REVIEW ARTICLE

Vaccine refusal – what we need to know

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Vaccination; Vaccine refusal; Vaccine hesitancy; Vaccine confidence; Vaccine acceptance

Abstract
Objective: Opposition to vaccines is not a new event, and appeared soon after the introduction of the smallpox vaccine in the late 18th century. The purpose of this review is to educate healthcare professionals about vaccine hesitancy and refusal, its causes and consequences, and make suggestions to address this challenge.
Source of data: A comprehensive and non-systematic search was carried out in the PubMed, LILACS, and ScieLo databases from 1980 to the present day, using the terms "vaccine refusal," "vaccine hesitancy," and "vaccine confidence." The publications considered as the most relevant by the author were critically selected.
Synthesis of data: The beliefs and arguments of the anti-vaccine movements have remained unchanged in the past two centuries, but new social media has facilitated the dissemination of information against vaccines. Studies on the subject have intensified after 2010, but the author did not retrieve any published studies to quantify this behavior in Brazil. The nomenclature on the subject (vaccine hesitancy) was standardized by the World Health Organization in 2012. Discussions have been carried out on the possible causes of vaccine hesitancy and refusal, as well as on the behavior of families and health professionals. Proposals for interventions to decrease public doubts, clarify myths, and improve confidence in vaccines have been made. Guides for the health care professional to face the problem are emerging.
Conclusions: The healthcare professional is a key element to transmit information, resolve doubts and increase confidence in vaccines. They must be prepared to face this new challenge.
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PALAVRAS-CHAVE
Vacinacao;
Recusa vacinal;
Hesitacao vacinal; 
Confianca nas vacinas; 
Aceitacao das vacinas

Recusa vacinal – o que é preciso saber

Resumo
Objetivo: Oposição às vacinas não é evento novo e surgiu logo após a introdução da vacina contra variola no fim do século XVIII. O objetivo desta revisão é esclarecer os profissionais de saúde sobre hesitação e recusa vacinal, suas causas e consequências e fazer sugestões para enfrentar esse desafio.

Fonte dos dados: Foi feita busca abrangente e não sistemática nas bases de dados PubMed, Lilacs e Scielo desde 1980 até o presente, utilizando os termos "recusa vacinal" "hesitação vacinal" e "confiança nas vacinas". Foram selecionados de forma crítica as publicações avaliadas como mais relevantes pela autora.

Síntese dos dados: As crenças e argumentos dos movimentos anti-vacinas mantiveram-se inalterados nos dois últimos séculos, mas as novas mídias sociais facilitaram a disseminação das informações contra as vacinas. Os estudos sobre o assunto se intensificaram depois de 2010, mas não foram identificados estudos publicados que permitam quantificar esse comportamento no Brasil. A nomenclatura sobre o tema (hesitação vacinal) foi uniformizada pela Organização Mundial de Saúde em 2012. Pesquisas têm sido feitas sobre as possíveis causas da hesitação e recusa vacinal, e também sobre o comportamento das instituições e da população em geral. Propostas de intervenções para diminuir as dúvidas da população, esclarecer mitos e melhorar a confiança nas vacinas tem sido feitas. Guias para o profissional de saúde enfrentar o problema estão surgindo.

Conclusões: O profissional de saúde é elemento fundamental para transmitir informações, combater as dúvidas e fortalecer a confiança nas vacinas. Eles devem se preparar para enfrentar esse novo desafio.

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Introduction

By fighting the devastating consequences that infectious diseases have inflicted on humankind for centuries, vaccines represent the most cost-effective health investment. In the last decades, the observed progress in the technology of production, improvement, and development of vaccines has resulted in a significant offer of new products, which are effective and safe; to fully achieve their public health potential, vaccines must be accepted, earn the trust of the target audience, and be broadly and adequately used.

The individual and collective benefits of vaccination are obtained at a high financial cost, and the commitment of a large structure of public vaccination programs and health authorities, as well as the individual actions of healthcare professionals. The National Immunization Program (Programa Nacional de Imunizaçao [PNI]) in Brazil is serious and competent: It relies on the trust of healthcare professionals and the population, and has achieved vaccine coverage of more than 90% for almost all the immunobiological agents whose vaccines are distributed in the public network in recent decades, distributing approximately 300 million of immunobiological doses annually. However, in 2016, in the states of Pernambuco and Ceará, after a decrease in immunization rates, the country recorded the first measles outbreak since 2000; moreover, the polio immunization rate in 2016 was the lowest of the last 12 years (84.4%) in Brazil. Although it is not yet possible to define whether this is a temporary vaccination coverage oscillation or if there is an actual decrease, these data are of concern.

