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# The impact of government policy on female HPV vaccination rates: A global perspective

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# ABSTRACT

**Introduction:** Human papillomavirus (HPV) is a major cause of cervical and other cancers. Vaccination is key to primary prevention, but uptake varies globally.

**Purpose:** To analyse the impact of government policy on HPV vaccination rates among women worldwide.

**Material and methods:** A literature review was conducted (2000–2025) using PubMed, Scopus, and Google Scholar. Inclusion criteria covered peer-reviewed articles, systematic reviews, modelling studies, and policy analyses.

**Brief description of the state of knowledge:** Despite broad access to vaccines, global disparities persist. EU countries publicly fund vaccination, but only some meet WHO targets. Australia achieves high coverage via a school-based model. U.S. state policies significantly affect uptake. In Africa, Asia, and Latin America, barriers include access, trust, and cultural factors. Policy design and implementation strongly influence outcomes.

**Conclusion:** Effective HPV prevention depends on coordinated national policies, public education, and accessible vaccination programmes.

Keywords: "HPV vaccination"; "cervical cancer"; "vaccine uptake"; "public health policy";

"Europe"; "Asia"; "Africa"; "Latin America"; "school-based programs"; "vaccine hesitancy"; "health promotion."

## **INTRODUCTION AND PURPOSE**

Human papillomavirus (HPV) is one of the most common sexually transmitted infectious agents responsible for the development of cervical cancer and other anogenital and orofacial cancers (1). The introduction of HPV vaccination is a key element of the primary prevention strategy for these cancers. In the context of the increasing burden of HPV-related cancers, it is necessary to increase public awareness of the benefits of vaccination and to implement effective education and prevention programmes. Only through integrated action will it be possible to achieve a significant reduction in the incidence of HPV-related cancers on a global scale. Despite the availability of effective vaccines, vaccination rates among women vary widely between countries, suggesting a significant impact of government policies on vaccination rates. The aim of this review is to analyse the impact of state policies on HPV vaccination rates among women, with a focus on European countries.

#### **MATERIAL AND METHODS**

This review was conducted using a narrative literature review methodology, aimed at synthesizing the most relevant international and national research concerning the implementation, effectiveness, and challenges of human papillomavirus (HPV) vaccination programs. The literature search was carried out between November 2023 and May 2025 using databases including PubMed, Scopus, and Google Scholar. Keywords applied in various combinations included: "HPV vaccination," "cervical cancer," "vaccine uptake," "public health policy," "Europe," "Asia," "Africa," "Latin America," "school-based programs," "vaccine hesitancy," and "health promotion." Inclusion criteria encompassed peer-reviewed original articles, systematic reviews, modeling studies, and health policy analyses published from 2000 to 2025. Particular emphasis was placed on recent publications (from 2018 onward) and those addressing regional and country-specific vaccination strategies, especially within Europe and Poland. Reports and fact sheets from the World Health Organization (WHO), as well as governmental and institutional sources (e.g., UCLA Health, Yale University), were also included to provide the most up-to-date policy and coverage data. A total of over 50 sources

were selected based on relevance to the topic, citation impact, and methodological rigor. Studies were grouped thematically: global HPV-related cancer burden, vaccination program implementation, policy-driven interventions, factors influencing vaccine uptake, and comparative effectiveness across countries and continents. Special attention was given to modeling studies assessing the timeframe for cervical cancer elimination and to national case studies illustrating policy successes or barriers. Bibliographic management was performed using Zotero software, and references were formatted according to the Vancouver style. The process of selection and categorization was independently verified to ensure the accuracy and relevance of included data.

