

Review

Barriers to the HPV Vaccination Program in the Eastern Mediterranean Region: A Narrative Review

Hakimi et al. Barriers to HPV Vaccination Program in Eastern Mediterranean Region

Sevil Hakimi¹, Faris Lami², Leil Allahqoli³, Ibrahim Alkatout⁴

¹Research Center of Psychiatry and Behavioral Sciences Tabriz University of Medical Science. Tabriz

²Department of Community Medicine, College of Medicine, University of Baghdad. Baghdad

³Ministry of health and medical education, Tehran, Iran

⁴Department of Obstetrics and Gynecology, University Hospital Schleswig-Holstein Campus Kiel, Kiel, Germany

Abstract

The human papillomavirus (HPV) vaccine is regarded as one of the most effective ways of preventing cervical cancer. Despite the massive burden of this disease, only two countries in the Eastern Mediterranean Region (EMR) have implemented the HPV vaccination program. The aim of the present study was to assess the main barriers to the integration of HPV vaccination in the national vaccination programs of EMR countries. We performed a narrative review with no inclusion and exclusion criteria. The electronic databases we searched included Medline (PubMed), Scopus, Embase, and Web of Science (last update December 2021). The search was not subject to any limitation in terms of time or method. Studies that dealt with the obstacles or the needs of vaccination programs in EMR countries were included in the investigation. After a full-text screening, the report comprised 31 studies from 15 EMR countries. All of the studies were descriptive. The most common barriers to the HPV vaccination are the following: a) lack of knowledge and awareness, b) economic barriers in terms of the cost-effectiveness of the HPV vaccination program, c) social insecurity in conflict zones, d) cultural norms and religion. EMR countries should focus on modifiable barriers to the vaccination program. Steps to improve HPV vaccination coverage in these countries should include enhancing social awareness and mobilization, ensuring the support of the GAVI Alliance (Global Alliance for Vaccines and Immunization) in eligible countries, using national resources in an optimal way, and addressing the HPV vaccination in undergraduate medicine and paramedic curriculums.

Keywords: Barriers to vaccination, cervical cancer, Eastern Mediterranean region countries, HPV vaccine

Address for Correspondence: Leila Allahqoli
e.mail: lallahqoli@gmail.com

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Introduction

Cervical cancer is the fourth most common cancer among women worldwide (1). The prevalence of cervical cancer in the Sub-Saharan region is 11.4 % and the consequent fatality rates are considerable (2). The human papillomavirus (HPV) is one of the most significant risk factors for cervical cancer. HPV can be transmitted through sexual contact, including vaginal or oral sex with an infected person (3). HPV has more than 100 strains, of which HPV16 and HPV18 account for about 70% of invasive cervical cancers (4, 5). The HPV vaccine can prevent cervical cancer effectively. The World Health Organization (WHO) recommends routine HPV vaccination for girls aged 9-14 years (prior to sexual activity) through national immunization programs, “catch-up vaccinations” for unvaccinated adults older than 15 years with high-risk behaviors, and for HIV-positive women (6). A minimum six-month interval must be ensured between the first and the second dose. The WHO currently does not recommend the HPV vaccination for boys (7). Since 2007 the HPV vaccine is approved in the United States and the European Union (8). National HPV vaccination programs have been implemented in at least 107 countries worldwide (9). The HPV vaccination is a part of the routine immunization program in many high-income countries (8).

The HPV vaccination rate for women in the USA and Australia is about 37.6% and 32%, respectively (10), but is lower in Asian countries (3). Implementation of the HPV vaccination program is probably the most effective way of reducing the burden of cervical cancer (11), especially when screening tests are not available, limited, or of poor quality (12). According to the WHO, no study has reported major adverse effects of the HPV vaccine (13).

However, the HPV vaccine is not affordable in those countries that need it the most. In fact, cervical cancer mirrors health inequity more than any other female cancer (8, 14); approximately 90% of deaths due to cervical cancer occur in low-income countries (1).

The Eastern Mediterranean Region (EMR) of the WHO extends from Iran to Djibouti, covers 22 countries (Table 1) and a population of 680 million (15). Although some nations, including those of the Persian Gulf have common roots, the EMR countries differ significantly in terms of their geopolitical status, cultural backgrounds, income levels, and health expenditure rates. Moreover, some countries such as Afghanistan, Yemen and Syria are experiencing prolonged social instabilities and conflicts. A considerable part of the population of EMR countries has been displaced in recent years due to internal wars. Despite the huge burden of cervical cancer especially in low- and middle-income countries (LMIC) (16), only two nations in the EMR have implemented HPV vaccination in their national vaccination program (NVP) (17). The present study aimed to assess the barriers experienced in incorporating HPV vaccination in the NVP of EMR countries.

Methods

Published articles which addressed HPV vaccination were searched for a narrative review.

Determining the research question

The review was based on the following research question: What are the main barriers to the HPV vaccination in EMR countries?

Identifying relevant studies

We performed a systematic search in a range of electronic databases, including Medline (PubMed), Scopus, Embase, and Web of Science (WOS) (initial search in June 2021; last update in December 2021).

The following keywords were used: “HPV”, “vaccine” “vaccine strategy”, “barrier”, “obstacle”, and “Eastern Mediterranean region countries”. The names of 22 member states of EMR were searched separately. The classification of EMR countries is summarized in Table 1.

