

SPECIAL ARTICLE

Personal and parental acceptance of human papillomavirus vaccination prior to and during the economic crisis among women in Greece

Vagia Siamanta¹, Kimon Chatzistamatiou², Dimitrios Vavilis³, Evangelia Nena⁴, Ekaterini Chatzaki⁵, Theodoros C. Constantinidis⁶, Anastasia Kitsou⁷, Athena Tsertanidou⁸, Alexandros F. Lampropoulos⁹, Theodoros Agorastos¹⁰

¹4th Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Hippokratio General Hospital, Thessaloniki, Greece; ²1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Papageorgiou Hospital, Thessaloniki, Greece; ³1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Papageorgiou General Hospital, Thessaloniki, Greece; ⁴Laboratory of Hygiene and Environmental Protection, Medical School, Democritus University of Thrace, Alexandroupolis, Greece; ⁵Laboratory of Pharmacology, Medical School, Democritus University of Thrace, Alexandroupolis, Greece; ⁶Laboratory of Hygiene and Environmental Protection, Medical School, Democritus University of Thrace, Alexandroupolis, Greece; ⁷4th Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Hippokratio General Hospital, Thessaloniki, Greece; ⁸4th Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Hippokratio General Hospital, Thessaloniki, Greece; ⁹1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Papageorgiou General Hospital, Thessaloniki, Greece; ¹⁰4th Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Hippokratio General Hospital, Thessaloniki, Greece

Summary

Purpose: To assess personal and parental human papillomavirus (HPV) vaccination acceptance and how it is influenced by demographic factors prior to (2005-2010) and during (2011-2016) the economic crisis in Greece.

Methods: During 2005-2016, 6,401 women aged 18-65 years, living in different areas of Greece filled in a questionnaire covering demographic characteristics, knowledge of HPV infection's natural history and its consequences and assessing their intention to receive the HPV vaccine for themselves and their children.

Results: Women's intention to get vaccinated before the economic crisis was higher (86.2%) than during it (82.8%). In addition, the intention of women to vaccinate their children was higher for girls during 2005-2010 (78.3%), while there

was no statistically significant difference concerning boys. HPV vaccination acceptance per year showed a statistically significant variation. The initially high acceptance decreased following vaccine's release, mainly due to fear of side effects, increased following objective public education, and declined again. Demographic characteristics affected HPV vaccination acceptance at the time period before the economic crisis in Greece, but not during it.

Conclusion: Demographic factors affecting a woman's attitude towards vaccination prior to the economic crisis in Greece, stopped playing a significant role during the crisis, reflecting its devastating effect on most parts of the population.

Key words: demographic factors, economic disparities, economic Greek crisis, HPV vaccination acceptance

Introduction

Cervical cancer is the fourth most common cancer and the third most common cause of cancer death among women worldwide [1]. Currently, it is fully accepted that the cause of cervical cancer is

the persistent genital infection with HPV [2]. The HPV infection, however, is considered to be a necessary, but not sufficient cause for the development of cancer [3,4].

Correspondence to: Kimon Chatzistamatiou, MD, PhD. 1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Papageorgiou Hospital, Thessaloniki, Greece.
Tel: +30 6973321162, Fax: +30 2310892140, E-mail: kimon.chatzistamatiou@gmail.com
Received: 02/07/2018; Accepted: 30/07/2018

The etiological association between HPV and cervical cancer has been the basis towards research for the development of HPV vaccines [5]. In 2008, two HPV vaccines were released gradually in more than 110 countries worldwide: the bivalent vaccine against HPV types 16 and 18 and the quadrivalent vaccine against types 16, 18, 6 and 11 [6]. Recently, a nonavalent HPV vaccine (9vHPV) was released against types 6, 11, 16, 18, 31, 33, 45, 52 and 58 [7,8].

Since licensure, most countries have been providing the HPV vaccine free of charge; however, its acceptance is still less than expected. The highest coverage rate is noted in Australia (83% for at least one dose). Furthermore, England and Portugal present high population coverage rates (90% and 81% respectively), while the lowest rates are seen in Luxembourg (17%) and France (24%) [9].

In Greece, the vaccine became available in 2007 and was included in the National Vaccination Program in 2008. From 2005 to 2011, we conducted the "LYSISTRATA" study, a nationwide project aiming to assess HPV infection prevalence, public awareness of HPV vaccination and screening, as well as the knowledge of Greek women on primary and secondary prevention of cervical cancer. From 2011 the study questionnaire has been available online to Greek women [6].

Since 2010 an economic crisis affected Greece and resulted in extremely unpleasant consequences, from an economic and psychological point of view, for the Greek population. Many facts and parameters of the daily life have been affected. The objective of this study was to investigate HPV vaccination acceptance by Greek women for both, themselves and their alleged 13-year old daughter or son, as well as to investigate the parameters affecting the acceptance during the two distinct periods of the past decade, namely the period prior to the financial crisis (2005-2010) and after the onset of the crisis (2011-2016). The fact that this study began 5 years before the onset of the economic crisis in Greece and continued until 2016 was a sufficient condition to investigate possible consequences on primary cervical cancer prevention in Greece.