Despite every effort to ensure the distribution and application of vaccines, aiming at individual and collective benefits, people and groups who have concerns about the safety and need for vaccine application are present worldwide. This is not a recent phenomenon – it arose soon after the introduction of the smallpox vaccine at the end of the 18th century, and has continued throughout time. The arguments and beliefs of anti-vaccination groups have not changed much in the last two centuries, but the ability to disseminate information has increased in effectiveness and speed in the last decades.

The loss of confidence in vaccines and immunization programs can lead to a decrease in vaccine coverage, with all its consequences. The occurrence of doubts about the need for vaccines, the fear of possible adverse events, the dissemination of misinformation, in addition to philosophical and religious beliefs, have created situations in which families and even healthcare professionals have doubts about the need for vaccines. At the same time that the World Health Organization (WHO) expresses concern that one in ten infants worldwide (12.9 million children) did not receive any vaccine doses in 2016, with most of them living in regions of conflict and poverty, without access to health services, healthcare professionals still have to address children who, although having the resources and easy access to health services, are no longer vaccinated due to the decision of their parents/guardians.
Vaccine hesitancy/refusal

In 2012, the World Health Organization (WHO) created a special group to characterize, discuss, and establish strategies to address issues related to vaccine refusal: the SAGE Working Group on Vaccine Hesitancy. This group categorized factors that influence the decision to accept vaccines, and defined “vaccine hesitancy” as the delay in the acceptance or refusal to vaccinate despite the availability of vaccine services; it considers that vaccine hesitancy is a complex, context-specific phenomenon that varies in time, places, and regards specific vaccines. The aims of this group include: monitoring vaccine confidence and vaccine refusal, and developing communication interventions to address vaccine confidence failures, preventing their public health consequences.

The concept of vaccine hesitancy has been used in recent years, both in the academic scenario and in public health settings, raising concerns about the possibility of resurgence of already controlled infectious diseases, in addition to ethical and behavioral discussions. The effects of this behavior vary regionally and have stimulated the development of researches to better understand and address this issue, resulting in a growing number of studies and scientific articles published on the subject in the last ten years.

The confidence in vaccines and in healthcare professionals is crucial to maintain the demand and use of vaccines both in developed and developing countries. Most of the population follows the vaccination schedule recommended by their physician or healthcare institutions, but the challenge remains when one must address groups that refuse or delay the application of vaccines. These groups include parents of children and adolescents, pregnant women, the elderly, and healthcare professionals who decide not to be vaccinated, not to vaccinate their children or do not recommend that their patients be vaccinated.

Vaccine acceptance is the final result of a decision-making process influenced by several factors. For the SAGE Working Group on Vaccine Hesitancy, the determinants of this behavior can be characterized by the 3C model: Confidence (trust in healthcare professionals, vaccines, and their effectiveness), Complacency (low awareness of the risks of vaccine-preventable diseases and the importance of vaccines), and Convenience (availability of and accessibility to vaccines and healthcare services). Thus, vaccine refusal cannot be defined as a dichotomous behavior of acceptance versus refusal, but rather as a continuum between the two situations, with individuals who refuse all vaccines at one end, those who accept all vaccines at the other, and those who accept some but refuse others between the two groups.

A study carried out in 2016 to assess people's perceptions about the safety, efficacy, and importance of vaccines, as well as compatibility with their religious beliefs, collected data from 65,819 people in 67 countries, including Brazil. The data disclosed that, in general, confidence in vaccines is high, but varied in different regions; European countries showed the highest levels of negative responses on the importance, safety, and efficacy of vaccines, and France was the country with the most negative feelings about vaccine safety (41%).

Among the nine countries evaluated in the Americas, Brazil ranked among those with the highest confidence levels in vaccines. Countries whose populations had better access to health services and better levels of schooling had higher rates of negative feelings about vaccines, indicating an inverse association between positive feelings about vaccines and socioeconomic status.

