

RESEARCH PAPER



HPV vaccine acceptability in high-risk Greek men

Lea Hoefler, BA, BS^a, Savas Tsikis, BS^a, George Bethimoutis, MD^b, Electra Nicolaidou, MD^b, Vassilios Paparizos, MD^b, Christina Antoniou, MD^b, Antonios Kanelleas, MD^b, Leonidas Chardalias^c, Georgios-Emmanouil Stavropoulos^c, John Schneider, MD, MPH^{d,e}, and Angella Charnot-Katsikas, MD^f

^aBiological Sciences Division, University of Chicago Pritzker School of Medicine, Chicago, USA; ^b1st Department of Dermatology and Venereology, National and Kapodistrian University of Athens School of Medicine, “Andreas Syggros” Hospital, Athens, Greece; ^cNational and Kapodistrian University of Athens School of Medicine, Athens, Greece; ^dUniversity of Chicago Medicine, Department of Medicine, Chicago, USA; ^eUniversity of Chicago, Medicine, Department of Public Health Sciences, Chicago, USA; ^fUniversity of Chicago Medicine, Department of Pathology, Chicago, USA

ABSTRACT

HPV is associated with malignancy in men, yet there is a lack of data on HPV knowledge, vaccine acceptability, and factors affecting vaccine acceptability in Greek men. This study aims to identify determinants of knowledge and willingness to vaccinate against HPV among high-risk Greek men. Men ($n = 298$) between the ages of 18 and 55 were enrolled from the STI and HIV clinics at “Andreas Syggros” Hospital in Athens, Greece from July–October 2015. Participants completed a survey on demographics, economic factors, sexual history, HPV knowledge, and vaccine acceptability. The majority of participants were younger than 40 (76.6%) and unmarried (84.6%). Our sample was 31.2% MSM (men who have sex with men), and 20.1% were HIV-positive. Most participants (>90%) were aware that HPV is highly prevalent in both men and women; however, fewer identified that HPV causes cancers in both sexes (68%) and that vaccination protects men and women (67%). Amongst participants, 76.7% were willing to vaccinate themselves against HPV, 71.4% an adolescent son, and 69.3% an adolescent daughter. HIV-positive men were more likely to be willing to vaccinate themselves (OR 2.83, $p = .015$), a son (OR 3.3, $p = .015$) or a daughter (3.01, $p = .020$). Higher income levels were associated with increased willingness to vaccinate oneself (OR 1.32, $p = .027$), a son (1.33, $p = .032$) or daughter (1.34, $p = .027$). Although there is a HPV knowledge gap, HPV vaccine acceptability is high despite lack of vaccine promotion to Greek men. Future studies should include lower-risk men to adequately inform public health efforts.

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Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) worldwide, infecting the majority of sexually active men and women over the course of their lives.¹ Although cervical cancer in women is the best known HPV related malignancy, infection with high-risk HPV has been associated with other cancers in both sexes.¹ A recent study of the US population suggested that HPV is associated with 90% of anal cancers, 70% of oropharyngeal cancers, 60% of penile cancers, and nearly 70% of vulvar cancers.² A systematic review of HPV prevalence in men looking at studies globally found that infection rates in men range from 1.3%–72.9%. The same review found that men who have sex with men (MSM) and men with more than three lifetime partners were at greater risk for HPV.³ In the Greek context, data on HPV prevalence in the male population is unfortunately much less robust. Available data on Greek women suggest that infection rates may be up to 43% in certain populations.⁴