Methods

Study setting and participants

The present analysis utilized data on vaccination acceptance from the "LYSISTRATA" project, conducted between 2005 - 2011, aiming to assess the knowledge, views and habits of women regarding cervical cancer prevention, as well as data derived from the study questionnaire, which had been available online at www.hpv-society.gr, the Hellenic HPV Society website, from 2011 to 2016. It should be noted that the HPV vaccine was

released in Greece in 2007, thus the first Greek women who were enrolled in the study during 2005-2007 replied on a hypothetical basis concerning HPV vaccination acceptance.

Inclusion criteria had been female sex, age 18-65 years, Greek as main language and permanent residence in Greece. Women were enrolled in the study after providing their written informed consent when they visited healthcare provision settings for the routine Pap test or during various awareness campaigns across the country regarding HPV and cervical cancer prevention and then anonymously filled in the questionnaire, and were subsequently sampled for HPV DNA testing.

Study design

During the first years of the study, from January 2005 to December 2010, women were invited by announcements made on local printed and electronic media to visit local healthcare provision units, where cervical smear was obtained by healthcare professionals for HPV DNA testing and genotyping. Each woman also filled in the study questionnaire. The following years, until December 2016 the questionnaire had been accessed online.

Study questionnaire

Each participating woman filled in the study questionnaire which consisted of questions grouped into sections relating to the following: demographics, knowledge of cervical cancer natural history and current prevention methods, the woman's participation in these methods, her knowledge of HPV infection and its importance in the occurrence of cervical cancer, and the acceptance of HPV vaccination for herself and her children. Demographic data included age, educational level, profession, spouse's profession, marital status, size of residence area, monthly family income as well as lifestyle parameters such as smoking, oral contraceptives use, and frequency of visits to the gynecologist.

Statistics

This survey aimed to investigate: 1) HPV vaccination acceptance for oneself, for the daughter or the son, in the decade 2005-2016 as well as the comparison of the acceptance rates for the periods prior to (2005-2010) and during (2011-2016) the economic crisis, and, 2) the effects of the demographic factors on HPV vaccination acceptance during the abovementioned periods.

Descriptive statistical methods were used. At first, a normality test was performed for all the parameters by means of Kolmogorov-Smirnov analysis and parametric and non-parametric methods were employed accordingly. Values are referred as mean value \pm standard deviation, unless there is any special reference. For the comparison of mean values between subgroups, the Student's t-test or ANOVA were used depending on the subgroup size, whereas for the comparison between rates the chi-square test was employed. The value of statistical significance was set at $p < 0.05$.

Concerning possible associations between sample demographics and HPV vaccination acceptance, a

comparison was made between the latter for women themselves as well as for their children by means of a list of demographic factors, namely, age (<25 vs. 25-45 vs. >45), residence area (rural vs. semirural vs. urban), educational level (elementary school vs. high school vs. higher education), marital status (single vs. married vs. widowed vs. divorced) and profession (unemployed vs. employed), and a basic model was developed to assess each factor individually as well as the relation thereof to HPV vaccination acceptance.

A second analysis concerned women who expressed a negative attitude to HPV vaccine and the main reasons for refusal (inadequate information on HPV and the vaccine vs fears of possible side effects due to vaccination vs other reasons). In an effort to observe the possible change of the women's attitude over time a further analysis was conducted on the effect of demographic factors on the decision of a Greek woman to receive a HPV vaccine and on the main reasons for non-acceptance of vaccination concerning two time periods, 2005-2010 and 2011-2016, namely the years prior to and during the Greek economic crisis. Statistical analysis was performed with IBM SPSS v17.0.

Results

Demographics

Sample demographics are presented in Table 1. In total 6,401 women were enrolled, 15% being <25 years old, 56% between 25 and 45 and 29% above 45 years old. Concerning place of residence, most of the women reported residing in semi-rural or urban areas. Furthermore, more than 80% of the participants reported having attended at least high-school. Just less than half of the participants were married and concerning employment 38% of them reported not having a job.

Vaccination acceptance

Overall acceptance of vaccination for women enrolled in the study was 85.7% (5,166/6,401). Figure 1 shows the variation of HPV vaccination acceptance during the last decade. There is a statistically significant difference between the years ($p<0.001$). The highest rate of vaccination acceptance for the women themselves was observed in 2008 (91.5%) and the lowest in 2010 (69.8%). Comparison of time periods prior to (2005-2010) and during (2011-2016) the economic crisis revealed statistically significant difference ($p=0.009$). The overall acceptance of individual HPV vaccination during the economic crisis reached 82.8% with a statistically significant differentiation from the previous period, during which the respective rate was 86.2% (Figure 2).

