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To cite this article: Federico Marchetti, Luz Maria Vilca & Irene Cetin (2019): Insights and expectations for Tdap vaccination of pregnant women in Italy, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: [10.1080/14767058.2019.1659240](https://doi.org/10.1080/14767058.2019.1659240)

To link to this article: <https://doi.org/10.1080/14767058.2019.1659240>



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Published online: 04 Sep 2019.



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Insights and expectations for Tdap vaccination of pregnant women in Italy

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ABSTRACT

Background: Pertussis is a widespread vaccine-preventable disease, associated with an increasing trend to hospitalization among newborns. Pertussis in newborns can be fatal, and the most effective way to prevent it is maternal immunization (MI) with a reduced antigen content tetanus, diphtheria, and acellular pertussis vaccine (Tdap). In Italy, the National Immunization Plan (NIP) 2017–2019 introduced *de novo* Tdap vaccination during each pregnancy at no cost for the recipient. Despite this, vaccination coverage is suboptimal. This survey of pregnant women across Italy was conducted to investigate their knowledge and expectations of Tdap.

Methods: A cross-sectional survey was conducted. Pregnant women up to 28th gestational weeks were interviewed by Telephone using a questionnaire with 16 questions. Statistics were descriptive.

Results: The final sample recruited 600 respondents evenly distributed across Italy. The average duration of pregnancy at the time of the interview was 20.8 weeks (standard deviation [SD] 6.0). Most women (60.7%) were between 30 and 40 years of age. About half were aware of the risks of pertussis for newborns (54.5%) and the increased risk of hospitalization (59.8%); 47.2% were aware that Tdap MI was offered free of charge under the NIP. Safety information regarding the mother and newborn was considered the most important information in deciding whether to be vaccinated (47.4%), followed by safety information related only to the newborn (29.5%). About half (52.2%) stated that they would “certainly” accept MI, and 25.3% would like to receive more information. Gynecologists were the preferred healthcare providers (HCPs) for the provision of MI information (34.3%), followed by pediatricians (25.5%). Two-thirds of the respondents would prefer to be informed about MI before getting pregnant (66.0%). Vaccines investigated specifically for use in pregnancy were preferred by respondents. Overall, no relevant differences were observed between women pregnant for the first time and those with more than one pregnancy, nor between geographical regions.

Conclusions: The results show room for improving the awareness and understanding of the risks of pertussis for infants and the protective role of MI. The pregnant women preferred to receive advice on MI from an HCP, primarily their gynecologist. They were most interested in information on the safety profile of Tdap during pregnancy, on the mother, fetus, and newborn. The potential impact of this study to support clinical practice of Healthcare Providers is highlighted in the Focus on the Patient section.

ARTICLE HISTORY

Received 20 March 2019
Accepted 20 August 2019

KEYWORDS

Bordetella pertussis; Italy; maternal immunization; pregnancy; vaccination

Focus on the Patient

What is the context?

Whooping cough, also called pertussis, is a highly contagious infectious disease that can be prevented through vaccination. Although a high proportion of adults are vaccinated, pertussis continues to raise concern as it presents an important risk, even death, among infants below 6 months of age. The World Health Organization recognizes that the most effective way to prevent pertussis in infants is vaccination of mothers during pregnancy i.e., maternal immunization, as part of a combined tetanus, diphtheria, and acellular pertussis (Tdap) vaccine. Maternal immunization protects the mother from acquiring the infection and prevents the risk of neonatal infection. It also offers protection via antibodies transfer from the mother to the fetus and therefore immunizes the infant during the first months of life. In Italy, pregnant woman's vaccination against pertussis is recommended by the Ministry of Health in the National Immunization Plan and the Italian Society of Gynecology and Obstetrics (SIGO). It is offered to all pregnant women free of charge. Due to its recent introduction in Italy, the percentage of pregnant women to whom the pertussis vaccine is offered and who are vaccinated with the pertussis vaccine is still negligible. In this context, a survey was carried out to record insights and expectations regarding maternal immunization against pertussis.

What is new?

