





## ORIGINAL

# Knowledge, attitudes and practices towards HPV infections, complications of HPV infections and the HPV vaccine among students of Medical Science in North Macedonia

*Conocimientos, actitudes y prácticas respecto a las infecciones por VPH, las complicaciones de las infecciones por VPH y la vacuna contra el VPH entre los estudiantes de Ciencias Médicas de Macedonia del Norte*

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**Abstract**

**Introduction:** Human papillomavirus (HPV) is one of the most common causes of sexually transmitted diseases. The HPV vaccine is crucial in the primary prevention of HPV infection and associated diseases and complications. This objective of the study was to determine the knowledge, attitude and practices of the Medical students in North Macedonia towards HPV infections, complications of HPV infections and the HPV vaccine.

**Materials and methods:** In the period of November 2022 – December 2022 a study using a semi - structured questionnaire was conducted in Medical Faculties in North Macedonia, covering 728 people over 18 years old that are medical students. Standard descriptive statistics were used to summarize the demographic characteristics.

**Results:** A total of 728 participants took part in the survey, predominantly female (n=601, 82.5%). Around one third of all respondents (36.4%) have received the HPV vaccine. We established a statistically significant difference between the vaccinated and non-vaccinated respondents in terms of gender ( $\chi^2=22.231$ ,  $p<0.001$ ) and this proved to be the strongest predictor for vaccination in the logistic regression analysis. The main driver for hesitation regarding the HPV vaccine was the fear of possible side effects and there was an association between the fear of possible side effects and the probability for vaccination (15.1% (n=40) vaccinated vs. 41.2% (n=191) non-vaccinated students,  $\chi^2=73.020$ ,  $p<0.001$ ). The students who didn't agree with the statement that recommending the HPV vaccine to teenagers will send a message that it is okay to become sexually active at an early age were 1.89 times more likely to have been vaccinated.

**Conclusions:** The current study demonstrated that medical students in North Macedonia had a suboptimal uptake of the HPV vaccine. To increase the coverage, it is essential that people get the right information. Having doubts about the vaccine's safety and effectiveness is the main cause of vaccination hesitancy.

**Key words:** HPV, vaccine, knowledge, attitudes, practices.

**Resumen**

**Introducción:** El virus del papiloma humano (VPH) es una de las causas más frecuentes de enfermedades de transmisión sexual. La vacuna contra el VPH es crucial en la prevención primaria de la infección por VPH y de las enfermedades y complicaciones asociadas. El objetivo del estudio era determinar los conocimientos, la actitud y las prácticas de los estudiantes de Medicina de Macedonia del Norte en relación con las infecciones por VPH, las complicaciones de las infecciones por VPH y la vacuna contra el VPH.

**Materiales y métodos:** Entre noviembre de 2022 y diciembre de 2022 se llevó a cabo un estudio con un cuestionario semiestructurado en las facultades de medicina de Macedonia del Norte, que abarcó a 728 personas mayores de 18 años estudiantes de medicina. Se utilizaron estadísticas descriptivas estándar para resumir las características demográficas.

**Resultados:** Un total de 728 participantes tomaron parte en la encuesta, predominantemente mujeres (n=601, 82,5%). Alrededor de un tercio de todos los encuestados (36,4%) han recibido la vacuna contra el VPH. Establecimos una diferencia estadísticamente significativa entre los encuestados vacunados y los no vacunados en términos de género ( $\chi^2=22,231$ ,  $p<0,001$ ) y esto demostró ser el predictor más fuerte para la vacunación en el análisis de regresión logística. El principal impulsor de la indecisión respecto a la vacuna contra el VPH fue el miedo a los posibles efectos secundarios y hubo una asociación entre el miedo a los posibles efectos secundarios y la probabilidad de vacunación (15,1% (n=40) estudiantes vacunados frente a 41,2% (n=191) no vacunados,  $\chi^2=73,020$ ,  $p<0,001$ ). Los estudiantes que no estaban de acuerdo con la afirmación de que recomendar la vacuna contra el VPH a los adolescentes enviará el mensaje de que está bien ser sexualmente activo a una edad temprana tenían 1,89 veces más probabilidades de haberse vacunado.