Inclusion and Exclusion Criteria

All types of studies dealing with HPV vaccination in EMR countries, published exclusively in the English language, were included. Reports that were not in line with the purpose of the study or did not provide their full text were excluded.

Selection of studies

We reviewed all types of articles published in EMR countries. The search was not subject to any limitations in terms of time or methodology. Reference lists of all identified studies were screened manually. Vaccination-related guidelines published by the ministry of health in each EMR country and the WHO-EMRO were searched. The review process consisted of two screening steps: a) reviewing the title and summary of the articles, and b) reviewing the full texts.

Collating, summarizing, and reporting the results

We reviewed studies that included data concerning programs, strategies, barriers, and implementation of the HPV vaccination program in EMR countries. As we aimed to identify existing gaps and guide future research, we dispensed with quality assessment or an extensive data synthesis of the published reports.

Results

Search results

We reviewed investigations from 2012 to 2021 based on various methodologies. Of 85 publications found in the various databases, 10 were duplicate articles. After reviewing the titles and abstracts of the remaining reports, 45 were excluded. Finally, 31 studies from 15 EMR countries (Arab states $n = 23$, African countries $n = 3$, and non-Arab countries $n = 5$) were included in a narrative review. The characteristics of the studies are summarized in Table 2.

Cervical cancer and HPV prevalence

We lack precise statistics regarding the incidence and prevalence of cervical cancer for any EMR member state. Currently, in Afghanistan about 862 women have been identified with cervical cancer and 570 die from the disease every year (18). Cervical cancer ranks second after breast cancer in some countries, such as Yemen, Djibouti, Somalia and Afghanistan (19). An increase in life expectancy has been registered in all EMR countries. The risk of cancer is increasing with age. Both, population growth and population aging have led to more numerous cases of cancer. Changes in lifestyle are regarded as one of the most important risk factors for cervical cancer. The HPV infection is increasing at an alarming rate in recent times due to unsafe sexual activity (20). The overall prevalence of HPV in Egypt was estimated at 10-23% (21, 22). Bansal et al. estimated an HPV prevalence of 5.8% among women in Qatar with a normal cytology, and 18.4% in women with an abnormal cervical cytology (23). In Kuwait, the prevalence of HPV was reported to be about 2.5% and higher than 50% in women with a normal and abnormal cytology, respectively (24, 25).

HPV vaccination status in EMR countries

According to the report of the WHO, at the annual workshop of the EMRO held in Lebanon in 2019 it was noted that only Libya and the United Arab Emirates (UAE) had integrated the HPV vaccination in their national vaccination programs, while a third country (Morocco) plans to do so (26, 27). In some countries such as Iran, the private sector is responsible for providing vaccines. Therefore, the HPV vaccine is neither affordable nor available to all persons (28).

Barriers to HPV vaccination in EMR countries

Knowledge and awareness

Lack of knowledge is a fundamental obstacle to the HPV vaccination. Adequate knowledge about the role of HPV as a risk factor for cervical cancer is crucial. In a study comprising 746 female students in Pakistan, Gul et al. reported that nearly 85% had no information about the HPV vaccine and, surprisingly, more than 95% would like to receive it (29). Knowledge of

the HPV vaccination was moderate or poor in Bahrain, Morocco, Oman, and Lebanon, expressed in a distrust of the vaccine (30-34).

Due to the absence or paucity of public education, the majority of the residents in the EMR countries are unaware of the availability of the HPV vaccine. Recommendations for the HPV vaccination by physicians and the workforce in the health sector are very important, as these will influence parents' acceptance of the vaccine for their daughters (35). However, health care providers themselves do not have sufficient knowledge about the vaccine. Studies performed in Saudi Arabia and Iraq showed that physicians and medical students are poorly informed about the subject (36-39).

About 54% of student nurses in Sudan were aware of the HPV vaccine (40). The studies revealed that the main sources of information for medical and nursing students were mass media, including TV and web pages, as well as self-learning (36).

Published studies reveal that there is concern about the long- and short-term side effects of the HPV vaccine (30). Women are afraid of its potential side effects (20). In a study in Syria, Al Saad et al. (41, 42) reported that mothers were unwilling to vaccinate their daughters against HPV due to concerns about the adverse effects and safety of the vaccine.