The results show a good awareness and understanding of the risks of pertussis for infants and the protective role of maternal immunization. Survey respondents mostly would like to have safety information on the vaccine. Facebook was the most important source of information on maternal immunization, followed by YouTube. In this survey, mothers with more than one pregnancy are more confident on the role of pertussis maternal immunization in protecting the newborn as compared to women who are pregnant for the first time. Pregnant women who responded to the survey expect primarily their gynecologists to recommend maternal immunization, and to provide them with adequate information to answer their concerns regarding safety of the vaccine for the mother, the fetus and the newborn.

What is the impact?

This study points out the importance of the role of healthcare professionals as a trusted source of information for pertussis vaccination. Such information might be used to strengthen the pertussis vaccination rate among pregnant women and therefore prevent the pertussis risk during the sensitive periods of infancy and childhood.

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All authors participated in the interpretation of the study results and the development of this manuscript. All authors had full access to the data and gave final approval before submission.

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Introduction

Pertussis, a highly contagious infectious disease caused by *Bordetella pertussis* [1,2] is a widespread vaccine-preventable disease [3]. Concerns were recently expressed by public health experts on the resurgence of pertussis in Italy and a trend toward increasing hospitalization of infants [4–7]. Moreover, in Italy, pertussis is underdiagnosed and underreported, therefore the epidemiological burden of disease among young infants still needs to be identified [3,6,8,9]. An analysis of Italy's national hospital discharge data showed that more than half of hospitalizations are due to pertussis involving infants aged under 1 year [7]. The hospitalization rate for pertussis in this age group increased from 46.4% in 1999 to 66.9% in 2009 [7]. Moreover, in a case-series study in children aged under 3 months, hospitalized with respiratory symptoms at a children's hospital in Rome, one in four children was diagnosed with pertussis [8]. Paroxysmal cough, absence of fever, absolute lymphocyte count $>10,000$ n/mm³, apnea and symptom duration longer than 5d, were the clinical characteristics significantly associated with pertussis [8]. In the first phase of pertussis development, i.e. the catarrhal phase, symptoms are common to the symptoms of a common cold. When the disease progresses to the paroxysmal phase, symptoms of spasmodic coughing fits with subsequent whoops or emesis may last for up to 10 weeks. Pertussis symptoms in newborns are more serious [1] and can be fatal; in 2017, six deaths were reported in Italy involving children under 3 months of age admitted to tertiary pediatric centers; none of the mothers of the deceased had received pertussis vaccination before or during pregnancy [10].

Because neither natural- nor vaccine-induced protection against pertussis last long, booster vaccination is important throughout life [11]. Therefore, the National Immunization Plan 2017–2019 (NIP) of the Ministry of Health (MoH) declares that periodic vaccine boosters are required [12]. It is therefore important to provide the full pediatric schedule, of the primary vaccine doses series ending at 6 months of age and then proceed to the booster doses [3,5,13,14].

Pertussis in newborns who are too young to be vaccinated can be effectively prevented by maternal immunization (MI) during pregnancy with a combined reduced antigen content tetanus, diphtheria, and acellular pertussis (Tdap) vaccine [13]. As indicated by the World Health Organization (WHO) [13], and as shown in safety surveillance reports [15,16] and in available randomized controlled study results either including a very small sample size [17] or in a large phase IV study

enrolling more than 300 pregnant women in each study group [18], MI with Tdap has consistently proven to meet standards of safety and in routine use to be effective in protecting newborns who are especially vulnerable to develop serious illness [19–22]. MI, via transplacental antibody transfer from mother to the fetus [13,23], confers protection to newborns until they complete their primary vaccination and, it also protects the mother from acquiring the infection, and thus from seriously affecting herself and her child's health [13,22,23].

In 2017, Tdap free-of-charge vaccination of all pregnant women was introduced in the NIP [12] and it was recently recommended by the Italian Society of Gynecology and Obstetrics (SIGO) [24]. The optimum timing for Tdap MI is considered to fall between the 28th and the 32nd week of gestation [12]. Despite the current maternal pertussis vaccine recommendation, national vaccination coverage among pregnant women is still negligible [25,26]. Different barriers to achieving better MI rates have been identified, including demographic factors such as age, socioeconomic and education levels [25]. However, the main barriers identified, are concerns about vaccine safety during pregnancy for the mother, the fetus, and the newborn [26], lack of knowledge about disease severity, and lack of recommendation by healthcare providers (HCPs) [25,26].