**Conclusiones:** El presente estudio demostró que los estudiantes de medicina de Macedonia del Norte tuvieron una aceptación subóptima de la vacuna contra el VPH. Para aumentar la cobertura, es esencial que las personas reciban la información adecuada. Tener dudas sobre la seguridad y eficacia de la vacuna es la principal causa de indecisión en la vacunación.

**Palabras clave:** VPH, vacuna, conocimientos, actitudes, prácticas.

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## Introduction

One of the most common causes of sexually transmitted viruses is the human papillomavirus (HPV). HPV consists of a family of small, double-stranded DNA viruses with more than 200 distinct types. Research shows that more than 90% of all sexually active men and women will acquire at least one type of HPV in their lifetime<sup>1</sup>. HPV is an unavoidable part of life for the majority of people. Condyloma is the consequence of low-risk HPV types, while malignancies of the genital areas, head and neck are the result of high-risk HPV types.

Up to 14 million people get a new HPV infection each year, and 45,300 of them could develop malignancies as a result of the infection<sup>2,3</sup>. Cervical cancer is the most common cause of cancer death among African women<sup>4</sup>. In North Macedonia the incidence of cervical cancer for 2020 is estimated at 10.9 per 100 000 women<sup>5</sup>. In Spain a 14% rise in the overall number of cancers, specifically resulting in a notable increase in cases of cervical and oropharyngeal cancer caused by HPV infection is reported<sup>6</sup>. The cumulative number of deaths due to cervical cancer for 2019 for North Macedonia is 68 of overall 12 100 deaths registered among women<sup>7</sup>. Regarding the therapeutic options for reducing the risk of an infection with the HPV virus to progress to cervical cancer there have been several options: cryosurgery, laser surgical removal, loop electrosurgical excision procedure and cold knife conization. A novel non-invasive approach that enhances the elimination of the HPV virus and promotes the healing of the cervix's epithelium involves the application of a gel containing *Coriolus versicolor*, a fungus rich in polysaccharidopeptides<sup>8</sup>. This approach has been studied in an observational non-comparative open-label prospective pilot study (EPICERVIX). The researchers reported that the application of the gel for 21 consecutive days had a favourable effect on cervix epithelization and vaginal microbiota which could prevent the clinical course of HPV-related lesions<sup>9</sup>.

The HPV vaccine is crucial in the primary prevention of HPV infection and associated diseases and complications. Three vaccine types –2-valent, 4-valent, and 9-valent– have been shown to be safe and effective against HPV and it has been discovered that the HPV vaccine alone reduces HPV infection by 70% and cervical cancer by 48%<sup>1</sup>. HPV vaccine is recommended for routine vaccination for both girls and boys at age 11 or 12 years and can be started at age 9.<sup>7</sup> The Advisory Committee on Immunization Practices (ACIP) also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger and vaccination is not recommended for everyone older than age 26 years<sup>10</sup>. Some adults ages 27 through 45 years might decide to get the HPV vaccine based on discussion with their clinician, if they did not get vaccinated when they were younger and HPV vaccination of people in this age range provides less benefit, for several reasons, including

that more people in this age range have already been exposed to HPV<sup>10</sup>.

To increase the awareness regarding HPV infection and HPV vaccine the public should have good knowledge about the risk factors, prevention methods, early diagnosis, screening, and treatment. Even though the HPV vaccine has been shown to reduce the frequency of infections and malignancies that may be associated with the virus, only 47.0% of adults between the ages of 18 and 26 had received at least one dose in 2019 in USA (811). In North Macedonia a national program for HPV vaccination was introduced in 2009. In 2020 every 3 in 10 girls turning 15 years old have received their final vaccination dose in 2020. The overall coverage with an HPV vaccine among women in 2020 was estimated to be 30 %<sup>7</sup>.

The present study aimed to determine the knowledge, attitude and practices of the students of Medical Science in North Macedonia towards HPV infections, complications of HPV infections and the HPV vaccine.

## Materials and methods

### Study design and participants

In the period of November 2022 - December 2022 a cross-sectional study using a semi - structured questionnaire was conducted in North Macedonia. The questionnaire was sent among three Medical universities in North Macedonia- Ss. Cyril and Methodius University (UKIM), Skopje, University of Tetova, University "Goce Delcev".

For recruiting the participants, we used a random convenience sampling method using social media to distribute the questionnaire. The sample size was calculated using G\* Power version 3.1.9.7. The margin of error (the maximum difference between the sample results and the total population) and the confidence interval (the probability that the sample accurately reflects the attitudes of the targeted population) were set at 5% and 95%, respectively. The number of participants needed for our study was estimated to be 602. The total sample size during our study was 728 respondents over 18 years of age.

