Excerpt from the ePaper of the Pharmaceutical Report 2024 on the topic of 'HPV vaccination'

Solutions for improving the HPV vaccination rate

The first ePaper of the Pharmaceutical Report 2024 deals with the topic of 'HPV vaccination - protection against HPV-related cancers'. In 2022, 10.2 per 100,000 BARMER-insured women were diagnosed with cervical cancer. Although HPV vaccination has been proven to prevent the occurrence of this disease, what is the current vaccination status and regional differences? The BARMER Institute for Health Systems Research (bifg) summarised the possible solutions for improving the vaccination rate in a recently published ePaper (1).

>> The team of authors, consisting of Daniel Grandt, Veronika Lappe and Ingrid Schubert, have summarised the main topic 'HPV vaccination - protection against HPV-related cancers' in this ePaper on the BARMER Drug Report 2024, which has been published for the first time.

After an introduction to the background (see box on the right) and an explanation of the importance of HPV vaccination for cancer prevention, the authors first discuss the WHO and STIKO recommendations. According to the authors, in order to eliminate cervical cancer in the next century, the WHO is aiming for a complete vaccination rate of 90 per cent of girls worldwide by 2030 (WHO, 2020), a goal that the European Union has adopted in the ECCO & European Beating Cancer Plan (European Commission, 2022). With the aim of reducing the transmission of HPV pathogens to women and reducing the development of cancers of the anus, penis or mouth and throat in men, the STIKO has also recommended the HPV vaccination for boys aged 9 to 14 years since August 2018 in line with international recommendations (Robert Koch Institute, 2018c), according to the team of authors. The authors point out that since 2020, BARMER has also been offering the HPV vaccination to women and men between the ages of 18 and 25 as a statutory benefit: 'In addition to the direct benefits for the vaccinated male adolescents, the vaccination can also contribute to herd immunity, which is extremely useful, especially in view of the low vaccination rate among girls in Germany.'

In order to find out the vaccination status of BARMER policyholders and what regional differences there are, the authors analysed the vaccination rate against HPV among female and male adolescents insured by BARMER before and during the Covid-19 pandemic. Aspects such as age at first vaccination, the specialisms of the vaccinating doctors, vaccination rates after participation in the 20 to 29-year-old women over time for the years 2011 to 2022.

The analyses follow on from the investigations

Background

Malignant tumours can be caused by various triggers. Viral infections are responsible for 16% of malignant tumours worldwide and 7% in developed countries (de Martel et al., 2012). The human papillomavirus (HPV) is responsible for half of all virus-related malignant tumours and for almost 100 percent of carcinomas of the female cervix - cervical cancer (McBride, 2024). Infection with the human papillomavirus is one of the most common sexually transmitted diseases. 90 per cent of HPV infections heal spontaneously, but in 10 per cent of cases a chronic infection occurs. Infection with low-risk HPV types can lead to the development of genital warts, which are bothersome but harmless. However, persistent infection with one of the 13 oncogenic HPV types carries the risk of developing carcinoma, which can occur in the anogenital region (anus, cervix, penis, vagina, vulva) or in the oropharynx (mouth and throat area) after a latency period of up to several decades (McBride, 2024). The quantitative significance of HPV infection for the development of malignant tumours has been clearly proven by studies in Germany and is highly relevant. A study from Germany published in 2010 reported a prevalence of HPV infections in 22.3 per cent of women between the ages of 10 and 30 (Iftner et al., 2010). This means that almost one in four women was affected.
According to the Centre for Cancer Registry Data, 4,640 women were diagnosed with cervical cancer in 2020 and 1,546 died from it. New cases of cancer in the oral cavity and throat infections with HPV type 16 are a major risk factor here - occurred in 4,050 women and 9,140 men in 2020, 1,397 women and 3,955 men died from them (Robert Koch Institute & Society of Epidemiological Cancer Registries in Germany e. V., 2023).

Note: Literature in the original paper, see link at the end of the article.