Overall vaccination acceptance for the woman's daughter reached 78.3% (4,592/6,401). There

Table 1. Demographic characteristics of the study population

Characteristics	n=6,401 n (%)
Age group, years	
<25	958 (15)
25-45	3587 (56)
>45	1856 (29)
Place of residence	
Rural	1288 (20.1)
Semirural	2745(42.9)
Urban	2094(32.7)
Educational level	
Elementary school	810 (12.6)
High school	2766 (43.2)
Higher education	2630 (41.1)
Marital status	
Single	1645 (25.7)
Married	2991 (46.7)
Widowed	75 (0.2)
Divorced	237 (3.7)
Employment status	
Unemployed	2483 (38.8)
Employed	3668 (57.3)
Year of recruitment	
2005	474 (7.4)
2006	1304 (20.4)
2007	1012 (15.8)
2008	1280 (20.0)
2009	808 (12.6)
2010	501 (7.8)
2012	237 (3.7)
2013	199 (3.1)
2014	204 (3.2)
2015	102 (1.6)
2016	280 (4.4)

was a statistically significant difference in the variation of this parameter over the years ($p<0.001$). The highest acceptance rate was noted in 2015 (85.9%), whereas the lowest in 2010 (61.5%) (Figure 1). Comparison of time periods prior to (2005-2010) and during (2011-2016) the economic crisis in Greece did not reveal statistically significant difference (Figure 2).

The overall HPV vaccination acceptance for the son during the decade 2005-2016 was 77.4% (4,419/6,401), and the variation presented statistically significant changes during the study period ($p<0.001$). The highest acceptance rate of HPV vaccination for the son was documented in 2015 (84.4%), whereas the lowest (60.1%) was observed in 2010 (Figure 1). Comparison of time periods

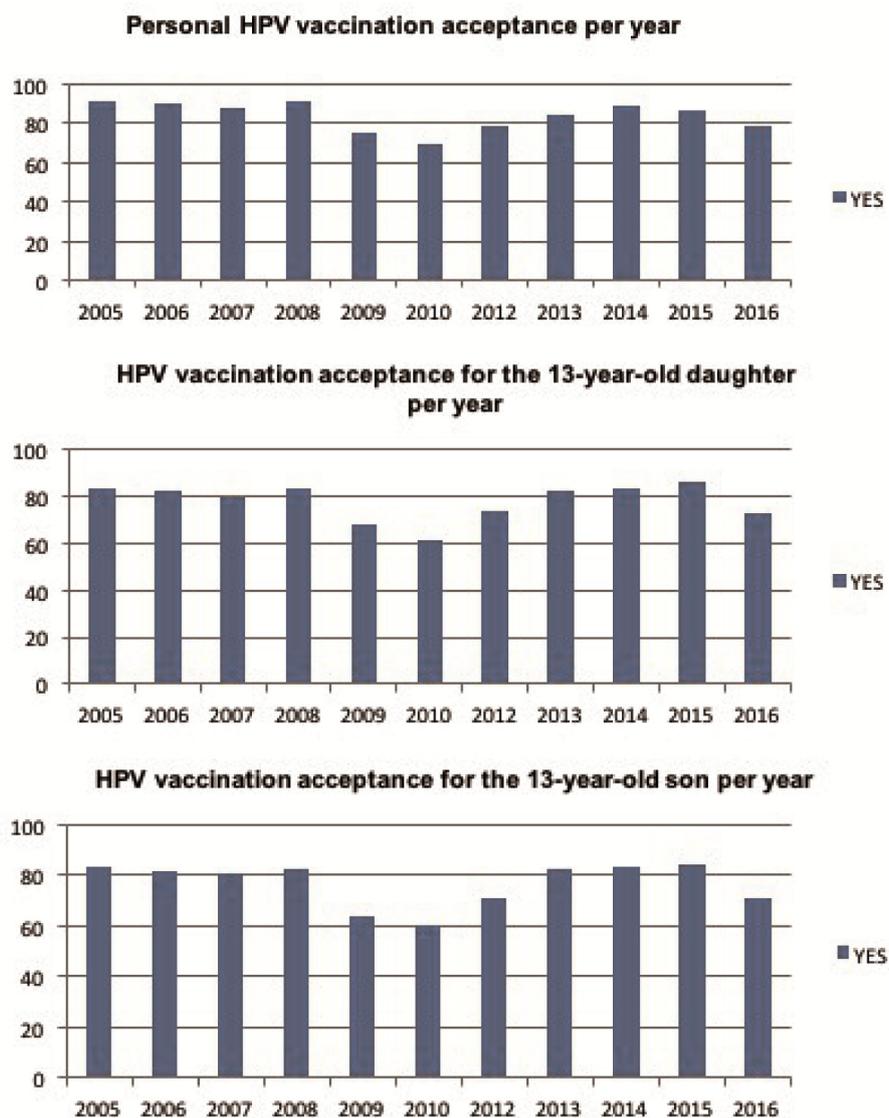


Figure 1. Personal HPV vaccination acceptance and HPV vaccination acceptance for the 13-year old daughter or son during the years of the study.

prior to (2005-2010) and during (2011-2016) the economic crisis in Greece did not reveal statistically significant differences (Figure 2).

