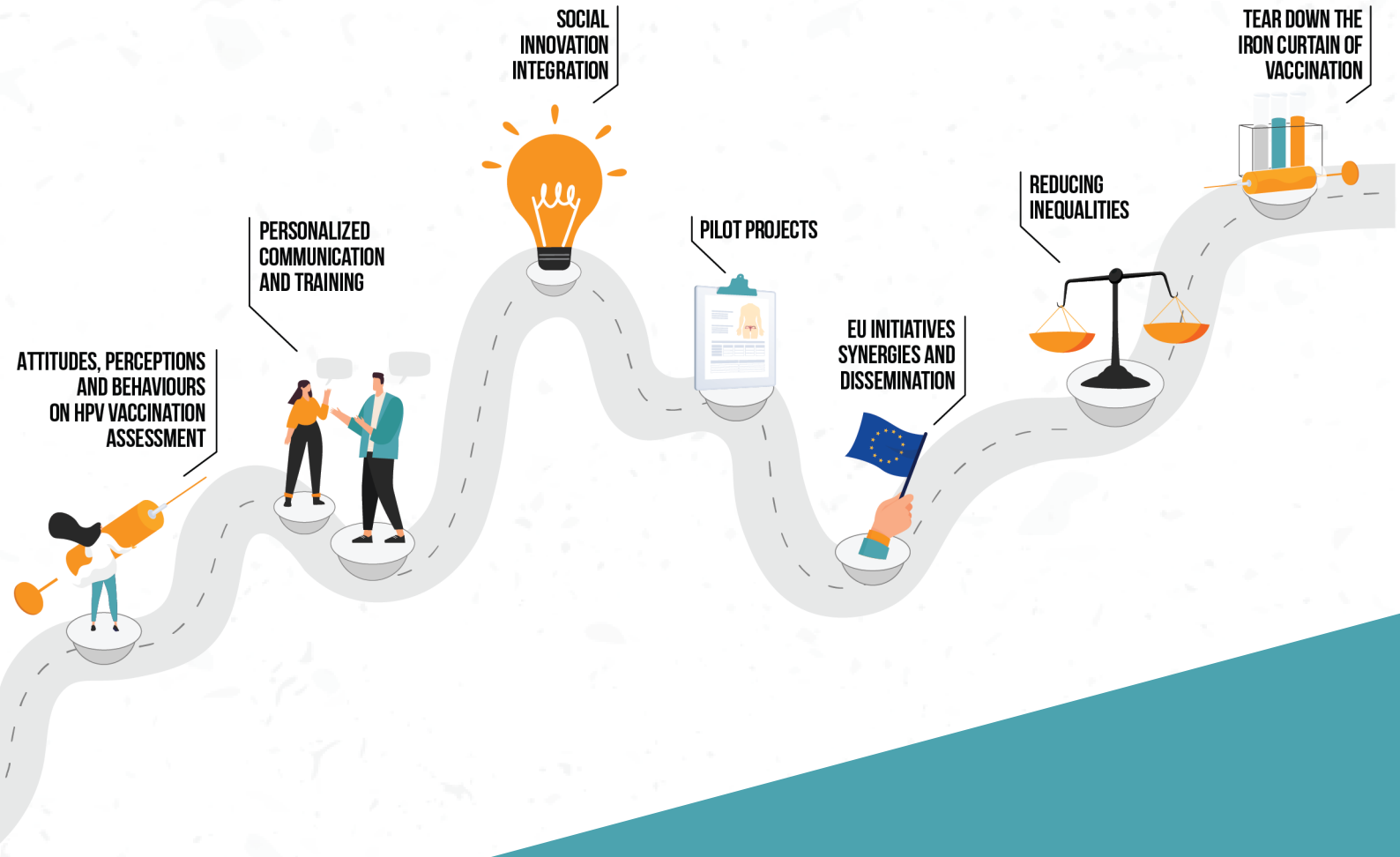
Rethink and Reduce inequalities in HPV vaccination through personalized communication and training, based on social innovation and behavioural determinants of health

D2.1 KNOWLEDGE CENTRE ON HPV VACCINATION & COMMUNICATION FOR EUROPEAN COUNTRIES WITH LOW VR

OCTOBER 2023



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LIST OF ABBREVIATIONS

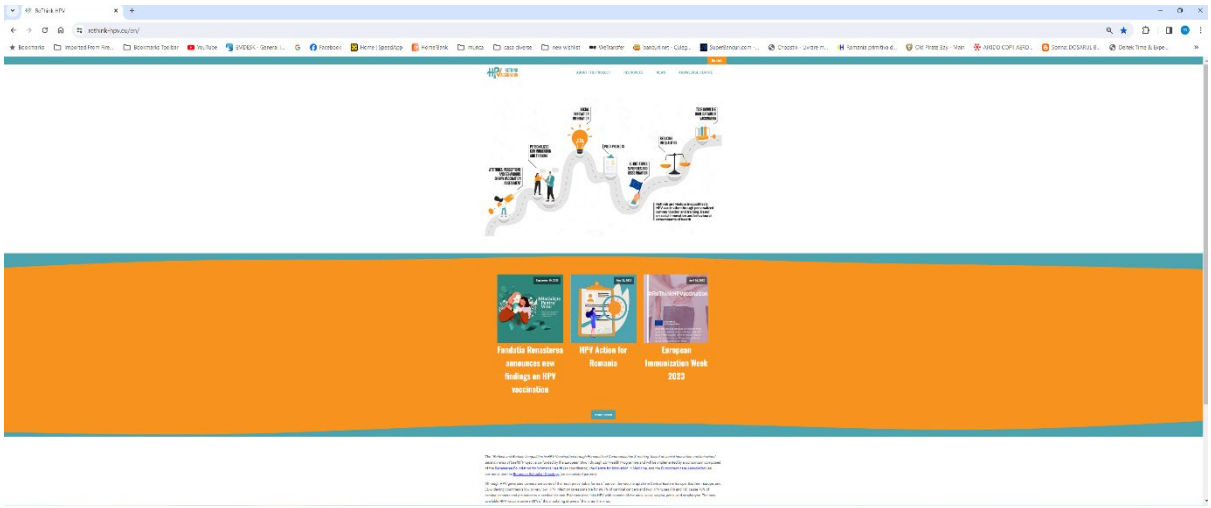
Acronym	Description
EU	European Union
WP	Work Package
GA	Grant Agreement
T	Task
D	Deliverable

LIST OF FIGURES

WEBSITE ADRESS AND SCREENSHOT

The Knowledge centre can be found at this address:

https://rethink-hpv.eu/



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EXECUTIVE SUMMARY

The Deliverable D2.1 'Knowledge Centre on HPV Vaccination & Communication for European Countries with Low VR' represents a pivotal point of the ReThinkHPVaccination project. It combines rigorous data accumulation, expert validation, and state-of-the-art platform development, intending to provide a robust informational base for countries with lagging HPV vaccination rates. Overall, the Deliverables covers multiple tasks in WP2.

It can be accessed here: https://rethink-hpv.eu/

Data and Information Gathering (T2.1)

Drawing from the momentum where isolated studies in Romania indicate soaring intentions for HPV vaccination, our bilingual (Romanian and English) platform emerges as a reservoir of invaluable information about HPV prevention through vaccination. Users can access a wealth of knowledge, aimed not just at highlighting the importance but also at demystifying misconceptions.

This data foundation sets the tone for future content personalization and refinement, especially once we integrate insights from Deliverable 2.2 – an exhaustive study on attitudes, perceptions, and behaviours towards HPV vaccination in the Romanian population. As we move forward, the subsequent Deliverable 2.3, the HPV Vaccination Personalized Communication Matrix, will serve as a guidepost for tailoring the content to address specific behavioural determinants and communication needs of the audience.

Our dedicated team synthesized valuable scientific data and information that bolster the significance of HPV vaccination for cancer prevention. By studying the success models from countries such as the UK and Australia, we gained in-depth insights into their efficacious communication strategies. This served as a foundation, allowing us to draw parallels and understand best practices that can be replicated across European countries with low vaccination rates.

Content Validation (T2.2)

To ensure the integrity and credibility of our gathered information, we initiated a content validation phase. This involved partnering with leading Scientific Societies at both

National and European levels. The validation process ensured that the Knowledge Centre would only house accurate, up-to-date, and scientifically vetted information.

Online Platform Creation (T2.5)

Bringing our vision to fruition, we designed, implemented, and launched an online platform dedicated solely to the Knowledge Centre. This platform is a testament to our commitment to the cause, as it not only offers data but also showcases the best communication practices. Recognizing the enduring challenge of elevating HPV vaccination rates in Central and Eastern European (CEE) countries, we've pledged to sustain and evolve the platform beyond the project's lifespan, leveraging our resources and other available funds. All the details are in Annex 1 to this document.

INTRODUCTION

At the heart of the ReThinkHPVaccination project, the 'Knowledge Centre on HPV Vaccination & Communication for European Countries with Low VR' was developed with a clear vision. Our primary goal was to offer structured knowledge and essential information to individuals. By doing so, we aimed to support their confidence in making informed decisions about getting vaccinated against HPV. Such a collective, informed choice has ripple effects, potentially guiding countries on how best to utilize and allocate their resources for public health.

However, the path to our goal wasn't without its hurdles. Recently, the Ministry of Health in Romania introduced a significant change to the HPV vaccination distribution method. Instead of only procuring it from family doctors, people were to be granted the option to access the vaccine from pharmacies with a medical prescription. This unforeseen change prompted us to realign our strategies and timelines.

We had initially strategized to incorporate insights from Deliverable 2.2, a comprehensive study focusing on Romanian attitudes towards HPV vaccination. This would have allowed us to tailor our content meticulously based on these perceptions. However, due to the reshuffling in the vaccination program and other administrative challenges, the release of that study was deferred.

To ensure that our mission didn't lose momentum, we pivoted. We gleaned valuable insights from smaller, yet impactful recent studies spearheaded by Fundatia Renasterea, coupled with rich discussions with vaccination experts and general practitioners. While this wasn't our initial blueprint, the insights gathered are pivotal and actionable.

In essence, though our journey witnessed a few detours, our mission's essence remained untouched: to furnish individuals and countries with reliable, actionable information on HPV vaccination. This platform stands as a testament to that commitment, poised to drive a significant change in HPV vaccination attitudes and actions.

1. METHODOLOGY

The primary aim was to establish an online Knowledge Centre that would serve as a comprehensive source of information on HPV vaccination, focusing on European countries with low vaccination rates. The centre would address barriers to vaccination, dispel myths, and offer validated and credible information about HPV and its associated risks.

We employed specialized search strategies tailored to extract comprehensive data on HPV vaccination. Online academic databases such as PubMed, Elsevier's Scopus, Springer, and Web of Science served as our primary sources. Articles were included based on their relevance to HPV vaccination, recentness, and the credibility of their source. To ensure we were gleaning insights from the most authoritative sources, we prioritized data from journals such as The Lancet, New England Journal of Medicine, Journal of the American Medical Association, and the British Medical Journal. Web scraping tools, with built-in AI capabilities, were used to extract specific data points from larger datasets available online. This allowed for a vast array of data to be funnelled down into usable and relevant insights.

The "ReThinkHPVaccination" project, through a blend of traditional research methods and cutting-edge AI tools like ChatGPT, provides a holistic, up-to-date, and accessible knowledge platform. This platform aims to bolster understanding and influence HPV vaccination uptake in regions of Europe where it's critically needed. Leveraging AI tools such as ChatGPT, raw data was synthesized into coherent, concise information segments. ChatGPT also aided in filtering out redundant data, ensuring only relevant, and significant data points were considered.

The content was classified under several overarching topics such as HPV vaccine basics, efficacy, safety, misconceptions, and the role of communication in vaccination. This organization allows users to navigate through the Knowledge Centre seamlessly.

To cater to varied user preferences, data was presented in different formats, such as articles, infographics and more types of content will follow.

Data Collection: Sourced peer-reviewed articles, studies, and publications primarily from databases such as PubMed, Springer, MDPI, and other reputable academic platforms. Articles ranged from 2012 to 2022 and provided insights into HPV awareness, knowledge, vaccination rates, and barriers in Romania and other European countries. A

specific emphasis was placed on articles that targeted different demographic groups, including medical professionals, students, parents, and the general public.

Data Extraction: Relevant information was extracted from these articles, including statistics on awareness levels, perceptions about the vaccine, rates of vaccination, and identified barriers to vaccination. The information obtained was categorized under themes such as awareness and knowledge levels, attitudes towards the vaccine, cultural and societal beliefs, trust in healthcare, media influence, etc.

Translation (Romanian) and Integration: Building upon the extracted data, translations previously provided about HPV were integrated to ensure cultural and regional relevance. This integration aimed to ensure that the Knowledge Centre's content was accessible, relatable, and comprehensible to the target audience, especially in regions with low vaccination rates.

Knowledge Centre Development: An interactive online platform was chosen, which would enable easy navigation, search functionality, and the ability to frequently update the content based on emerging research and feedback.

Content Creation and Organization: Topics were organized under broad categories. Multimedia elements, including infographics, videos, and interactive quizzes, will be introduced to engage a diverse audience and cater to different learning preferences.

Promotion and Outreach: In collaboration with health organizations, educational institutions, and media partners, a promotional campaign will be designed to increase the visibility of the Knowledge Centre among target demographics.