In this context, the primary objective of this survey was to record insights and expectations regarding MI with Tdap in a sample of pregnant women in Italy. Secondary objectives included the documentation of demographic features of survey respondents, information on the level of knowledge regarding pertussis severity and Tdap MI, and the type, source, and timing of information pregnant women would require in order to accept MI.

Materials and methods

In May 2017, at the request of GSK, Italy, Datanalysis srl conducted a survey as market research. Datanalysis is a health research institute that, over the last 30 years, has developed an electronic database of patients and families. The database was searched using the keyword “pregnant women” to retrieve records of pregnant women up to the 28th week of gestation (because vaccination is recommended in the 28th–32nd week of pregnancy). Pregnant women identified by systematically searching the database for women on “pregnancy” status were contacted by telephone and were asked to participate in the survey.

The aim was to recruit at least 600 participants evenly distributed across Italy in the Macro areas defined by the Italian National Institute of Statistics (ISTAT).

Survey design

The interview schedule formulated for this survey included 16 questions. Seven questions could be answered by choosing one or more answers from a preset list, eight could be answered by “yes,” “no,” or “no response,” and one asked for the exact week of pregnancy. The questions covered the participants’ knowledge about the severity of pertussis and, in relation to Tdap MI recommendations, their information needs in deciding whether to undergo vaccination (content, preferred source, and timing). There were also questions on the sibling history of vaccination against pertussis, and the participants’ demographic information. The interviewers were trained in conducting telephonic interviews. Being a market research, no Ethics Committee approval was required.

Analysis

Statistics were descriptive. Data were analyzed for the whole country (Italy) and by ISTAT regions Northwest, Northeast, Central, and South & Islands. Frequencies, percentages, and mean scores with standard deviations (SD) were calculated for each question. Subgroup analyses by parity and by geographical region were also conducted. A chi-square test for homogeneity was applied to determine whether two or more subgroups shared the same distribution of a categorical response variable. Due to the nature of the survey, no control group was needed.

Results

Participants

Records of 850 pregnant women up to the 28th week were retrieved from the database. Of these, 600 women (150 from each of the four ISTAT regions) agreed to take part in the survey.

Half (52.8%) of the respondents were in the second trimester of their pregnancy, and for two-thirds (66.2%) this was not the first pregnancy. The average duration of pregnancy at the time of the interview was 20.85 weeks (SD 6.05). Two-thirds of the women (60.7%) were between 30 and 40 years of age, and secondary school was the most frequent educational level in three-quarters of the patients (lower and upper secondary school: 452/600, 75.3%).

Overall results for Italy

Table 1 shows that the majority of women who were not pregnant for the first time had got their children vaccinated against pertussis (85.9%). Slightly more than half of the respondents (54.5%) were aware of the pertussis risks for the newborn, the increased risk of hospitalization (59.8%), and 47.2% were aware that Tdap vaccination for pregnant women was offered free of charge by the NIP (Table 1). Two-thirds of the women (401/600, 66.8%) considered that Tdap MI was either “certainly necessary” or “useful” to protect the newborn. However, a quarter of the sample felt that Tdap MI might be useful, but even so, did not feel that they needed to be vaccinated.

Safety information regarding the mother and the newborn was considered the most important information in deciding whether to be vaccinated (47.4%), followed by safety information related only to the newborn (29.5%) when referred to the total answers (694) to this multiple-choice question; figures increased up to 54.8 and 34.2%, respectively when answers were considered for the number of respondents (600). Gynecologists were the preferred HCPs for the provision of MI information, followed by pediatricians, and local health unit staff (Table 1). Ideally, two-thirds of the respondents would wish to be informed about MI before getting pregnant (66.0%). Respondents most frequently used Facebook to retrieve information, followed by YouTube (Table 1).

About half of the respondents stated that they would “certainly” accept MI, and 25.3% would like to receive more information. However, 13.2% of women were opposed to MI for different reasons. 64.2% of the sample would feel more reassured if they knew that the Tdap vaccine available had been tested for this specific indication in clinical studies.

Number of pregnancies

Overall, the only relevant differences between the answers given by the women with previous pregnancies and those with their first pregnancy were for two questions (Figure 1). One question dealt with the respondents’ attitude toward MI based on the information they had received so far, and another question that was asking the respondents to indicate the most important points in convincing pregnant women to receive pertussis vaccination. More than half (58.4%) of the women with multiple pregnancies responded that MI was “certainly necessary” for the protection of the newborn. Half of the women in their first pregnancy (50.7%) felt that MI would be potentially useful

Table 1. Main results of the survey.