Methodology

The analyses are based on anonymised insurance data from BARMER, which was available until 2022, excluding insured persons from the former Deutsche BKK, as corresponding data was not available for all observation years. Insured persons between the ages of 9 and 26 were included with information on gender, year of birth and federal state of residence. The age reached in the respective calendar year was calculated from the year of birth. Persons were considered to be continuously insured if their gaps in insurance were a maximum of 30 days and if they were continuously insured until their death in the respective year.
The HPV vaccination was identified via the billing of the fee codes for the vaccination service, which are defined in Annex 2 of the G-BA's vaccination guidelines: 89110A and 89110B (G-BA, 2024). In addition, special codes were taken into account that only applied to certain Associations of Statutory Health Insurance Physicians (KV) and only for certain periods. The letters at the end of the billing code indicate whether the vaccination is part of an ongoing vaccination series (A) or a completed vaccination series (B). As the letter suffixes are not reliably used correctly (Rieck et al., 2014) and the special digits sometimes do not allow any allocation to a vaccination series that has been started or the last vaccination, they were not used to determine complete vaccination cycles. In addition, it is not possible to determine whether the vaccination series started is the first vaccination. Therefore, the first vaccination of a calendar year was defined as the first vaccination if no HPV vaccination had been billed for the child/adolescent in the five preceding years.
The incidence of incident cervical cancer (ICD-10 code C53) was determined. This was counted as incident in the year of observation if neither an outpatient diagnosis with the addition 'confirmed' nor an inpatient main or secondary diagnosis was documented in the previous four calendar years. In the year of incidence, a main inpatient diagnosis of C53 had to be documented. BARMER Children and Adolescents Programme (KJP) and the development of the number of vaccinations administered. The incidence of cervical cancer among BARMER policyholders was also recorded and a special focus was placed on the age group of 20 to 29-year-old women over time for the years 2011 to 2022.

carried out as part of the BARMER Arzneimittelreport 2019, which showed that almost half of the girls insured with BARMER (who were twelve years old in 2011 and could be observed until 2017) did not have full vaccination protection against HPV infections. The lowest rate of HPV vaccination at that time was found in Bavaria, where 60 per cent of girls had no or insufficient protection against HPV infection through vaccination (Grandt et al., 2019).

Results

Since cervical carcinomas are practically always attributable to HPV infection, the authors assume that these carcinomas are a good indicator of HPV-related tumours, even if they only represent a subset of HPV-related malignancies. In their analysis, they shed light on the frequency of incident cervical carcinomas and their differentiation by age group (Fig. 1).

According to the authors, the differentiation of incident cervical carcinomas according to age groups of affected women illustrates the usually decades-long and variable latency between HPV infection, which often occurs in young adults, and the occurrence of cervical carcinoma. The team of authors: 'Cervical carcinoma manifests itself most frequently between the ages of 40 and 49, but can occur at any age. Screening is therefore recommended throughout life.'

As vaccination against HPV was only introduced for girls in Germany at the end of 2007 and for boys at the end of 2018, changes in the incidence of cervical cancer can only be expected in young women so far. Figure 2 shows the development of the incidence of cervical cancer in 20 to 29-year-old women compared to 30 to 39-year-old women in the period from 2011 to 2022. The 30 to 39-year-old women serve as a comparison group here, as they have not yet been able to benefit from a vaccination programme. Due to the generally long latency between infection and tumour development, the incidence of cervical cancer in the 20 to 29 age group is low; protective effects in this age group are an indicator of an even greater benefit, which only becomes clear and quantifiable when the vaccinated women are older.

If the average incidences of cervical cancer are compared for the periods 2011 to 2017 and 2018 to 2022, i.e. periods before and after the introduction of the vaccination, the effect of the vaccination becomes even clearer. While there was even a slight increase in the incidence of cervical cancer in the group of 30 to 39-year-old women, a decrease from 2.51 to 1.18 incidences of cervical cancer per 100,000 women would be visible in the group of 20 to 29-year-old women. This corresponds to a 53 per cent reduction in the incidence of cervical cancer in this age group.

At what age are girls and boys first vaccinated against HPV and has this changed over time ? The authors answer these questions by analysing the data. This shows that the STIKO vaccination recommendation made at the end of 2014 to bring forward the vaccination age from 12 to 17 years to 9 to 14 years has only been implemented hesitantly and insufficiently. Although the proportion of girls vaccinated for the first time at the age of nine tripled between 2015/2016 and 2021/2022, it is still very low at 7.1 per cent in 2022. In 2015, 78.8 per cent of girls who received an HPV vaccination were first vaccinated between the age of nine and the year they turned 15; in 2022, the figure was 89.3 per cent.