The methodology adopted for the "ReThinkHPVaccination" project ensures a systematic and comprehensive approach to gathering, synthesizing, and presenting information on HPV vaccination. Through the Knowledge Centre, the project aims to foster improved understanding and positively influence vaccination rates in European countries with historically low uptake.

2. CONTENT

The content is bilingual, as well as the ReThinkHPVaccination Project website (see Annex 1 for the Visual Deliverable). The general structure of the Knowledge Centre category is presented in Figure 1 and described below in detail.

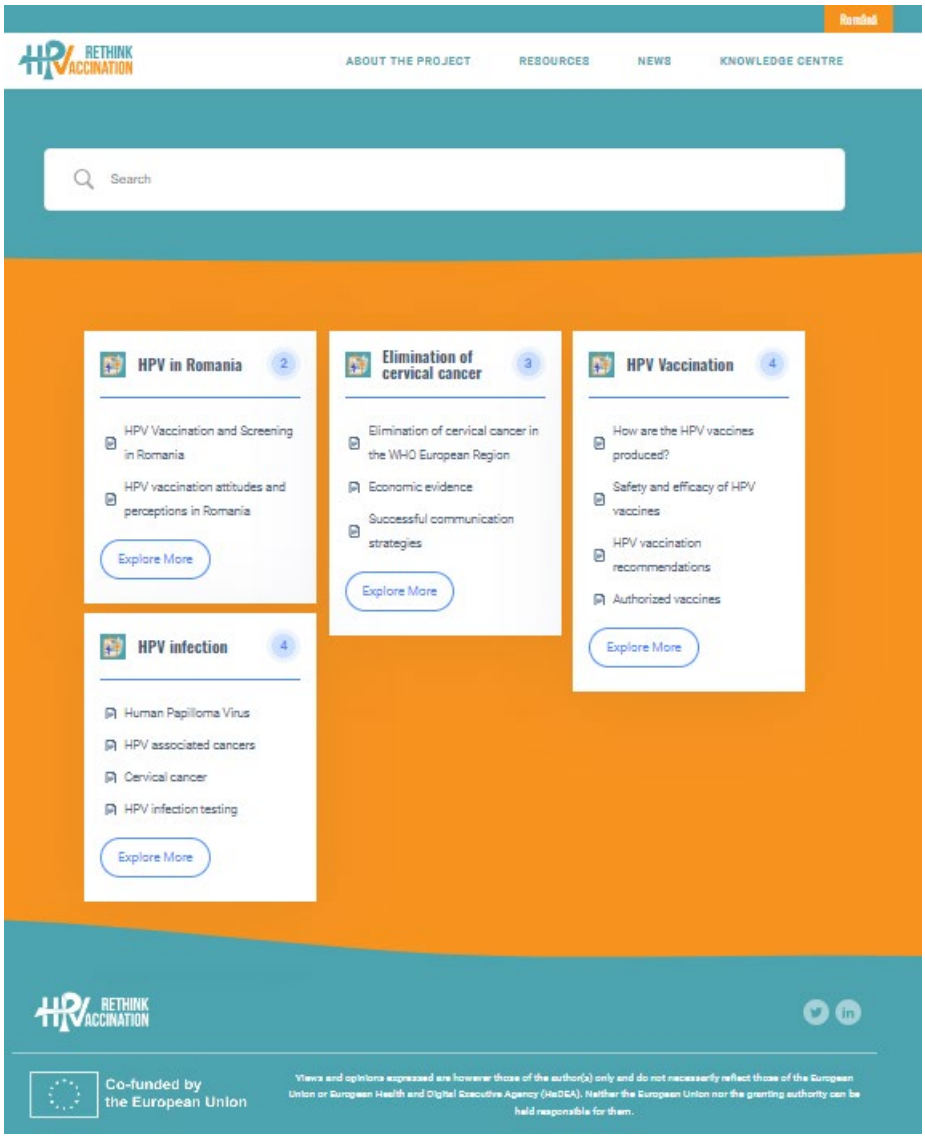

Figure 1 Knowledge Centre

2.1. English content

**Please note that this is the first version of our Knowledge Centre. We are dedicated to ensuring the most accurate and personalized information for our readers. As we gather data from our upcoming survey, we will be refining and updating the content to better suit the needs of different types of readers. We appreciate your understanding and patience as we work towards enhancing our platform and delivering an innovative approach to communication about HPV vaccination.*

Main sections

1.1. HPV infection background

Human Papilloma Virus

HPV (Human papillomavirus) is a family of over 200 related viruses (the Papillomaviridae family) that can infect the skin and mucous membranes. A significant portion of the global population is exposed to HPV at some point in their lives [1]. HPV types can be classified by their potential to induce cancer (high risk vs low-risk types). Types of HPV with low oncogenic risk are associated with warts (genital warts) and in most cases are associated with transient infections [2]. High-risk types of HPV are also associated with infections, usually transient, but with a higher likelihood of persistence. Along with other risk factors, high-risk types of HPV can integrate into the DNA of the host cells, which over time can transform into malignancies.

The viruses are highly tissue-specific and infect the basal cells of the skin and mucous membranes. HPV enters the host cell through micro-abrasions or lesions in the skin or mucous membranes. Once inside the host cell, the viral genome is transported to the nucleus. Viral DNA replicates and transcription of viral genes occurs, leading to the synthesis of early and late proteins. The viral genome is organized into three regions: early (E), late (L), and long control region (LCR) [3]. The early region encodes proteins involved in viral replication, transcriptional regulation, and modulation of host cell functions, while the late proteins enter the structure of the viral capsid. Based on the genomic sequence of L1, the gene encoding the principal capsid protein, over 200 HPV types have been identified and characterized, of which at least 12 are associated with cancers [4].

HPV subtype 16 is associated with about 55-60% of cervical cancers, and HPV subtype 18 is involved in a percentage of 10-15% of cases. Another eight subtypes (31, 33, 35, 45, 51, 52, 56 and 58) are associated with most other cases of cervical cancer. HPV infection subtypes 16 and 18 may increase the risk of developing cervical intraepithelial neoplasia by 11 to 17 times [5].

Understanding the molecular and cellular biology of HPV is critical for developing targeted therapies, vaccines, and diagnostic tools to prevent and manage HPV-related diseases, including cancers and warts.

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- [2] https://www.mdpi.com/1422-0067/23/3/1818
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- [4] https://karger.com/books/book/224/chapter/5152522/Human-Papillomavirus-Genomics-Past-Present-and
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HPV associated cancers

HPV infection is responsible for approximately 5% of the total global cancer cases. Among HPV-related cancers in women, cervical cancers constitute 93% [1]. In 90% of cases, the body controls the infection so those who develop lesions mount an effective cell-mediated immune (CMI) response, and the lesions regress. Failure to develop such a response result in persistent infection and, in the case of the high-risk HPVs, an increased probability of progression to CIN 2+. Regular screenings and HPV vaccinations can significantly reduce the risk of HPV-related cancers. HPV is known to cause several types of cancer. The following are the most common types of cancer that can be caused by HPV:

- Cervical cancer: HPV infection is the main cause of cervical cancer.
- Anal cancer: HPV infection is a significant risk factor for anal cancer, especially in men who have sex with men. Especially types 16 and 18, can cause anal cancer.
- Oropharyngeal cancer: HPV infection is the main cause of oropharyngeal cancer, a type of throat cancer that develops in the back of the tongue, tonsils and throat.
- Penile cancer: HPV infection is a risk factor for penile cancer, which is a rare cancer.
- Vaginal cancer: HPV infection can cause vaginal cancer, a rare cancer that affects the vagina.
- Vulvar cancer: HPV infection can cause vulvar cancer, a rare cancer that affects the external female genitalia [1].

Cervical cancer was the fourth leading cause of cancer and cancer deaths in women in 2020, with an estimated 604 000 new cases and over 340 000 deaths (8% of all female cancer deaths). HPV16 and HPV18 together are responsible globally for 71% of cases of cervical cancer. HPV45 accounts for 6%, HPV31 for 4%, HPV33 for 4%, HPV52 for 3% and HPV58 for 2% of cervical cancer cases [2]. Together, these 7 HPV types account for approximately 90% of the squamous-cell carcinomas that are positive for HPV DNA. Most cervical cancer cases in 2020 (88%) occurred in LMICs, where they account for 17% of all cancers in women, compared with only 2% in high-income countries (HICs).

HPV types 16 and 18 are associated with 85% of HPV-related head and neck cancers and 87% of all anal cancers – the second and third most frequent HPV related cancers with, respectively, 52 000 and 29 000 estimated cases in 2018.
A multicenter clinical trial in heterosexual men showed a prevalence of HPV (all types) of 19% at the penis, 13% at the scrotum, 8% at the perineal/perianal region and 21% at any site. A systematic review of genital HPV prevalence in men aged over 18 years concluded that prevalence peaked at slightly older ages than in women and then remained constant or decreased slightly with increasing age.

HPV6, HPV11 and other types can also cause a rare condition (incidence <4 cases per 100 000 persons) known as recurrent respiratory papillomatosis (RRP), in which warts form on the larynx or other parts of the respiratory tract with the risk of airway obstruction [4].

References:

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- [2] https://infectagentscancer.biomedcentral.com/articles/10.1186/s13027-023-00499-7
- [3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086430/
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Cervical cancer

HPV is the most common viral infection of the reproductive tract. Most HPV infections are asymptomatic and resolve spontaneously, but persistent infection with oncogenic HPV types may lead to cervical intraepithelial neoplasia (CIN), which untreated can progress to invasive cervical cancer. Cervical cancer is a type of cancer that starts in the cervix, the lower part of the uterus that connects to the vagina. The cervix constantly undergoes changes depending on the menstrual cycle. During these physiological changes, cervical cells can undergo various mutations, favoring the appearance of abnormal (precancerous) cells [1].

Epidemiological studies have shown that the main etiological factor for the development of cervical carcinoma is persistent HPV (Human Papilloma Virus) infection. The types of HPV that favor the appearance of cervical cancer are usually transmitted through sexual contact. HPV infection is spread through contact with infected genital skin, mucous membranes, or bodily fluids, and can be transmitted through sexual intercourse, including oral sex [2]. Not all HPV infections lead to cancer. Most HPV infections are eliminated by themselves, without treatment (70–90% are asymptomatic and resolve spontaneously within 1–2 years). However, persistent HPV infection can lead to the development of cancer over time. Persistent HPV infection is defined by the presence of type-specific HPV DNA on repeated clinical biological samples over a period (usually 6 months) [3].

The interval between the acquisition of HPV infection and progression to invasive carcinoma is usually 15–20 years or longer. HPV vaccination is an effective way to prevent HPV-related

cancers. Regular screening for cervical cancer can also help in the early detection of abnormal cells, which can be treated to prevent the development of cancer.

Risk factors for cervical cancer

The incidence of cervical cancer depends on the prevalence of high-risk types of HPV in the population, along with other factors such as:

- Immunosuppression: immunosuppressive therapy, HIV/AIDS infection;
- Smoking;
- Multiparity: three or more term pregnancies seem to increase the risk of developing cervical cancer. In addition, women whose first term pregnancy occurred before 17 years of age are almost twice as likely to develop cervical cancer compared to women whose first pregnancy occurred at 25 years of age or older;
- Consumption of oral contraceptives over long periods of time seems to increase the risk of cervical cancer;
- Sexual behavior: early onset of sexual activity, before 18 years; the existence of several sexual partners; the existence of a male partner who has had multiple sexual partners;
- Body weight: overweight women have a 25% higher risk of developing cervical cancer, and women with moderate obesity have a 70% higher risk. Also, overweight and obese women have a higher risk of death from cervical cancer;
- Hereditary history of cervical cancer: women whose mother or sister had cervical cancer have a 2-3 times higher risk of developing the disease;
- History of sexually transmitted diseases (STI, hepersvius, chlamydia, gonococcal infections);
- Poor socio-economic status [4].

Abnormal transformation of the cells of the cervix is asymptomatic, and signs of HPV infection may or may not be present (warts in the oral or genital area). The symptoms of cervical cancer are not always obvious and there may not be any warning sign until the disease has reached an advanced stage. For this reason, it is very important to have regular testing in order to detect certain potentially cancerous lesions and to perform the Pap smear.

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- [3] https://academic.oup.com/jid/article/198/7/971/2192193?login=false
- [4] https://www.cancer.org/cancer/types/cervical-cancer/causes-risks-prevention/risk-factors.html

HPV infection testing

HPV (Human Papillomavirus) infection can be detected through various types of tests, and the choice of test depends on the purpose of screening or diagnosis. HPV is a common sexually transmitted infection that can lead to cervical cancer, so early detection is important. The primary tests used for cervical HPV infection detection include:

HPV-induced changes in the cervical epithelium can be detected by microscopic examination of exfoliated cells, known as the Papanicolaou (Pap) cytology test or Pap Smear (Pap Test):

A Pap smear is a routine screening test used to detect abnormal changes in cervical cells, often caused by HPV infection. During a Pap smear, a healthcare provider collects a sample of cervical cells using a speculum and a brush or spatula. The cells are then sent to a laboratory where they are examined under a microscope to check for any abnormalities or signs of HPV infection.