Age

The participants were divided into three groups: women <25 years old, 25-45 years old and >45 years old. The age group significantly influenced her decision to be vaccinated against HPV ($p=0.002$). Specifically, women aged 25-45 presented the highest acceptance rate (87.3%), followed by women below 25 years old (84.9%) and women aged more than 45 (83.5%). Concerning the comparison between the time periods prior to and during the economic crisis, it was shown that in the years 2005-2010 the age affected the decision of a woman to be vaccinated against HPV ($p=0.001$) and, in detail, women aged between 25 and 45 presented

higher acceptance for vaccination (87.7%) followed by younger women (<25 years old) (85.3%). The lowest acceptance rate was observed in women of older than 45 (83.3%). The opposite was noted in the period 2011-2016, when age did not seem to affect the decision of a woman to be vaccinated (Table 2).

Regarding HPV vaccination acceptance for the daughter, it was shown that age statistically significantly influenced the woman's attitude ($p=0.01$). Women aged between 25 and 45 were more positive (79.8%), followed by women older than 45 years (77.2%) and women younger than 25 years (75.1%). In the period preceding the economic crisis in Greece, age still affected the decision of a woman to vaccinate her daughter ($p=0.018$). The highest acceptance rate of HPV vaccination for daughters was observed in women aged between

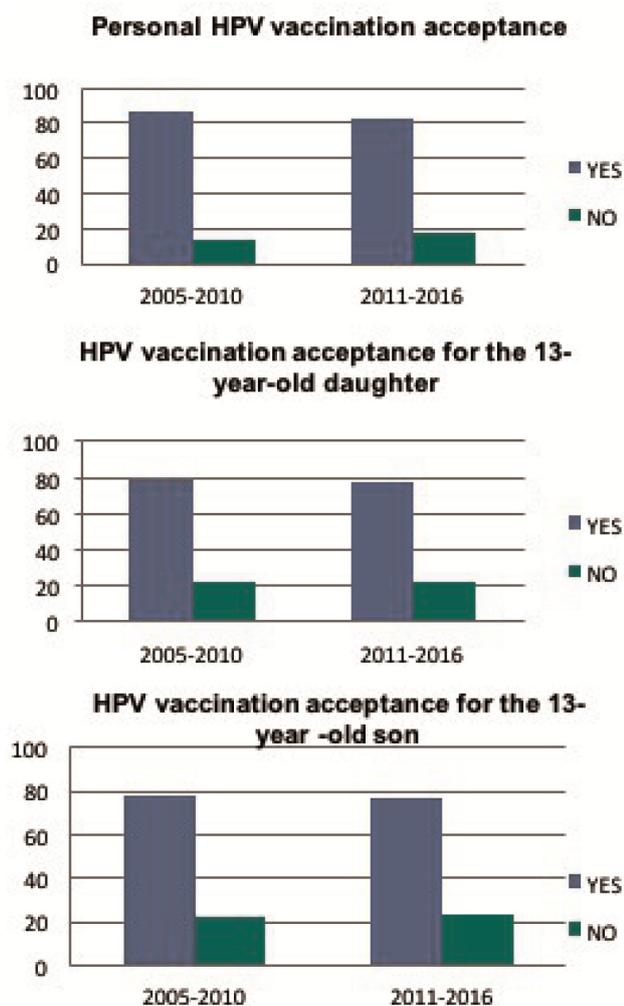


Figure 2. Comparison of personal HPV vaccination acceptance and HPV vaccination acceptance for the 13-year-old daughter or son prior to and during the economic crisis in Greece.

25 and 45 (79.7%), while the lowest in women aged <25 (75.3%). On the contrary, no correlation of age with the acceptance of HPV vaccination for the daughter was noted during the economic crisis in Greece, namely the period 2011-2016 (Table 3).

In relation to HPV vaccination acceptance for the son, the mother's age did not play a significant role during the two time periods investigated, 2005-2010 ($p=0.09$) and 2011-2016 (Table 4).

Place of residence

The women participating in the study were divided into three groups based on their place of residence: 1) women living in villages, 2) women living in towns 3) women living in large cities.

The analysis showed that the place of residence affected the decision of a woman to be vaccinated against HPV ($p=0.000$). Specifically, women living in villages were more willing to be vaccinated (88.2%), followed by women living in provincial

cities/towns (87%) and women living in large cities of Greece (82.4%). During the period 2005-2010 the place of residence affected the decision of a woman to be vaccinated ($p=0.000$). Women living in villages were more positive (88.3%), followed by those living in provincial cities/towns (87.3%) and in large cities (83%). On the contrary, during the economic crisis, the place of residence did not appear to affect the decision of a woman to be vaccinated (Table 2).