Potential causes of vaccine hesitancy/refusal

The determinants of vaccine refusal/hesitancy are complex and can be attributed to the confluence of several sociocultural, political, and personal factors; doubts about the actual need for vaccines, concerns about vaccine safety, fear of possible adverse events, misconceptions about the safety and efficacy of vaccines, concerns over a possible “immune system overexposure,” past negative experiences with vaccines, mistrust of the seriousness of the vaccine industry and the healthcare system, heuristic thinking, and philosophical and religious issues may be involved.

Vaccines can be considered victims of their own success. With the availability of new and effective vaccines, the epidemiology of infectious diseases has undergone major changes. Doctors who graduated from medical school less than 20–30 years ago have scarcely seen or cared for patients with polio, diphtheria, meningitis caused by Haemophilus influenzae; those who graduated less than 40 years ago did not see cases of smallpox. The lack of memory of these diseases, their severity and their sequelae, makes the need to prevent them less conspicuous.

The decision to vaccinate is influenced by social factors that include personal experience, family history, and friends’ opinions, together with so many other decisions to be made about one’s children; thus, the relevance of vaccination may lose its meaning and importance.

The access to information (and misinformation) on vaccines released by the media influences decision-making on whether or not to vaccinate. The information is not always correct, which leads to conflicting feelings – parents with insufficient knowledge about vaccine-preventable diseases may show negative attitudes toward vaccines and healthcare professionals.

The changes that occurred in the last decades in the doctor–patient relationship and the concept of sharing decisions, giving autonomy to the patient and their parents, have modified the health decision-making process, which includes the option of being vaccinated.

Importance of health professionals

Healthcare professionals, especially pediatricians, who maintain direct and frequent contact with parents, play a key role in maintaining vaccine confidence and are considered the main and most reliable source of information for patients. With the increasing availability of new vaccines and the frequent updates of vaccine schedules, keeping up-to-date and knowing the indications, precautions, and possibility of adverse events are constant challenges for these professionals. Moreover, considering their occupational exposure, they are susceptible to acquiring and transmitting infectious diseases, which requires
them to keep their own vaccination schedule updated, which does not happen as desired.\textsuperscript{14,15}

It is crucial to be prepared to answer the parents’ concerns about vaccines. A qualitative research carried out in Australia with healthcare professionals (doctors and nurses) working in regions with high rates of vaccination objections revealed that practitioners reported challenging and conflicting relationships – it is important to be aware of the challenges faced by healthcare workers when addressing this issue and the strategies available to them.\textsuperscript{20}

Another Australian study that interviewed 165 pediatricians online showed that although 61\% of them reported discussing immunization aspects frequently or “almost always,” \textsuperscript{15} 15\% reported that such discussions rarely occur; although time restriction was considered the main barrier to this activity, 25\% of them reported lack of confidence in their knowledge related to the topic, and 62\% showed a desire for training in the area.\textsuperscript{17}

The healthcare professionals’ vaccination, their knowledge about the subject and their own confidence in vaccines are essential to guide their behavior when indicating vaccines to their patients.\textsuperscript{18,19}

A review of 185 articles on vaccination hesitancy among health professionals carried out in 2016\textsuperscript{20} showed that knowledge about vaccines, their efficacy and safety increase the professionals’ confidence and the prescription of these immunobiological agents; most articles revealed that an appropriately vaccinated professional is more likely to prescribe vaccines, which makes more evident the need for continuing education and training.

Having the opportunity to experience infectious diseases, their consequences and sequelae can influence the professional’s attitude and willingness to recommend vaccines. A study carried out with American physicians at different time intervals since graduation from medical school demonstrated a 15\% decrease in confidence on vaccine safety for every five-year interval since graduation, showing that the perception of the risks and benefits of immunization differs among physicians trained in recent years when compared to their older colleagues, which certainly reflects on the way they recommend vaccines to their patients.\textsuperscript{27}