Cervical HPV infection can be detected through an HPV nucleic acids amplification test (NAAT) (DNA or mRNA) performed on cervical or vaginal samples.
HPV DNA tests identify the virus by detecting its genetic material, specifically the viral DNA. On the other hand, HPV mRNA tests identify transcripts of the viral E6 and E7 oncoproteins, which play a crucial role in the process of HPV-induced oncogenic transformation of epithelial cells [2].

The HPV DNA test detects the presence of high-risk HPV strains (types associated with cervical cancer) in cervical cells. Similar to a Pap smear, a healthcare provider collects a cervical cell sample, but this sample is specifically tested for the presence of HPV DNA. This test is often used with a Pap smear or as a primary screening method for women over the age of 30.

HPV mRNA test detects the presence of HPV by measuring the presence of HPV messenger RNA (mRNA) in cervical cells. It is primarily used in conjunction with Pap smears to assess the risk of cervical cancer in certain cases.

Visual Inspection with Acetic Acid (VIA) and Visual Inspection with Lugol's Iodine (VILI) involve the application of acetic acid (VIA) or Lugol's iodine (VILI) to the cervix. Abnormalities in cervical tissue can be visualized by changes in color and texture after the application of these substances. While not as sensitive as molecular tests, VIA and VILI are low-cost methods that can be used in resource-limited settings for initial screening [3].
HPV NAATs, cervical cytology, and visual inspection with acetic acid are used to identify women who have, or are at risk of, cervical precancerous lesions and early invasive cancer.

Colposcopy is a procedure used when abnormal results are obtained from a Pap smear or HPV test. A colposcope, which is a magnifying instrument, is used to closely examine the cervix and vaginal walls. If abnormal areas are identified, a biopsy may be taken for further evaluation .
If abnormal cervical tissue is detected during a colposcopy or other screening test, a biopsy may be performed. During a biopsy, a small sample of tissue is removed from the cervix and examined under a microscope to confirm the presence of HPV-related changes and assess their severity.

WHO recommends the use of validated HPV DNA NAATs on self-collected vaginal or provider-collected cervical samples in a screen-and-treat approach, or in a screen, triage and treat approach, starting at the age of 30 years and repeated at 5–10-year intervals [2].
The new European Union cervical cancer recommendations prioritize HPV (human papillomavirus) testing among women aged 30 to 65 every 5 years, taking into account vaccination status. In addition to updating screening programs, for HPV eradication it is recommended to ensure vaccination coverage in the eligible population under 15 years of age [4].

References:

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- [3] https://www.jogcr.com/article_697368.html
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1.2. HPV Vaccination

How are the HPV vaccines produced?

Human papillomavirus (HPV) is responsible for a significant number of cancers globally, including the majority of cervical cancers. Biotechnological advancements have allowed the development of vaccines that not only curb the prevalence of this virus but also promise a future with a reduced burden of HPV-associated diseases [1].

Recombinant DNA Technology

The foundational technology behind HPV vaccines is recombinant DNA technology. Instead of using live viruses, which can be risky, the HPV vaccines utilize virus-like particles (VLPs). These VLPs are non-infectious as they don't contain the viral DNA necessary for replication, but they closely mimic the structure of the virus. This resemblance ensures that when introduced into the body, the immune system recognizes these VLPs as foreign invaders, leading to the production of antibodies against HPV [2]. To produce these VLPs, scientists identify and isolate the genes in HPV responsible for producing the outer protein shell of the virus. These genes are then inserted into yeast or insect cells, which act as factories, producing vast quantities of the VLPs. This method bypasses the need to handle or produce the actual HPV virus, ensuring both safety and scalability in vaccine production [3]. The HPV vaccines, with Gardasil 9 at the forefront, represent a confluence of advanced molecular biology, genetics, and immunology.

While its predecessors (Cervarix and the original Gardasil) offered protection against a limited number of HPV types, Gardasil 9 broadened this protection spectrum. It covers nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52, and 58. This inclusion is not just a numbers game; it's a calculated enhancement to provide protection against HPV types responsible for approximately 90% of cervical cancers and a significant percentage of other HPV-related cancers.

Moreover, the success of the HPV vaccines offers a blueprint for tackling other infectious diseases. The methodologies used, from VLP production to multi-valent vaccine development, can potentially be repurposed to address other global health threats.

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Safety and efficacy of HPV vaccines

HPV vaccines have been studied for a long time and have been shown to be safe and effective in preventing infection with the types of HPV that are most associated with cancer and genital warts. Vaccines have been in use for at least 15 years, and clinical trials have already demonstrated safety and efficacy. [1]

Studies have shown that HPV vaccines are very **effective in preventing infection** with the types of HPV included in the vaccine. Vaccines have been shown to provide protection against the development of cervical, oropharyngeal, penis, vaginal and vulvar cancers, as well as genital warts. Vaccines are most effective when administered before exposure to HPV, which is why vaccination is recommended for girls and boys before they become sexually active [2].

The nonavalent vaccine is designed to protect against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. The vaccine's efficacy in preventing infections and diseases associated with these types has been demonstrated in clinical trials. It showed nearly 97% efficacy in preventing cervical, vulvar, and vaginal cancers caused by the five additional high-risk HPV types (31, 33, 45, 52, 58) that were not covered by the original quadrivalent vaccine. It continued to demonstrate almost 100% efficacy against diseases caused by HPV types 6, 11, 16, and 18, which were already covered by the original vaccine [3].

While the exact **duration of protection** of Gardasil 9 is not yet fully known, studies indicate that it provides sustained protection. The antibodies produced in response to the vaccine remained at levels expected to provide protection for at least six years after the initial vaccination, and the duration is likely much longer based on ongoing studies [4].

HPV vaccines have an excellent safety profile. Vaccines have been widely tested in clinical trials involving thousands of participants. The most common side effects are mild and include pain, redness, or swelling at the injection site, and occasionally fever, headache, or muscle pain. Serious side effects are rare and have not been directly related to the HPV vaccine. The benefits of vaccination far outweigh the risks, and the HPV vaccine is safe for most people [4].

In clinical trials involving tens of thousands of participants, the nonavalent vaccine demonstrated **a safety profile c**onsistent with that of the quadrivalent vaccine, which had been extensively studied and was in use for several years prior to the introduction of Gardasil 9.
The most common side effects of the Gardasil 9 vaccine are similar to other vaccines and include injection site reactions (pain, swelling, and redness at the injection site are common but generally mild and short-lived) and general side effects, which might include fatigue, headache, fever, and nausea.

HPV vaccines are not effective against all types of HPV and vaccines do not provide protection against HPV infections that a person may already have. Therefore, it is still important that people who have been vaccinated continue to have a responsible sex life and regularly participate in screening for cervical cancer [5].

In countries where high vaccination rates are recorded, there are also real-world data on the impact of vaccination: reducing infections, and preventing precancerous cervical lesions and genital warts, both in men and women. For example, Australia, which has been a frontrunner in HPV vaccination, saw a significant decrease in the prevalence of vaccine-related HPV types among young women. Within a decade of the vaccine's introduction, infections with HPV types 16 and 18 (the types responsible for the majority of cervical cancers) decreased by over 80% among women aged 18-24. Also, there was a 90% reduction in genital warts among young women aged less than 21 years within eight years of the vaccine's introduction [6]. In Scotland, within a decade of introducing the vaccine, there was an 89% reduction in CIN3+ (a high-grade cervical abnormality) in women who were vaccinated at age 12-13 [6].

Countries with high HPV vaccination rates have also seen reductions in HPV infections among unvaccinated individuals, suggesting the presence of herd immunity. This was observed in both Australia and the U.S., where declines in HPV prevalence were noted not only among vaccinated individuals but also among those who had not been vaccinated [7]. These real-world outcomes reaffirm the importance and effectiveness of HPV vaccination programs. By providing evidence of the vaccine's impact beyond clinical trials, these findings underscore the vaccine's role in reducing the burden of HPV-associated diseases on a population level. As HPV vaccination programs continue and coverage rates increase, further reductions in HPV-related diseases are anticipated worldwide.

Ongoing post-marketing surveillance in various countries has consistently found the safety profile of HPV vaccines in real-world settings to align with clinical trial data. The vast majority of reported side effects are non-serious.

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HPV vaccination recommendations

In Europe, recommended HPV vaccination programmes vary by country. All EU /EEA have introduced HPV vaccination into national vaccination programs and many countries have moved or are about to move from a strategy to vaccinate girls to a one-size-fits-all strategy for girls and boys as well [1].

The most common programs are as follows:

- *Program with two doses:* This program involves the administration of two doses of HPV vaccine every 6-12 months. The European Medicines Agency (EMA) has approved a two-dose programme for girls and boys aged 9 to 14 years.
- *Program with three doses:* This program involves the administration of three doses of the HPV vaccine. The first dose is followed by a second dose 1-2 months later, and the third dose is administered 6-12 months after the first dose. This program is recommended for girls and boys aged between 15-26 years.
- *Catch-up Schedule*: This program is dedicated to people who did not receive the HPV vaccine during the routine vaccination program. The alternative scheme may involve the administration of two or three doses of the HPV vaccine, depending on the age of the individual.

The HPV vaccine is recommended for both girls and boys in Europe. The age range for routine HPV vaccination varies by country but generally falls between 9-14 years for girls and 11-14 years for boys. Vaccination by recovery is usually recommended up to the age of 26 for both girls and boys.

Multiple HPV vaccines are available. The bivalent vaccine covers HPV types 16 and 18, the quadrivalent vaccine covers HPV types 6, 11, 16, and 18, and the nonavalent vaccine covers HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. The nonavalent vaccine is the most comprehensive and offers protection against a broader range of HPV types.

While the primary goal of the HPV vaccination programs was the prevention of cervical cancer, the vaccine also prevents other cancers and conditions caused by HPV.

Updated WHO recommendations on HPV vaccination

In a new position paper published in December 2022, WHO updated the recommendations for vaccination against human papillomavirus (HPV). Notably noteworthy, the paper states that a single-dose vaccination program, referred to as an alternative, off-label in the single dose program can provide comparable efficacy and protective durability at a two-dose regimen [2]

The recommendation for single dose alternative programming was initially made by the WHO's independent expert advisory group, SAGE, in April 2022.
The position paper is important in the context of a significant decrease in vaccine coverage against HPV globally. Between 2019 and 2021, coverage of the first dose of HPV vaccination decreased by 25% to 15%. This means that an additional 3.5 million girls missed out on the HPV vaccination in 2021 compared to 2019.

Optimising the HPV programme is expected to improve access to the vaccine, giving countries the opportunity to expand the number of girls who can be vaccinated and alleviating the burden of the often complicated and costly monitoring required to complete the vaccination series. It is vital that countries strengthen their HPV vaccination programmes.

WHO recommends:

- A one- or two-dose schedule for girls aged 9-14 years
- A one- or two-dose program for girls and women aged 15-20 years
- Two doses with an interval of 6 months for women over 21 years of age

Given the extensive burden of HPV-related diseases globally, the vaccine has the potential to prevent a substantial number of cancers and improve global public health.
While screening can detect precancerous and cancerous changes, it requires regular intervals of testing and follow-up, and there's room for errors. On the other hand, vaccination offers more consistent protection against the most dangerous types of HPV.

Treating HPV-related conditions and diseases is costly, both in terms of direct medical costs and the broader socioeconomic impact (like loss of work). Preventing these diseases through vaccination can result in significant savings for healthcare systems worldwide. With high vaccination coverage combined with effective cervical screening, there's potential to drastically reduce, and possibly eliminate, cervical cancer in the future.

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Authorized vaccines

The first vaccine for the prevention of HPV-related disease was licensed in 2006. Currently 6 prophylactic HPV vaccines are licensed. All are intended to be administered, if possible, before the onset of sexual activity, i.e. before exposure to HPV [1].

All vaccines are prepared, using recombinant DNA and cell-culture technology, from the purified L1 structural protein, which self-assembles to form HPV type-specific empty shells, termed virus-

like particles (VLPs). HPV vaccines do not contain live biological products or viral DNA and are therefore non-infectious. HPV vaccines use different expression systems, contain adjuvants and do not contain antibiotics or preservative agents [2].

All HPV vaccines contain VLPs against high-risk HPV types 16 and 18; the nonavalent vaccine also contains VLPs against high-risk HPV types 31, 33, 45, 52 and 58. The quadrivalent and nonavalent vaccines contain VLPs to protect against anogenital warts causally related to HPV types 6 and 11 [4].

All HPV vaccines are indicated for use in females aged 9 years or older and are licensed for use up to 26 or 45 years of age. Some HPV vaccines are also licensed for use in males. All HPV vaccines are indicated for the prevention of cervical premalignant lesions and cancers caused by high-risk HPV types, which vary by vaccine product. As per their product labels, selected vaccines have indications against another HPV-related disease. HPV vaccines are available as a prefilled syringe or in single or 2-dose vials [3].

There are three HPV (human papillomavirus) vaccines that have been approved for use in Europe:

- Gardasil: This vaccine is manufactured by Merck and is approved for use in individuals aged 9 to 45 years. It provides protection against HPV types 6, 11, 16, and 18 [5].
- Cervarix: This vaccine is manufactured by GlaxoSmithKline and is approved for use in individuals aged 9 to 25 years. It provides protection against HPV types 16 and 18.
- Gardasil 9: This vaccine is also manufactured by Merck and is approved for use in individuals aged 9 to 45 years. It provides protection against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. Gardasil 9 is licensed for girls and boys aged 9–14 years as a 2-dose schedule (5–13 months apart). From age 15, a 3-dose schedule should be followed (at 0, 1–2 and 4-6 months) [4].