The decision of a woman to vaccinate her alleged under-aged children was affected by the place of residence ($p=0.001$ for the daughter and $p=0.000$ for the son). In detail, women living in villages were more willing to vaccinate their children (81.8% for daughter and 82% for son) compared with those living in provincial cities/towns (78.2% for daughter and 77.3% for son) and those living in large cities (76.2% for daughter and 75.1% for son). The same trend was observed in the analysis of the years 2005-2010 ($p=0.000$). During that period women residing in villages were more positive towards HPV vaccination for their children (82.5%), followed by those residing in provincial cities/towns (77.7% for daughter and 77% for son) and those residing in large Greek cities (76% for daughter and 74.9% for son). No correlation of the residence area with the acceptance of vaccination was noted in the following years (Tables 3 and 4).

Marital status

The women of the sample were divided in four groups: 1) single, 2) married, 3) widows and 4) divorced.

The marital status did not have an impact on the acceptance of personal HPV vaccination neither in the overall analysis ($p=0.057$) nor in the analysis of the period 2011-2016 ($p=0.467$). However, there was a significant correlation during the period 2005-2010 ($p=0.009$) and, particularly, the highest acceptance of the vaccine was observed for single women (87%), followed by married women (83.7%), divorced women (80.9%), and widows (76.1%) (Table 2).

Concerning HPV vaccination acceptance for the daughter and son, it was shown that marital status did not play a significant role either for the whole sample or for each one of the time periods investigated (Tables 3 and 4).

Educational level

The women enrolled in the study were divided into three groups according to their educational level. The first group consisted of women who attended only primary school, the second included

Table 2. Association of demographic characteristics of women with personal HPV vaccination acceptance

<i>Parameters</i>	<i>Total</i>	<i>Before the economic crisis</i>	<i>During the economic crisis</i>
Age group, years			
<25	84.9	85.3	75
25-45	87.3	87.7	83.8
>45	83.5	83.3	90.9
	p=0.002	p=0.001	p=0.276
Place of residence			
Rural	88.2	88.3	86.8
Semirural	87	87.3	85
Urban	82.4	83	80.5
	p=0.000	p=0.000	p=0.173
Educational level			
Elementary school	86	86.1	81.8
High school	84.3	84.6	80.6
Higher education	86.6	87.7	83.4
	p=0.000	p=0.017	p=0.645
Marital status			
Single	85.9	87	83.2
Married	83.4	83.7	81.3
Widowed	77.1	76.1	100
Divorced	82.5	80.9	100
	p=0.057	p=0.009	p=0.467

Table 3. Association of demographic characteristics of women participating in the study with HPV vaccination acceptance for their alleged 13-year-old daughter

<i>Parameters</i>	<i>Total</i>	<i>Before the economic crisis (2005-2010)</i>	<i>During the economic crisis (2012-2016)</i>
Age group, years			
<25	75.1	75.3	71.9
25-45	79.8	79.7	80.5
>45	77.2	77.1	81.5
	p=0.01	p=0.018	p=0.498
Place of residence			
Rural	81.8	82.5	71.4
Semirural	78.2	77.7	80.7
Urban	76.2	76	77.1
	p=0.001	p=0.000	p=0.177
Educational level			
Elementary school	81.3	80.8	90
High school	75.1	75.7	71.7
Higher education	80	80	79.8
	p=0.001	p=0.001	p=0.03
Marital status			
Single	78	78	77.8
Married	76.7	76.7	76.6
Widowed	72.3	72.6	66.7
Divorced	75.7	71.3	94.9
	p=0.577	p=0.22	p=0.068

Table 4. Association of demographic characteristics of women participating in the study with HPV vaccination acceptance for their alleged 13-year old son

Parameters	Total	Before the economic crisis	During the economic crisis
Age group, years			
<25	74,9	74,9	74,2
25-45	78,6	78,5	79,5
>45	76,7	76,6	83,3
	p=0.065	p=0.09	p=0.692
Place of residence			
Rural	82	82,5	73,9
Semiural	77,3	77	32,7
Urban	75,1	74,9	38,4
	p=0.000	p=0.000	p=0.386
Educational level			
Elementary school	83	81	100
High school	73,9	74,6	69,2
Higher education	79,2	79,2	79
	p=0.000	p=0.000	p=0.004
Marital status			
Single	77,8	77,9	77,4
Married	75,6	75,7	75,1
Widowed	73,1	73,4	66,7
Divorced	74,5	71	89,2
	p=0.355	p=0.201	p=0.255

those who were senior high school graduates and the third group those who received tertiary education.