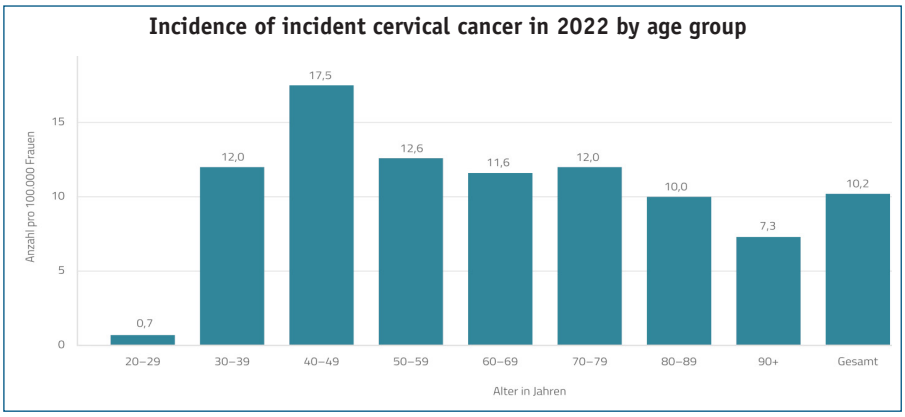


Fig. 1: *Incidence of incidental cervical cancer in 2022 by age group. Note: Age groups 0-9 and 10-19 are not shown as no cases are available. Proportion of women with an incident diagnosis of cervical cancer in 2022 (main hospital diagnosis) n = 412 of women continuously insured from 2018 to 2022 or continuously insured until death in 2022, total n = 4,023,339. Source: BARMER data, 2018-2022 Source: bifg ePaper 'HPV vaccination - protection against HPV-related cancers'.*

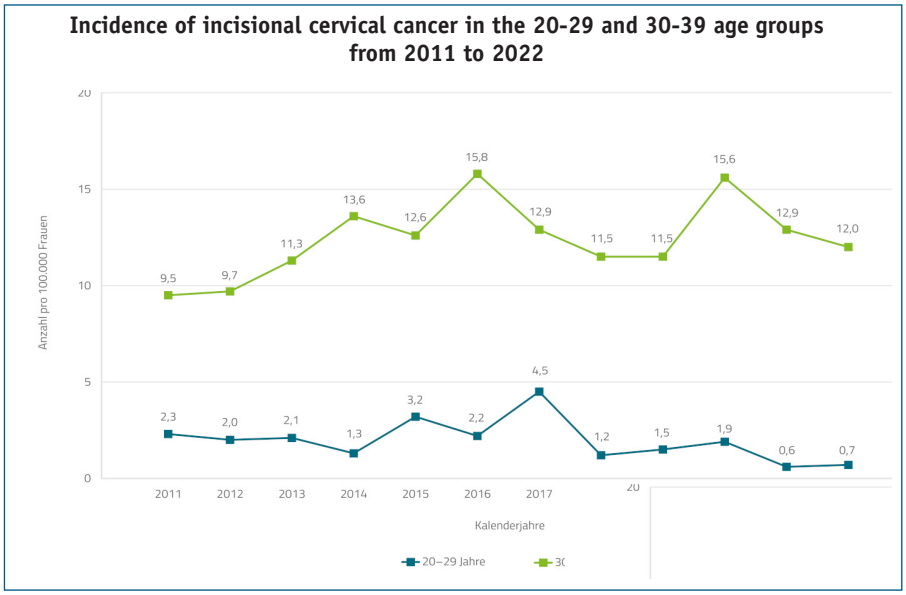


Fig. 2: *Incidence of incisional cervical cancer in the 20-29 and 30-39 age group from 2011 to 2022. Note: Women, 20-29 and 30-39 years, continuously insured in the calendar year of incidence or until death in this year and the four previous years. Source: BARMER data, 2007-2022. Source: BARMER data, 2018-2022 Source: bifg ePaper 'HPV vaccination - protection against HPV-related cancers'.*

As the HPV vaccination of boys only began at the end of 2018, the team of authors can understand why older boys were initially vaccinated. But here too, only 6.4 per cent were vaccinated at the age of nine in 2022. However, the recommendation issued in 2014 that the vaccination should be given from the age of nine has increased the importance of paediatricians in administering the HPV vaccination. They are the most important doctors vaccinating against HPV for both sexes. In the authors' opinion, this should be taken into account when developing strategies to improve the vaccination rate.