## A BRIEF DESCRIPTION OF THE STATE OF KNOWLEDGE:

#### The importance of HPV vaccination

Until 2000, cervical cancer was the second most common malignancy in women worldwide, with an annual mortality rate of about 50% (2). During their lifetime, 80% of sexually active men and women have been or will be infected with HPV (3,63). The virus is mainly transmitted during sexual contact, but infection can also occur through contact with the skin or mucous membranes of the person carrying the virus. According to the World Health Organisation, cervical cancer ranks fourth among the most commonly diagnosed cancers in women worldwide. More than 500 000 women are affected by the disease each year, and about 250 000 of them die (4). The implementation of widely available HPV vaccination programmes is a fundamental step towards more effective cancer prevention (5). Despite proven efficacy and safety, global vaccination coverage remains inadequate, with alarming declines in vaccination rates in some countries (6). According to an analysis by Giannone and co-authors, human papillomavirus (HPV) vaccination has the potential to lead to the first ever case of cancer elimination through preventive action. However, achieving this goal requires a coordinated approach at a global level, including adaptation of vaccination programmes to the infrastructural circumstances of individual countries and optimisation of the vaccination strategies used (7). In the context of women, Høgh and co-authors discuss the importance of HPV vaccination as a key element in the prevention of cervical cancer. They emphasise that, despite the availability of vaccines, vaccine uptake among women is still not reaching optimal

levels, requiring increased education and prevention efforts (8). A systematic review of studies by Mortensen and co-authors analyses the psychological, social and structural factors influencing the decision of women living in Europe to receive the human papillomavirus (HPV) vaccine. Based on 26 qualitative and quantitative studies, the authors showed that the most important determinants were the level of knowledge about HPV and vaccination, attitudes towards the vaccine (including safety concerns and beliefs about promoting early sexual activity), trust in healthcare professionals, the social influence of the environment (family, peers, teachers), and government policies regarding vaccine availability and funding. Of particular importance were the recommendations given by doctors and the organisation of vaccination in schools, which significantly increased vaccination rates. The authors emphasise that effective interventions should be culturally appropriate and based on sound health education and systemic solutions to increase vaccine availability (9). The highest incidence of cancers associated with HPV infection occurs in low- and middle-income countries, yet many of these countries have still not started HPV vaccination programmes (10).

#### Vaccination policies in EU countries

An analysis of the implementation strategies for HPV vaccination programmes in EU countries shows a wide variation in approaches. All 27 EU countries provide public funding for HPV vaccination, of which 26 offer free vaccination for both girls and boys (11). Most countries use a nine-valent vaccine and the main criterion for selecting a vaccine provider in tenders is the lowest price. In May 2018, the World Health Organisation (WHO) called for the elimination of cervical cancer as a public health problem and set a target of 90% HPV vaccination coverage by 2030 in the Global Strategy to Eliminate Cervical Cancer as a Public Health Problem developed in 2019. (12). As outlined in the Global Strategy for the Elimination of Cervical Cancer, developed by the World Health Organisation (WHO), member states have been required to meet the so-called 90-70-90 targets by 2030. The strategy calls for (13):

- to cover at least 90% of girls with the full human papillomavirus (HPV) vaccination schedule before the age of 15,
- to ensure access to high quality cervical cancer screening in at least 70% of women for the first time at the age of 30-35 and then before the age of 45,

• implementing effective treatment in 90% of women diagnosed with pre-cancerous lesions or cervical cancer, regardless of the stage of the disease.

According to projections based on mathematical models developed by the World Health Organisation, consistent implementation of these interventions in the coming decades could reduce the global incidence of cervical cancer by 42% by 2045 and by as much as 97% by 2120 (14).

The aim of the study by Gountas and co-authors was to estimate when 22 European countries would reach a 90% vaccination rate against human papillomavirus (HPV) among 15-year-old girls, in line with the World Health Organisation's (WHO) 2030 target (15). The authors used regression models based on WHO data on vaccination rates to predict when countries would reach 90% vaccination coverage. The average vaccination coverage rate for the countries analysed was 62.2% (SD = 18.3%). The predictive models indicate that only nine countries - including Iceland, Norway, Portugal, Ireland, Hungary, Spain, Sweden, Denmark and Switzerland - have a high probability of reaching the WHO target by 2030. Another group of countries, including Estonia, Cyprus, the Netherlands, France, Germany and Italy, are likely to meet the target between 2030 and 2040, while seven countries, including Belgium, Bulgaria, Finland, Latvia, Luxembourg, Malta and Slovenia, are unlikely to achieve the required vaccination coverage by 2030. These results highlight the need to intensify vaccination efforts in much of Europe to meet the goals of the global cervical cancer elimination strategy.

