

Statistical Study: Vaccination Against HPV Among Dental Students in Romania

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Abstract: *Vaccination against Human Papilloma Virus continues to remain a highly complex public health issue, as there are many countries or regions that show increasing reluctance. Romania is among the countries that do not provide HPV vaccine in the national vaccination scheme, but offers the opportunity to young girls between 11 and 18 years of age to benefit from free vaccination. It is the responsibility of health professionals in all health sectors to inform themselves correctly, but also to instruct patients in a prophylactic approach against infection with both HPV and other types of microorganisms. Accurate information and a thorough knowledge of the prophylactic means are achieved from the years of study.*

Our study focuses on the following aspects: the degree of vaccination among dental students, the willingness of students to get vaccinated if they have not done it so far, the degree of information about Human Papilloma Virus infection, including ways of transmission and methods of diagnosing the infection, the perception of students on how this topic has been promoted, the sources of information they access in order to obtain information about Human Papilloma Virus.

Keywords: *vaccine; HPV; Gardasil; Cervarix; education; prevention.*

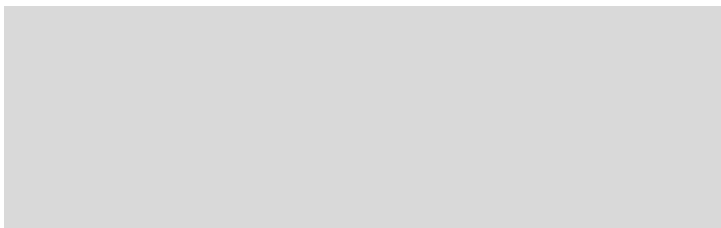
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Introduction

Vaccination has been and continues to be the main means of preventing infectious diseases (Haviari et al., 2015). Over time, vaccines have proven their effectiveness in reducing morbidity and mortality (Haviari et al., 2015). However, vaccine administration is a complex process in which specialists from many fields contribute: physicians, government institutions, medical researchers, public authorities (Ulrich, 2013; Van den Hoven & Verweij, 2013; Zimmerman, 2013). Awareness of the need for vaccination is both an individual and a collective responsibility. Healthcare workers are often under great stress due to the rigorous criteria for the development and optimal storage of vaccines (Zheng et al., 2018), as well as the increasing reluctance of the population towards the immunization through vaccination (Galanakis et al., 2014).

The onset of the Covid19 pandemic and recommendations for vaccination or even in some countries, mandatory vaccination, have led to increased reluctance to vaccinate, as evidenced by recent cases of poliomyelitis in India (Choudhary et al., 2021) (which was eradicated around 2000 from most countries, with Africa remaining the last continent to declare on 25th of August 2020 that it had eradicated the disease) (Bahl et al., 2018). Another example is the dramatic drop in the number of measles vaccines administered across Europe in the post-pandemic period of Covid19 (Giubilini, 2021). Currently, Europe is facing a tripling of measles cases (Giubilini, 2021). Refusal to vaccinate initially occurs in narrow groups of individuals such as those with religious beliefs who are against certain medical acts (Salmon et al., 2005), individuals who promote a natural lifestyle (Hough-Telford et al., 2016), individuals with anxiety about the potential adverse effects of vaccination (Salmon et al., 2005; Wang et al., 2014).

HPV Vaccine: Beginnings, Myths, Present

The HPV vaccine was first used in the United States in 2006 (Bednarczyk, 2019). At the beginning of the vaccination campaign, it was recommended to young girls, teenagers and women (Bednarczyk, 2019), but in 2009 the recommendations were reversed and men were included (Centers for Disease Control and Prevention, 2010). Also in the early stages of the vaccination campaign, there were voices that tried to downplay the importance of this vaccine in favour of the Pap test which we already know has proven its effectiveness over time in preventing cervical cancer (Bednarczyk, 2019). A strong argument against this claim is that the HPV

vaccine is not only for cervical cancer prevention, but also provides the necessary prophylaxis for the following cancers: head and neck cancer (Bergman et al., 2019), oropharyngeal cancer (de Martel et al., 2017), anal, vulvar or penile cancer (Brotherton & Bloem, 2018; de Martel et al., 2017).