Economic barriers regarding the cost-effectiveness of HPV vaccination program

Given the population structure (large and growing young population) in EMR countries, the large number of persons eligible for vaccination, and the number of required doses (3 doses), the provision of a sufficient budget for public vaccination is a challenging issue for many countries in the region (34). The HPV vaccine is almost as expensive as other vaccines (35). The cost of each dose ranges from 13 to 100 US\$ (43), making vaccination programs unaffordable for many low-income countries. The cost of one dose of HPV vaccine (Gardasil 4) is about 13 US\$, as the cost is not covered completely or even partially by the insurance companies (44). Therefore, the majority of eligible persons in Iran do not receive the vaccine (28). However, in a secondary analysis of the Iranian Ministry of Health data, Mohammadpour et al. (26) concluded that the use of Gardasil has increased very markedly in the last 5 years. Shaykh et al. reported that the cost of vaccination is a barrier in Pakistan: the surveyed persons said they refrained from HPV vaccination because it was not affordable. A correlation was observed between income levels and HPV vaccination (45). The Global Alliance for Vaccine and Immunization (GAVI) could negotiate with the industry to provide a low-cost vaccine, or co-finance its provision. In 2011 Merck Company announced that a single dose of the HPV vaccine will be distributed on behalf of the GAVI for 5 US\$ (43). Similar programs could be devised to provide affordable HPV vaccines. It should be noted that the HPV vaccine is affordable for countries with a gross domestic product just below 1000 US\$ when each dose is supplied for 1-2 US\$ (8). Some EMR nations, including Saudi Arabia, Oman and Qatar are not low-income countries, but their governments doubt the cost-effectiveness of HPV vaccination on a nationwide basis (28). It appears that the opinion of the government about the missing cost benefit of Gardasil is the main factor underlying the integration of the HPV vaccine in the NVP of each country (46). Health economy experts assessed the cost benefit, cost effectiveness, and affordability of the vaccine in Oman. They also evaluated the burden of HPV and stated that the integration of the HPV vaccine in the NVP of Oman is not cost effective (47).

The paucity of data about the burden of cervical cancer, its annual incidence, as well as the direct and indirect costs of treatment impairs the development of an up-to-date guideline and decisions about the HPV vaccine in EMR countries. The cost-effectiveness of mass vaccination against HPV depends on the incidence of cervical cancer and the cost of vaccine (48). To make an appropriate decision, experts would need to obtain valid data about the direct and indirect costs of treating precancerous lesions and invasive carcinoma. Vaccination

is obviously a cost-effective measure in countries with a high incidence of cervical cancer (48).

Social insecurity in conflict zones

Timely delivery of the HPV vaccine in conflict zones is very challenging. It requires a reliable infrastructure, such as an uninterrupted cold chain. Schools are one of the appropriate places for the HPV vaccine. However, a very large number of girls in poor and conflict-ridden societies do not attend school or drop out after primary school (49). Of the 22 member states of the EMR, nearly six suffer from internal wars and insecurity.

Cultural norms/religion

EMR countries have a relatively young population. Given social taboos, the age of sexual debut in this region is not clear. However, it is estimated that the usual age is 19-23 years (50). There is evidence of changing sexuality and gender relations in EMR countries. The age of marriage and the prevalence of premarital sexual activity are increasing (51). The HPV vaccine is known to prevent STDs and this raises cultural as well as religious concerns in the society. Given that all EMR member states are predominantly Muslim, a considerable proportion of the population in some countries are conservative in regard of sexual activity. Islam does determine the sexual behavior of individuals in EMR countries; sexual activity should occur within the context of marriage. In the same vein, religious activists may oppose the HPV vaccine because they believe it encourages premarital sexual activity (52). Cultural circumstances cause mothers to believe that their daughters are not at risk for HPV and do not need the vaccine (41). According to religious authorities, given that young people have no premarital sexual contact, they do not need the HPV vaccine (49). In a study comprising 600 women in the UAE, Ortashi et al. noted that 17% of women believed the HPV vaccine may not be culturally acceptable (53).

Discussion

Cervical cancer is regarded as one of the leading causes of death among women in EMR countries (19). This review summarizes the HPV vaccination program in the Eastern Mediterranean region. Barriers to vaccination were mainly lack of knowledge and awareness, doubts about the cost-effectiveness of the HPV vaccination program, social insecurity in conflict zones, and cultural norms or religious beliefs. Lack of knowledge about the HPV vaccine was one of common barriers in EMR countries. Lack of knowledge creates a vacuum and encourages the spread of misinformation in social networks (54). Educational initiatives aimed at women may be most successful if designed to increase awareness of their susceptibility to HPV infection and transmission. School-based meetings would serve as a useful sensitization strategy to enhance the quantity and quality of knowledge about cervical cancer and the HPV vaccine. Vaccine safety is one of the prime concerns of parents and young persons. We need culturally sensitive training programs addressing parents and emphasizing the absence of side effects of the vaccine (55). Inclusion of the HPV vaccination in the curricula of undergraduate-level medicine and paramedics is also essential. A change in policies regarding the HPV vaccine is essential because we anticipate an increase in the burden of cervical cancer over the coming years (56).

Our analysis showed that the cost and cost-effectiveness of the vaccine are further barriers to its acceptance in the target population. Previous studies reported the highest vaccination coverage rates for HPV in countries where vaccines are funded by the national budget (57). Providing HPV vaccine free of charge or at a low cost will be essential in low-income countries. In view of the fact that the GAVI Alliance covers the provision and delivery of the HPV vaccine for low- and lower-middle income countries, upper- and middle-income countries are confronted with serious challenges in purchasing the vaccine (58).

Male guardianship is an issue in EMR countries. As the male-dominated culture requires the spouse's consent to a woman's vaccination, men's education should be included in the agenda of the health system. Women's access to the vaccination would depend on men being sufficiently informed about it (59). Advocacy programs will be needed for introducing the HPV vaccine. Addressing the burden of cervical cancer is a critical issue and requires a suitable cancer registry system (60).

Strong partnership and collaboration with all stakeholders will be needed to implement the HPV vaccination program (61). All of the involved parties should be aware of their clear roles from the point of distribution to implementation. In some countries, we need to identify specific needs such as technical or financial support, a suitable plan of action, and appropriate monitoring.