Fortunately, many HPV infections and HPV-related cancers can be prevented through vaccination. Originally licensed for women, HPV vaccine recommendations have since been expanded in some countries to include boys ages 11–12, as

well as catch up vaccination for young men.⁵ Vaccination in men has shown to be effective in preventing persistent infection associated with malignancy.⁶ MSM, and especially HIV positive MSM, are more likely to be affected by HPV, and are also less likely to benefit from herd immunity that may protect unvaccinated men who have sex with vaccinated women.⁷ Additionally, specifically vaccinating men who have sex with men may be highly effective at preventing anal cancer, as well as being a cost-effective intervention in general.^{8,9} However, vaccine uptake depends partially upon vaccine acceptability. To date, there have been several HPV vaccine acceptability studies that have focused on men from around the world. A systematic review and meta-analysis of HPV vaccine acceptability in 8360 men across 22 studies from various countries found a mean acceptance rate of 50.4 on a 100-point scale. Overall, the study suggested that there are generally lower rates of HPV vaccine acceptance among men when compared to women, in part due to less support for vaccination of men and boys.¹⁰

The current vaccination schedule recommended and funded by the Greek National Health System only includes HPV vaccination for females up to age 18, with catch up

vaccination until age 26. Vaccination for males is currently not funded and is not specifically endorsed by the Greek National Health System.¹¹ Despite the fact that the HPV vaccine is provided by the Greek health service, uptake of the vaccine among women has been surprisingly low; one study found a 25.82% vaccination rate in female higher-education students in Athens.¹² Given that there has been limited uptake of the HPV vaccine amongst Greek women, herd immunity for Greek men who have sex with women (MSW) is likely also suboptimal. Moreover, uptake of multiple vaccinations is generally low among Greek adolescents,¹³ and a recent study suggests that vaccine coverage rates in Greek youth are associated with socioeconomic factors.¹⁴

The LYSISTRATA study followed over 5000 women between the ages of 18 to 59 from 2005 to 2011, revealing a significant decrease in vaccination acceptance among women for themselves, for their daughters, and for their sons following the 2008 introduction of the vaccine in Greece. When asked about their willingness to vaccinate themselves or their adolescent child against HPV, acceptance rates dropped from over 80% to around 60% by 2011.^{15–17} A subsequent paper from this study found that low income was associated with low vaccine acceptability rates for a son, but not for themselves or for an adolescent daughter, raising the question that cost may play a larger role in the decision to vaccinate Greek men and boys as the cost of the HPV vaccine is not currently covered under the Greek immunization schedule. To explain the 20% drop in acceptability amongst Greek women considering vaccination for themselves and their children, some have suggested that highly publicized media stories about negative side effects of the vaccine have contributed to fears of vaccinating.^{16,18} Importantly, the LYSISTRATA study did not include men, and therefore no data is currently available on the acceptability of the HPV vaccine among Greek men.

The high prevalence of HPV in Greek women, the low vaccination rate, and the current economic crisis, suggest that HPV may be a serious epidemic among Greek men.¹⁹ Expanding HPV vaccination programs to men could play an important role in preventing anal, penile, and oropharyngeal cancers. With the results of the LYSISTRATA study indicating that vaccine acceptance among women has dropped after licensure in Greece, investigating vaccine acceptability among men will be a key step in informing future public health efforts. The objectives of this study are therefore to identify determinants of knowledge and willingness to vaccinate against HPV among high-risk Greek men.

Results

Study population demographics

In total, 298 men were enrolled in this study, 237 from the STI clinic and 61 from the HIV Infection Unit (Table 1). Four of the 302 patients (1.3%) who initially agreed to hear about the study then declined to participate. The mean age of the patients included in the study was 33 years. Our population had a wide range of income and education level, and the majority were unmarried men. Thirty-three percent of participants reported being currently unemployed, and 66% reported being unemployed within the last five years. Sixty-nine percent of the population reported a current

Table 1. Patient demographics.