## Variation and dynamics of HPV vaccination coverage in the target population

Between 2008 and 2020, approximately 3.3 million women received at least one dose of human papillomavirus (HPV) vaccine, corresponding to 61.69% of the target population. In countries with high implementation rates of HPV vaccination programmes, the percentage of vaccinated women was significantly higher than for men (45.48% vs. 8.45%). At the same time, there was a decrease in vaccination rates between 2015 and 2020 compared to the period 2006-2014 (41.48% vs 89.03%). In countries with low vaccine uptake, vaccination levels were low among both women and men (5.31% and 2.93%, respectively), but an increase was observed in the most recent period analysed (2015-2020) compared to earlier years (5.22% vs 0.76%). Importantly, in countries with high levels of implementation, demonstration programmes were

more effective than routine programmes, achieving a higher percentage of the population vaccinated (89.94% vs 59.74%) (16-18).

#### Factors influencing vaccination coverage

Analysis of psychological factors influencing the decision to receive human papillomavirus (HPV) vaccination among European women showed a significant impact of knowledge level and attitudes towards preventive health care on vaccination rates. Knowledge of the risks of HPV infection significantly increased the likelihood of vaccination (OR = 1.82; 95% CI: 1.27-2.61), as did declared intention to participate in cervical cancer screening (OR = 1.68; 95% CI: 1.37-2.07). In contrast, the most frequently identified barriers included fear of side effects of vaccination, lack of sufficient information and the belief that personal risk of infection was low, which limited willingness to take preventive action (19). A systematic review and meta-analysis by Jiboc et al. indicates that HPV vaccination rates among women and adolescents in Europe are influenced by factors such as knowledge about HPV, attitudes towards vaccination, trust in the healthcare system and availability of vaccines. Lack of adequate health education and concerns about vaccine safety are the main barriers to increasing vaccination rates (19). Analysis of factors influencing women's decisions regarding HPV vaccination indicates the important role of recommendations from physicians, especially paediatricians, and the belief that the vaccine is effective in preventing cancer (19). In addition, the introduction of vaccination programmes in schools and the extension of vaccination competence to pharmacists, as has been done in France, can significantly increase the availability and acceptance of vaccination among the population (20). Experience from Bremen, Germany, shows that vaccination programmes implemented in schools can significantly increase vaccination rates. In an article published in the journal Vaccine, Singer and co-authors analysed the effectiveness of a human papillomavirus (HPV) vaccination programme implemented in schools in Bremen, Germany (21). The programme, which started in the 2013/14 school year, offered vaccination to all eighth-grade students, initially to girls and from the 2022/23 school year also to boys. The aim was to increase vaccination rates in the context of low coverage in Germany, which is mainly based on vaccinations performed in medical practices. The retrospective analysis included data from 2015/16-2018/19 for girls and from 2022/23 for both sexes, covering a total of 13,550 pupils from 56 schools. Among previously unvaccinated pupils, 26-35% of girls and

39% of boys accepted the vaccination as part of the school programme each year. Higher vaccination uptake was observed in schools of lower socio-economic status (SSI 5: 37%) compared to schools of higher status (SSI 1: 30%; p = 0.022). Vaccination uptake rates among unvaccinated pupils remained stable over time, with around one-third of pupils receiving at least one dose of vaccine at school. The remaining two-thirds did not take up the offer of school vaccination, which may be due to hesitation towards vaccination or a preference for vaccination in medical practices. The introduction of vaccination in educational institutions, with the support of local health services, allowed more young people and their parents to be reached, resulting in higher vaccination rates (21). Structural aspects of the health system also have an impact on the effectiveness of vaccination programmes. In many countries, such as France, the UK and Switzerland, policy decisions regarding the integration of HPV vaccines into the health care system are crucial. Julia et al. discuss the possibility of extending vaccination competence to pharmacists, which could enable easier access to vaccines in the community. Such actions could help to lower barriers related to vaccine access, especially in more remote regions (20). A study by Mlakar and co-authors assessed acceptability and factors influencing uptake and completion of the human papillomavirus (HPV) vaccination schedule among women aged 25-45 years in Slovenia. The analysis included 607 participants from two centres, of whom 49.6% (301 women) consented to the vaccination, with statistically significant differences noted between centres (p < 0.0001) (22). Women who chose not to be vaccinated were more likely to have a higher education (p = 0.0068) and to be in stable relationships or marriages (p = 0.01). Health professionals were the most trusted source of medical and vaccination information (55.2%). The main reasons for accepting vaccination included protection against HPV-related diseases (93.4%), perceived seriousness of preventable diseases (82.7%), safety of the vaccine (66.8%), availability of free vaccine (62.8%) and existence of vaccination recommendations (55.5%). On the other hand, the main reasons for refusing vaccination were the need for additional information about the vaccine (31.4%) and concerns about its safety (29.4%). The authors emphasise the need for widespread dissemination of information on the benefits and safety of HPV vaccination to healthcare professionals and the general public. The results of this study may be useful for other countries in the region that face a high burden of cervical cancer and a lack of data on the acceptability of vaccination among adult women.