The educational level seemed to have an impact on the decision of a woman both overall ($p=0.000$) and during the period 2005-2010 ($p=0.017$). In the analysis of the whole sample it was found that women with tertiary education had a more positive attitude towards HPV vaccination, presenting an acceptance rate of 86.6%. The corresponding rate for the period 2005-2010 was 87.7%. Acceptance rates for women who were senior high school graduates were 84.3% and 84.6% for the two above-mentioned instances respectively. No correlation between the educational level and the acceptance of individual HPV vaccination was observed for the period 2011-2016 ($p=0.645$) (Table 2).

Educational level affected the decision on vaccination of the alleged children in both periods prior to ($p=0.001$ for daughter and $p=0.000$ for son) and during the economic crisis ($p=0.03$ for daughter and $p=0.004$ for son). The highest acceptance rates were presented for women with elementary educational level (80.8% for the daughter and 81% for the son, between the years 2005-2010 and 90% for the daughter and 100% for the son between the

years 2011-2016). Women with tertiary education presented rates of 80% and 79.8% for both time periods for daughters (79.2%) and for sons (79%) respectively. The most negative attitude was shown by women with secondary education with the corresponding rates being 75.7% for daughters and 74.6% for sons between 2005 and 2010 and 71.7% for daughters and 69.2% for sons between 2011 and 2016 (Tables 3 and 4).

Discussion

According to our findings, overall vaccination acceptance for women themselves was 85.7%, for their minor daughters 78.3% and for their minor sons the corresponding rate reached 77.4%. These rates are in line with the main LYSISTRATA study conducted until 2011 [10], however, acceptance of personal vaccination was higher (86.2) in the latter and this decline could be attributed to the Greek economic crisis and the loss of health insurance. Furthermore, concerning real HPV vaccination coverage in Greece results from a study conducted on Greek students showed that only 25.8% had actually been vaccinated with all three doses [11]. This rate was 8.9% for Greek girls (11 to 14) according to

a study conducted between 2008 and 2014 [12]. The low rates of vaccination coverage in Greece are attributed mainly to the lack of a national organized vaccination school-based campaign. This vaccination system has been successful in Australia, where in 2007 the government provided the quadrivalent vaccine to schools initially for girls aged between 12 and 18 and, then, in 2013 for boys aged 12 and 13 too. As a result, an 83% vaccination coverage for girls (one dose at least) and above 70% (three doses) was achieved [13]. The school-based approach for HPV vaccination has been successful in other countries as well, such as Spain, Scotland (81%) and England (76%) [14]. In Greece, HPV vaccination initially was offered to the female population aged 11 to 26 but recently the upper limit declined to 18. Concerning male population, vaccination has been scheduled only for men who have sex with men (MSM).

The willingness of women to vaccinate themselves and their minors was immense before the vaccine's release and its incorporation in the National Vaccination Program. Despite this, personal and parental acceptance of HPV vaccination has fallen significantly after the vaccine's release with the lowest acceptance rates being noted in 2010. The sharp drop in vaccination acceptance coincided with the increase in women's concern regarding side-effects of the vaccine despite the fact that there were numerous data confirming its safety and efficacy [15,16]. The importance of the media on that has been shown by a previous study conducted by our group, which found that 35.1% of Greek women are informed about medical topics by the media [5,10]. Therefore, the main reason for this decline seemed to be the negative publicity for the vaccine and the alleged side effects by media [17-20].

From 2012 onwards, there has been a new increase in the acceptance of vaccination for the women themselves and their minors and again a decrease in the last two years of the study. The initially increased acceptance could be attributed to the more substantiated information from doctors and other health professionals on matters pertaining to the vaccine as well as to the fact that the media stopped reporting and debating on possible side effects of the vaccine, enabling the public opinion to decide on a more objective basis. The doctor's opinion is crucial to whether a mother will reach a positive decision on HPV vaccination. It has been reported that 60% of mothers who did not want to vaccinate their daughters stated that they had not received any recommendation from their doctor to be vaccinated [21,22]. Moreover, medical students informed by the media showed lower acceptance

rates for the vaccine in relation to those informed by their doctor [23].

The decline in the acceptance of the vaccine over the last two years could be attributed to the economic crisis in Greece. A large part of the population is now without any insurance and does not have access to state-provided health care. It has been shown that, due to economic difficulties, the access to medical care declined and the health of the population deteriorated [24].

The main reasons for refusing both personal vaccination and vaccination for minors have shifted significantly between the two time periods, prior to and during the economic crisis. During the former period, the main reason for refusal of vaccination was lack of information. During the economic crisis however, it seems that insufficient information has been replaced by the fear of possible side effects of the vaccine.