Some factors, such as the level of income, knowledge, and the employment of mothers facilitate the acceptance of the HPV vaccine. Recommendations about the vaccine by health care authorities and its approval by decision-makers in each country would encourage mothers to accept the vaccine (41).

Conclusions

There is an urgent need for greater social awareness about the necessity of HPV vaccination. Addressing the HPV vaccination in undergraduate medicine and the paramedic curriculum is an essential step towards improving HPV vaccination coverage in these countries. The burden of cervical cancer should be publicized on the basis of robust data proving the significance of HPV vaccination and justifying its cost-effectiveness. Policy-makers should be sensitized to the economic benefits of the vaccination. Ensuring the support of the GAVI in eligible countries will be a crucial step in achieving high vaccination coverage. Non-GAVI countries should be encouraged to allocate national resources to HPV vaccination in an optimal way (62).

References

1. Serrano B, Brotons M, Bosch FX, Bruni L. Epidemiology and burden of HPV-related disease. *Best practice & research Clinical obstetrics & gynaecology*. 2018;47:14-26.
2. Bruni L, Diaz M, Castellsagué M, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. *Journal of Infectious Diseases*. 2010;202(12):1789-99.
3. Kristina SA, Permitasari NPAL. Knowledge, attitudes and barriers towards human papillomavirus (HPV) vaccination in developing economies countries of South-East Asia region: a systematic review. *Systematic Reviews in Pharmacy*. 2019;10(1):81-6.
4. Jalil AT, Karevskiy A. The Cervical Cancer (CC) Epidemiology and Human Papillomavirus (HPV) in the Middle East. *International Journal of Environment, Engineering & Education*. 2020;2(2):7-12.
5. Forman D, de Martel C, Lacey CJ, Soerjomataram I, Lortet-Tieulent J, Bruni L, et al. Global burden of human papillomavirus and related diseases. *Vaccine*. 2012;30:F12-F23.
6. WHO. Comprehensive cervical cancer control Geneva. Available at: <https://www.who.int/reproductivehealth/topics/cancers/hpv-vaccination/en/> Accessed on September 2021. 2009.
7. WHO. Guide to introducing HPV vaccine into national immunization programmes: World Health Organization; 2016.
8. Agosti JM, Goldie SJ. Introducing HPV vaccine in developing countries—key challenges and issues. *New England Journal of Medicine*. 2007;356(19):1908-10.

9. Bruni L, Saura-Lázaro A, Montoliu A, Brotons M, Alemany L, Diallo MS, et al. HPV vaccination introduction worldwide and WHO and UNICEF estimates of national HPV immunization coverage 2010-2019. *Preventive medicine*. 2021;144:106399.
10. Group FIIS. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *The BMJ*. 2010;341.
11. Karimi-Zarchi M, Allahqoli L, Nehmati A, Kashi AM, Taghipour-Zahir S, Alkatout I. Can the prophylactic quadrivalent HPV vaccine be used as a therapeutic agent in women with CIN? A randomized trial. *BMC public health*. 2020;20(1):274.
12. Kind AB, Pavelyev A, Kothari S, El Mouaddin N, Schmidt A, Morais E, et al. Assessing the epidemiological impact on cervical cancer of switching from 4-valent to 9-valent HPV vaccine within a gender-neutral vaccination programme in Switzerland. *BMC public health*. 2020;20:1-13.
13. WHO. HPV Information sheet—Observed Rate of Vaccine Reactions human papillomavirus vaccine. 2017.
14. Salehiniya H, Momenimovahed Z, Allahqoli L, Momenimovahed S, Alkatout I. Factors related to cervical cancer screening among Asian women. *European review for medical and pharmacological sciences*. 2021;25(19):6109-22.
15. WHO. <https://www.emro.who.int/countries.html>. 2022.
16. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2018;68(6):394-424.
17. Dochez C, Al Awaidy S, Mohsni E, Fahmy K, Bouskraoui MJV. Strengthening national teams of experts to support HPV vaccine introduction in Eastern Mediterranean countries: Lessons learnt and recommendations from an international workshop. 2020;38(5):1114-9.
18. Anwari P, Debellut F, Vodicka E, Clark A, Farewar F, Zhwak ZA, et al. Potential health impact and cost-effectiveness of bivalent human papillomavirus (HPV) vaccination in Afghanistan. *Vaccine*. 2020;38(6):1352-62.
19. Kulhánová I, Bray F, Fadhil I, Al-Zahrani AS, El-Basmy A, Anwar WA, et al. Profile of cancer in the Eastern Mediterranean region: The need for action. *Cancer epidemiology*. 2017;47:125-32.
20. Al-Azri MH, Al-Saidi M, Al-Mutairi E, Panchatcharam SM. Knowledge of Risk Factors, Symptoms and Barriers to Seeking Medical Help for Cervical Cancer among Omani Women Attending Sultan Qaboos University Hospital. *Sultan Qaboos University Medical Journal*. 2020;20(3):e301.
21. Youssef MA, Abdelsalam L, Harfoush RA, Talaat IM, Elkattan E, Mohey A, et al. Prevalence of human papilloma virus (HPV) and its genotypes in cervical specimens of Egyptian women by linear array HPV genotyping test. *Infectious agents and cancer*. 2016;11(1):1-10.
22. Shaltout MF, Sallam HN, AbouSeeda M, Moiety F, Hemeda H, Ibrahim A, et al. Prevalence and type distribution of human papillomavirus among women older than 18 years in Egypt: a multicenter, observational study. *International Journal of Infectious Diseases*. 2014;29:226-31.
23. Bansal D, Elmi AA, Skariah S, Haddad P, Abu-Raddad LJ, Al Hamadi AH, et al. Molecular epidemiology and genotype distribution of Human Papillomavirus (HPV) among Arab women in the State of Qatar. *Journal of translational medicine*. 2014;12(1):1-9.