#### The role of education and public awareness

Health education is a key element of a state policy strategy that can significantly influence vaccination rates. Research results show that information campaigns and the involvement of public opinion leaders are extremely important in shaping positive public attitudes towards vaccination. The example of Slovenia, where a vaccination programme for girls aged 12-13 years has been implemented, shows how combining vaccination with educational programmes in schools can result in positive health outcomes. Irzaldy et al. in their study documented that five years after the introduction of the vaccination programme, rates of cervical cancer and other anogenital lesions decreased in this age group (23). In the Netherlands, the country has invested in public education and extensive campaigns to promote HPV vaccination. Luttjeboer et al. (2023) conducted an analysis of vaccine efficacy in this country, showing that the vaccination programme was highly effective in reducing the long-term incidence of cervical cancer (24). In Germany, HPV health policy has been more focused on educational campaigns and changes in vaccine availability. A study by Sharma et al. (2022) noted that despite widespread access to vaccines, awareness of HPV among the German population was relatively low. This speaks to the need for continued awareness campaigns, which should focus not only on the availability of vaccines, but also on educating the public about the risks of HPV infection and the benefits of vaccination (25). However, the level of HPV awareness is not equal in different countries. For example, in countries such as Italy and France, vaccination policies are often more comprehensive, including the promotion of vaccination for adult women. Cherif et al. (2025) presented the results of a cost-benefit analysis of extending vaccination to adults in Italy. According to their study, expanding the target group could significantly reduce the cost of treating HPV-related cancers, providing an additional argument in favour of extensive vaccination programmes (26).

## Parental motivations and social attitudes

Parents' motivations in deciding whether to vaccinate their children are a key element of health policy. In a study by Štrbaca et al. (2023) on parents' attitudes towards HPV vaccination in Serbia, it was noted that although parents show a high sensitivity to doctors' recommendations, factors such as education, vaccine availability and socio-cultural attitudes have a decisive influence on the decision to vaccinate (27). State policy in this context should include programmes that not only promote vaccination, but also involve families in the education process.

#### **Barriers to the implementation of vaccination programmes**

Despite the availability of vaccines, there are barriers to the implementation of HPV vaccination programmes. These include lack of confidence in the vaccines, safety concerns, low public awareness and lack of reminder systems. In addition, the COVID-19 pandemic disrupted vaccination programmes, leading to declining implantation rates in many countries (27). In response to these challenges, some countries have introduced strategies to catch up on vaccination, such as awareness campaigns and increased availability of vaccination.

#### Vaccination policy in the United States

Individual state health policies in the US have a significant impact on human papillomavirus (HPV) vaccination rates. Studies indicate that making HPV vaccination mandatory as a condition of school admission significantly increases the number of vaccinated adolescents. For example, in Rhode Island, where such legislation is in place, the percentage of adolescents vaccinated with at least one dose was 91%, compared to an average of 78% in neighbouring states without mandatory vaccination (28). The socio-political context is also significant, with states with higher levels of religiosity and conservative political values, such as Utah and Mississippi, recording lower vaccination rates (29). The decision to vaccinate is also influenced by regulations that allow minors to self-consent - in states that allow this step, the rate of vaccination with at least one dose was 67.9 per cent, compared to 61.4 per cent in states with a more restrictive approach (30). Introducing easier access to vaccination - e.g. by allowing it to be administered in pharmacies or by participating in public programmes such as Vaccines for Children - also significantly supports increased implantation rates (31). These findings suggest that thoughtful legislative and organisational action at the state level can be effective in increasing acceptance of HPV vaccination and reducing the risk of associated cancers. Ma GX et al.conducted a study evaluating the effectiveness of a multilevel, culturally tailored

intervention to increase HPV vaccination among Asian-American adolescents. The intervention included parent and adolescent education, outreach to clinics and schools, and media campaigns involving community leaders, with educational materials available in participants' native languages. Results showed a significant increase in vaccination coverage in the intervention group compared to the control group, confirming the effectiveness of the integrated approach in overcoming language, cultural and systemic barriers (32-34).

