-of-Hours and General Dental Practices. *Antibiotics* 9, 575
54. Sarason, B.R. and Duck, S., eds. (2001) *Personal Relationships: Implications for Clinical and Community Psychology*, John Wiley & Sons Ltd
55. Jason, L.A. *et al.* (2019) Introduction to the field of Community Psychology. In *Introduction to Community Psychology* (Jason, L. A. et al., eds), pp. 3–22, Rebus Foundation Publishers

56. Hernando-Amado, S. *et al.* (2020) Antibiotic Resistance: Moving From Individual Health Norms to Social Norms in One Health and Global Health. *Front Microbiol* 11, 1914
57. Michel-Lepage, A. *et al.* (2013) Cross-sectional survey: risk-averse French GPs use more rapid-antigen diagnostic tests in tonsillitis in children. *BMJ Open* 3, e003540
58. Rolain, J.M. and Baquero, F. (2016) The refusal of the Society to accept antibiotic toxicity: missing opportunities for therapy of severe infections. *Clin Microbiol Infect* 22, 423–427
59. Little, P. *et al.* (1997) Reattendance and complications in a randomised trial of prescribing strategies for sore throat: the medicalising effect of prescribing antibiotics. *Brit Med J* 315, 350–352
60. Wang, K.Y. *et al.* (2009) Which practices are high antibiotic prescribers? A cross-sectional analysis. *Br J Gen Pract* 59, e315–e320
61. Charani, E. *et al.* (2010) Antibiotic stewardship programmes—what's missing? *Journal of Antimicrobial Chemotherapy* 65, 2275–2277
62. Shallcross, L. *et al.* (2017) Antibiotic prescribing frequency amongst patients in primary care: a cohort study using electronic health records. *Journal of Antimicrobial Chemotherapy* 72, 1818–1824
63. Macfarlane, J. *et al.* (1997) Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. *BMJ* 315, 1211–1214
64. Sirota, M. *et al.* (2017) Expectations for Antibiotics Increase Their Prescribing: Causal Evidence About Localized Impact. *Health Psychol* 36, 402–409
65. Dekker, A.R.J. *et al.* (2015) Inappropriate antibiotic prescription for respiratory tract indications: most prominent in adult patients. *Fam Pract* 32, 401–407
66. Denny, K.J. *et al.* (2019) Appropriateness of antibiotic prescribing in the Emergency Department. *Journal of Antimicrobial Chemotherapy* 74, 515–520
67. Fuertes, M. *et al.* (2020) Maternal sensitivity and mother-infant attachment are associated with antibiotic uptake in infancy. *J Health Psychol* DOI: 10.1177/1359105320941245
68. Bowlby, J. (1969) *Attachment and loss.*, I, Penguin Book
69. Beeghly, M. *et al.* (2011) Maternal sensitivity in dyadic context: Mutual regulation, meaning-making, and reparation. In *Maternal sensitivity: A scientific foundation for practice.* (Davis, D. W. and Logsdon, M. C., eds), pp. 59–83, Nova Science Publishers

70. Cassidy, J. and Shaver, P.R. (2018) *Handbook of Attachment - Theory, Research, and Clinical Applications*, ((3rd edn)), Guilford Press
71. Barbosa, M. *et al.* (2018) Robust Stability and Physiological Correlates of Infants' Patterns of Regulatory Behavior in the Still-Face Paradigm at 3 and 9 Months. *Dev Psychol* 54, 2032–2042
72. Ainsworth, M.D.S. *et al.* (1978) *Patterns of attachment - A Psychological Study of the Strange Situation.*, Lawerence Erlbaum Associates
73. Fuertes, M. *et al.* (2022) The Impact of Low Birthweight in Infant Patterns of Regulatory Behavior, Mother-Infant Quality of Interaction, and AttachmentAvailable at http://dx.doi.org/10.2139/ssrn.4115177
74. Belsky, J. (1999) Interactional and contextual determinants of attachment security. In *Handbook of attachment: Theory, research, and clinical implications.* (Cassidy, J. and Shaver, P. R., eds), pp. 249–264, The Guilford Press
75. DeWolff, M.S. and van Ijzendoorn, M.H. (1997) Sensitivity and attachment: A meta-analysis on parental antecedents of infant attachment. *Child Dev* 68, 571–591
76. Lucassen, N. *et al.* (2011) The Association Between Paternal Sensitivity and Infant-Father Attachment Security: A Meta-Analysis of Three Decades of Research. *J Fam Psychol* 25, 986–992
77. Braungart-Rieker, J.M. *et al.* (2001) Parental sensitivity, infant affect, and affect regulation: Predictors of later attachment. *Child Dev* 72, 252–270
78. Mesman, J. *et al.* (2012) Parental sensitivity to infant distress: what do discrete negative emotions have to do with it? *Attach Hum Dev* 14, 337–348
79. Stern, J.A. *et al.* (2020) Beyond Early Adversity: The Role of Parenting in Infant Physical Health. *J Dev Behav Pediatr* 41, 452–460
80. Bosley, H. *et al.* (2022) Understanding antibiotic-seeking behaviour: A qualitative case study of mothers of children aged 5 and under. *Journal of Advanced Nursing* 78, 3772–3781
81. Franco, V. *et al.* (2017) A National Early Intervention System as a Strategy to Promote Inclusion and Academic Achievement in Portugal. *Frontiers in Psychology* 8
82. Barbosa, M. *et al.* (2021) Emerging patterns of infant regulatory behavior in the Still-Face paradigm at 3 and 9 months predict mother-infant attachment at 12 months. *Attachment & Human Development* 23, 814–830