The position of parents and caregivers

Communication with parents and caregivers about child vaccination is one way to address vaccine refusal; such communication must be a two-way process (from professional to the caregiver and vice versa), supporting vaccination in a creative and ethical way.\textsuperscript{15} In addition to discussing vaccines (their benefits and challenges) and the diseases that can be prevented by vaccination, it is necessary to provide information about vaccination sites available and, moreover, the healthcare professional must welcome the experiences, fears, and beliefs that parents and caregivers have on vaccines to adequately assess what kind of communication should be established to guide the decision to vaccinate. It is necessary to consider that currently, in addition to the recommendations provided by healthcare professionals, the search for information about vaccines among friends and on the internet (on Twitter, Facebook, Google, and YouTube, among others) is the rule, allowing a rapid gathering of information outside the scientific environment, thus increasing the chance of spreading information that lacks scientific quality.\textsuperscript{2,9,23}

A longitudinal North-American study interviewed mothers at three different times – at birth, at 6 months, and at 24 months – and found that both the hesitancy rate and the proportion of hesitant mothers significantly decreased from birth to 24 months;\textsuperscript{24} considering that confidence in the safety and efficacy of vaccines is a dynamic process that increases over time, it suggests that pregnancy and the postpartum period may be the ideal time to clarify and ensure information on the infant’s vaccines. In Australia, a cross-sectional study carried out in 2012 with 452 parents concluded that although 92\% reported that their children were vaccinated, 52\% reported concerns; factors related to hesitancy included concerns about the safety of vaccines and obtaining information from sources other than the healthcare professional.\textsuperscript{25}

A North-American study interviewing 9354 parents of children aged 19–35 months, in whom a vaccine confidence scale was applied, demonstrated that 15\% of them reported a history of vaccine refusal and 27\%, a delay in vaccine application.\textsuperscript{26} Using periodic surveys by the American Academy of Pediatrics of 2006 and 2013 to verify the perception of pediatricians about the prevalence of vaccine refusal and delay,\textsuperscript{27} the proportion of pediatricians who reported vaccination refusal increased from 74.5\% in 2006 to 87.0\% in 2013. The main reason stated by parents for vaccine refusal was the perception that vaccines are unnecessary and the discomfort and “immune system overload” for vaccine delay.

Engaging vaccine-confident parents to act as advocates for immunization in their communities was shown to be a useful method to reduce vaccine hesitancy in a study carried out in the United States.\textsuperscript{36}

Another issue to be considered is the option for parents to follow an “alternative vaccination schedule” that differs from that proposed by the official immunization programs. Such schedules, in addition to not being tested for efficacy and safety, increase the time that children remain unprotected; studies indicate that up to 25\% of families are adopting these alternative schedules.\textsuperscript{37,38}

The role of the pregnant woman

Decisions on infant vaccines appear to start in the prenatal period.\textsuperscript{39,40} Women adhering to vaccination schedules during pregnancy, in addition to protecting themselves and their offspring from infectious diseases, appear to have an attitude of confidence toward similar vaccines for their offspring. A study conducted in Australia with recommendations on vaccination during pregnancy and infant vaccination follow-up showed that primiparous women have more doubts about vaccines, and this can be correlated with the vaccination rates of their children.\textsuperscript{39} A study carried out with over 4000 American pregnant women found that mothers who reported having received the influenza vaccine during pregnancy were significantly more likely to complete their children’s vaccination schedule.\textsuperscript{40} These findings reinforce the need to provide information on vaccines during pregnancy.
Role of the medical student and resident physician

There has been little research on the teaching of vaccines in medical schools and their consequences on vaccine confidence. Preparing medical students and residents to identify and treat vaccine-preventable infectious diseases is an important tool to prepare them to provide guidance on the importance of vaccines for the control of such diseases. A study of 385 pediatric residents in the United States showed that more than 25% of them did not feel comfortable and confident in identifying and treating some of these diseases. Most residents reported extreme concern about dealing with parents who refused vaccines and more than 95% of them reported that they would benefit from better training in the area. A recent study with pediatric residents in the United States showed that most of them not only felt insecure when diagnosing vaccine-preventable diseases, but were also concerned that they were not able to adequately argue aspects of vaccine refusal with parents. Studies carried out in France with medical students and in Korea with family medicine residents to evaluate vaccine knowledge disclosed a lack of knowledge on the subject and lack of training for the medical practice, particularly regarding the discussion of adverse events, healthcare professional vaccination, and strategies to address vaccine refusal. In both studies, the authors suggest that the teaching on vaccines is insufficient and that it is necessary to invest in the area.