All three vaccines are highly effective at preventing HPV infections and related diseases, such as genital warts and certain cancers.

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1.3. Elimination of cervical cancer

Elimination of cervical cancer in the WHO European Region

As part of its mission to promote health and well-being, the World Health Organization (WHO) European Region has prioritized the elimination of cervical cancer, which largely hinges on effective strategies to combat HPV.

More than 66,000 women are diagnosed with cervical cancer and more than 30,000 deaths are recorded annually in the Region. In the last decade, access to HPV vaccination in the European Region has increased. Over 80% of the member states in the WHO European Region have introduced the HPV vaccine into their national immunization programs. Vaccines are currently recommended for girls between the ages of 9 and 14 in 38 of the 53 countries in the region. Early vaccination before contact with the virus is essential to achieve the maximum benefits of vaccination.

In countries with established vaccination programs, coverage for the first dose among target groups ranged between 70% to 90%, though there were variances from country to country. However, Eastern Europe lags behind Western and Northern Europe in terms of HPV vaccination coverage. While some Western European countries boast coverage rates above 80%, many Eastern European nations struggle to achieve even 20% coverage among the target population.

The **World Health Organization** (WHO) launched a global strategy in November 2020 to accelerate the elimination of cervical cancer as a public health problem. The strategy is based on three key pillars, often referred to as the "90-70-90 targets" to be achieved by every country by 2030 [1]:

Prevention

- **Target**: Vaccinate 90% of girls with the HPV vaccine by the age of 15.
- **Action**: The WHO recommends the introduction and scaling-up of the HPV vaccination in national immunization programs. Given that persistent infection with specific high-risk HPV types is the primary cause of cervical cancer, vaccinating pre-adolescent girls (and, where feasible, boys) can significantly reduce the risk.

Screening and Diagnosis

- **Target**: Screen 70% of women using a high-performance HPV DNA test at 35 and 45 years of age.
- **Action**: The WHO recommends that women undergo screening at key ages to detect and treat precancerous lesions before they become invasive cancers. The emphasis on HPV DNA testing, which detects the presence of the virus rather than changes in cervical cells, is due to its higher sensitivity and longer-lasting negative predictive value compared to traditional cytology-based methods like the Pap smear.

Treatment and Care

- **Target**: Treat 90% of women identified with cervical disease.
- **Action**: This includes:
    - Treating 90% of women with precancerous lesions through methods like cryotherapy, LEEP (Loop Electrosurgical Excision Procedure), or cold coagulation.

- Providing 90% of women diagnosed with invasive cervical cancer access to more advanced treatments such as surgery, radiotherapy, and chemotherapy.

The European Commission launched **Europe's Beating Cancer Plan** in February 2021, which aims to tackle the entire disease pathway, from prevention to quality of life of survivors. Cervical cancer, being one of the most preventable forms of cancer when adequate measures are in place, is specifically addressed within the plan [2].
Key objectives and actions related to cervical cancer in the Europe's Beating Cancer Plan include:

Prevention through Vaccination: The plan emphasizes the importance of vaccination against HPV, which is responsible for the vast majority of cervical cancer cases.
Aiming to vaccinate at least 90% of the EU target population of girls (and, where feasible, boys) by 2030.
Efforts will also be made to promote catch-up vaccination for those who did not receive it at the target age.

Screening: The goal is to screen 90% of the EU target population of women for cervical cancer by 2030. Screening plays a vital role in the early detection of precancerous lesions, allowing for timely treatment.
The plan promotes the implementation and improvement of population-based screening programs, ensuring they adhere to the best practices and guidelines. Improving access, quality, and diagnostics of screening programs is emphasized, especially utilizing HPV DNA-based tests, which are more effective than traditional cytology in detecting high-risk HPV strains.

Successful models in eliminating HPV infection
The UK's experience with HPV vaccination demonstrates that cervical neoplasm is a preventable disease. In the United Kingdom, one of the first countries in the WHO European Region to introduce HPV vaccination, it has been shown that through the immunisation programme cervical cancer is almost eliminated in women born after 1 September 1995. They were vaccinated at the age of 12-13 years. In these women, the incidence of high-grade precancerous cervical lesions (CIN3) was significantly reduced.

The UK's strategy has several components:

- HPV Vaccination: The UK introduced the HPV vaccination program in 2008, and since then, girls aged 12 to 13 have been offered the HPV vaccine for free as part of the school-based vaccination program. In 2019, the UK expanded the HPV vaccination program to include boys aged 12 to 13 as well, with the aim of protecting them against HPV-related cancers and diseases.
- Cervical Cancer Screening: The UK's cervical screening program has been in place since the 1980s and offers free cervical screening tests to women aged 25 to 64. In 2019, the UK introduced a more sensitive test for HPV as part of its cervical screening program, which aims to detect HPV infection and cervical cancer earlier.

- Public Health Campaigns: The UK government and various health organizations have launched public health campaigns to increase awareness about the importance of HPV vaccination and cervical screening. The campaigns aim to address the misconceptions surrounding HPV and encourage more people to take up the HPV vaccine and cervical screening.

Through these components, the UK aims to eliminate cervical cancer as a public health problem, with a goal to reduce the number of cervical cancer cases by 90% by 2035. The success of the UK's HPV elimination strategy can already be seen, with the HPV vaccination program and cervical screening program contributing to a significant decrease in the incidence of cervical cancer and related deaths.

References:

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Economic evidence

Several studies have shown that the feasibility of HPV vaccination is high, which means that the vaccine's benefits in terms of disease prevention outweigh the costs of administering the vaccine. The cost-effectiveness of HPV vaccination varies depending on several factors, including the vaccinated population, the cost of the vaccine, the effectiveness of the vaccine, and the cost of treating HPV-related diseases. However, most studies have shown that HPV vaccination is feasible and even reduces costs in the system, especially when it is given to girls and boys before they start their sex lives [1].

As recommended by the WHO in 2019, all countries should conduct research to determine the cost-effectiveness of HPV vaccination before implementing national programs. Programs dedicated to HPV vaccination and studies on the subject adapted for low- and middle-income countries are needed to increase vaccination coverage [2].
Multiple studies across various countries and settings have consistently shown that the HPV vaccine is cost-effective, especially when considering the long-term healthcare costs associated with treating HPV-related diseases, such as cervical cancer, other anogenital cancers, and oropharyngeal cancers.

Cost of Illness: Treating HPV-associated diseases is expensive. For instance, in the United States, the annual direct medical cost of treating cervical diseases and cancers caused by HPV is estimated to be over $1 billion.

Vaccine Cost vs. Treatment Cost:

- A study conducted in the U.S. found that the cost of vaccinating 12-year-old girls was less than the lifetime costs associated with treating new cases of cervical cancer and genital warts [3].

- According to the World Health Organization (WHO), in low-resource settings where cervical cancer screening and treatment are limited or absent, HPV vaccination of girls has shown to be highly cost-effective [4].

Modeling Studies:

- Various modeling studies have found HPV vaccination to be cost-effective, particularly when vaccination coverage is high and provided at younger ages, usually before sexual debut.
- A study in the UK found that the HPV vaccination program, targeting 12-year-old girls, would prevent up to 400 deaths from cervical cancer annually. The program's cost-effectiveness was even more pronounced when considering the broader spectrum of HPV-related diseases.
- A study from Australia, which has one of the earliest and most comprehensive HPV vaccination programs, found that the program was cost-saving when considering the cumulative costs of cervical cancer screening and treatment over a lifetime.

Inclusion of Boys:

Several analyses have assessed the cost-effectiveness of expanding HPV vaccination to boys. The results vary based on settings, HPV types in the vaccine, coverage in girls, and other factors. However, many studies, especially those from settings where vaccine uptake in girls is low, suggest that vaccinating boys can be cost-effective [5].

The cost-effectiveness of a one-dose vaccination scheme:

Reviews of the available scientific data have shown that a single dose of the vaccine is just as effective as two doses at preventing HPV-related cancers. A single-dose vaccination offers comparable health advantages to a two-dose regimen, streamlining the vaccination process, lowering expenses, and easing vaccine supply limitations. If protection from a single dose has a shorter lifespan, and if there are more affordable vaccine options, efficient delivery methods, and a significant incidence of cervical cancer, then a second dose might become economically viable [7].

Health and Economic Benefits:

Beyond the direct medical costs saved, HPV vaccination has broader societal and economic benefits. Preventing cervical and other HPV-associated cancers means fewer years of life lost to the disease, improved quality of life, reduced pain and suffering, and decreased work and productivity losses.

Catch-Up Vaccination Programs:

Some studies have assessed the cost-effectiveness of catch-up vaccination programs for older adolescents and young adults. While the cost-effectiveness generally decreases with age (due to prior HPV exposure), these programs can still be deemed cost-effective, especially in settings where the vaccine coverage among younger cohorts has been low [6].

It's essential to note that while HPV vaccination has a front-loaded cost (the cost of buying and administering the vaccine), the benefits — both in terms of health outcomes and cost savings from averted treatment — accrue over the long term. Overall, the consensus in the public health community is that HPV vaccination provides excellent value for money, especially when considering the full range of HPV-associated diseases it can prevent.

Understanding the costs associated with different strategies for large-scale vaccination implementation is key to identifying opportunities to optimize current vaccination programs. For example, the stigma associated with vaccination for a sexually transmitted disease is a factor influencing vaccination coverage in many regions. In this context, interventions are needed to target citizens' behaviour.

Given the current public attitude towards vaccination, the cultural and historical aspects of each region must be taken into account when implementing vaccination strategies. The inclusion of community representatives in the initial phases of the planning of these strategies can facilitate the creation and promotion of safe, personalized and coordinated public health messages.

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Successful communication strategies

According to WHO Communication resources centre, increasing community awareness through timely, complete and appropriate communication is the key to successful and sustainable HPV vaccine introduction. With a unique target group of young girls and links to both sexual activity and cancer, the HPV vaccine calls for multifaceted communications strategies [1].
In part 1 of the most recent HPV communication guideline published by WHO (2017), the authors emphasize the following:

- changing human behaviour is a process in multiple steps: unaware of HPV vaccine; gain awareness through communication; consider HPV vaccination; take action; pro-actively vaccinate the other children; become a voice in the community
- communication principles (health communication should adhere to key principles and be grounded in a human rights approach) are based on the following basics: communication team; technical programme objectives; situation analysis; communication objectives; target audiences; define the right messages, and finally,

mixing all elements to personalise the communication for each community; build a crisis communication plan; have a monitoring and evaluation plan, with indicators and outcomes [2].

Country context is very important: there is no silver bullet to achieve 90% HPV vaccination rate, but to ensure that the particularities of each country are understood, following the situation analysis and identifying the strong and weak points could be the best starting point.
A list with the European countries reporting some of the highest HPV vaccination coverage in girls:

1. United Kingdom: The UK has consistently maintained high HPV vaccination coverage for girls since the introduction of the programme in 2008. As of 2021, the coverage rate for the two-dose HPV vaccine in the UK was over 80% for 12-13-year-old girls.
2. Denmark: Denmark has also shown impressive results in HPV vaccination coverage. In recent years, the country has achieved high vaccination rates, close to or above 90%, among eligible girls.
3. Norway: Norway has reported relatively high HPV vaccination coverage rates, with percentages close to or above 90% for girls eligible for the vaccine.
4. Sweden: Sweden has made significant progress in increasing HPV vaccination coverage, reaching rates close to or above 80% for eligible girls.
5. Netherlands: The Netherlands has consistently reported high HPV vaccination coverage, with percentages close to or above 80% for eligible girls.
6. Finland: Finland has been successful in achieving high HPV vaccination coverage, with rates close to or above 90% for eligible girls.

UK's case, as being the country that started the first HPV vaccination campaign in the same time as Romania (2008)

A qualitative study from 2017, based on interviews with key experts at the national level highlighted that: "Effective planning and data management were key for successful service provision of HPV vaccination, as well as close collaboration between commissioners, service providers and data system managers, a team skill mix with experienced staff, pro-active engagement with schools and service providers equipped to respond to parental concerns."
UK went full in with the communication efforts to complement the vaccination effort. Here is a timeline of communication strategies and efforts regarding the HPV vaccination programme in the UK starting 2008:

- Educational Materials and Public Awareness: The National Health Service (NHS) and the UK government launched educational materials and public awareness campaigns to inform parents and young girls about the benefits and safety of the HPV vaccine.
- School-Based Vaccination Programme: The HPV vaccine was primarily administered through a school-based vaccination programme. Health professionals and school nurses played a crucial role in disseminating information and addressing concerns from students and parents.

- Information for Healthcare Professionals: The UK health authorities provided information and training to healthcare professionals, including general practitioners and nurses, to help them understand the vaccine's importance and address any misconceptions.
- Media Campaigns and Information Dissemination: The government and health authorities used various media channels, such as television, radio, newspapers, and online platforms, to reach a broader audience and promote the vaccination programme.
- Addressing Misinformation: In response to concerns and misinformation about the HPV vaccine's safety, health authorities actively worked to debunk myths and provide evidence-based information.
- Expansion to Boys: In 2019, the UK government announced the extension of the HPV vaccination programme to include boys as well. This move aimed to protect them from HPV-related diseases and reduce transmission.
- Community Engagement: Community engagement initiatives were implemented to involve local communities, religious leaders, and community organizations in promoting vaccination and dispelling any misconceptions.
- Research and Monitoring: Continuous research and monitoring of the vaccination programme's effectiveness and safety were conducted to inform future communication strategies and maintain public trust [3].