Answers to the survey questions	Respondents, number (%)
Vaccinated before pregnancy	532 (88.7%)
Vaccinated their children against pertussis	341 (85.9%)
Did not vaccinate their children against pertussis	36 (9.1%)
For what reasons did they not vaccinate their children?	
Vaccination was not mandatory	6 (14.3%) ^a
I do not consider pertussis a clinically relevant disease	9 (21.4%) ^a
I am against vaccines	26 (61.9%) ^a
No response	1 (2.4%) ^a
Aware of the risk of pertussis for the newborn	327 (54.5%)
Aware that pertussis involves high number of hospitalization amongst newborns	359 (59.8%)
Aware of MI for protecting newborn	315 (52.5%)
Aware of the free offer of Tdap vaccine during pregnancy	283 (47.2%)
In light of the information you received, MI is:	
Certainly necessary to protect the newborn	286 (47.7%)
Potentially useful for the newborn but not enough to justify MI	150 (25.0%)
Useful for protecting the newborn	115 (19.2%)
Certainly harmful to the newborn	24 (4.0%)
Possibly harmful to the newborn	12 (2.0%)
No response	13 (2.2%)
Information considered relevant	
Safety for the mother and the newborn	329 (47.4%) ^b
Safety for the newborn	205 (29.5%) ^c
Effectiveness in protecting the newborn	83 (12.0%)
Recommended by my gynecologist	35 (5.0%)
Recommended by the MoH	21 (3.0%)
Use in other countries	9 (1.3%)
No response	12 (1.7%)
Preferred HCP for MI consultation	
Gynecologist	206 (34.3%)
Pediatrician	153 (25.5%)
Local health unit staff	116 (19.3%)
Midwife	91 (15.2%)
Family doctor	11 (1.8%)
No response	23 (3.8%)
Optimum time to receive information on MI	
Before pregnancy	396 (66.0%)
In the first trimester	91 (15.2%)
In the second trimester	25 (4.2%)
In the third trimester	34 (5.7%)
No response	54 (9.0%)
Mothers' information sources	
Facebook	205 (34.2%)
YouTube	158 (26.3%)
Specialist health magazines	90 (15.0%)
Newspapers	49 (8.2%)
Radio	17 (2.8%)
Television	41 (6.8%)
No response	29 (4.8%)
Other	11 (1.8%)
Feels secure and relieved knowing that the vaccine has undergone clinical testing and is authorized for this specific indication	385 (64.2%)
Willing to accept MI	
Yes, certainly	313 (52.2%)
Yes, but I would like to have more information	152 (25.3%)
Yes, but I would like to have the advice of a doctor	56 (9.3%)
No, because I'm against vaccines	25 (4.2%)
No, because it is not a mandatory vaccine	7 (1.2%)
No response	47 (7.8%)

^aPercentage of the 42 total responses given by the women who had not had their children vaccinated.

^b54.8% when the cumulative answers were considered for the number of respondents (600).

^c34.2% when the cumulative answers were considered for the number of respondents (600).

HCP: healthcare provider; MI: maternal immunization; MoH: Ministry of Health; Tdap: diphtheria and acellular pertussis (vaccine).

for protecting newborns, but they were not convinced that MI should be done. Providing information on safety issues related to the newborn scored higher amongst the women with multiple pregnancies (32.8%) than amongst those with their first pregnancy (22.6%).

Regional variation

No important differences between the four ISTAT regions were observed and similarly, none were seen between the group of regions with previous regional MI recommendations and those without previous regional Tdap MI recommendation.