Another concern of many females was the fear that this vaccine could affect fertility (Bednarczyk, 2019). In contrast to this concern, we can only emphasize, rather, the harmful effects of HPV infection on fertility and pregnancy (Souho et al., 2015). Numerous studies have shown a direct link between the presence of HPV infection in the mother and the onset of disorders in the gynaecological and neonatal sphere: premature birth, miscarriage (Gomez et al., 2008; Hermonat et al., 1997). In general, infections of any type, viral, bacterial or parasitic produce a strong imbalance in the normal development of the foetus and are considered an etiological factor of miscarriage (Skoczyński et al., 2011). During pregnancy many hormonal changes occur, but immunological changes should not be neglected. As far as HPV is concerned, pregnancy is a favourable time for the virus to replicate (Skoczyński et al., 2011). HPV has also been shown to be present in the umbilical cord (Puranen et al., 1996; Syrjänen, 2010) and in the placenta (Syrjänen, 2010). Thus, there is a risk that HPV infection may be contracted at birth, which again raises the issue of properly informing women who wish to become pregnant about immunisation by vaccination.

At the same time, we emphasize that HPV infection can be transmitted non-sexually, as evidenced by the increasing incidence of papillomatous lesions of the tegument or mucous membranes among children (Syrjänen, 2010). This again raises alarm bells among health workers and highlights the importance of vaccination against HPV from childhood onwards (Fu et al., 2014).

HPV Vaccine in the World and in Romania

By 2020, both the American and European continents had introduced the HPV vaccine in more than 75% of states (WHO, 2020). In this subchapter we will make a comparative analysis of the HPV vaccination rate in different EU Member States for women. Accurate data on the percentage of individuals vaccinated by state/region was obtained by accessing the World Health Organization's online platform (WHO, 2020). It is worth mentioning that in our country the HPV vaccine is not included in the national vaccination scheme, but it is free for young people aged between 11 and 18 years. Other countries in Romania's situation that have not included the HPV vaccine in the national vaccination scheme are: India, China, Indonesia, Bangladesh, Nigeria, Pakistan, Russia.

Table 1. Comparative analysis of the vaccination rate against the HPV virus among the member countries of the European Union. The information was extracted from the WHO platform (2020).

Country	HPV vaccination rate in 2021 (3 doses)
Romania	Do not provide an official report
Bulgaria	5,28%
Germany	47,2%
Greece	Do not provide an official report
Belgium	Do not provide an official report
Netherlands	66,44%
Luxembourg	14%
Spain	77,3%
Hungary	Do not provide an official report
Sweden	83%
Slovenia	49,8%
Slovakia	Do not provide an official report
Austria	Do not provide an official report
Denmark	80,2%
Finland	60,3%
Croatia	Do not provide an official report
Lithuania	66,2%
Cyprus	Do not provide an official report
Malta	99,52%
Poland	Do not provide an official report
Czech Republic	Do not provide an official report
Georgia	23,76%
Estonia	44,64%
Portugal	76,4%

Immunological Aspects of HPV Vaccine

Understanding how the HPV vaccine modulates immunity has an essential role in promoting prophylaxis through immunization with this

serum (Licciardi et al., 2021). The HPV vaccine is characterized by a major potential to trigger an optimal immune response (Hoes et al., 2022; Turner & Huh, 2016). The immunological efficacy of this vaccine can only be properly assessed if the vaccination scheme is complete (all three doses) (Hoes et al., 2022). As with other vaccines, it is necessary to measure the neutralizing antibody titre, with the caveat that to date no minimum antibody titre has been established to ensure protection and induce long-lasting immunity (Hoes et al., 2022; Schiller & Lowy, 2012). The measurement of antibody levels is performed in the laboratory using various techniques, the most common being ELISA (Hoes et al., 2022).

Worldwide through FDA approval there are three types of HPV vaccines which are marketed and used in current medical practice: Gardasil, Gardasil9 and Cervarix. All three vaccines are based on virus-like particles (VLPs), but benefit from different adjuvant systems (Hoes et al., 2022). It is also mentioned that aluminium salts are present in the composition of the vaccines to slowly release the antigen in order to activate the innate immune system (Didierlaurent et al., 2009; Hoes et al., 2022). Following serum injection, the body starts to produce antibodies against HPV. The injected serum composed of L1 VLP induces an important production of antibodies that provide the necessary protection against infection. L1 is the major capsid antigen of the HPV virus (Buck et al., 2013). Numerous studies over time have demonstrated that immunity gained from vaccination results in a significantly increased neutralizing antibody titre compared to immunity gained from infection (Stanley, 2006; Pattyn et al., 2019).

Types of HPV Vaccines and their Characteristics

Table 2. Characteristics of different types of HPV vaccine.