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1.4. HPV in Romania

HPV Vaccination and Screening in Romania

Romania ranks first in terms of incidence and mortality for cervical cancer: the incidence is 2.5 times higher than the European average, and the mortality rate is over 4 times higher. According to the „Attitudes and perceptions on cancer in Romania" national survey organised in 2018 by the Centre for Innovation in Medicine, according to Renasterea Foundation Surveys and National Institute for Public Health data:

- (2018) 48% of women respondents said that in the last 3 years they were not tested for HPV;
- (2018) Although 1 in 2 got informed on HPV vaccination, only 2% decided to get the vaccine;
- (2018-2020) no less than 67% of women and girls from rural areas, aged 15-65, have genital
  infections;

- (2020) only 36% of Romanian women have heard of the HPV virus and only 31% associate this infection with cervical cancer.

Romania initiated its first cervical cancer screening program in 2012, aiming to cover around 6 million women aged between 25 and 63 over a span of five years. Yet, by 2015, a scanty 7% of the intended audience had been tested.

Romania was an early adopter of the HPV vaccination, introducing it in 2008 for 10–11-year-old girls, coinciding with the UK's initiative. Unfortunately, this effort was largely unsuccessful; merely 2.6% of the eligible girls received the vaccine, leading to the suspension of the program. 2009 saw the commencement of an awareness campaign, followed by another vaccination drive aimed at girls aged 12–14. An additional initiative allowed adult women to be vaccinated for free through healthcare providers. However, with the vaccine's low adoption rate, the school-centric program was halted by the end of 2011. Subsequent launches of the program occurred in April 2013 and again in 2019.

Preliminary figures from 2020 and 2021 indicate that less than 50,000 girls got vaccinated. No region in Romania has achieved a vaccination rate surpassing 5% of its target demographic, with the national average for 2020/2021 lingering at 2%. In stark contrast, the UK's HPV vaccination efforts have reaped significant results, witnessing a staggering 90% decrease in cervical cancer incidence.

Starting December 1, 2023, according to the Ministry of Health, Romania will finally implement one of the largest programs in Europe to eliminate cancers caused by HPV:

- Adolescent girls and boys aged 11-14 will be able to get anti-HPV vaccination free of charge.
- Women between 19 and 45 years old will benefit from the anti-HPV vaccination in a 50% compensated regime.

More details will follow.

HPV vaccination attitudes and perceptions in Romania

We conducted a brief review of scientific articles published from 2012 to 2022 to see how the perceptions and attitudes towards HPV vaccination in Romania varied. According to the materials found, over the last decade, awareness of HPV and its vaccine has generally increased in Romania. However, the level of knowledge and the quality of information varied. Misconceptions, fueled in part by media and pseudoscientific sources, persisted. This led to hesitancy and low vaccination rates, even among those aware of HPV. The role of medical professionals was consistently highlighted as crucial for disseminating accurate information and influencing positive attitudes towards HPV vaccination.

Evolution of Attitudes Towards HPV Vaccination in Romania (2012-2022):

2012: Concerns were high, with predominant reasons being the perceived riskiness of the vaccine, conspiracy theories, and general mistrust in the health system. The need for clear and factual information was highlighted.

- 2013: Online forums showed mixed views, with evidence-based positive views competing against pseudoscientific and emotional anti-vaccine views. The vaccine was seen by critics as dangerous and part of a conspiracy. Supporters viewed it as beneficial.
- 2014: Media coverage was mixed. While almost a third were neutral, a slightly lesser percentage were negative or extremely negative. Only 23.6% were positive. Concerns included side effects and inadequate testing. Media was often not comprehensive or accurate.
- 2015: Knowledge among adolescents was extremely low. Most were unaware of HPV, its vaccine, or the Papanicolau smear test. Yet, there was a significant interest in receiving more information.
- 2018: Awareness among Romanian women was moderate, but with minimal and often incomplete knowledge. The majority had heard of the vaccine, but only half had a positive attitude. Concerns included side effects, risk perception, and financial barriers. (North-eastern Romania): Among vaccinated women, knowledge was good. There was strong awareness of HPV and its relation to cervical cancer. The decision to vaccinate was majorly influenced by healthcare professionals.
- 2019: Vaccine hesitancy (VH) was evident, with media being a major negative influence. The HPV vaccine, among others, induced hesitation.
- 2022: A large survey revealed confusion. Despite a high awareness of HPV and its related cancers, a small fraction was vaccinated. Most respondents did not receive their HPV information from medical professionals.
- 2022 (data from 2021): Awareness was high among medical students, doctors, and a significant portion of parents. However, the knowledge quality varied. Many believed vaccination should be considered after 18 years. There was a noted gap in detailed knowledge about HPV among students and parents. Most respondents believed that doctors and healthcare professionals should provide accurate HPV information.

The sources used for the analysis above:

- 2012 “Who will take the blame?”: Understanding the reasons why Romanian mothers decline HPV vaccination for their daughters [1]

Results show as main reasons for not vaccinating their daughters perceiving the vaccine as risky, the belief that the vaccine represents an experiment that uses their daughters as guinea pigs, the belief that the vaccine embodies a conspiracy theory that aims to reduce the world's population and general mistrust in the ineffective health system. Mothers stated they would need clear, factual information about the HPV vaccine and its link to cervical cancer in order to motivate them to accept it for their daughters.

- 2013 Dangerous Agent or Saviour? HPV Vaccine Representations on Online Discussion Forums in Romania [2]

Twenty discussion forums, with a total sample size of 2,240 comments (2007–2012), were included.

- Positive discourses relying on evidence-based arguments or cancer-related experiences battled with negative discourses that focused mostly on pseudo-scientific information and affect-based testimonials.
- Both camps made use of appeals to authority in order to provide powerful messages.
- Critics expressed high levels of mistrust in the health system and perceived the vaccine as dangerous, as part of a conspiracy, as unnecessary or as a promoter of promiscuity.
- By contrast, supporters considered the HPV vaccine to be helpful and criticized the irrationality of opponents.
- Ambivalence and uncertainty also emerged, along with criticism toward the suboptimal organization of the vaccination programmes.

Findings highlight ways in which views about the vaccine are embedded in broader perspectives about science, the national medical system, society development and economic inequality.

- 2014 Mass media coverage of HPV vaccination in Romania: a content analysis [3]

Content analysis of 271 media reports (from newspapers, magazines, videos and informational websites) published online between November 2007 and January 2012. Overall, results indicated that :

- 31.4% of the materials were neutral,
- 28% were negative or extremely negative,
- 17% were mixed,
- while 23.6% were positive towards the vaccine.

The most dominant vaccine-related concerns were side effects and insufficient testing. Elementary information about the vaccine and HPV was constantly left out and sometimes inaccuracies were found. Negatively disposed reports were more likely to contain incorrect data about vaccine efficacy and less likely to provide comprehensive information about the vaccine and HPV-related diseases. Some dimensions of media coverage varied across time and media outlets. The present findings suggest that educational interventions are greatly needed as a response to suboptimal and incomplete media coverage of HPV vaccination.

- 2015 Romanian adolescents' knowledge and attitudes towards human papillomavirus infection and prophylactic vaccination [4]

A total of 524 adolescents aged 16–18 years old were recruited from the first two general highschools in Bucharest (according to the admission grade) and completed a self-administered questionnaire including demographics, HPV related and Papanicolau smear test knowledge
Of the adolescents interviewed, a very small proportion had heard of HPV infection, HPV vaccine and Papanicolau smear test, that is, 20.22%, 67.92% and 22.9%, respectively. The overall vaccination rate for this group was 2.3%. The most common reason for not receiving the HPV vaccine was the lack of information (80.6%) followed by parents' concerns regarding safety (11%), fear of pain (5.59%) and not being sexually active (2.7%). However, 97.7% of the respondents declared interest in receiving more information about HPV.

- 2018 Awareness and Knowledge About HPV and HPV Vaccine Among Romanian Women [5]

69.2% of women were aware about HPV but their knowledge was minimal and incomplete. While 62.3% had heard about HPV vaccine, only 50.7% had a positive attitude toward it. The main barriers to vaccination were the fear of side effects, the perception that is risky, and the financial concerns.

Deficiencies in knowledge were noted for vaccine, genital warts, or risks factors for HPV infection like the early onset of sexual life. The information regarding HPV and vaccine is not always accurate and complete, and only 50.7% of women have a positive attitude toward the vaccine.

- 2018 HPV and HPV vaccine knowledge among HPV-vaccinated women in North-eastern Romania [6]

Among the participants (n = 120), knowledge of HPV, HPV vaccine, and cervical screening was good. Most respondents were aware of the causal relationship between HPV and cervical cancer (83.3%), the sexual transmission of HPV (81.6%), and its asymptomatic nature (68.3 %). The women with a high knowledge score were more likely to have attained a high educational level, to work in the healthcare system, and to consult more health information sources. A major role in deciding to get the vaccination was the physician (gynaecologist or general practitioner) who proposed the vaccination and explained the importance of being immunized with the HPV vaccine.

- 2019 Qualitative Assessment of Vaccine Hesitancy in Romania Cluj [7]

Human Papillomavirus (HPV) 24.1%. One-third of the investigated population had expressed VH, and a further one-third of these had refused a vaccine for their child. Chicken Pox, Measles, Mumps, Rubella (MMR), and HPV vaccines generated the most hesitation. ***Negative information from the media was the most frequently evoked reason for VH.***

- 2022 Barriers and Facilitators of Romanian HPV (Human Papillomavirus) Vaccination [8]

1122 responders were interviewed; mean age 36.39 ±10.7 years (limits: 19–62), majority women, 999 (89.04%), and from urban areas, 930 (82.89%). Most of the participants in the survey (684 (60.96%)) had university and post-university studies, and 459 (40.91%) participants were related to the medical domain.

Out of the 666 parents, only 67 (5.97%) parents were themselves vaccinated against HPV, and 91 (8.11%) had the intention to vaccinate themselves against HPV in the future. The participants with children eligible for HPV vaccination had one, two, three, or even four children. Altogether, there were 609 children, but 303 were aged 9 to 15 years. Out of these 303 children, 75 (24.75%) children were HPV vaccinated: 69 girls and 6 boys.

The ***Romanian population is very confused when it comes to the importance of the HPV vaccine****. Although the majority of interviewed Romanians are aware of HPV and related cancers (1023 (91.18%)) and believe that the HPV vaccine poses no risk (823 (73.35%)), only 324 (28.88%) received their HPV information from the medical doctors, and only 118 (10.51%) are HPV vaccinated.*

- 2022 Assessing the Level of Knowledge, Beliefs and Acceptance of HPV Vaccine: A Cross-Sectional Study in Romania [9] (data from 2021)

Awareness on HPV infection:

- *Almost 86% of all parents (6th-8th pupils) in Targu Mures (Northern Romania)*
- *89.7% medical students and 100% doctors*
- *70.4% boys in the 11th–12th grades, 74.3% girls in the 11th-12th grades and 82.8% of their mothers*

Awareness on HPV vaccination:

- *The level of information about HPV infection was satisfactory for almost half of the doctors (47.3%)*
- *A* ***good level of information was identified in 32.1% doctors*** *and 28.9% medical students.*

- *The degree of information on HPV vaccination was satisfactory for 44.6% doctors, while for the other categories of respondents the poor level of information was predominant*

Optimal administration age opinions

- *69.0% of the medical students, 72.3% doctors and 30.9% boys in the 11th–12th grades considered that optimal vaccination should occur between 12–14 years,*
- *while 44.5% of the parents of pupils in the 6th–8th grades and 50.6% of the mothers of high-school students in the 11th–12th grades believed that vaccination should be considered after the age of 18 years.*
- *50.6% girls in the 11th–12th grades believed that vaccination should be administered before becoming sexually active.*

Overall, there was a very low level of knowledge among students and their parents regarding the clinical signs, methods of transmission, infection site, infection consequences, risk factors and prophylaxis of HPV infection.

Very few respondents sought information from their general practitioner or HPV specialist, at the same time considering that accurate information about HPV should be provided by physicians and healthcare professionals.

Overall, the HPV vaccination barriers in Romania are related to:

- Lack of awareness and knowledge: Studies highlighted a general lack of awareness and knowledge about HPV and its associated risks, as well as the benefits of vaccination. This lack of understanding could lead to hesitancy or refusal among parents and adolescents.
- Misperceptions and fears: Misconceptions and fears regarding the safety and efficacy of the HPV vaccine. Rumors and misinformation about adverse effects or unfounded beliefs may play a role in vaccine refusal.
- Cultural and social factors: Cultural norms and societal attitudes towards sexual health discussions and vaccination can influence decisions about HPV vaccination. Conservative views or stigma associated with discussions about sexually transmitted infections might hinder vaccine acceptance.
- Trust in healthcare providers: The level of trust and confidence that individuals have in healthcare providers and authorities may impact their decision to vaccinate. If there are doubts about the credibility of healthcare advice, vaccination rates could be affected.
- Access and availability: Challenges in accessing healthcare facilities or concerns about the cost and availability of the vaccine could be barriers to vaccination.
- Media influence: The media's portrayal of HPV vaccination, including both positive and negative coverage, can influence public perception and decisions about vaccination.
- Vaccine education campaigns: The effectiveness of educational campaigns promoting HPV vaccination might be assessed to understand their impact on vaccine acceptance.