The questionnaire included 40 questions, 1 of which with more than one possible answer. The questions were divided in 5 sections: demographic information - 7 questions, assessment of the knowledge about cervical cancer - 8 questions, assessment of the knowledge about HPV infection - 11 questions, assessment of the knowledge about HPV vaccine - 6 questions, the attitudes for HPV immunization - 7 questions. An anonymous survey was generated through the web - based platform provided by Google Forms. The questionnaire was distributed in Macedonian since it is the native language of the country.

### Data analysis

The SPSS programme, version 25.0 (IBM Corp, Armonk, NY, USA), was used to enter and analyse the data. The respondents' demographics were analyzed using descriptive statistics. Numbers/totals and percentages (n, %) are used to represent qualitative factors in data. P-values lower than 0.05 were regarded as statistically significant. The distribution of the sampled participants was determined using the Kolmogorov-Smirnov test. Any discrepancies between the observed and hypothesized distributions were checked using the chi-square test for independence. The z-test was used to test for differences between proportions. To examine the impact of the various variables on the likelihood of immunization, a logistic regression was utilized.

## Results

### Demographic

A total of 728 students took part in the study, predominantly female (n=601, 82.5%). The median age of the respondents was 22 years. Approximately 94,9% (n = 691) were students at Ss. Cyril and Methodius University in Skopje and 92,2% (n = 671) were students of the Medical Faculty. A minority were smokers (20,9%, n = 152). (Table I).

When asked whether they have received the HPV vaccine 36.4% (n=265) participants gave a positive answer. As the programme for immunization with the HPV vaccine in North Macedonia targets girls above the age of 12 years expectedly the uptake with the vaccine was higher in females (40.3% for females vs. 18.1% for males). We established a statistically significant difference between

the vaccinated and non-vaccinated respondents in terms of gender ( $\chi^2=22.231$ ,  $p<0.001$ ). Regarding the other demographic variables, no statistically significant differences were observed between the two groups (Table I).

### Knowledge

The respondents showed an overall good knowledge of the characteristics of the HPV virus in terms of contagiousness, risk groups and complications due to the HPV infection (Table II). Six hundred and sixty-two (90,9%) correctly identified that there are specific types of HPV that can cause cervical cancer and 97,3% (n = 708) were aware that HPV is a sexually transmitted virus. Only 26,9% (n = 196) were not familiar with the fact that more than 50% of sexually active men and women become infected with HPV at some point in their lives. Most of the students were aware that HPV is associated with oropharyngeal cancer, genital warts and lung carcinoma and 81,3% (n = 592) answered correctly that you can be infected with HPV for many years without having any symptoms and 87,1% (n = 634) responded that HPV can affect both men and women. Only 9,8% (n = 71) were not aware that condoms are effective in protecting against HPV infection.

Just 50,5% (n = 368) of the participants answered that HPV vaccine is in the calendar for regular immunization and there was statistically significant difference between the vaccinated and non-vaccinated students in regards to this question (69.8% for vaccinated vs. 39.5% for non-vaccinated  $\chi^2=61.845$ ,  $p<0.001$ ). Further when asked what is the preferred age for administration of the HPV vaccine we estimated statistically significant difference among the vaccinated and non-vaccinated respondents ( $\chi^2=29.915$ ,  $p<0.001$ ).

Table I: Demographics of the respondents (n=728).

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
<b>Age</b>	22 y.o (21 y.o.; 23 y.o.)			
<b>Gender</b>				
Male	127 (17.5)	23 (8.7)	104 (22.5)	0.000
Female	601 (82.5)	242 (91.3)	359 (77.5)	
<b>University</b>				
Ss. Cyril and Methodius University in Skopje	691 (94.9)	258 (97.3)	433 (93.5)	0.054
University of Tetovo	33 (4.5)	7 (2.7)	26 (5.6)	
Goce Delcev University	4 (0.6)	0 (0)	4 (0.9)	
<b>Faculty</b>				
Medicine	671 (92.2)	242 (91.3)	429 (92.6)	0.600
Dentistry	19 (2.6)	9 (3.4)	10 (2.1)	
Pharmacy	38 (5.2)	14 (5.3)	24 (5.3)	
<b>Year of study</b>				
1 <sup>st</sup> year	86 (11.8)	24 (9.0)	62 (13.4)	0.368
2 <sup>nd</sup> year	94 (12.9)	34 (12.8)	60 (12.9)	
3 <sup>rd</sup> year	218 (29.9)	89 (33.6)	129 (27.9)	
4 <sup>th</sup> year	141 (19.4)	54 (20.4)	87 (18.8)	
5 <sup>th</sup> year	104 (14.3)	34 (12.8)	70 (15.1)	
6 <sup>th</sup> year	85 (11.7)	30 (11.4)	55 (11.9)	
<b>Smoking</b>				
Yes	152 (20.9)	53 (20)	99 (21.4)	0.659