The data were collected based on the information provided by the manufacturer (European Medicines Agency, n.d.a; n.d.b)

Vaccine type	Cervarix	Gardasil4	Gardasil9
HPV Type	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Dose	2 doses: 9-14 years 3 doses: over 15 years	2 doses: 9-13 years 3 doses: over 14 years	2 doses: 9-14 years 3 doses: over 15 years
Vaccination scheme	2 doses: 0, 5 months 3 doses: 0, 1, 6 months	2 doses: 0, 6 months 3 doses: 0, 2, 6 months	2 doses: 0, 6-12 months 3 doses: 0, 2, 6 months

Precautions	- blood clotting disorders - thrombocytopenia	- blood clotting disorders - thrombocytopenia	- blood clotting disorders - thrombocytopenia
Common side effects	- pain, rash at the injection site - headaches - fever - myalgia - arthralgia - gastrointestinal complaints (nausea, vomiting, diarrhoea)	- pain, erythema, oedema, haematoma at the injection site - fever - pain in the extremities - nausea	- pain, erythema, oedema at the injection site - headache - dizziness - nausea - fever - fatigue

Materials and Methods

For this study, we developed a questionnaire comprising a total of 12 questions with a simple complement. The questionnaire was distributed to a sample of 554 dental students from the University of Medicine and Pharmacy of Craiova and the University of Medicine and Pharmacy 'Carol Davila' Bucharest, Romania. The questionnaire was developed by three teaching staff and consultations were carried out with specialists from the educational field, but also psycho-social in order to implement it. The questionnaire was distributed to students in electronic format. After the questionnaire was created using Google Forms application, the teaching staff from the two universities distributed it in the form of a link to the leader of the year, and the leader of one distributed it to his colleagues. The study was carried out with the Google forms application, the data were processed in Excel 2021, and the graphics were made in PowerPoint 2021.

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the University of Medicine and Pharmacy Craiova (approval reference no. 45/24.03.2022).

Informed consent was obtained from every student involved in the study.

The questions were about: the degree of vaccination against Human Papilloma Virus infection among dental students, the willingness of unvaccinated students to be vaccinated in the near future, the need to introduce a course on HPV in the university curriculum, the sources of information, the degree of information of students about HPV infection (means of transmission, diagnostic methods and treatment).

Results

Of the total respondents, 88.9% are female and 11.1% are male. The distribution by age group is as follows: 18-25 years 64.8%; 25-40 years 31.5%; over 40 years 3.7%.

The results of the study conducted among dental students highlighted the insufficient or absent information on the subject of HPV infection and vaccination. A significant percentage of students (89%) stated that they are unvaccinated, but the encouraging situation is given by their increased willingness to get vaccinated in the near future. Among the students vaccinated against HPV, the majority chose the Gardasil 9 vaccine, as it is already known that it is the most effective one, because it protects against nine types of the HPV virus.

Regarding the students' sources of information on this topic, we observe that most of them collect their information from medical books, scientific articles. Also, the majority of student respondents consider that the topic of HPV vaccination is insufficiently addressed in Romania. Regarding the students' degree of information on this topic again, we notice that the majority consider that they are insufficiently informed or even not informed at all, which is a worrying situation, especially considering the fact that they are students in the medical field. Following the discussions with the students, after completing the questionnaire, it was noted their request to learn more information about HPV.

In the case of vaccinated students, it is particularly important that they check the titer of antibodies obtained after vaccination against HPV. The measurement of antibody levels is performed in the laboratory using various techniques, the most common being ELISA.

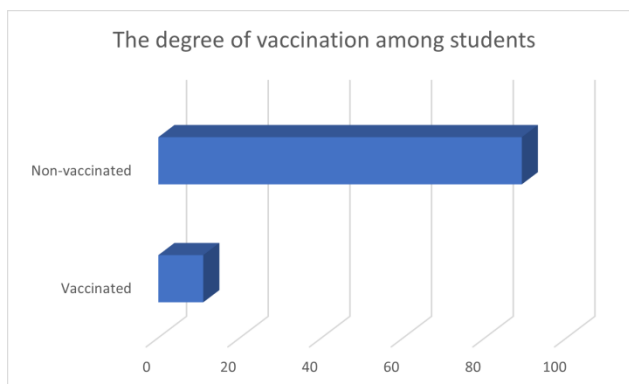


Figure 1. Degree of vaccination among dental students.
Source: Authors' own conception

It is observed that the majority of students are not vaccinated against HPV infection (89%). Although the profile of the specialty studies is medical, there are still large gaps in terms of methods to prevent the contraction and transmission of Human Papilloma Virus infection.