24. Al-Awadhi R, Chehadeh W, Jaragh M, Al-Shaheen A, Sharma P, Kapila K. Distribution of human papillomavirus among women with abnormal cervical cytology in Kuwait. *Diagnostic cytopathology*. 2013;41(2):107-14.
25. Al-Awadhi R, Chehadeh W, Kapila K. Prevalence of human papillomavirus among women with normal cervical cytology in Kuwait. *Journal of medical virology*. 2011;83(3):453-60.
26. WHO. The work of WHO in the Eastern Mediterranean Region: annual report of the Regional Director 2019. 2020.
27. Gallagher KE, LaMontagne DS, Watson-Jones D. Status of HPV vaccine introduction and barriers to country uptake. *Vaccine*. 2018;36(32):4761-7.
28. Mohammadpour F, Mansouri A, Hadjibabaie M. Utilization Evaluation of Human Papilloma Virus Vaccine (GARDASIL®) in Iran; A Cross-Sectional Study. *Iranian journal of pharmaceutical research : IJPR*. 2020;19(1):68-76.
29. Gul S, Javed A, Mall S. Awareness about cervical cancer, human papilloma virus and acceptability of its vaccine among female university students of Peshawar Pakistan. *Asian J Agri Biol*. 2015;3(3):90-6.
30. Husain Y, Alalwan A, Al-Musawi Z, Abdulla G, Hasan K, Jassim G. Knowledge towards human papilloma virus (HPV) infection and attitude towards its vaccine in the Kingdom of Bahrain: cross-sectional study. *BMJ open*. 2019;9(9):e031017.
31. Jassim G, Obeid A, Al Nasheet HA. Knowledge, attitudes, and practices regarding cervical cancer and screening among women visiting primary health care Centres in Bahrain. *BMC public health*. 2018;18(1):1-6.
32. Selmouni F, Zidouh A, Nejjari C, Bekkali R. Acceptability of the human papilloma virus vaccine among Moroccan parents: a population-based crosssectional study. *EMHJ-Eastern Mediterranean Health Journal*. 2015;21(8):555-63.
33. Zouheir Y, Daouam S, Hamdi S, Alaoui A, Fechtali T. Knowledge of human papillomavirus and acceptability to vaccinate in adolescents and young adults of the Moroccan population. *Journal of pediatric and adolescent gynecology*. 2016;29(3):292-8.
34. Abou El-Ola MJ, Rajab MA, Abdallah DI, Fawaz IA, Awad LS, Tamim HM, et al. Low rate of human papillomavirus vaccination among schoolgirls in Lebanon: barriers to vaccination with a focus on mothers' knowledge about available vaccines. *Therapeutics and clinical risk management*. 2018;14:617.
35. Jumaan AO, Ghanem S, Taher J, Braikat M, Al Awaidy S, Dbaibo GS. Prospects and challenges in the introduction of human papillomavirus vaccines in the extended Middle East and North Africa region. *Vaccine*. 2013;31:G58-G64.
36. Al-Darwish AA, Al-Naim AF, Al-Mulhim KS, Al-Otaibi NK, Morsi MS, Aleem AM. Knowledge about cervical cancer early warning signs and symptoms, risk factors and vaccination among students at a medical school in Al-Ahsa, Kingdom of Saudi Arabia. *Asian Pacific Journal of Cancer Prevention*. 2014;15(6):2529-32.
37. Sait KH. Knowledge, attitudes, and practices regarding cervical cancer screening among physicians in the Western Region of Saudi Arabia. *Saudi Med J*. 2011;32(11):1155-60.
38. Hwaid AHJAJPHR. Knowledge and awareness of papillomavirus and cervical cancer among college students and health care workers women in Diyala, Iraq. 2013;1(8):221-5.
39. Ibrahim WA, Daniel S, Hussein NR, Assafi MS, Othman RJWsHB. Knowledge of Human Papillomavirus (HPV) and the HPV Vaccine Among Medical and Nursing Students of Duhok, Iraq. 2019;6(1):1-6.