**Table II:** Knowledge of the respondents regarding the characteristics of the HPV virus and the HPV infection.

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
<b>HPV is a sexually transmitted infection.</b> Correct	708 (97.2)	255 (96.2)	453 (97.8)	0.200
<b>There are specific types of the HPV virus that cause cervical cancer.</b> Correct	662 (90.9)	245 (92.4)	417 (90.1)	0.280
<b>More than 50% of sexually active men and women become infected with HPV after starting sexual activities.</b> Correct	532 (73.1)	194 (80.2)	338 (73.0)	0.952
<b>HPV can cause oropharyngeal cancer.</b> Correct	520 (71.4)	190 (71.7)	345 (74.5)	0.360
<b>HPV is associated with genital warts.</b> Correct	562 (77.2)	201 (75.8)	361 (77.9)	0.512
<b>HPV can cause lung cancer.</b> Correct	207 (28.4)	71 (26.8)	136 (29.3)	0.458
<b>You can be infected with HPV for many years without having symptoms.</b> Correct	592 (81.3)	217 (81.9)	375 (81.0)	0.766
<b>HPV can infect both women and men.</b> Correct	634 (87.1)	227 (85.7)	407 (87.9)	0.385
<b>Condoms are effective in protecting against HPV infection</b> Correct	657 (90.2)	236 (89.0)	421 (90.9)	0.413
<b>For whom is the HPV vaccine recommended?</b> Men Women Men and women	5 (0.7) 359 (49.3) 364 (50.0)	0 (0) 135 (50.9) 130 (49.1)	5 (1.1) 224 (48.4) 234 (50.5)	0.206
<b>At what age should the HPV vaccine be administered?</b> 9-14 y.o. 15-17 y.o. 18-26 y.o. Regardless of age	226 (48.8) 84 (18.1) 68 (14.8) 85 (18.3)	153 (57.7) 69 (26.0) 23 (8.7) 20 (7.6)	73 (37.2) 15 (7.7) 43 (21.9) 65 (33.2)	<b>0.000</b>
<b>Is the HPV part of the immunization calendar of North Macedonia?</b> Yes	368 (50.5)	185 (69.8)	183 (39.5)	<b>0.000</b>

As in North Macedonia the HPV vaccine is administered free of charge to females since 2009 we wanted to assess the knowledge and the practices of our female respondents regarding the HPV virus and the HPV vaccine.

Variables	Vaccinated female respondents (n=242)	Non-vaccinated female respondents (n=359)	p-value
<b>Cervical cancer is a common oncological disease in women</b> Correct	236 (97.5)	343 (95.5)	0.205
<b>Cervical cancer is most commonly diagnosed in women aged between:</b> 25-35 y.o. 35-45 y.o. 45-55 y.o.	50 (20.7) 138 (57.0) 54 (22.3)	64 (17.8) 220 (61.3) 75 (20.9)	0.552
<b>What is the most common method used for screening for cervical cancer?</b> Pap test Vaginal smear Colposcopy	220 (90.9) 12 (5.0) 10 (4.1)	325 (90.5) 14 (3.9) 20 (5.6)	0.614
<b>Have you ever been screened for cervical cancer?</b> Yes	89 (36.8)	113 (31.5)	0.177
<b>Which are the risk factors for cervical cancer?</b> HPV infection Multiple sexual partners Smoking Low socio-economic status Early sexual activity	240 (99.2) 218 (90.1) 206 (85.1) 186 (76.8) 187 (77.2)	347 (96.6) 333 (92.7) 284 (79.1) 242 (67.4) 271 (75.5)	0.182 0.184 0.070 0.013 0.611