(n = 298)	N	(%)
Age		
18–29	123	41.335.2
30–39	105	15.8
40–49	47	7.7
50+	23	
Country of Birth		
Greece	245	83.3
Other	49	16.7
Education		
Elementary or middle school	30	10.1
High school	80	26.8
Post Secondary	188	63.1
Marital Status		
Married	46	15.4
Not married	252	84.6
Employment Status		
Currently employed	198	66.4
Currently unemployed	100	33.6
Unemployed in previous 5 years, including now	198	66.4
Monthly Income		
0–233 Euro (0–265 USD)	77	25.8
234–432 Euro (266–491 USD)	41	13.8
433–1000 Euro (492–1137 USD)	132	44.3
> 1000 Euro (> 1137 USD)	48	16.1
HIV+	60	20.1%
MSM	93	31.2%
Self-reported history of genital warts	206	69.1%

MSM- Men who have sex with men

Participants were asked to select income levels in Euro amounts. Conversions were made using the exchange rate available on June 7th, 2016.

or past history of genital warts, 31% of the patients identified as MSM, and 20% as HIV positive. Additionally, over half (52.7%, n = 49) of MSM were also HIV positive.

Knowledge about HPV infection and HPV vaccine

Overall, 71% of participants had heard of HPV prior to the study, with 47% of participants reporting that they felt “familiar” with the HPV vaccine. All participants then chose from sources from which they had heard about the vaccine, regardless of whether or not they reported feeling familiar with the vaccine: 10.4% heard about it from their doctor, 14.1% from the media, 14.1% from friends or family, and 14.8% from another source. The remainder of participants answered that they had never heard of the vaccine, or were “unsure” if they had ever heard of it.

The majority of participants, including those who had not heard of HPV prior to the study, correctly identified that HPV is a common STI (92.6%), and nearly all identified that HPV affects both sexes (98%). However, a two-tailed chi-squared test demonstrated a statistically significant gap in knowledge between the percentage of patients who correctly responded to the former two questions and those who correctly responded to the following questions: that HPV is involved in cancers in men and women (68%, $p < 0.0001$) and that the HPV vaccine can protect both men and women (67%, $p < 0.001$)

HPV vaccine acceptability

Over three quarters of participants were willing to vaccinate against HPV (76.7%), with 79.4% of those reporting being

Table 2. Factors associated with vaccine acceptability for oneself in Greek men attending outpatient STI & HIV clinics at “Andreas Syggros” Hospital in Athens, Greece, 2015.

	N (= 277)	Adjusted Odds Ratio (p =)	Adjusted 95% Confidence Interval
Willingness to vaccinate self			
HIV+	60	2.8 (p = 0.02)*	[1.23–6.51]
History of genital warts	206	1.6 (p = 0.07)	[.96–2.73]
Increasing income levels		1.3 (p = 0.03)*	[1.03–1.68]
Increasing number of days hungry		.7 (p = 0.04)*	[.51–.98]
Increasing difficulty making ends meet		.7 (p = 0.09)	[0.47–1.06]

*p < .05

Notes: Models were adjusted for age, birth country, education level, income, MSM status, and HIV status. Values were considered statistically significant at p = .05.

Only factors with p-values less than p = .1 were included in the table.

277 participants were included in each model, participants not included were dropped due to missing variables.

MSM- men who have sex with men.

willing to vaccinate even if the vaccine would cost. Only 7.7% answered that they were unwilling to vaccinate, with 15.5% being unsure. Vaccine acceptability for adolescent sons (71.4%) and daughters (69.3%) was also high.

Multivariate ordinal regression models demonstrated that willingness to vaccinate was positively associated with HIV-positivity (aOR 2.8, CI [1.23 – 6.51]), higher income levels (aOR 1.3, CI [1.03 – 1.68]), and a history of genital warts (aOR 1.6, CI [.96–2.73]). Measures of decreased economic stability demonstrated a negative association with willingness to vaccinate, namely a higher number of reported days of going hungry (aOR .7, CI [.51 – .98]) and increasing difficulty making ends meet (aOR .7, [0.47 – 1.06]) (Table 2). All of the above factors demonstrated statistical significance (p < 0.05). Age and identifying as MSM were not statistically significant factors for vaccine acceptability.

In identical models looking at willingness to vaccinate a hypothetical adolescent daughter or son, statistically significant positive associations were seen if participants were HIV positive (daughter: aOR 3.0, CI [1.17–7.73, son: aOR 3.3, CI [1.26–8.60]), had higher income levels (daughter: aOR 1.3, CI [1.03–1.74], son: aOR 1.3, CI [1.02–1.75]), or were married (daughter: aOR 2.4, CI [.94–5.91], son: aOR 2.3, CI [.91–5.83]) (Table 2).