Conclusions and proposed solutions

According to the team of authors, national and international studies have identified factors that may contribute to inadequate vaccination rates against HPV.

1. insufficient knowledge of adolescents about the risks of HPV infection and the possibility of protection through HPV vaccination

A study on the quality of articles on HPV vaccination in the German media shows that there are considerable deficits in quality, especially with regard to the presentation of the evidence on vaccination (Niewald et al., 2019). The fact that the press has a significant influence on the willingness of girls and their parents to be vaccinated is impressively demonstrated by a study from Canada (Perez et al., 2016). An older survey conducted in 2010 among 19 to 35-year-old female students at the largest German university showed that only 62.5 per cent of the women surveyed were aware of the HPV vaccination (Kuznetsov et al., 2013). A survey of young male trainees in 2014 with a response rate of 10.8 per cent shows that around 74 per cent would have been willing to be vaccinated. A good 92 per cent stated that their parents had a positive attitude towards vaccinations. However, 93 per cent of respondents also stated that they had not been informed about HPV-associated diseases by their doctors (Schwarz et al., 2016).

2. Unfounded fear of side effects

Based on the analysis of two prospective randomised studies and a systematic review, HPV vaccination is considered safe and well tolerated (Takla et al., 2018). There were numerically more severe side effects in the placebo group than in the vaccinated group.

No causal relationship was seen between the reported severe side effects and the vaccination (Takla et al., 2018). Nevertheless, fear of side effects is the most common reason given by girls surveyed via Facebook for refusing the HPV vaccination (Takla et al., 2018). Another survey of girls aged 9 to 17 from 4,747 households in Germany in 2007 showed that of the 1,906 girls who took part, 4.7 per cent refused the HPV vaccination in principle after receiving information about the HPV vaccination and 16.3 per cent were unsure. Although 61.5 per cent were positive about the vaccination, only 17.4 per cent were actually vaccinated (Schülein et al., 2016).

3. lack of a precise vaccination date

Sometimes necessary vaccinations are simply forgotten by the person to be vaccinated or the doctor treating them. The risk is probably particularly high if there is no clearly defined vaccination date, but only a time corridor and also no precisely defined vaccination interval if several vaccinations are required. The HPV vaccination is an example of a situation where a period of several years is recommended for vaccination rather than an exact vaccination date and there is no link to a routine visit to the doctor. The lack of a fixed recommended interval for the follow-up vaccination can further increase the inadequate acceptance of the HPV vaccination. The available analyses show that 11.9 per cent of fully vaccinated girls have an interval of more than twelve months between the first and second vaccination.

4. lack of a reminder system for HPV vaccination

To ensure that vaccinations are not forgotten by those to be vaccinated or by the doctors treating them, an automatic recall system that reminds those to be vaccinated and those treating them of the first and subsequent vaccinations can help. Such a system has not yet been established across the board in Germany.

Solutions for improving the HPV vaccination rate

According to the bifg ePaper, numerous projects to increase the HPV vaccination rate have been initiated in Germany, as a systematic review published in 2024 shows (Schott et al., 2024). Most of the educational projects have focussed on teaching vaccination in the school context, but projects aimed at parents and healthcare professionals have also been carried out. However, as evaluation reports were not available for most of the projects, the review was unable to compare the effectiveness of the various interventions (Schott et al., 2024). However, international studies point to effective ways of increasing vaccination rates:

1. introduction of an early detection examination for children aged nine to ten (U10) in accordance with Section 26 SGB V with HPV vaccination programme
2. vaccination reminder system for those not yet and not yet fully vaccinated against HPV
3. communicate vaccination as a gender-neutral vaccination
4. indication of HPV vaccination for non-HPV vaccinated twelve-year-olds by health insurance companies. <<

by: MVF editor-in-chief Peter Stegmaier

You can find the complete bifg ePaper here: https://t1p.de/jr5og

Citation

Stegmaier, P.: 'Solution approaches for improving the HPV vaccination rate', in „Monitor Versorgungsforschung“ (05/24), S. 18–20. http://doi.org/10.24945/MVF.05.24.1866-0533.2646