## Attitudes

The respondents in our study showed an overall positive attitude towards the HPV vaccine. Statistically significantly higher is the share of vaccinated respondents who believe the vaccine is effective in preventing cervical cancer (80.4% (n=213) vaccinated vs. 59.1% (n=275) non-vaccinated students,  $\chi^2=34.180$ ,  $p<0.001$ ) and who are on the opinion that the vaccine should be recommended to all

teenagers (85.7% (n=227) vaccinated vs. 57.9% (n=268) non-vaccinated students,  $\chi^2=82.339$ ,  $p<0.001$ ). The main driver for hesitation regarding the HPV vaccine was the fear of possible side effects and there was an association between the fear of possible side effects and the probability for vaccination (15.1% (n=40) vaccinated vs. 41.2% (n=191) non-vaccinated students,  $\chi^2=73.020$ ,  $p<0.001$ ).

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
<b>The HPV vaccine is effective in preventing cervical cancer.</b> Completely agree/Agree	488 (67.0)	213 (80.4)	275 (59.1)	<b>0.000</b>
<b>Getting the HPV vaccine can protect you from HPV infection.</b> Completely agree/Agree	497 (68.3)	194 (73.2)	303 (65.2)	<b>0.027</b>
<b>I am worried about the side effects of the HPV vaccine.</b> Completely agree/Agree	231 (31.7)	40 (15.1)	191 (41.2)	<b>0.000</b>
<b>I believe that HPV vaccine should be recommended to all teenagers.</b> Completely agree/Agree	495 (68.0)	227 (85.7)	268 (57.9)	<b>0.000</b>
<b>Getting the HPV vaccine will send a message to the teenagers that it is okay to have unprotected sex.</b> Completely agree/Agree	135 (18.5)	50 (18.9)	85 (18.3)	0.599
<b>I would recommend the HPV vaccine to family and friends.</b> Completely agree/Agree	436 (59.9)	214 (80.7)	222 (47.7)	<b>0.000</b>

Model	Unstandardized Coefficients		Wald	df	Sig.	Exp (B)	95% Confidence Interval for B	
	B	Std. Error					Lower Bound	Upper Bound
(Constant)								
<b>Faculty</b>								
Faculty of Medicine (baseline)								
Faculty of Dental Medicine	1.063	0.559	3.615	1	0.057	2.896	0.968	8.669
Faculty of Pharmacy	0.162	0.420	0.149	1	0.700	1.176	0.516	2.679
<b>Year of study</b>								
1 <sup>st</sup> year of study (baseline)								
2 <sup>nd</sup> year of study	0.172	0.403	0.181	1	0.670	1.187	0.538	2.618
3 <sup>rd</sup> year of study	0.086	0.348	0.061	1	0.804	1.090	0.551	2.156
4 <sup>th</sup> year of study	-0.099	0.371	0.072	1	0.789	0.905	0.437	1.875
5 <sup>th</sup> year of study	-0.771	0.400	3.707	1	0.054	0.463	0.211	1.014
6 <sup>th</sup> year of study	-0.954	0.413	5.333	1	<b>0.021</b>	0.385	0.171	0.866
<b>Gender</b>								
89/Male gender (baseline)								
Female gender	1.627	0.298	29.768	1	<b>0.000</b>	5.087	2.836	9.125
<b>Worried about possible side effects of the HPV vaccine</b>								
Strongly disagree (baseline)								
Disagree	-0.605	0.367	2.717	1	0.099	0.546	0.266	1.121
Neither agree nor disagree	-0.808	0.361	5.021	1	<b>0.025</b>	0.446	0.220	0.904
Agree	-1.575	0.404	15.193	1	<b>0.000</b>	0.207	0.094	0.457
Completely agree	-2.479	0.631	15.445	1	<b>0.000</b>	0.084	0.024	0.289
<b>Believe the HPV vaccine should be recommended to all teenagers</b>								
Strongly disagree (baseline)								
Disagree	-1.808	1.108	2.663	1	0.103	0.164	0.019	1.438
Neither agree nor disagree	-1.662	0.869	3.659	1	0.056	0.190	0.035	1.042
Agree	-1.161	0.856	1.841	1	0.175	0.313	0.059	1.676
Completely agree	-0.106	0.867	0.015	1	0.903	0.900	0.165	4.920
<b>Getting the HPV vaccine can effectively protect you</b>								
Strongly disagree (baseline)								
Disagree	0.686	0.994	0.476	1	0.490	1.985	0.283	13.929
Neither agree nor disagree	0.068	0.942	0.005	1	0.943	1.070	0.169	6.781
Agree	-0.144	0.930	0.024	1	0.877	0.866	0.140	5.357
Completely agree	-0.663	0.951	0.486	1	0.486	0.516	0.080	3.321
<b>Getting the HPV vaccine will send a message to teens that it is okay to become sexually active from an early age</b>								
Strongly disagree (baseline)								
Disagree	0.641	0.295	4.718	1	<b>0.030</b>	1.889	1.065	3.387
Neither agree nor disagree	0.427	0.283	2.275	1	0.131	1.532	0.880	2.667
Agree	0.355	0.344	1.066	1	0.302	1.426	0.727	2.796
Completely agree	0.326	0.482	0.457	1	0.499	1.386	0.538	3.565
<b>I would recommend the HPV vaccine to family and friends</b>								
Strongly disagree (baseline)								
Disagree	-0.147	1.344	0.012	1	0.913	0.863	0.062	12.013
Neither agree nor disagree	0.187	1.288	0.021	1	0.885	1.205	0.097	15.051
Agree	1.019	1.303	0.611	1	0.434	2.769	0.215	35.606
Completely agree	0.816	1.337	0.373	1	0.541	2.262	0.165	31.065