Willingness to vaccinate also closely correlated with participant’s beliefs about general vaccine safety and efficacy. In all cases, belief in general vaccine safety and efficacy positively correlated with increased willingness to vaccinate. When it came to an adolescent son or daughter, both disbelief and uncertainty in

vaccine safety or efficacy decreased willingness to vaccinate. However, when it came to vaccinating themselves, it was not participants who *did not believe* in vaccine safety and efficacy that had statistically significantly lower rates of acceptance, but participants who reported being *unsure* about these things (Table 3).

The most commonly participant-selected factors that would increase willingness to vaccinate included belief that it would protect against disease (73.2%), recommendation from a healthcare provider (44.6%), and belief that side effects would be minimal (45%). Common reasons selected that would make a participant less willing to vaccinate were fear of adverse side effects (55.7%), healthcare provider does not suggest or recommend (47.3%), and insufficient knowledge about the vaccine (36.9%). Interestingly, 25% of participants reported that a high cost for the vaccine would make them less likely to vaccinate.

Discussion

To our knowledge, this is the first study that has examined HPV vaccine knowledge, acceptability, and factors affecting willingness to vaccinate amongst high-risk men in Greece. Over 70% of participants had heard of HPV prior to the study. In addition, the majority of participants were easily able to identify that HPV is a common STI and infects both men and women. This demonstrates an increased awareness of the virus amongst Greek men when compared to similar studies performed in countries such as Italy and Peru in which 40–60% of participants were aware of HPV.^{20–22} One potential explanation for the increased awareness shown amongst our study population is that they were enrolled through STI and HIV clinics, and many of our patients had been previously exposed to the virus (69%). However, similar to the findings of a study of MSM in New York City, fewer participants in our study were able to identify that HPV can cause cancers in men as well as women.²³

We find that high-risk Greek men have a fairly high rate of vaccine acceptance for themselves (76.7%), as well as for an adolescent son (71.4%) or daughter (69.3%). This is despite a lack of prior promotion of the vaccine towards men and a drop in acceptance amongst women after formal licensure in Greece.¹⁵ One important factor that may be impacting the high rate of vaccine acceptability is the study population. As this study was conducted at a STI and a HIV clinic, a high-risk population was sampled. Their experience with human papillomavirus (69% with history of genital warts) and the perceived

Table 3. Relationship between HPV vaccine acceptability and prior beliefs about vaccines.

	Willingness to vaccinate self (adjusted OR, p-value, CI)	Willingness to vaccinate adolescent daughter (adjusted OR, p-value, CI)	Willingness to vaccinate adolescent son (adjusted OR, p-value, CI)
Believe vaccines effective	2.8 (p < .001)* [1.68–4.56]	3.1 (p < .001)* [1.87–5.35]	2.7 (p < .001)* [1.59–4.82]
Unsure of vaccine efficacy	.4 (p = .001)* [.262–.718]	.5 (p = .01)* [.292–.870]	.5 (p = .03)* [.312–.945]
Believe vaccines ineffective	.5 (p = .1) [.212–1.14]	.3 (p = .002)* [.101–.60]	.3 (p = .005)* [.112–.672]
Believe vaccines safe	2.8 (p < .001)* [1.67–4.57]	4.0 (p < .001)* [2.29–6.90]	3.7 (p < .001)* [1.99–6.05]
Unsure of vaccine safety	.3 (p < .001)* [.2–.58]	.4 (p = .001)* [.227–.694]	.4 (p = .004)* [.247–.768]
Believe vaccines unsafe	.8 (p = .64) [.34–1.93]	.3 (p = .001)* [.107–.570]	.3 (p = .003)* [.121–.643]

*p < .05

Notes: Models were adjusted for age, birth country, education level, income, MSM status, and HIV status. Values were considered statistically significant at p = .05.