References:

- [1] https://www.sciencedirect.com/science/article/abs/pii/S0264410X12013266
- [2] https://link.springer.com/article/10.1007/s12529-013-9340-z
- [3] https://academic.oup.com/her/article/29/6/977/2804290
- [4] https://www.sciencedirect.com/science/article/abs/pii/S0301211515003346
- [5] https://link.springer.com/article/10.1007/s13187-016-1130-2

- [6] https://www.imrpress.com/journal/EJGO/39/3/10.12892/ejgo3773.2018
- [7] https://www.mdpi.com/1648-9144/55/6/282
- [8] https://www.mdpi.com/2076-393X/10/10/1722
- [9] https://www.mdpi.com/1660-4601/19/11/6939

2.2. Romanian content

Content is generated based on the adaptation of the English content to Romanian.

3. TECHNICAL DETAILS

The website is fully responsive, and the architecture is as follows:

- About the project
  - *Background*
  - *Objectives*
  - *Structure*
- Resources
  - *Approved Deliverables and Milestones*
- News
  - News (Press releases and Events)
- Knowledge Center

The website is built with a customized WordPress approach, allowing those responsible for uploading the content (latest news, press releases, events, details about the project) to have access to the classic, flexible and user-friendly WordPress dashboard. The dashboard will be personalized in order to have access to different metrics and performance indicators regarding the user's interactions. As the development of the website is still in its early phase, not all the categories and pages are completely formatted according to the visual guidelines.

The website will be integrated with Google Analytics and Google Search Console, providing the partners with comprehensive metrics to track and analyze various aspects such as the number of visitors, demographic information, user's behavior (the number of interactions, sessions, the duration of the visit, the most accessed categories etc), the traffic source and so on. These metrics can inform content development, to find best ways to promote the project and to learn more about the targeted audiences.

4. CONCLUSION

In summary, the Deliverable 'Knowledge Centre on HPV Vaccination & Communication for European Countries with Low VR' represents a key resource of the project, striving to enhance HPV vaccination drives, offering comprehensive data, validated content, and effective communication strategies curated from successful global models.

Based on the platform and content, we'll build synergies with other projects and initiatives and seek to promote our resources to as many organisations as possible – all for the common good of reaching the elimination of HPV infections in the European Union and beyond.

The Deliverable D2.1, titled 'Knowledge Centre on HPV Vaccination & Communication for European Countries with Low VR,' stands as a testament to the ReThinkHPVaccination project's unwavering dedication to address the pressing issue of lagging HPV vaccination rates in specific European regions.

By drawing inspiration from global success stories and blending it with rigorous scientific validation, the ReThinkHPVaccination project ensures that the Knowledge Centre becomes a beacon of trusted information in the realm of HPV vaccination. As the platform continues to grow and evolve, it promises to be a pivotal tool in the collective endeavour to elevate vaccination rates, demystify misconceptions, and drive a healthier European future.

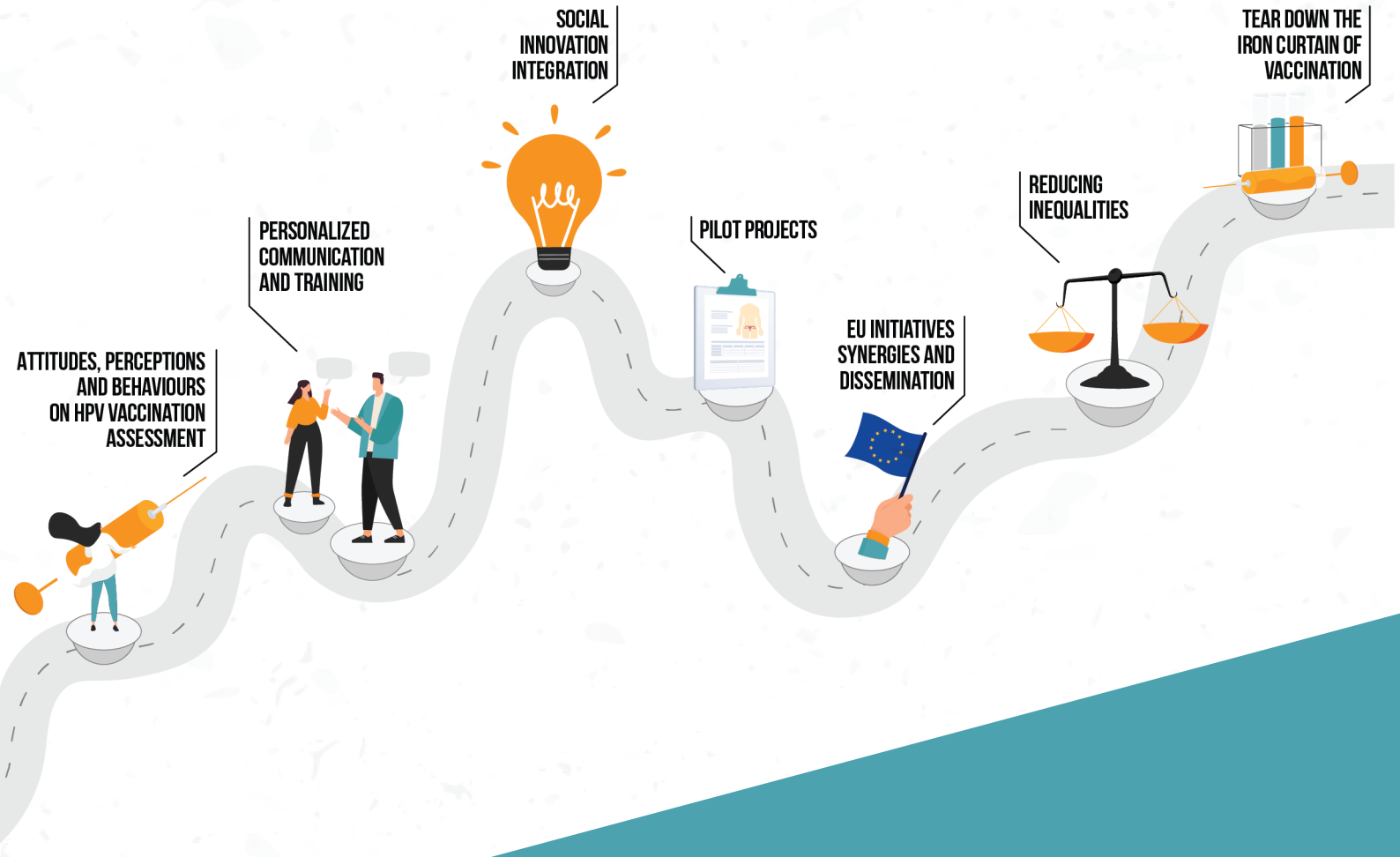
This culmination of effort, expertise, and intent crystallizes the project's overarching mission: to catalyse change through knowledge, collaboration, and innovation.

ANNEX 1. VISUAL IDENTITY MANUAL AND PROJECT WEBSITE

Rethink and Reduce inequalities in HPV vaccination through personalized communication and training, based on social innovation and behavioural determinants of health

VISUAL IDENTITY & WEBSITE

AUGUST 2023



Co-funded by the European Union

Co-funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

Project number: 101080000
Project name: Rethink and Reduce inequalities in HPV vaccination through personalized communication and training, based on social innovation and behavioural determinants of health
Project acronym: ReThinkHPVaccination
Call: EU4Health

VERSION TRACKER

Date	Version	Author	Description
30.07.2023	0.1	Ruxandra Schitea	Table of Contents
01.08.2023	0.2	Ruxandra Schitea	First Draft
30.08.2023	0.3	Adriana Boata	Final Review

LIST OF ABBREVIATIONS

Acronym	Description
EU	European Union
WP	Work Package
GA	Grant Agreement
WHO	World Health Organisation

LIST OF FIGURES

TABLE OF CONTENTS

EXECUTIVE SUMMARY

This deliverable aims to provide an overview of the visual aspects and guidelines used in communicating and disseminating information regarding the ReThinkHPVaccination project. The present document summarizes the output of the ReThinkHPVaccination's Task 8.1 – Project Branding.

The following pages contain a detailed overview of the project's main assets that have been developed in order to support and enhance communication and stakeholder engagement activities. More precisely, this document contains briefs on ReThinkHPVaccination's visual identity (such as logo & patterns), online and print templates (Word & PowerPoint) used for disseminating news and for sharing insights, social media activity (Twitter & LinkedIn) and website development.

All the assets created have been briefly detailed inside this deliverable and every template can be found attached in the Annex section. All the templates are in harmony with the project's visual guidelines in order to consolidate its bold and proactive message.

INTRODUCTION

The "*Rethink and Reduce Inequalities in HPV Vaccination through Personalized Communication & training, based on social innovation and behavioral determinants of health"* Project is co-funded by the European Union through EU4Health Programme and will be implemented by a consortium composed of the Renasterea Foundation for Woman's Health (as coordinator), the Centre for Innovation in Medicine, and the Eurocomunicare Association (as partners), and the European School of Oncology (as associated partner).

Although HPV-generated cancers are some of the most preventable forms of cancer, the vaccine uptake in Central Eastern Europe, Southern Europe, and EU-widening countries is low or very low. HPV infection is responsible for 99.7% of cervical cancers and two HPV types (16 and 18) cause 70% of cervical cancers and pre-cancerous cervical lesions. Evidence also links HPV with cancers of the anus, vulva, vagina, penis, and oropharynx. The now-available HPV vaccine covers 90% of the circulating strains of the virus. the virus.

In this context, vaccination of the female and male populations should be one of the public health priorities. Theoretically, it is, but practically the results are missing in many countries – Romania, Bulgaria, Greece, Poland, Republic of Moldova, Ukraine, Belarus, Georgia, Albania and so on are the best examples on how lack of access to the right information, misinformation/fake-news, unrealistic communication strategies and the infodemic related to vaccination in general (including Covid-19 vaccination) can generate thousands of avoidable deaths. These countries, with Romania being one of the worst, have the highest rate of preventable and treatable deaths in European Region.

The ReThinkHPVaccination Project aims at changing this narrative and reducing inequalities in HPV vaccination between and within countries through personalized communication & training, based on social innovation and assessment and targeted interventions on the behavioral determinants of health. The main goal of this project is to support Member States and EU-widening countries to **ReThink** and **ReStart** their **HPV vaccination** campaigns and so take a step closer to achieving Europe's Beating Cancer Plan and Cancer Mission objectives with regards to HPV vaccination and cancer prevention.

1. RETHINKHPVACCINATION LOGO

Through a simple and unique design, ReThinkHPVaccination logo highlights the need of re-shaping old approaches. Revitalizing and optimistic, the design invites the viewer to a dimension of open communication and clarity of thought. With an underlying sense of community, it opens the way to a joint action that needs to be taken in order to Rethink and Reduce the inequalities in HPV vaccination through personalized means.

At a first glance, the logo can be perceived as typographic, with a clean, bold, and straightforward typeface, delivering a clear message ”Rethink Vaccination”. However, the design also figures the well-known ribbon – the key graphical element of the logo, a symbol of awareness and support for different types of cancer – framed by two carefully modified letters, all three building the structure ”HPV”.

Figure 1 ReThink HPVaccination favicon

Figure 2 ReThink HPVaccination logo

1.1. Visual identity

ReThinkHPVaccination’s Visual Identity Manual *(see Annex 1)* includes the main guidelines on how to best use graphic and typography assets when communicating and displaying the project. The manual contains the logo and some of its variations, color palette, graphics and patterns, as well as typography guides.

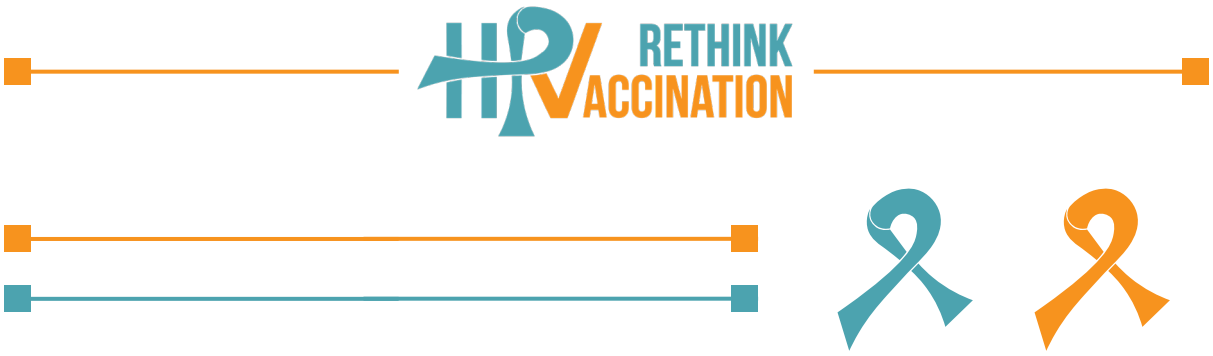


Figure 3 Graphical elements

Figure 4 Pattern variations

The central element of the pattern can be either the ribbon (representing a sign of support for oncologic patients), or the logo itself. The two horizontal lines direct the viewer's attention to the central element, while providing a stable framework for any composition.