We performed a logistic regression to determine the effects on the likelihood of receiving the HPV vaccine. The logistic regression model was statistically significant ( $\chi^2 = 247.558$ ,  $p < 0.001$ ). The model correctly classified 39.5% of the cases. In terms of demographic characteristics respondents who were in the 6<sup>th</sup> year of their study were 0.385 less likely to have received the HPV vaccine whereas the female students were 5.1 times more likely to have been vaccinated. Regarding the attitudes of the respondents who were afraid of possible adverse events following the administration of the HPV vaccine were less likely to have received the vaccine. On the contrary the students who didn't agree with the statement that recommending the HPV vaccine to teenagers will send a message that it is okay to become sexually active at an early age were 1.89 times more likely to have been vaccinated.

## Discussion

To the best of our knowledge this is the first study to assess the knowledge, practices and attitudes towards the HPV vaccine among students in medical universities in North Macedonia. As future healthcare providers it is critical that students are thoroughly educated about the HPV virus and the vaccines available for and the recommendations for vaccination.

North Macedonia has a population of 2,065 million, 890,171 of them women aged 15 years or older. Current estimates suggest that every year 113 women are diagnosed with cervical cancer and among them 62 die from the disease and for 2023 the incidence from cervical cancer is 10.9<sup>5</sup>. North Macedonia has introduced a national screening program for cervical cancer since 2021 which is covering women 24 through 60 years of age and it is reported that 6 in 10 women have been screened for cervical cancer in the last 5 years<sup>7</sup>.

HPV vaccination is the primary and the most effective way to prevent HPV and its potentially serious complications and malignancy. Currently, three HPV vaccines are available and shown to be effective worldwide<sup>1</sup>. The quadrivalent HPV vaccine has been found to be successful in preventing genital warts and external genital lesions in males. Additionally, both the quadrivalent and ninevalent HPV vaccines have been shown to provide comparable levels of protection against precancerous lesions and cancer in the cervix, vagina, and vulva in young women<sup>12</sup>.

Our students demonstrated good knowledge about some aspects of the HPV virus and the risk of cervical cancer, but there were substantial gaps in their knowledge regarding other HPV-related oncological diseases. This supports the necessity of advocating for educational initiatives targeting young individuals and implementing modifications to the existing curriculum of university

students enrolled in health sciences schools. These measures aim to enhance the knowledge and awareness of future healthcare professionals regarding HPV. In comparison, a study in Serbia also proved that students involved in medical studies or those that attended medical high school had the highest knowledge about cervical cancer<sup>13</sup>. The level of knowledge about cervical cancer (CC) and human papillomavirus HPV virus is generally inadequate in other Balkan countries. A study conducted in Romania revealed that although most women were familiar with HPV, their understanding of the risk factors for infection was limited<sup>14</sup>. In Greece, adolescents were also found to have insufficient knowledge about the risk factors and methods of protection against cervical cancer<sup>15</sup>. Similarly, Hungary and Slovenia also reported a similar situation with regards to cervical cancer and HPV knowledge<sup>16,17</sup>.