277 participants were included in each model, participants not included were dropped due to missing variables.

need to prevent against related disease is likely skewed from that of the general population. We also find that being HIV-positive, another high-risk group, is correlated with higher levels of vaccine acceptability. This population also included large numbers of young men and men with high levels of education, which may have also influenced willingness to vaccinate.

One question that may be of interest for future studies is whether or not Greek men have been prejudiced against the HPV vaccine by negative media coverage. Previous studies in Greek women have found that coverage of negative side effects after the vaccine's licensure may be contributing to low rates of acceptability and vaccination amongst Greek women and girls.¹⁶ As the vaccine has only been licensed for women at this point, it is possible that this negative publicity has not been as influential to Greek men. Additionally, the results of our study suggest that few Greek men are hearing about the HPV vaccine from their physicians, potentially due to the fact that the vaccine is not licensed for men currently. Education from physicians and other healthcare personnel could have an important impact on the perception of the vaccine amongst men, even before it becomes licensed for men in Greece.

Several economic indicators correlate with participants' reported willingness to vaccinate. In all cases, higher levels of income increased willingness to vaccinate by an odds ratio of 1.3. Two other measures looking specifically at economic stress, a higher number of "hungry days" per week and reported difficulty making ends meet, decreased participant willingness to vaccinate themselves. A quarter of participants also indicated that a higher cost would make them less likely to vaccinate. The HPV vaccine is currently only provided free of charge for women and girls under the Greek National Health System.¹⁸ Reports from the LYSISTRATA study of over 5000 Greek women investigating HPV epidemiology and vaccine acceptability from 2004–2011, demonstrated that income was only a significant factor when considering vaccination for a son. The authors of this study hypothesize that this effect may be due in part to a perception that HPV vaccination is not as important for boys as it is for girls, as well as the fact that the vaccine is not provided free of cost to boys and men in Greece.¹⁸ However, recent studies have suggested that the ongoing economic crisis has impacted the completion of vaccination schedules in both boys and girls.¹⁴ It may be that in the context of high unemployment levels and the ongoing Greek economic crisis, financial questions play a more important role when vaccination is being considered by, and for, Greek men and boys. Notably, our study was partially conducted during the summer of 2015, when Greek banks shut down for a period of time given the uncertain situation surrounding the Greek national debt. Participants' answers may have reflected an increased focus on financial factors given that this was a time of heightened economic stress. In contrast, the LYSISTRATA study was conducted before the height of the financial crisis and economic issues may not have carried as much weight for people during that time period.

Participant's responses to questions on what would make them more or less willing to vaccinate reveal that patient knowledge of the vaccine and its side effects is an important factor contributing to vaccine acceptability. This is consistent with previous studies in Greece finding that information about

side effects plays an important role in vaccination decisions.²⁴ Additionally, this study finds that lower rates of vaccine acceptance for themselves were more significant among participants who felt "unsure" about vaccine safety and efficacy than amongst participants who felt vaccines were outright unsafe or ineffective. In the case of vaccinating a hypothetical adolescent son or daughter, beliefs about general vaccine safety or efficacy also significantly affect willingness to vaccinate. Additional education on HPV and the HPV vaccine, as well as endorsement by healthcare providers, could all serve to expand acceptability of the HPV vaccine amongst high-risk Greek men.

Though this study asked about a hypothetical son or daughter and did not specifically consider men who are parents, the results are consistent with studies of parents in other European countries, including several where current vaccination schedules also do not include male children. Parents generally report high acceptance for vaccinating an adolescent son, with knowledge about the role of HPV disease in males and beliefs about the safety and efficacy of vaccines being important factors affecting their acceptance of the HPV vaccine.^{25,26} Should the vaccine coverage be expanded to include men in Greece, public health education efforts may play an important role in providing vaccine education in order to reach high rates of coverage, especially given that physician recommendations were indicated as a factor that would increase willingness in nearly half of participants.