40. AbdAllah A, Hummeida M, Elmula I. Awareness and attitudes of nursing students towards prevention of cervical cancer. *Cervical Cancer*. 2016;1(1):106.
41. Al Saad M, Jadoo SAA. Syrian mothers, why to accept or to refuse HPV vaccine for their teen girls. *Journal of Ideas in Health*. 2018;1(1):7-13.
42. Alsaad MA, Shamsuddin K, Fadzil FJAPJoCP. Knowledge towards HPV infection and HPV vaccines among Syrian mothers. 2012;13(3):879-83.
43. Wigle J, Coast E, Watson-Jones D. Human papillomavirus (HPV) vaccine implementation in low and middle-income countries (LMICs): health system experiences and prospects. *Vaccine*. 2013;31(37):3811-7.
44. Yousefi M, Hasanzadeh M, Rostaminezhad V, Gaffarean M, Mousavi ASJJoO, Gynecology, Research C. Human Papillomavirus Vaccination: Is it Cost-Effective in Iran? 2017;2(1):0-.
45. Shaikh MY, Hussaini MF, Narmeen M, Effendi R, Paryani NS, Ahmed A, et al. Knowledge, Attitude, and Barriers Towards Human Papillomavirus (HPV) Vaccination Among Youths of Karachi, Pakistan. *Cureus*. 2019;11(11).
46. Khatibi M, Rasekh HR, Shahverdi Z. Cost-effectiveness evaluation of quadrivalent human papilloma virus vaccine for HPV-related disease in Iran. *Iranian journal of pharmaceutical research: IJPR*. 2014;13(Suppl):225.
47. Al Awaidy S. The National Committee for Vaccines Regulation and Surveillance of Vaccine-Preventable Diseases in the Sultanate of Oman: evidence-based approach and consensus decision-making. *Vaccine*. 2010;28:A39-A41.
48. Jit M, Brisson M, Portnoy A, Hutubessy R. Cost-effectiveness of female human papillomavirus vaccination in 179 countries: a PRIME modelling study. *The Lancet Global health*. 2014;2(7):e406-e14.
49. Kane MA. Delivering HPV vaccine in the industrial and developing world: the role of the ob-gyn community. *International Journal of Gynecology & Obstetrics*. 2006;94:S89-S94.
50. Seoud M. Burden of human papillomavirus-related cervical disease in the Extended Middle East and North Africa—A comprehensive literature review. *Journal of lower genital tract disease*. 2012;16(2):106-20.
51. El-Kak F. Sexuality and sexual health: constructs and expressions in the extended Middle East and North Africa. *Vaccine*. 2013;31:G45-G50.
52. Hamdi S. The impact of teachings on sexuality in Islam on HPV vaccine acceptability in the Middle East and North Africa region. *Journal of epidemiology and global health*. 2018;7:S17-S22.
53. Ortashi O, Shallal M, Osman N, Raheel H. Knowledge, attitude and practice of school nurses in the United Arab Emirates about HPV infection and vaccine. *Asian Pacific Journal of Cancer Prevention*. 2012;13(12):6481-4.
54. Zimet GD, Rosberger Z, Fisher WA, Perez S, Stupiansky NWJPM. Beliefs, behaviors and HPV vaccine: correcting the myths and the misinformation. 2013;57(5):414-8.
55. Gee J, Weinbaum C, Sukumaran L, Markowitz LEJHv, immunotherapeutics. Quadrivalent HPV vaccine safety review and safety monitoring plans for nine-valent HPV vaccine in the United States. 2016;12(6):1406-17.
56. de Sanjosé S, Serrano B, Castellsagué X, Brotons M, Muñoz J, Bruni L, et al. Human papillomavirus (HPV) and related cancers in the global Alliance for vaccines and immunization (GAVI) countries: a WHO/ICO HPV information Centre report: Elsevier; 2012.
57. Owsianka B, Gańczak M. Evaluation of human papilloma virus (HPV) vaccination strategies and vaccination coverage in adolescent girls worldwide. *Przegląd epidemiologiczny*. 2015;69(1):53-8, 151-5.