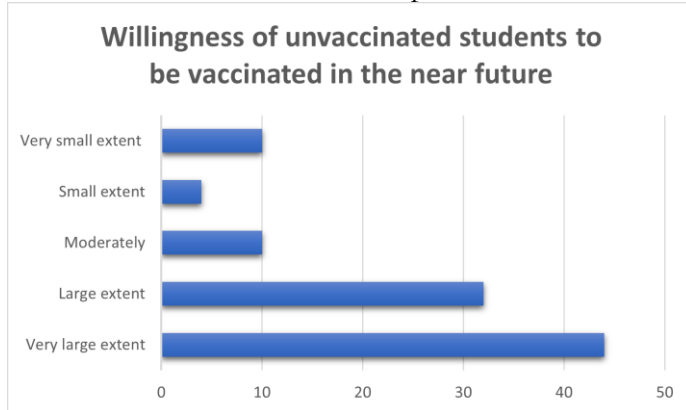


Figure 2. Willingness of unvaccinated students to be vaccinated in the near future.
Source: Authors' own conception

Although there is a significantly increased percentage of an unvaccinated student, the result is encouraging as more than 40% of students are willing to get vaccinated soon. However, there remains a high percentage of those who are unwilling or not fully convinced to get vaccinated. In this situation, the implementation of a national information programme could change this mentality and encourage vaccination against HPV.

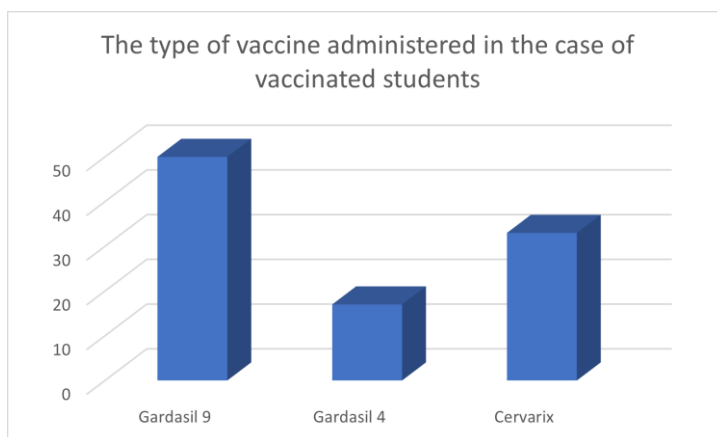


Figure 3. The type of vaccine administered in the case of vaccinated students
Source: Authors' own conception

Among the students who were administered the full HPV vaccination scheme we note that half of them (50%) were inoculated with Gardasil 9 serum which is nonavalent, 33% chose Cervarix vaccine which is bivalent (against HPV variants 16 and 18) and only 17% chose Gardasil 4 tetravalent vaccine. Of the total number of students vaccinated against HPV, all are female.

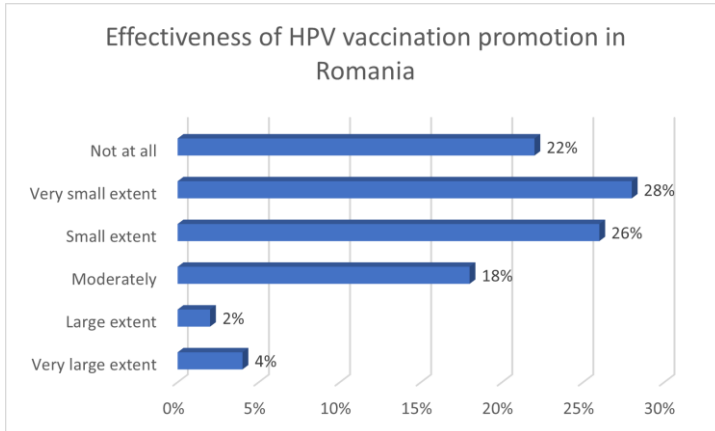


Figure 4. Effectiveness of HPV vaccination promotion in Romania.
Source: Authors' own conception

In this question the students appreciated the fact that the issue of HPV vaccination, as well as informing the citizens of the country about the ways of transmission/diagnosis/treatment of HPV infection were either not promoted enough (26%) or very little (28%), or not at all (22%).