2. STANDARD PROJECT TEMPLATES

In order to have a structured and cohesive approach when communicating and disseminating information regarding the project both internal and external, there has been created a series of Word document templates and a PowerPoint presentation that follow ReThinkHPVaccination's visual identity guidelines. The templates have been made available to all the project's partners.

2.1. Deliverable template

The deliverable template *(see Annex 1)* will be used for preparing all project deliverables.

2.2. PowerPoint presentation template

A PowerPoint presentation template for ReThinkHPVaccination *(see Annex 3)* has been developed in order to ensure a visually pleasing, uniform and data-centric design. The template was developed not to be text heavy, but data-driven, the use of icons, vectors and shapes supporting the design. The brand's vibrant colors help deliver a clear and impactful message.

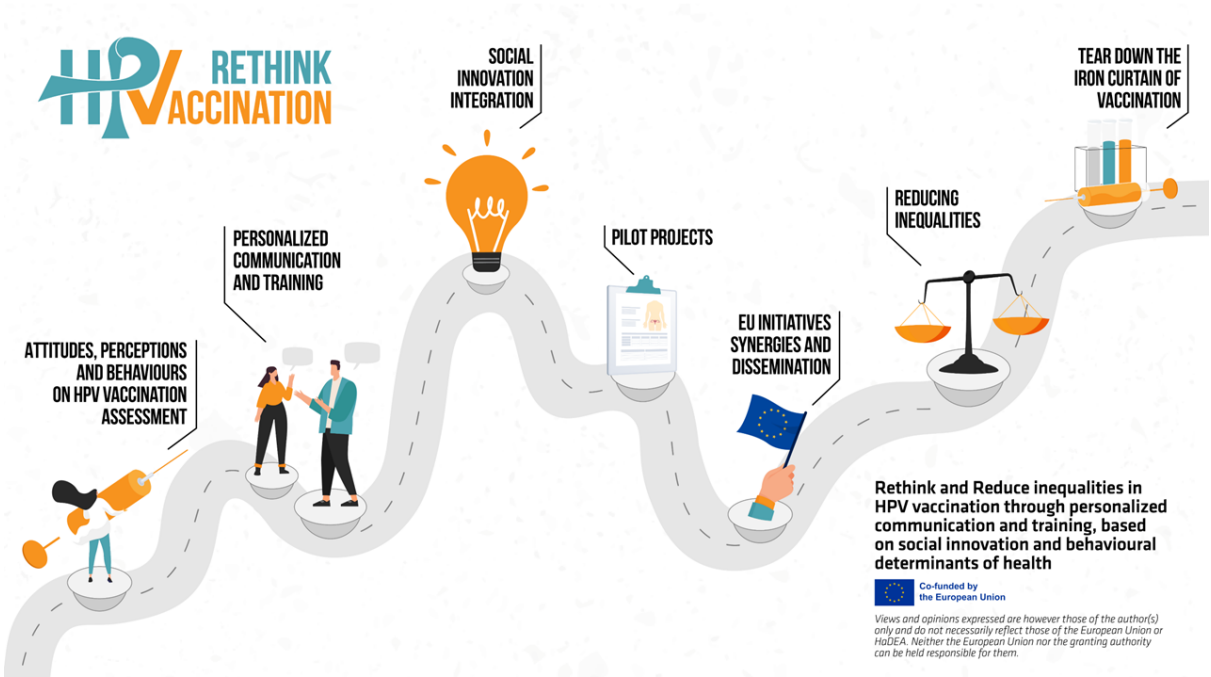


Figure 5 Examples of PowerPoint presentation slides

2.3. Internal documents template

The internal document template resembles the deliverable template *(see Annex 1)*, following the same visual and typographic guidelines that can be found in the project's visual identity manual.

2.4. Press release Template

A standard news release template *(see Annex 3)* has been created with the purpose of sharing the latest information regarding the ReThinkHPVaccination project. The template can be used in both online and print communications.

3. SOCIAL MEDIA

Social Media (SM) is one of the key actors in promoting and disseminating information regarding ReThinkHPVaccination's latest developments. SM channels allow the project to break the boundaries of The Eastern European block, and to spread its message to the whole world.

Through these means of communication, ReThinkHPVaccination will be able to share accurate and engaging updates, announcements, and developments, highlighting its message and position towards HPV vaccination.

ReThinkHPVaccination is available both on Twitter (**@rethinkhpv**, *Figure 6*) and LinkedIn (**rethink-hpvaccination**, *Figure 7*). Besides these two, there won't be any other social media channel used for communicating the project's developments, as Twitter and LinkedIn are the best ways amplify the visibility and impact of our project. Both accounts have been created a few days before the Kickoff Meeting Event, on March 10th, Bucharest, Romania, and the first posts have been uploaded right on the event day.

Both SM channels display the same profile picture – the project's logo. There have been developed two different banners, illustrated in the following pages – the first one being a customized version of the project's main poster, and the second one being a collage of three images picturing different gestures or objects related to HPV and vaccination. Both banners have been created in accordance with the project's visual guidelines. The main banner used was the one displaying the collage, as it was more approachable and user friendly.

For the moment, there aren't many posts on either channels, as the project is only at the beginning, but as it develops further there will be shared more announcements, press releases and engaging visuals.

3.1. Twitter

ReThinkHPVaccination's Twitter channel (Figure 6) was launched in March 2023 and is available via the social media handle **@rethinkhpv**. The Twitter highlights the description of the project *"A EU4Health funded project to reduce HPV vaccination inequalities in Central and Eastern European (CEE) countries".*

Figure 6 ReThink HPVaccination Twitter Social Media Channel (As of August 2023)

As described previously the project's logo acts as the profile picture, so the Twitter account should be easily recognized and accessed. The account's banner is a collage made of three images – a person being vaccinated (left), the HPV ribbon (middle), and several women holding their hands in union (right). The banner aims to accentuate the project's message, standing together to face the same goal – the need to rethink and reduce HPV inequalities through personalized means, and through teamwork and community aid.

Until now, the present posts link the Twitter account to the LinkedIn one, highlighting the project's dedicated hashtag **#ReThinkHPVaccination**, which aims to raise more visibility. Social media content will cover the latest information on the project's development and press releases, as well as infographics containing accurate scientific data on the HPV subject or vaccination status, not only in the Eastern European Block, but also worldwide.

As soon as it is ready, the Twitter channel will be updated with a direct link to ReThinkHPVaccination's official website.

3.2. LinkedIn

ReThinkHPVaccination's LinkedIn channel (*Figure 7*) was launched in March 2023 and is available via the social media handle **rethink-hpvaccination**. The LinkedIn highlights the same description of the project as the Twitter channel – *"A EU4Health funded project to reduce HPV vaccination inequalities in Central and Eastern European (CEE) countries".*

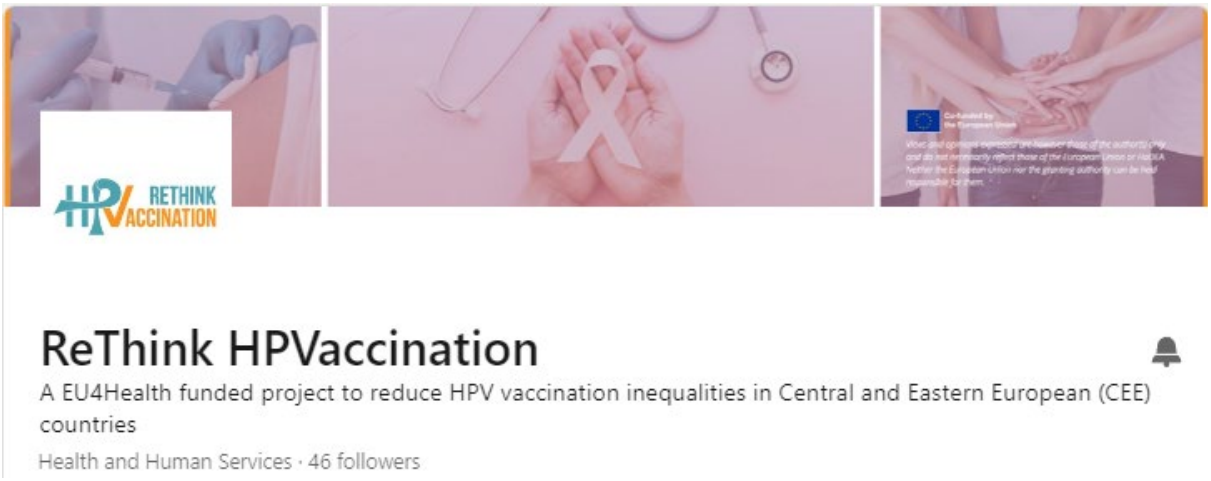


Figure 7 ReThink HPVaccination LinkedIn Social Media Channel (As of August 2023)

Between Twitter and LinkedIn, the latter is regarded as the main source of communication as it has a broader audience interested in health services and developments. However, just like in the former's case, there are only two posts until now – one highlighting the project's mission and objectives over the course of the next following two years, and the other one made during the European Immunization Week.

Although the LinkedIn channel has a direct link to ReThinkHPVaccination's official website, the website isn't ready to be made public yet.

4. VISUALS AND INFOGRAPHICS

As it is stipulated in Article 17 - Communication, Dissemination and Visibility of the Grant Agreement (101080000), communication activities must acknowledge EU Support and funding by the grant through the display of the European flag and translated disclaimer into local languages where appropriate.

With this requirement in action, each and every visual destined to the ReThinkHPVaccination project contains the European flag (either monochrome or colored, *original vectors downloaded from the official European center for visual elements* *https://ec.europa.eu/regional_policy/information-sources/logo-download-center_en*), as well as the following disclaimer: *Co-funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.*

4.1. General information

A series of visuals, social media banners, visual cards, collages, and infographics destined to social media channels have been developed so far. Further visual content will be developed based on the project's needs, during its lifetime. The visuals are approached from both a vectorial point of view, as well as a standard image-text-overlay point of view.

4.2. Image templates for online platforms

Two templates *(Figure 8)* for online platforms such as Teams, Zoom, Skype etc, have been developed.

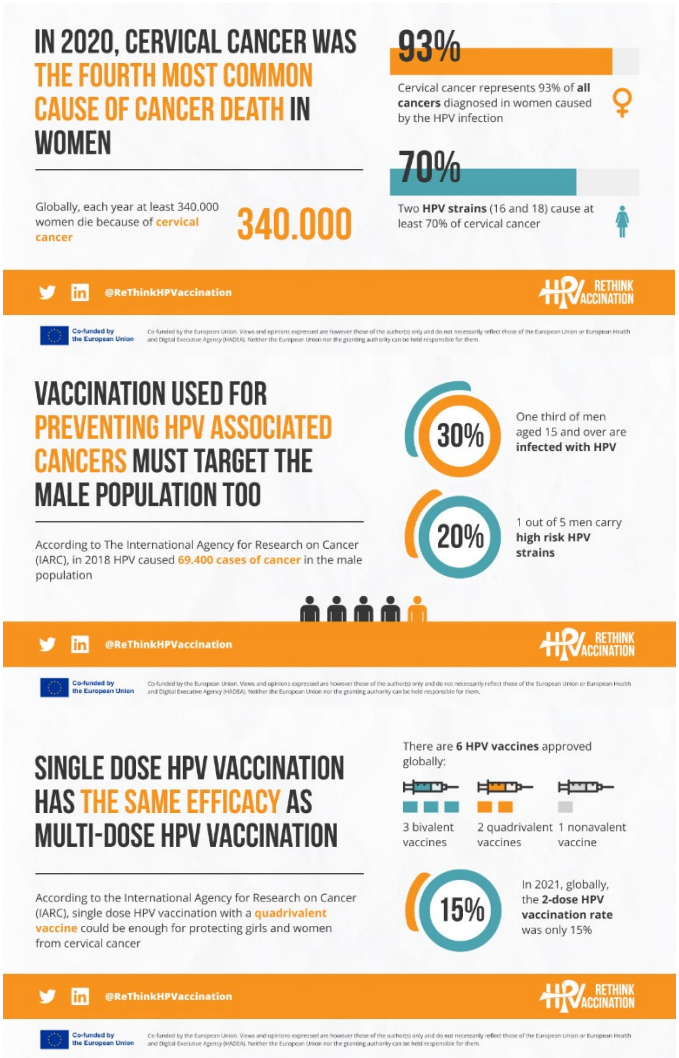
Figure 8 Image templates for online platforms or events

Both images are supposed to be used during online calls or webinars, to emphasize the project's visibility and to offer a sense of community and teamwork towards a common goal. While the first visual depicts in depth the project's objectives, the second visual is more user friendly and easier to be perceived and remembered.

The first picture is derived from the project's main poster, adapted in a way that it can have a customizable title, depending on the event it's used for. The second image cannot be easily personalized; it displays a collage of two photos – one envisioning the well-known ribbon for cancer awareness, and the other one portraying a group of women holding hands.

4.3. Infographics

A series of infographics for communication purposes was created, in Romanian and English based on the information gathered for the Knowledge Centre.