58. Tsu VD, LaMontagne DS, Atuhebwe P, Bloem PN, Ndiaye C. National implementation of HPV vaccination programs in low-resource countries: Lessons, challenges, and future prospects. *Preventive medicine*. 2021;144:106335.
59. Jradi H, Bawazir A. Knowledge, attitudes, and practices among Saudi women regarding cervical cancer, human papillomavirus (HPV) and corresponding vaccine. *Vaccine*. 2019;37(3):530-7.
60. Termrungruenglert W, Havanond P, Khemapech N, Lertmaharit S, Pongpanich S, Khorprasert C, et al. Cost and effectiveness evaluation of prophylactic HPV vaccine in developing countries. *Value in Health*. 2012;15(1):S29-S34.
61. Tsu VD, LaMontagne DS, Atuhebwe P, Bloem PN, Ndiaye C. National implementation of HPV vaccination programs in low-resource countries: Lessons, challenges, and future prospects. 2021;144:106335.
62. WHO. Summary Report on the Meeting of the Eastern Mediterranean Regional Technical Advisory Group [RTAG] on Immunization, Muscat, Oman 14 December 2017. World Health Organization, Regional Office for the Eastern Mediterranean; 2018.
63. Grabieli M, Reutzel TJ, Wang S, Rubin R, Leung V, Ordonez A, et al. HPV and HPV vaccines: the knowledge levels, opinions, and behavior of parents. 2013;38(6):1015-21.
64. Aljuwaiheli A, Al-Jarallah A, Al-Busairi H, El-Shazly MKJGJoMS. Awareness of HPV and cervical cancer vaccine among PHC physicians in Kuwait. 2013;3(4):152-9.
65. Wigle J, Coast E, Watson-Jones D. Human papillomavirus (HPV) vaccine implementation in low and middle-income countries (LMICs): health system experiences and prospects. *Vaccine*. 2013;31(37):3811-7.
66. Ortashi O, Raheel H, Shalal MJAPJoCP. Acceptability of human papilloma virus vaccination among women in the United Arab Emirates. 2014;15(5):2007-11.
67. Khatibi M, Rasekh HR, Shahverdi Z, Jamshidi HR. Cost-Effectiveness Evaluation of Quadrivalent Human Papilloma Virus Vaccine for HPV-Related Disease in Iran. *Iranian journal of pharmaceutical research : IJPR*. 2014;13(Suppl):225-34.
68. Al-Darwish AA, Al-Naim AF, Al-Mulhim KS, Al-Otaibi NK, Morsi MS, Aleem AM. Knowledge about cervical cancer early warning signs and symptoms, risk factors and vaccination among students at a medical school in Al-Ahsa, Kingdom of Saudi Arabia. *Asian Pacific journal of cancer prevention : APJCP*. 2014;15(6):2529-32.
69. Saqer A, Ghazal S, Barqawi H, Babi JA, AlKhafaji R, Elmekresh MMJAPjocpA. Knowledge and awareness about cervical cancer vaccine (HPV) among parents in Sharjah. 2017;18(5):1237.
70. Alwahaibi N, Alsalami W, Alramadhani N, Alzaabi AJAPjocpA. Factors influencing knowledge and practice regarding cervical cancer and pap smear testing among Omani women. 2018;19(12):3367.
71. Abi Jaoude J, Saad H, Farha L, Dagher H, Khair D, Kaafarani MA, et al. Barriers, attitudes and clinical approach of Lebanese physicians towards HPV vaccination; A cross-sectional study. 2019;20(10):3181.
72. Sallam M, Al-Fraihat E, Dababseh D, Yaseen A, Taim D, Zabadi S, et al. Dental students' awareness and attitudes toward HPV-related oral cancer: a cross sectional study at the University of Jordan. 2019;19(1):1-11.
73. Anfinan NM. Physician's knowledge and opinions on human papillomavirus vaccination: a cross-sectional study, Saudi Arabia. *BMC health services research*. 2019;19(1):963.

74. AlMansoori LS, AlKatheeri MS, AlHallami AA, AlMarzooqi MY, Al-Tatari MJJoCR, Review. Physicians' knowledge, attitude, and practices toward HPV disease and vaccination in Al Ain city, UAE. 2019;10(06):20741-50.
75. Almazrou S, Saddik B, Jradi H. Knowledge, attitudes, and practices of Saudi physicians regarding cervical cancer and the human papilloma virus vaccine. Journal of infection and public health. 2020;13(4):584-90.
76. Rezqalla J, Alshatti M, Ibraheem A, Omar D, Houda A-F, AlHaqqan S, et al. Human Papillomavirus (HPV): unawareness of the causal role of HPV infection in cervical cancer, HPV vaccine availability, and HPV vaccine uptake among female schoolteachers in a Middle Eastern country. 2021;14(5):661-7.

Table 1. Classification of EMR countries	
EMR subregions	Countries
Arab states	Bahrain, Iraq, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, United Arab Emirates (UAE), Yemen, Occupied Palestinian Territory (OPT)
African countries	Djibouti, Egypt, Somalia, Sudan (North-East African nations)
	Libya, Morocco, Tunisia (North-West African nations)
Non-Arab countries	Iran, Afghanistan, Pakistan

Table 2. Characteristics of studies					
Author/year	Origin of the target population	Study type	Sample size	Study population	Results
Alsaad /2012 (42)	Syria	Descriptive/cross-sectional	345	Women	Less than a third of the participants were aware of HPV and the HPV vaccine.
Ortashi/2012 (53)	United Arab Emirates	Descriptive/cross-sectional	356	University students	46% of the participants said they accept the HPV vaccine. Fear of side effects (85%) and the absence of obvious benefits (38%) were among the most important factors hindering its acceptance.
Hwaid/ 2013 (38)	Iraq	Descriptive/cross-sectional	198	Women	Knowledge about the availability of the HPV vaccine was inadequate. Only 23.2% of the participants were aware of it.
Gabriel/ 2013 (63)	Jordan	Descriptive/cross-sectional	129	Parents	The mean knowledge score about HPV and the HPV vaccine was 36 (range 0-80). 40% of parents mentioned the cost of the vaccine as a barrier to vaccination.
Aljuwaihel/2013(64)	Kuwait	Descriptive/cross-sectional	206	Primary health care physicians	Information about the HPV vaccine was moderate. The percentage knowledge score was 63.4%.
Wigle/2013 (65)	Low- and middle-income countries	Review article	-	-	Social insecurity, internal wars and conflicts are barriers to HPV vaccination.
Ortashi/2014 (66)	United Arab Emirates	Descriptive/cross-sectional	640	Women	Knowledge about the HPV vaccine was low (37%) in the study population. However, 80 % of women would be willing to receive the vaccination. 69% of participants were willing to be vaccinated. 17% of the women believed it might not be culturally acceptable. Vaccine safety was one of the foremost concerns of women.
Khatibi/2014(67)	Iran	Descriptive modelling study	-	-	The cost of the vaccine may be viewed as a barrier in countries with limited resources.