Interventions when dealing with the problem

Despite the great impact of vaccines on individual and collective health, the number of individuals and groups who question their importance and, therefore, choose alternative vaccine schedules or refuse their application has grown in recent years. In Brazil, it is still not possible to correctly quantify these groups, but concerns with this issue among health professionals is increasing. In 2013, Dr. Guido Carlos Levi, an infectologist from São Paulo, Brazil, wrote a book on vaccine refusal and stated that, in addition to providing information and debates on the subject, he aimed to increase confidence in vaccines in those who already use them and raise some doubts in those who are opposed to them. In the United States, the American Academy of Pediatrics, using periodic surveys, found that the rate of parents refusing one or more vaccines recommended by pediatricians increased from 9.1% in 2006 to 16.7% in 2013; the rate of Americans who refuse all vaccines is estimated at 3%. The study by Larson et al., carried out in 2016, showed that European countries have the lowest confidence rates in vaccines; over 40% of the individuals surveyed declared to have negative feelings about vaccine safety, suggesting that vaccine refusal must be higher in those regions. The levels of vaccine refusal and the knowledge of the anti-vaccination groups in Brazil are still not well quantified.

Developing strategies that can improve vaccine confidence and decrease vaccine refusal rates with all its consequences is essential, but choosing the best way to pass on messages that effectively change people’s behavior toward vaccines is not an easy task. Some studies have been carried out to evaluate the strategies that should be used to turn vaccine-hesitant parents or patients into vaccine-confident. Leaflets containing information on vaccines have been used in an attempt to dispel myths about them, as well as leaflets explaining the lack of evidence between autism and the triple viral vaccine, leaflets showing pictures of children with severe manifestations of vaccine-preventable infectious diseases, and testimonies of mothers or physicians about children who became ill and had sequelae due to these diseases. Most studies, however, have failed to define the best strategy. Some researchers believe that focusing on interventions aimed at those showing vaccine hesitancy, which may respond positively, is more productive than at those showing vaccine refusal.

While there is no doubt that healthcare professionals need to be more involved in the dialog with parents and patients who are hesitant about vaccines, it is also necessary that the messages be effective. The decision to vaccinate is complex and it is important to consider this fact, mentioned by Dr. Heidi Larson of the Vaccine Confidence Project: “Healthcare professionals inform what they consider important, which does not necessarily correspond to the concerns that people have.” This suggests that listening to what patients and parents say is important to build arguments and decide on the form of communication that could improve vaccine confidence. Improving the knowledge on diseases and vaccines is an important strategy to reduce vaccine refusal, but the way this information is offered should be reassessed.

Recommendations and guidelines on the subject

The growing concern about vaccine refusal has led the World Health Organization, the United States Centers for Disease Control and Prevention, and medical associations to issue technical guidelines and manuals on the subject. These documents present the causes, reinforce the consequences, and suggest strategies for coping with vaccine hesitancy or refusal, including establishing principles for health professionals to provide answers when confronted in public with anti-vaccine groups.

The American Academy of Pediatrics, in addition to providing subsidies and material for pediatrics to keep up-to-date on vaccines and vaccine refusal, discusses the media exposure to which families are subject, the possibilities of vaccine exemption in the country, the possibility of pediatrics’ refusal to treat the children of parents who refuse vaccines, and the extreme importance of the pediatrician’s dialog with families to clarify doubts, eliminate myths, and facilitate interpersonal relationships. It also provides information, informative documents for professionals and for the public/parents, as well as educational videos and suggestions for the professionals’ conduct.

In Washington, United States, a public–private partnership has created an intervention called Immunity Community, which mobilizes parents who are confident in the value of vaccines and provides them with tools to engage in positive dialogs about immunization in their communities.
In Brazil, the Brazilian Society of Pediatrics (Sociedade Brasileira de Pediatria [SBP]) and the Federal Council of Medicine (Conselho Federal de Medicina [CFM]), concerned about the advent of the anti-vaccination movement, issued an alert on June 23, 2017 urging the population, physicians, and other healthcare professionals to counteract said movement. “Failing to vaccinate oneself or prevent children and adolescents from being vaccinated can result in immense problems for public health, such as the emergence of severe diseases or the return of epidemic diseases, such as poliomyelitis, measles, and rubella, among others” says the document.59 No other movements aimed at minimizing vaccine hesitancy and refusal in the country have been identified.