The HPV vaccine uptake in our study was 36.4% (40.3% for females vs. 18.1% for males). We established a statistically significant difference between the vaccinated and non-vaccinated respondents in terms of gender ( $\chi^2 = 22.231$ ,  $p < 0.001$ ) and in the binary logistic regression analysis being female was the strongest variable associated with the probability to have received the HPV vaccine. The vaccine development and implementation approach has been primarily targeted towards women with the goal of avoiding cervical cancer, which has led to the phenomenon of vaccination feminization<sup>18</sup>. Similarly, the HPV vaccine was introduced in 2009 in North Macedonia and the immunization program targets females above 12 years of age. The latest global guidelines for HPV vaccination now encompass a wider range of age groups. In addition to adolescents of both genders aged 11-12 years, females aged 13-26 years who have not received prior vaccination or completed the vaccine series are also recommended to be vaccinated. Furthermore, males aged 13-21 years and 22-26 years, who either have specific medical conditions or want to protect themselves against the disease, are also advised to receive the vaccine<sup>19</sup>. For 2021 the coverage with HPV vaccine among females has been estimated to be 32%<sup>5</sup>. In our study the uptake among females is higher-40.3% which can be explained that our respondents are students in medical universities and they have better knowledge regarding the HPV virus and are more motivated to receive the vaccine.

Our results for the vaccine uptake among our respondents (36.4%) are higher than the results of studies from India (6.8% uptake), Turkey (4.3% uptake) and similar to studies from Brazil (21% uptake), and USA (32.1% uptake)<sup>20-23</sup>. The variations in the adoption of the HPV vaccine across different countries can be attributed to barriers that impede the uptake of the vaccine. These barriers include insufficient understanding of HPV infection and its associated illnesses, concerns about the safety of the vaccine, the high cost of the HPV vaccine, logistical challenges in organising vaccine campaigns, and

difficulties in ensuring that both recipients and providers adhere to the recommended vaccine schedule.

When exploring the attitudes of the students regarding the HPV vaccine we found that there was a substantial part of respondents that were having doubts about the effectiveness (67 % of all respondents agree/completely agree with the statement that the HPV vaccine is effective in preventing cervical cancer), and safety of the vaccine (31.7% of respondents were concerned about possible side effects after HPV vaccination). The findings of this survey align with a previous study conducted in Spain, which reported that 66.5% and 65.4% of students agree or strongly agree that HPV can prevent cervical cancer and that the associated side effects are acceptable, respectively<sup>24</sup>. Furthermore, the fear of possible side effects after HPV vaccination proved to be negatively associated with the probability of vaccination.

The findings of our study continuously emphasise the necessity for further educational interventions to enhance understanding and consciousness regarding the prevention of cervical cancer. It is important to increase awareness of cervical cancer and screening programmes using various communication channels. These programs can take various forms, such as seminars, group discussions, and interactive sessions, and can involve both pharmaceutical companies and government initiatives. In addition, the media can play a significant role in increasing awareness about HPV and cervical cancer. This was confirmed by a Serbian study, which found that the media was the primary source

of information for participants<sup>25</sup>. Similarly, an American study involving young women also demonstrated the media's influence on public opinion. Overall, promoting accurate information about HPV and its prevention is crucial to increasing vaccination rates and preventing cervical cancer<sup>26</sup>.

## Conclusion

The medical students in the present study demonstrated an overall good knowledge of the HPV virus, cervical cancer, and vaccination, although exhibited deficiencies in their knowledge pertaining to HPV-related illnesses. The present investigation revealed that medical students in North Macedonia had suboptimal uptake of the HPV vaccine. To enhance the acceptance of the HPV vaccine, it is crucial for individuals to acquire accurate information, possess awareness of its existence, and obtain it from trustworthy sources. The primary factor contributing to vaccination hesitation is scepticism regarding the safety and efficacy of the vaccine. It is recommended to utilise diverse audio-visual platforms for carrying out educational programmes aimed at promoting vaccination within the community. These programmes should aim to enhance positive attitudes about HPV vaccines, raise information about vaccine availability, and bolster public trust in the safety of vaccines.

## Conflict of Interest

None.

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