Al-Darwish/2014 (68)	Saudi Arabia	Descriptive/cross-sectional	188	Medical students	67.7% of the participants were unaware of the availability of the HPV vaccine.
Gul/ 2015(29)	Pakistan	Descriptive/cross-sectional	764	Female university students	The information level of the young population about the HPV vaccine was not high.
Selmouni/ 2015 (32)	Morocco	Descriptive/cross-sectional	653 women 659 men	Parents of girls aged 6-12 years	The acceptance rate of the HPV vaccine was 76.8 (95% CI: 73.3–79.9%) among women and 68.9% (95% CI: 65.2–72.5%) among men.
Zouheir/2015 (33)	Morocco	Descriptive/cross-sectional	1044	Adolescents (12-17 years) and young persons (18-30 years)	The level of knowledge about the HPV vaccine was poor (20%). The acceptance rate of the HPV vaccine among the participants was 27%.
Abdallah/2016 (40)	Sudan	Descriptive/cross-sectional	246	Student nurses	A half of the participants (49.9%) lacked complete information about the HPV vaccine.
Saqer/2017(69)	United Arab Emirates	Descriptive/cross-sectional	400	Women	Near a third (36.5%) of the population had heard about the HPV vaccine. 76.6% of parents were willing to vaccinate their daughters. Vaccine recommendation by health care providers and greater awareness of the vaccine on the part of husbands could influence the rate of vaccinated girls.
Jassim/2018 (31)	Bahrain	Descriptive/cross-sectional	300 women	Primary health care attendees	11.3 % of the participants had heard about the HPV vaccine.
Alwahaibi/2018 (70)	Oman	Descriptive/ cross sectional	494	Patients attending an outpatient gynecology clinic, female staff of the clinic,	Patient awareness about the HPV vaccine was 5.9%. The awareness of staff members and students was 59.4% and 14.6%, respectively.

				university students	
Abou El Ola/2018 (34)	Lebanon	Descriptive/cross-sectional	1193	Women	The main barrier to HPV vaccination is lack of knowledge and information about it. 34% of the participants were aware of the availability of the vaccine to prevent cervical cancer.
Alsaad/2018 (41)	Syria	Descriptive/cross-sectional	400	Women	The cost of the HPV vaccine and lack of knowledge were major barriers hindering women's acceptance of the vaccine.
Hamdi/ 2018 (52)	Middle East and North Africa	Review article	-	-	Traditional norms and religious issues could serve as barriers to HPV vaccination.
Shaikh 2019 (45)	Pakistan	Descriptive/cross-sectional	400	Young adults (18-26 years)	Approximately a half of the responders considered the vaccine time consuming and expensive. Poor knowledge of the vaccine and its cost were among the main barriers to HPV vaccination.
Husain/ 2019 (30)	Bahrain	Descriptive/cross-sectional	408 (268 women and 140 men)	Primary health care attendees	Awareness about HPV and the HPV vaccine is limited.
Abi Jaoude/2019 (71)	Lebanon	Descriptive/cross-sectional	228	Doctors, parents	The main barrier to HPV vaccination is its cost. Further barriers include concern about its safety and efficacy, and lack of knowledge about HPV.
Ibrahim/2019 (39)	Iraq	Descriptive/cross-sectional	240	Medical and nursing students	The responders had sufficient knowledge about the availability of the HPV vaccine; 81.9% of medical students and 50.5% of nursing students were aware of it.
Sallam/2019 (72)	Jordan	Descriptive/cross-sectional	376	Dentistry students (pre-clinical and clinical)	Less than a half of the participants (44% of pre-clinical and 36% of clinical students) were aware of the HPV vaccine.

Jradi/2019 (59)	Saudi Arabia	Qualitative research	77	Women (general population, physicians, health care providers)	A small number of participants were aware of the HPV vaccine. Most of the population in Saudi Arabia did not know about the HPV vaccine and its efficacy. Lack of knowledge was among the most important barriers.
Anfinan/ 2019 (73)	Saudi Arabia	Descriptive/cross-sectional	2000	Physicians	Lack of knowledge about the HPV vaccine (21.1%) and being sexually inactive (14.7%) were the most common barriers.
Almansouri/ 2019 (74)	United Arab Emirates	Descriptive/cross-sectional	110	Physicians	The percentage of physicians who recommended the HPV vaccine was high, but they lacked comprehensive knowledge about the HPV vaccine.
Anwari/ 2020 (18)	Afghanistan	Cohort model	-	-	In Afghanistan, targeting a single cohort with the HPV vaccine was potentially cost-effective (0.7 times the GDP per capita of 586 US\$) from the perspectives of both, the government and society. Additional health benefits could be generated by a catch-up campaign, depending on the government's willingness to pay for the projected health outcomes.
Almazrou/2020 (75)	Saudi Arabia	Descriptive/cross-sectional		Physicians	More than a half of the participants were aware of HPV and the HPV vaccine. They believed that lack of knowledge among parents was one of the most important barriers to vaccination.
Mohammadpour/2020 (28)	Iran	Descriptive/cross-sectional	566	Vaccine recipients	The cost of the HPV vaccine could be regarded as a vaccination barrier
Rezqalla/2021 (76)	Kuwait	Descriptive/cross-sectional	1341	Female school teachers	Lack of knowledge about the availability of the HPV vaccine.