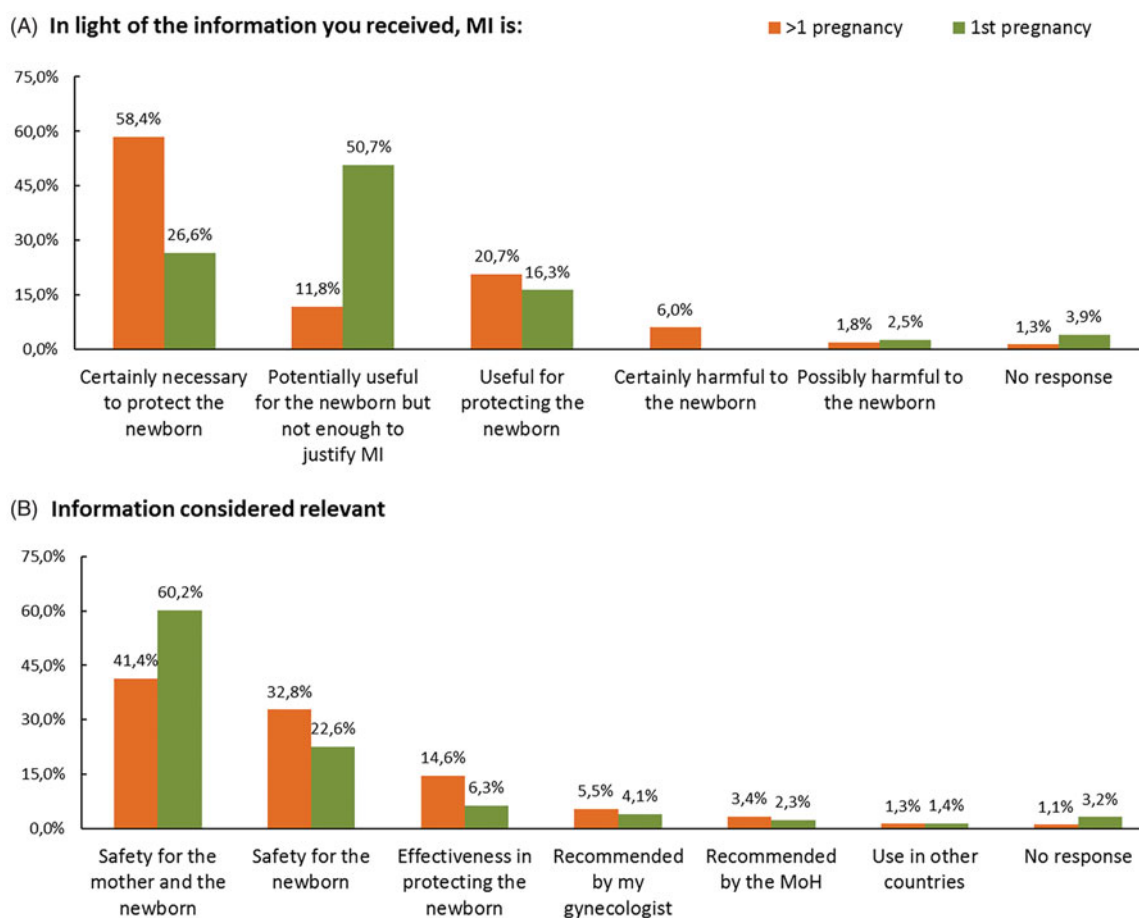


Figure 1. Responses related to MI information; (A) received so far, and (B) considered relevant. MI: maternal immunization; MoH: Ministry of Health.

Discussion

This survey was conducted across Italy with pregnant women to understand their state of knowledge about pertussis and their expectations regarding Tdap MI. The results show good awareness and understanding of the risks of pertussis for newborns and the protective role of MI.

Information type

The most important type of information the survey respondents would like to have is safety information on the vaccine, a finding in agreement with several previous studies in Italy [27–29] and elsewhere [26,30]. A study [27] investigating the type of information that pregnant Italian women searched for on the Internet between 2017 and 2018, showed that they were mainly concerned about safety issues with vaccines for themselves and their babies [27]. A survey [29] conducted in 2015 on 347 pregnant and postpartum women in Italy, showed that more than half of the women did not know that Tdap MI protected newborns. Three-quarters of the survey population did not

have Tdap vaccination because “nobody had recommended it” [29]. Unlike that study, the present survey showed that 52.5% of the respondents knew that MI Tdap protected the newborns from pertussis. This difference shows how much progress has been made since 2015 and after the 2017 NIP recommendation for *de novo* Tdap MI vaccination during each pregnancy [29]. However, what was evident in both surveys was the need to educate women about the safety profile of the vaccines administered for MI. In the 2015 survey [29], 28% of the women noted that they were “scared of side effects for both the mother and the fetus” and believed that “a vaccine was not safe”; in the present survey only few women shared the same opinion: 6% believed that MI was “certainly” or “possibly” harmful to the newborn. Women should, therefore, be offered comprehensive safety information. It can be worth noting that most of the safety data available were generated during vaccines’ routine use and thus based on passive surveillance. Only one Tdap vaccine was accompanied by prospectively collected safety data on more than 1000 pregnant women enrolled in clinical trials [18,31]. As stated by

SIGO [24], vaccine datasheets, further to MI educational materials and leaflets, may play a role in communicating information to pregnant women provided they include robust clinical data on MI.