## Vaccination policies in Asia

HPV vaccination policies in Asian countries are characterised by considerable variation, which translates into different vaccination rates among women. Countries such as Malaysia and Bhutan have implemented effective school-based vaccination programmes, achieving coverage rates of 83-91% and over 87%, respectively (35). In other countries in the region, such as Thailand and Japan, there was initially a high acceptance of vaccination, but in Japan, negative media campaigns about the safety of the vaccine caused vaccination coverage to drop to less than 1%, highlighting the importance of public trust and communication in health policy (36). Many countries face barriers such as limited funding, low awareness among health care workers and social and cultural norms favouring scepticism towards vaccination (37,38). Despite the implementation of vaccination programmes in about 70 per cent of East Asian countries, overall vaccination coverage remains low, particularly in less affluent countries, where it is around 10 per cent (39). Current strategies are focused on expanding vaccination in schools and extending programmes to larger population groups, including boys and older adults, with the aim of increasing vaccination coverage and reducing the burden of HPV (40). In addition, developing local vaccine production and combating misinformation are key to overcoming public distrust and improving the outcomes of vaccination programmes (36,40).

#### Vaccination policies in South America

HPV vaccination policies in South American countries are characterised by the introduction of vaccination programmes in most countries in the region, although vaccination coverage and implementation strategies vary. By 2022, sixteen of the nineteen Latin American countries (comprising the Spanish- and Portuguese-speaking countries south of the US) had introduced

HPV vaccination into their public health programmes, but only Mexico had achieved the target of 90% vaccination coverage for girls under 15 years of age (41,42). Vaccination programmes most often cover girls aged 9-14 years, are mainly implemented in schools and health centres, and the vaccination schedule has shifted from three doses to two, in line with WHO and local expert recommendations (41,43). Despite the availability and documented efficacy of vaccines, vaccination coverage is lower than expected, due to a number of barriers, such as limited public knowledge about HPV and the vaccine, safety concerns, cost, cultural barriers and the impact of the COVID-19 pandemic (41, 42, 44). In response to these challenges, effective policies include strong referrals from health care providers, provision of vaccines in both schools and health facilities, and consideration of a single-dose regimen that is as effective as two or three doses according to recent WHO recommendations, which may increase accessibility and acceptance of vaccination (41, 44). Although progress and support from international organisations such as PAHO, monitoring of vaccination programmes remains underdeveloped and data on vaccination coverage and its impact on cervical cancer incidence are limited (43). Therefore, further research and strengthening of surveillance systems are needed to more effectively address public health goals and reduce inequalities in access to vaccination in the region (41,43).

#### Australia as an example

Australia is widely regarded as a role model for HPV vaccination policy, with the introduction of a state-funded, nationwide vaccination program in 2007, initially for girls and, since 2013, for boys as well (45,46). This program, implemented mainly in schools, has achieved some of the highest vaccination rates in the world, reaching nearly 90% (46-48). Thanks to high vaccination coverage, a significant decrease in the incidence of genital warts and high-grade cervical lesions has been observed among those eligible for vaccination (45). In addition, studies indicate a potential reduction in the risk of adverse pregnancy outcomes in cohorts of women who received the HPV vaccine (50). The vaccination program in Australia was changed in 2018 from a 4-valent to a 9-valent vaccine and from a 3-dose to a 2-dose schedule, reducing costs and resource requirements (45). Analyses indicate that including people vaccinated with only one dose can raise vaccination rates to nearly 90% (53). Further measures to increase program effectiveness include minimizing school absenteeism and streamlining the process of obtaining consent for vaccination (45).