In the presented study, women aged 25-45 years were more willing to be vaccinated and to accept vaccination for their daughters (not for their sons), compared to women of other age groups. Previous studies revealed similar conclusions. Higher acceptance was observed in women younger than 30, 40 or 45 years old [6]. The same conclusions were drawn from the analysis of the period 2005-2010, during which age affected the decision on personal vaccination and vaccination for daughters. Young Greek women were less willing to vaccinate their children in relation to the 25-45 year-old ones, possibly because, for younger ages, the question had been hypothetical, since most participants did not have any children. The analysis of data during the economic crisis has shown that age did not affect a woman's decision to have herself or her daughter vaccinated. The necessity of covering basic needs for the families, along with the requirement to pay for the vaccine in case of insurance coverage loss could be a reason why women no longer gave priority to vaccinating their children. This has been shown in the USA too, in a study documenting the association of social insurance with acceptance of vaccination. In particular, vaccination acceptance rates were lower in women without any health insurance compared to those who were insured [25,26]. The analysis of vaccination acceptance for under-aged boys showed that there was no correlation of mother's age with it. One more reason for this observation is that many women have not associated HPV with men and believe that it only concerns women. They also think that their children will never get sick and, therefore, do not need to be vaccinated. A study showed that educational and informational sessions about the virus for parents and teenage boys was the most

effective way for under-aged boys to proceed to vaccination [27].

Women living in rural areas held a more positive attitude towards vaccination for themselves and their children and the same was noted in the years before the economic crisis. Moreover, women residing in provincial cities and towns in Greece appeared to be more willing than those living in large cities. No statistical significance was noted between the place of residence and vaccination acceptance during the period of economic crisis. The results contradict other studies, in which women residing in rural areas were less willing to be vaccinated and had lower vaccination coverage [28,29]. These studies observed that vaccine acceptance was higher in areas where there was more information provided by and greater willingness of doctors, accompanied by the corresponding informational material. In our study, the results could be attributed to the fact that women living in provincial areas are informed more frequently by their doctor and not by social media and also have easier and more direct access to the doctor than women living in large cities.

Marital status did not affect a woman's decision to have herself or her children vaccinated. The only effect of marital status on acceptance was found during the period 2005-2010, where single women were more positive towards personal vaccination. Married women accept the vaccine at a lower rate, as they believe that they have sexual stability and are not at risk of being infected by the virus.

As strengths of the presented study one can note that there was a relatively large number of participants who were personally contacted and answered the questionnaire, as well as the fact that they represented, more or less, the general female population in Greece, because the majority of them were residing in equal proportions in villages, country towns and large cities across the country. Opposite to that, the facts that the interpretation of answers during the years 2011-2016, i.e. during the economic crisis in Greece, is based on an electronic form of the questionnaire and that

women answering electronically were markedly less than the ones involved in the first period of the study (2005-2010), represent the main limitations of our study.

Conclusion

As a conclusion, the acceptance of HPV vaccination per year of study, presented a statistically significant variation during the decade 2005-2016, and the main reasons for refusal of vaccination were lack of information and fear of possible vaccine-related side effects, according to the women's belief. The personal and parental acceptance of HPV vaccination that was initially high, started to decrease following its release, mainly due to fear of side effects, rose after media stopped debating on side effects and women were more objectively informed by doctors, and declined again presumably in the context of a general public health deterioration due to the economic crisis. The demographic factors affecting a woman's attitude towards vaccination prior to the economic crisis in Greece, in general, stopped playing a significant role during the crisis, reflecting the devastating effect of it to most parts of the population.

Acknowledgements

The authors thank all the medical, paramedical, and technical personnel who voluntarily contributed to the realization of this study. The study was carried out under the auspice of the Hellenic Ministry of Health and Social Solidarity (GMN DYG5/au 93880/08.09.2005), the Hellenic Ministry of Macedonia and Thrace (MN 5912/22.07.05), the Rectorat of the Aristotle University Thessaloniki (MN 49214/22.06.2005), the Prefecture of Thessaloniki (MN GN 2327/22.06.2005), the Hellenic Cancer Society MN 819/21.06.2005), and local Authorities.

Conflict of interests

The authors declare no conflict of interests.

References

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer; J Int du Cancer*. 2010;127:2893-917.
2. Nour NM. Cervical cancer: a preventable death. *Rev Obstet Gynecol*. 2009;2:240-4.
3. zur Hausen H. Papillomaviruses causing cancer: evasion from host-cell control in early events in carcinogenesis. *J Natl Cancer Inst* 2000;92:690-8.
4. Conway MJ, Meyers C. Replication and assembly of human papillomaviruses. *J Dent Res*. 2009;88:307-17.