Ethical and legal aspects

Childhood vaccination involves balancing the autonomy of parents in deciding whether to immunize their children and the benefits for public health of mass vaccination campaigns.59 The balance between individual actions and their impact on collective health, as well as evaluation of the risks and benefits can generate ethical conflicts.59,60

In Brazil, a 1975 Federal Law, regulated by a 1976 decree,61 provides for the organization of Epidemiological Surveillance actions and the National Immunization Program, establishing in paragraph 27 that vaccination is mandatory throughout the national territory. Paragraph 29 of the same decree establishes that it is the duty of all citizens to submit to compulsory vaccination, as well as all minors under their custody or responsibility.

Moreover, the Child and Adolescent Statute (Estatuto da Criança e do Adolescente [ECA]) establishes that it is the duty of the family to ensure the children’s and adolescents’ health rights, which includes routine vaccination.62 From the doctor-patient relationship standpoint, family members who oppose the vaccination of their children can seriously impair this relationship, which may be enough to allow the physician to stop caring for this patient (Code of Medical Ethics – article 36).63

Based on the abovementioned facts, situations where physicians refuse to treat patients can occur, judges may determine the loss of parental rights, and parents can be held responsible for the crime of abandonment and omission if a child becomes ill as a result of vaccine refusal. Therefore, ethical and legal discussions should be part of clinical practice, which certainly helps physicians in their decision-making and in the recommendations provided to parents.

Final considerations

The safety, effectiveness, importance, and success of vaccines in individual and collective protection against infectious diseases and quality of life are unquestionable. However, doubts about the efficacy and necessity of vaccines, as well as myths about the possibility of harm caused by them have existed since vaccines were introduced, over two centuries ago.

Parents and caregivers want to provide the best for their children; in search of this “best,” they might seek information and support in friends, social media, and gray literature, resulting in controversy and doubts about the safety and efficacy of vaccines, their actual necessity, and even suggestions of a conspiracy among healthcare professionals and the pharmaceutical industry. Furthermore, personal experiences with health services and vaccines, access to safe information and vaccine, as well as philosophical, social, and religious issues, can have a significant importance in health decision-making.

Addressing these issues ethically and safely requires knowledge of the problem, its determinants, and the impact it has on public and individual health. Although the parents’ communication with physicians (especially pediatricians) is not uniform and not always productive, it is necessary for pediatricians to understand they play a key role in the parents’ decision regarding each act related to the care of their children. For this role to be played to its fullest extent, resulting in benefits for the child, it is important that the pediatrician be equipped with technical knowledge and communication skills, taking every opportunity to clarify the parents about the subject, ensuring that the healthcare professional has confidence in vaccines.

Therefore, frequent updates on available vaccines, changes in vaccination schedules, and on the occurrence and management of adverse events are indispensable. Such updates can be achieved through courses, scientific documents, and consultations with specialists, allowing physicians to answer the questions they are asked with safety and credibility.

Listening to parents and being available to answer questions makes a difference. Asking parents what they know or think about vaccines can be an interesting introduction. Discussing aspects of the vaccines at each pediatric visit is an excellent starting point. It is necessary to provide the information and ensure that it has been correctly understood; hearing and accepting doubts without judging their relevance. Discussing the benefits of vaccines, keeping an open mind to relay knowledge, and accepting cultural and intellectual differences are very important.

Offering information on the millions of lives saved by vaccine programs can be far more effective than presenting frightening data on the consequences, sequelae, and mortality of infectious diseases, as well as explaining that individual vaccination brings benefits to the community through herd protection, by clarifying that children with immunodeficiencies who cannot receive vaccines deserve our concern, and we should avoid their exposure to the occurrence and outbreaks of infectious diseases secondary to non-use of vaccines. It is important to suggest to parents that having access to safe information from healthcare professionals, the Ministry of Health, and medical societies is preferable to information from sources whose safety and credibility are debatable. Taking every opportunity to talk about vaccines, not just to the child, but to other family members, can have a significant impact, particularly when mothers are pregnant again.

It is important to consider that most parents trust the information offered by pediatricians and, although they might have some questions, they will follow the healthcare professional’s advice, including on vaccination.
Conflicts of interest

The author declares no conflicts of interest.

References