83. Faria, A. *et al.* (2014) Pais e mães protegem, acarinham e brincam de formas diferentes. *Analise Psicologica* 32, 419–438
84. van Ijzendoorn, M.H. and Sagi-Schwartz, A. (2008) Cross-cultural patterns of attachment: Universal and contextual dimensions. In *Handbook of attachment: Theory, research, and clinical applications.* (Cassidy, J. and Shaver, P. R., eds), pp. 880–905, The Guilford Press
85. Lamb, M.E. *et al.* (1982) Security of mother- and father-infant attachment and its relation to sociability with strangers in traditional and nontraditional Swedish families. *Infant Behavior and Development* 5, 355–367
86. Rauh, H. *et al.* (2000) Stability and change in infant-mother attachment in the second year of life: Relations to parenting quality and varying degrees of day care experience. In *The Organization of Attachment Relationships: Maturation, Culture, and Context* (Crittenden, P. M. and Claussen, A. H., eds)
87. Dickstein, Y. *et al.* (2019) Antimicrobial use trends, Israel, 2012 to 2017. *Euro Surveill* 24, 1900022
88. Mesman, J. *et al.* (2016) Cross-cultural patterns of attachment. *Handbook of attachment: Theory, research, and clinical applications*
89. Gloger-Tippelt, G. *et al.* (2000) "Strange-Situation"-Studies in German Speaking Countries: An Overview. In *Psychologie in Erziehung und Unterricht (PEU)* 47 (Crittenden, P. M. and Claussen, A. H., eds), pp. 87–98
90. Sturkenboom, M.C.J.M. *et al.* (2008) Drug use in children: cohort study in three European countries. *BMJ* 337, a2245
91. Hersh, A.L. *et al.* (2011) Antibiotic prescribing in ambulatory pediatrics in the United States. *Pediatrics* 128, 1053–1061
92. Chai, G. *et al.* (2012) Trends of outpatient prescription drug utilization in US children, 2002-2010. *Pediatrics* 130, 23–31
93. Stam, J. *et al.* (2012) Antibiotic use in infants in the first year of life in five European countries. *Acta Paediatrica, International Journal of Paediatrics* 101, 929–934
94. Holstiege, J. and Garbe, E. (2013) Systemic antibiotic use among children and adolescents in Germany: A population-based study. *European Journal of Pediatrics* 172, 787–795
95. McCallum, M.S. and McKim, M.K. (1999) Recurrent Otitis Media and Attachment Security: A Path Model. *Early Education and Development* 10, 517–534

96. Gonçalves, J.L. *et al.* (2020) Maternal pre and perinatal experiences with their full-term, preterm and very preterm newborns. *BMC Pregnancy and Childbirth* 20, 276
97. Andrews, N.E. *et al.* (2011) Adult attachment and reports of pain in experimentally-induced pain. *Eur J Pain* 15, 523–530
98. Feeney, J.A. (2000) Implications of attachment style for patterns of health and illness. *Child Care Hlth Dev* 26, 277–288
99. Meredith, P. *et al.* (2008) A review of the evidence linking adult attachment theory and chronic pain: Presenting a conceptual model. *Clin Psychol Rev* 28, 407–429
100. Deschepper, R. *et al.* (2008) Are cultural dimensions relevant for explaining cross-national differences in antibiotic use in Europe? *BMC Health Serv Res* 8, 123
101. Grigoryan, L. *et al.* (2008) Determinants of self-medication with antibiotics in Europe: The impact of beliefs, country wealth and the healthcare system. *Journal of Antimicrobial Chemotherapy* 61, 1172–1179
102. Hulscher, M.E. *et al.* (2010) Antibiotic prescribing in hospitals: a social and behavioural scientific approach. *The Lancet Infectious Diseases* 10, 167–175
103. Krockow, E.M. *et al.* (2022) Prosociality in the social dilemma of antibiotic prescribing. *Current Opinion in Psychology* 44, 164–169
104. Sroufe, L.A. (2005) Attachment and development: A prospective, longitudinal study from birth to adulthood. *Attachment & Human Development* 7, 349–367
105. ECDC (2022) *Antimicrobial consumption in the EU/EEA (ESAC-Net) - Annual Epidemiological Report 2021*.