Limitations of this study include that it was conducted using a high-risk population from a single center. This was a good representative sample of high-risk Greek men due to the fact that it was conducted at the primary referral center for men with STIs in southern Greece. However, results cannot be generalized to the broader Greek male population. Moreover, though declination to participate was infrequent among patients provided with study information (1.3%), additional data on patients who declined to participate was not gathered. This study also does not allow for direct comparison to HPV vaccination attitudes in a comparable population of Greek women. Finally, there is the possibility of participant recall bias regarding demographic and sexual history information.

In conclusion, this study shows that high-risk Greek men have high rates of HPV vaccine acceptability, both for themselves and for an adolescent son or daughter. Willingness to vaccinate against HPV may be influenced by economic factors, the current lack of support for male vaccination, and general beliefs about vaccine safety and efficacy. However, further studies are needed, especially large, multi-center studies with a more representative sample of the general population. Studies that include both men and women would also be useful for comparing vaccine acceptability between sexes. Lastly, studies on HPV vaccine cost-effectiveness are needed. Greek men, especially high-risk men, may benefit from expanded HPV vaccination in Greece. Expanding the body of knowledge on the HPV vaccine and Greek men is necessary to create public health initiatives to prevent HPV-related cancers.

Methods

Two hundred and ninety-eight men were enrolled in a single center, cross-sectional study conducted at "Andreas Syggros"

Hospital, a tertiary center specializing in Skin and Venereal Diseases located in Athens, Greece. This is the primary referral center in Athens for the care of men with STIs. Study participants were sequentially recruited from the HIV Infection Unit and from the general STI clinic between July 2015 and October 2015. It was determined by a two-sided Fischer's Exact test that a sample size of 300 would achieve 80% power to detect a 15% difference between groups. Eligible participants were Greek men between the ages of 18 and 55 seeing a physician at one of these two clinics. This study was approved by the University of Athens Ethics committee.

Participants were recruited during their routine clinic visits, provided with informed consent, and were asked to complete a four-part, Greek-language questionnaire. The questionnaire was computer-based and self-administered in a private room. Participants were assigned a unique study identifier number, which was used to preserve patient anonymity and confidentiality. The four parts of the survey asked participants about their basic demographic information, economic status, sexual history, and knowledge and attitudes regarding HPV vaccination. Survey questions were based on previously published studies to ensure validity, though we did not test internal consistency and reproducibility of the questionnaire.^{19,27–31}

Participants' knowledge about HPV infection in men was assessed using four True-False questions. This portion of the questionnaire was similar to that used by a study published by Donadiki et al of over 3,000 female higher-education students in Athens.¹² Next, participants were asked about general vaccine beliefs, willingness to vaccinate themselves against HPV, as well as their willingness to vaccinate a hypothetical adolescent son or daughter against HPV.^{15,32} Willingness to vaccinate oneself was measured using an ordinal scale including "not willing", "unsure", "willing only if free", and "willing even at cost". A simplified scale was used for willingness to vaccinate an adolescent son or daughter, encompassing "not willing", "unsure", and "willing". These questions were based on a study of HPV vaccine acceptability amongst over 10,000 Swedish young adults.³² Lastly, participants were asked to select from lists of factors that would influence their willingness to vaccinate.^{10,16}

All data analysis was performed using STATA version 13.0 (StataCorp corporation, College Station, Texas, USA) and Prism version 6.0 (GraphPad Software, La Jolla California USA). A two-tailed chi-squared test was used to assess differences in number participants correctly answering HPV knowledge questions. Adjusted ordinal logistic regression models were built to evaluate the impact of various demographic factors on willingness to vaccinate oneself, an adolescent daughter, or an adolescent son against HPV. Factors controlled for in all models were age, country of birth, education, income, identifying as MSM, and HIV status. These factors were chosen based on review of prior literature.^{10,12,15,18,32} All values were considered statistically significant at the $p = 0.05$ level.

Disclosure of potential conflicts of interest

The authors have no conflicts of interest to report.

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