5. Agorastos T, Chatzistamatiou K, Zafrakas M et al. Epidemiology of HPV infection and current status of cervical cancer prevention in Greece: final results of the LYSISTRATA cross-sectional study. *Eur J Cancer Prev* 2014;23:425-31.
6. Agorastos T, Chatzistamatiou K, Zafrakas M et al. Distinct demographic factors influence the acceptance of vaccination against HPV. *Arch Gynecol Obstet* 2015;292:197-205.
7. Joura E, Bautista O, Luxembourg A. A 9-Valent HPV Vaccine in Women. *New Engl J Med*. 2015;372:2568-9.
8. Simms KT, Smith MA, Lew JB, Kitchener HC, Castle PE, Canfell K. Will cervical screening remain cost-effective in women offered the next generation nonavalent HPV vaccine? Results for four developed countries. *Int J Cancer; J Int du Cancer*. 2016;139:2771-80.
9. Kessels SJ, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine* 2012;30:3546-56.
10. Sotiriadis A, Dagklis T, Siamanta V, Chatzigeorgiou K, Agorastos T, Group LS. Increasing fear of adverse effects drops intention to vaccinate after the introduction of prophylactic HPV vaccine. *Arch Gynecol Obstet* 2012;285:1719-24.
11. Donadiki EM, Jimenez-Garcia R, Hernandez-Barrera V, Carrasco-Garrido P, Lopez de Andres A, Velonakis EG. Human papillomavirus vaccination coverage among Greek higher education female students and predictors of vaccine uptake. *Vaccine* 2012;30:6967-70.
12. Mamas IN, Theodoridou M, Koutsaftiki C, Bertsiaris G, Sourvinos G, Spandidos DA. Vaccination against Human Papillomavirus in relation to Financial Crisis: The "Evaluation and Education of Greek Female Adolescents on Human Papillomaviruses' Prevention Strategies" ELEFThERIA Study. *J Pediatric Adolescent Gynecol* 2016;29:362-6.
13. Chow EP, Danielewski JA, Fehler G et al. Human papillomavirus in young women with Chlamydia trachomatis infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. *Lancet Inf Dis* 2015;15:1314-23.
14. Hopkins TG, Wood N. Female human papillomavirus (HPV) vaccination: global uptake and the impact of attitudes. *Vaccine* 2013;31:1673-9.
15. Cui Y, Baldwin SB, Wiley DJ, Fielding JE. Human papillomavirus vaccine among adult women: disparities in awareness and acceptance. *Am J Prev Med* 2010;39:559-63.
16. Agorastos T, Chatzigeorgiou K, Brotherton JM, Garland SM. Safety of human papillomavirus (HPV) vaccines: a review of the international experience so far. *Vaccine* 2009;27:7270-81.
17. Chatzistamatiou K, Sotiriadis A, Agorastos T. Letter to the editor referring to the manuscript entitled: "Increasing fear of adverse effects drops intention to vaccinate after the introduction of prophylactic HPV vaccine" reported by Sotiriadis et al. (*Arch Gynecol Obstet* 2012;285:1719-24). *Arch Gynecol Obstet* 2014;289:471-2.
18. Habel MA, Liddon N, Stryker JE. The HPV vaccine: a content analysis of online news stories. *J Womens Health (Larchmt)* 2009;18:401-7.
19. Keelan J, Pavri V, Balakrishnan R, Wilson K. An analysis of the Human Papilloma Virus vaccine debate on MySpace blogs. *Vaccine* 2010;28:1535-40.
20. Lower J. [Two unclear cases of death. Can we still recommend HPV vaccination?]. *MMW Fortschr Med* 2008;150:6.
21. Cheruvu VK, Bhatta MP, Drinkard LN. Factors associated with parental reasons for "no-intent" to vaccinate female adolescents with human papillomavirus vaccine: National Immunization Survey - Teen 2008-2012. *BMC Pediatr* 2017;17:52.
22. Warner EL, Lai D, Carbajal-Salisbury S et al. Latino Parents' Perceptions of the HPV Vaccine for Sons and Daughters. *J Community Health* 2015;40:387-94.
23. Papagiannis D, Rachiotis G, Symvoulakis EK et al. Vaccination against human papillomavirus among 865 female students from the health professions in central Greece: a questionnaire-based cross-sectional study. *J Multidiscip Healthc* 2013;6:435-9.
24. Simou E, Koutsogeorgou E. Effects of the economic crisis on health and healthcare in Greece in the literature from 2009 to 2013: a systematic review. *Health Policy* 2014;115:111-9.
25. Fisher H, Trotter CL, Audrey S, MacDonald-Wallis K, Hickman M. Inequalities in the uptake of human papillomavirus vaccination: a systematic review and meta-analysis. *Int J Epidemiol* 2013;42:896-908.
26. Pruitt SL, Schootman M. Geographic disparity, area poverty, and human papillomavirus vaccination. *Am J Prev Med* 2010;38:525-33.
27. Voss DS, Wofford LG. Human Papillomavirus Vaccine Uptake in Adolescent Boys: An Evidence Review. *Worldviews Evid Based Nurs* 2016;13:390-5.
28. Cunningham MS, Skrastins E, Fitzpatrick R et al. Cervical cancer screening and HPV vaccine acceptability among rural and urban women in Kilimanjaro Region, Tanzania. *BMJ Open* 2015;5:e005828.
29. Slattelid Schreiber SM, Juul KE, Dehlendorff C, Kjaer SK. Socioeconomic predictors of human papillomavirus vaccination among girls in the Danish childhood immunization program. *J Adolesc Health* 2015;56:402-7.