Brotherton et al (2014) reviewed the effects of Australia's state-funded HPV vaccination program, which has covered girls aged 12-13 since 2007, and a follow-up program for women up to age 26. The study described high vaccination coverage (>70% for 3 doses) and a rapid and significant reduction in the incidence of HPV infections, genital warts and cervical precancerous lesions (51). Skinner et al (2015) presented a protocol for a cluster randomized trial that evaluated the impact of educational interventions, decision support and logistical strategies on knowledge, attitudes and vaccination rates among students in Australian schools. This study is the first to comprehensively analyze the factors contributing to the effectiveness of school vaccination programs (47,48) Brotherton et al. (2018) in the VACCINE study assessed the prevalence of HPV genotypes covered by the vaccine in young Australian women after eight years of the program. The results confirmed high vaccination efficacy and significant reductions in HPV 6, 11, 16 and 18 infections in the vaccinated population (53). An estimation of HPV vaccination coverage in Australia using data from the Australian Immunisation Register (AIR) was reported in a 2022 paper. The analysis showed improved vaccination completion rates after switching from a 3-dose to a 2-dose regimen, and indicated persistent inequalities in access to vaccination by socioeconomic status and place of residence (52). These papers provide robust original data on the effectiveness, implementation strategies, and challenges of HPV vaccination policies in Australia, providing valuable insights for analyses of the impact of government policies on female vaccination rates.

#### Vaccination policy in Africa

HPV vaccination policies in African countries face a number of challenges, but also show positive examples of successful implementation, resulting in increased female vaccination rates. Between 2008 and 2020, many African countries introduced HPV vaccination, primarily covering girls aged 9-14, but overall vaccination coverage remains low, at around 33% in 2022, well below the global target of 90% (54). In response to vaccine availability and logistical constraints, some countries, such as Cameroon and Cape Verde, have adapted a single-dose regimen and expanded vaccination programs to include boys, supported by recommendations from national advisory groups (NITAGs) in 16 African countries (54). Studies indicate that strategies based on school-based vaccination and demonstration programs contribute to higher vaccination rates, as evidenced by experience in six African countries, where the use of class

instead of age to identify the target population facilitated the organization of vaccination and increased its effectiveness (55).

However, despite the growing number of countries introducing vaccination, many countries still face barriers such as limited public awareness, low knowledge among health care workers, misinformation, and lack of strong political support, all of which contribute to low acceptance and vaccination rates (56). For example, a survey of health care workers in Africa found that despite positive attitudes toward vaccination, there is a need for better training and communication to counter growing distrust and hesitancy toward vaccines, especially in the context of the COVID-19 pandemic (56).

## CONCLUSIONS

HPV vaccination is the most effective method of preventing cervical cancer and other HPVrelated cancers. The introduction of universal vaccination programs can significantly reduce the morbidity and mortality associated with these diseases. The level of HPV vaccination in Europe varies and in most countries is still insufficient to meet the targets set by the WHO. Only a few countries are likely to realize 90% vaccination coverage by 2030. The most important factors influencing vaccination decisions are the level of knowledge, trust in the health care system and recommendations of doctors. Educational activities, information campaigns and the organization of vaccination in schools also play a key role. The main barriers to increasing vaccination rates are concerns about vaccine safety, lack of reliable information and low awareness of the risk of HPV infection. Overcoming these barriers requires integrated education efforts and easier access to vaccination. Government policies, including funding for vaccination, organization of school-based programs and extension of vaccination competencies to pharmacists, significantly affect the effectiveness of vaccination programs. Countries that invest in extensive education and vaccine availability achieve higher vaccination rates. Implementing comprehensive, locally tailored vaccination strategies and intensifying outreach efforts are essential to achieving global cervical cancer elimination goals.

## **AUTHOR'S CONTRIBUTIONS**

The authors confirm contribution to the paper as follows: Conceptualization: Aleksandra Kujawa, Karolina Marrodán-Wojtczak Methodology: Aleksandra Kujawa, Paulina Krzeszowska, Software: Adrianna Zajączkowska, Kacper Stępniak Check: Jakub Zajączkowski, Karolina Krochmal Formal analysis: Wojciech Pisarek, Jan Wilk Investigation: Aleksandra Kujawa, Radosław Kuźma Resources: Karolina Marrodán-Wojtczak, Paulina Krzeszowska Data curation: Adrianna Zajączkowska, Radosław Kuźma Writing - rough preparation: Jakub Zajączkowski, Jan Wilk Writing - review and editing: Aleksandra Kujawa, Wojciech Pisarek Visualization: Kacper Stepniak, Karolina Krochmal Supervision: Paulina Krzeszowska, Aleksandra Kujawa Project administration: Paulina Krzeszowska, Karolina Marrodán-Wojtczak **PROJECT ADMINISTRATION:** All authors have read and agreed with the published version of the manuscript.

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