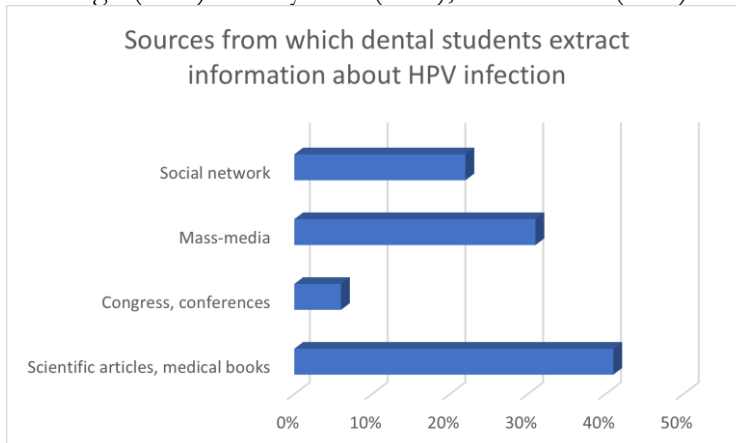


Figure 5. Sources from which dental students extract information about Human Papilloma Virus infection.
Source: Authors' own conception

Although most (41%) turn to scientific articles and textbooks for medical knowledge, we cannot help but notice that both the media (31%) and social networks (22%) are important sources of information. It is therefore particularly important that students are correctly informed and know how to distinguish between fake news and quality, scientifically proven and supported information.

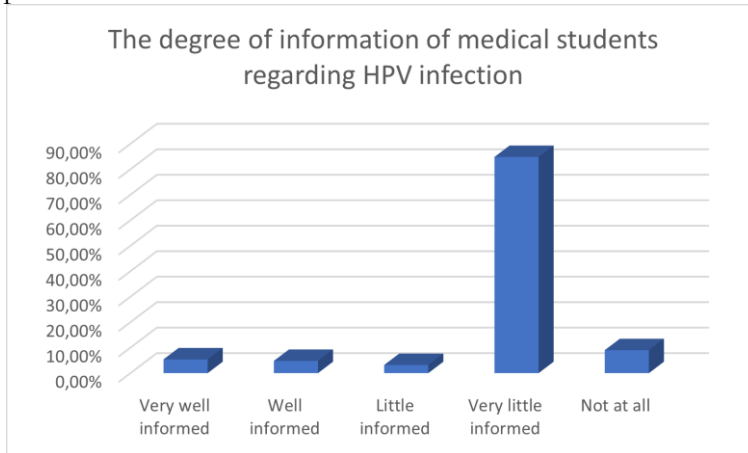


Figure 6. The degree of information of medical students regarding HPV infection.

Source: Authors' own conception

We notice that the majority of students reported that they are very little informed (470 students) regarding this subject. However, there is also a very small category of students who consider themselves very well informed (30 students) or well informed (27 students).

Discussions

Vaccination against Human Papilloma Virus infection remains a controversial topic especially in developing countries (Hardt et al., 2016). The dissemination of false information about this type of vaccination in the media and on social media has the effect of decreasing the population's confidence in the efficacy of the vaccine and amplifies the fear of adverse reactions frequently leading to the triggering of anxiety states (Pennycook & Rand, 2021; Teoh, 2019).

The impact of fake news is more pronounced for teenagers and young people, as they spend most of their time online and are also considered as target groups for misinformation (Watts et al., 2021). Also, the propagation of myths about the HPV vaccine has led many people considered to be at high risk of contracting the virus to choose not to be vaccinated. The high-risk group for HPV infection includes: females over 40

years of age among whom the incidence of cervical cancer is higher; people who have a family history of cervical/head and neck cancer, vulvar/penile/anal cancer; people with multiple sexual partners; healthcare workers (Arbyn et al., 2018; Sabatini & Chiocca, 2020; Symer, & Yeo, 2018). It is also necessary to inform the male population that they can benefit from this type of vaccination (Spînu et al., 2021).

Conclusions

Human Papilloma Virus infection continues to be extremely prevalent in developing countries that do not provide HPV vaccine in their national vaccination scheme. The implementation of a nationwide programme to inform the population about the benefits of the HPV vaccine is vital especially for high-risk groups. We also emphasize the importance of accurate, objective information that leaves no room for interpretation and does not attempt to hide the adverse effects that may arise from vaccine administration.

The introduction of courses in the university curriculum of medical schools would contribute to raising awareness among students (future doctors, dentists, nurses) about the importance of compliance with the rules of prophylaxis and mass immunisation through vaccination against HPV. Currently, in our country there is a low level of awareness among students about HPV infection, transmission, diagnosis and treatment.

The results of our study highlighted the fact that most dental students do not have basic information about Human Papilloma Virus infection. Due to poor information, the degree of immunization through vaccination is extremely low. Also, another particularly important aspect is that in the case of vaccinated students there are gaps regarding the importance of checking the post-vaccination antibody titer. However, the application of this questionnaire highlighted the students' desire to accumulate information about HPV infection. Preventive education should be a priority in the medical academic environment. If future doctors are correctly informed, they in turn can transmit vital information to patients.

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