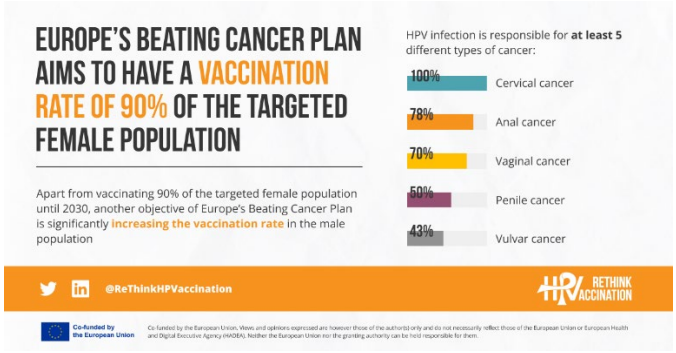


Figure 9 Infographics

4.4. Social Media images

Right now, there are in use two types of banners for social media, one poster, and two infographics. All of them follow the guidelines stipulated in the project's brand identity manual, and in Article 17 of the Grant Agreement. More visuals are going to be developed once the project runs its course.

The main poster (*Figure x)* has been used in the first two initial social media posts, representing the "face" of the project. Based on a vectorial approach, the poster displays the project's main objectives as a roadmap with several ups and downs that can be surpassed by cooperation, communication, and personalization. The poster comes in two different languages – English and Romanian.

Customized social media images will be developed once specific events occur, following the project's visual identity guidelines.

One of the social media banners has been adapted after the project's main poster, as it can be seen in Figure 10. The other one has been described above in this deliverable.

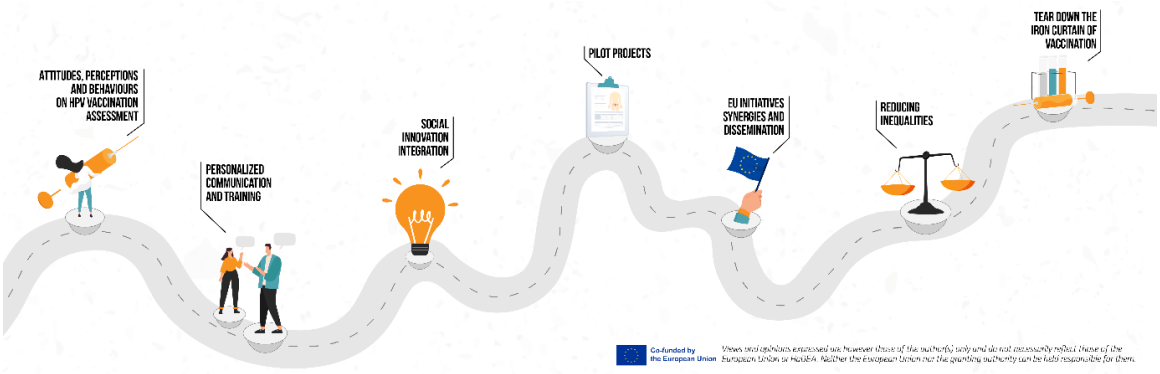


Figure 10 Social media banner variations for ReThink HPVaccination Twitter and LinkedIn pages

5. WEBSITE DESIGN AND DEVELOPMENT

The website is a work in progress and will be updated alongside the organic growth of the project and its activities.

The ReThinkHPVaccination website will be launched when submitting D2.1 Knowledge centre on HPV vaccination & communication for European countries with low VR, on October 2023, and it will be available at **www.rethink-hpv.eu**. The website will be maintained and updated regularly by Inomed.

5.1. Website structure and content

The website is fully responsive, and the architecture is as follows:

- About the project
  - *Background*
  - *Objectives*
  - *Structure*
- Resources
  - *Approved Deliverables and Milestones*
- News
  - News (Press releases and Events)
- Knowledge Center

The website is built with a customized WordPress approach, allowing those responsible for uploading the content (latest news, press releases, events, details about the project) to have access to the classic, flexible and user-friendly WordPress dashboard. The dashboard will be personalized in order to have access to different metrics and performance indicators regarding the user's interactions. As the development of the website is still in its early phase, not all the categories and pages are completely formatted according to the visual guidelines.

The website will be integrated with Google Analytics and Google Search Console, providing the partners with comprehensive metrics to track and analyze various aspects such as the number of visitors, demographic information, user's behavior (the number of interactions, sessions, the duration of the visit, the most accessed categories etc), the traffic source and so on. These metrics have the ability to inform content development, to find best ways to promote the project and to learn more about the targeted audiences.

The visuals below depict the website as of September 2023:

Homepage

The Homepage contains five sections – a navigation bar *(Figure 11)*, the hero section *(Figure 12)*, the news section *(Figure 13)*, details about the ReThinkHPVaccination projects *(Figure 14)* and a footer *(Figure 15)*.

Figure 11 Homepage

The navigation bar contains two rows – the first row allows the user to change the website's language from English to Romanian and the other way around; the second row contains the project's logo (on the left side) and the four categories – about the project, resources, news, and knowledge center.

The hero section displays an adapted version of ReThinkHPV's main visual, the roadmap that takes the viewer through the project's objectives. Apart from the official visual, this one doesn't contain the project's logo, EU's logo, and the disclaimer. The last two elements are to be found in the footer.

The news section contains three containers with the latest three news, or the most important news pinned.

The footer contains the logo, two social media buttons (for Twitter and LinkedIn), as well as the European Union's logo and the must-have disclaimer.

Figure 12 Navigation bar

Figure 13 News Section

Figure 14 Footer

About the project

The *About the project tab* allows the users to find more information on the mission, goals, and objectives of ReThinkHPVaccination, as well as the project's structure, as described in the Grant Agreement.

News

The news section displays several containers with the latest information available. Apart from the title and a brief description, each container displays the date on which it was posted. The users can access each one of them and navigate through their content, reading the latest details on ReThinkHPVaccination project.

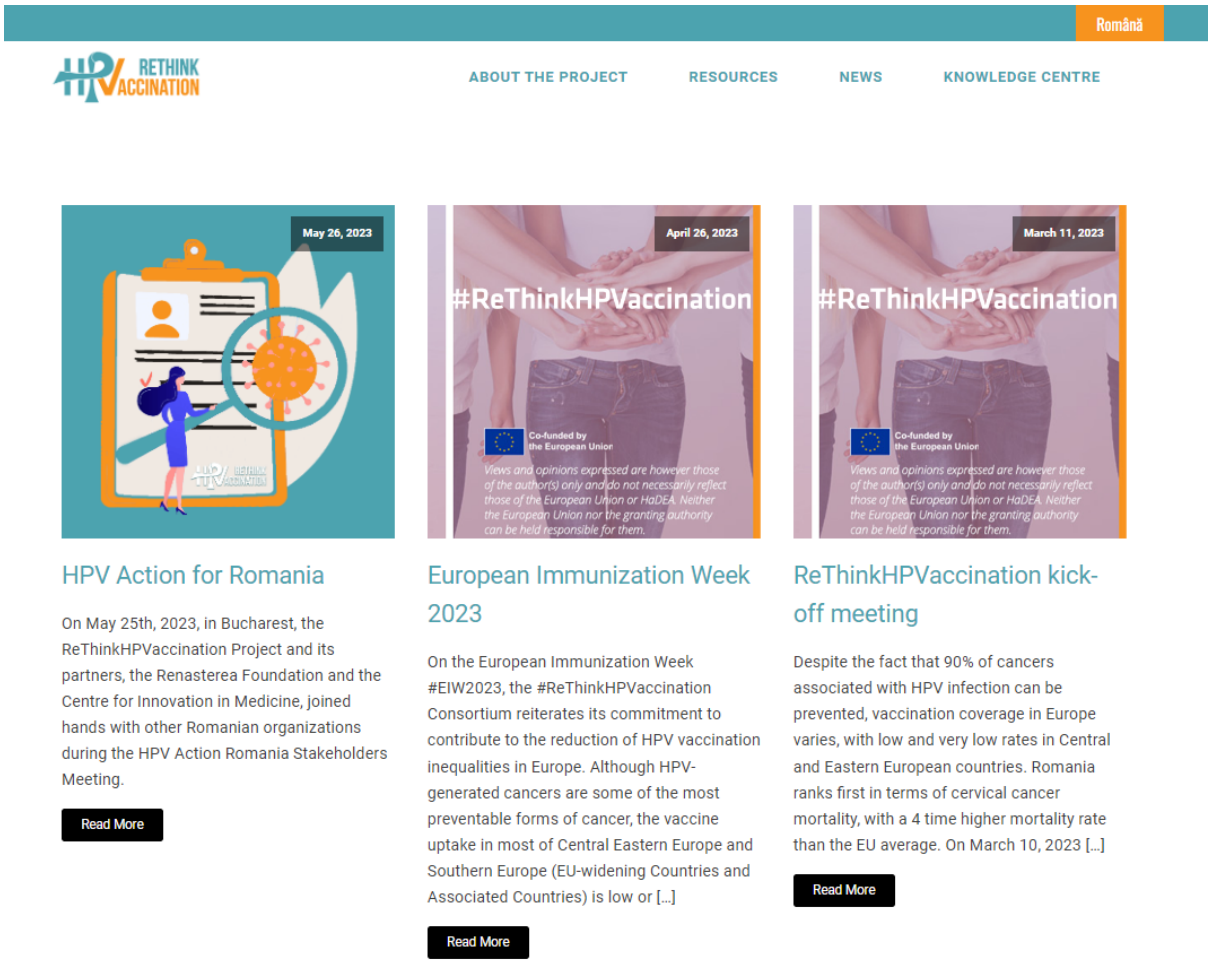


Figure 15 News section

Knowledge Centre

The Knowledge Centre is built upon a Wiki-like structure, with four main sections:

- HPV infection (covering subjects like what is HPV, the associated cancers, cervical cancer and testing)
- HPV vaccination (covering subjects like the safety and efficacy of EU approved vaccines, proposed vaccination schemes by WHO, production of vaccines and so on)
- Elimination of cervical cancer (covering the international and European initiatives)
- HPV in Romania (covering the situation of HPV infections, vaccination, and testing)

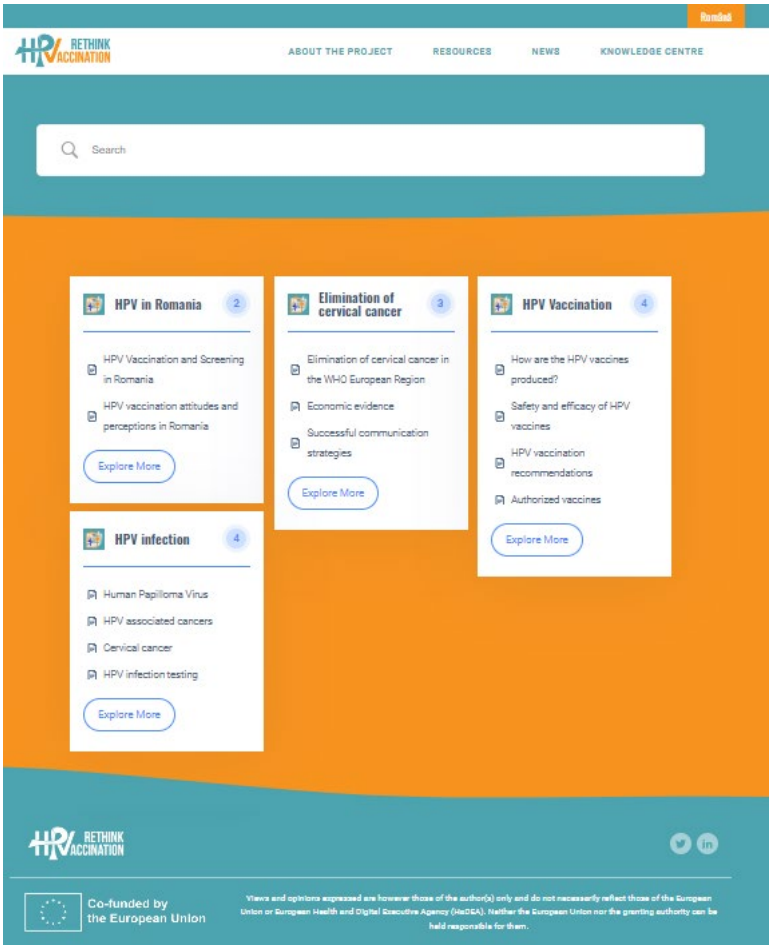


Figure 16 Knowledge Centre on HPV

CONCLUSIONS

The pressing challenge of increasing HPV vaccination uptake in several Central Eastern Europe, Southern Europe, and EU-widening countries is amplified by multiple factors - from misinformation campaigns to the current global infodemic surrounding vaccinations.

Within this intricate landscape, the ReThinkHPVaccination project emerges as a proactive response. Supported by visual assets and communication tools meticulously detailed in this deliverable, the project seeks to strategically engage stakeholders, disseminate credible information, and influence health behaviors for optimal outcomes.

These tools, designed in line with the project's visual identity, will play a pivotal role in amplifying its impact and ensuring cohesive message delivery. As countries grapple with the dire consequences of low HPV vaccination rates and the associated health risks, initiatives like ReThinkHPVaccination are of paramount importance.

Through its holistic approach, leveraging personalized communication, social innovation, and health behavioral determinants, the project aspires to bridge the existing gaps, inspire change, and pave the way for a healthier future in line with Europe's Beating Cancer Plan and Cancer Mission objectives.