Information sources

For nearly one-third of the survey respondents, Facebook was the most prominent source of information on MI, followed by YouTube. Previous studies [32–37] have also reported the use of social networking and social media as an easily and quickly accessible information resource for pregnant women [34]. However, a cross-sectional study conducted in 2017 in the UK, showed that women who used social networking sites to retrieve information on MI were less likely to receive Tdap vaccination during pregnancy [38]. Evidently, the Internet could be a valuable tool for disseminating scientific health information and for promoting immunization campaigns [38,39] but careful attention should be made when referring pregnant women to web sources. In a Belgian survey [26] including 250 pregnant women, the two main reasons for receiving Tdap MI were the recommendation by an obstetrician (33.2%) and the baby's safety (30.8%). In the same survey, lack of recommendation was the primary reason (12.0%) for not receiving Tdap MI [26].

Number of pregnancies

In this survey, mothers with more than one pregnancy were more confident about the role of Tdap MI in protecting the newborn. They were also more interested in receiving information on safety issues related to newborns, whereas women in their first pregnancy were more interested in receiving safety information related to both themselves and the newborn. An Australian survey on vaccine hesitancy amongst women attending antenatal clinics showed that first-time mothers were three times more likely to feel unsure and hesitant; a significantly higher percentage of first-time mothers had not made a decision up to the end of the second (35.5 versus 5.8%, $p = .0015$) and third trimester (14.9 versus 4.4%, $p = .0086$) compared with experienced mothers [40]. These findings indicate a need for more comprehensive counseling in the first pregnancy.

Strengths and limitations

The country-wide distribution of the survey respondents and the size of the sample significantly strengthen the

findings as does the choice of using telephone interviews by trained interviewers instead of using a web-based platform. Furthermore, this survey explored aspects of women's insights into MI which had not previously been assessed, such as the vaccination history of previous children, awareness of the disease epidemiological profile, and optimum time for consultation.

The main limitations of this survey were the use of a convenient sample and the absence of a control group. The use of a nonvalidated questionnaire might be viewed as a further limitation, although we consider the questionnaire adequate to fulfill the aims of the study. Some questions included a preset list of answers which might have introduced bias; the possibility of free wording in replying was given, however, although none of the women selected this choice. A further possible limitation might be enrolling only pregnant women up to the 28th week of gestation, thus excluding information from late-term pregnant women; however, from the survey, it turned out that most respondents wanted to be informed about MI before the start of their pregnancy.

Conclusions

In this sample of pregnant Italian women, one in two were aware of the risk of pertussis in newborns and expressed a positive attitude toward Tdap vaccination in pregnancy. However, the women expect HCPs, and primarily their gynecologist, to recommend MI, and to provide them with adequate information to respond to women's concerns regarding the safety of the vaccine for the mother, the fetus, and the newborn, and by referring them to vaccination centers. Future research in the field should explore further Tdap vaccine safety perceptions and associated concerns of pregnant women to increase acceptance of MI and further reduce the severe burden of pertussis in newborns.

Acknowledgments

The authors would like to thank Ivano Leonardi (Dataanalysis, Rome, Italy) for data collection and Business & Decision Life Sciences platform for editorial assistance and manuscript coordination, on behalf of GSK. Lyes Derouiche coordinated the manuscript development and editorial support, and Athanasia Benekou provided medical writing support.

Author contribution

All authors participated in the interpretation of the study results and the development of this manuscript. All authors had full access to the data and gave final approval before submission.

Disclosure statement

FM is an employee of the GSK group of companies. LMV declares to have received consulting fees outside of this work from the GSK group of companies. IC declares no conflicts of interest.

Funding

GlaxoSmithKline Biologicals SA funded this study and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also covered all costs associated with the development and publication of this manuscript.

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