



Advancing public health: a roadmap to eliminating HPV-related cancers and diseases in Belgium by 2030

White paper

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Glossary

| Abbreviation /Terminology | Description |
|---------------------------|---|
| HPV | Human Papillomavirus |
| RRP | Recurrent Respiratory Papillomatosis |
| WHO | World Health Organization |
| Fl. | Flemish Community |
| Fr. | French Community (“Fédération Wallonie-Bruxelles”) |
| W. | Walloon region |
| BCR. | Brussels-Capital Region |
| CIN | Cervical Intraepithelial Neoplasia or abnormal cells in the cervix categorized in three levels CIN1, CIN2, CIN3 |
| ONE | L’Office de la Naissance et de l’Enfance |
| SPSE | Les services de Promotion de la Santé à l’Ecole |
| CPMS (-CF) | Centres Psycho-Médico-Sociaux, (Communauté Française) |
| NIHDI | National Institute for Health and Disability Insurance |
| RIZIV | Rijksinstituut voor ziekte- en invaliditeitsverzekering |
| INAMI | Institut National d’Assurance Maladie-Invalidité |
| KCE | Federaal Kenniscentrum voor de Gezondheidszorg |
| HIV | Human Immunodeficiency Virus |
| CvKO | Centrum voor Kankeropsporing |
| CCR | Centre Communautaire de Référence pour le dépistage des cancers |
| ASCCP | American Society for Colposcopy & Cervical pathology |
| EFC | European Federation for Colposcopy |

About this white paper

This white paper is an evidence-based call to action for Belgian policymakers on how to eliminate HPV-related cancers and diseases in Belgium by 2030. The first version was published in November 2023 and an update was published in February 2025. It describes the current situation on vaccination, screening, and data collection, creates an overall ambition to eliminate HPV-related cancers and diseases in Belgium by 2030, and gives recommendations on how to achieve this ambition. The recommendations in this baseline plan ensure that all people are protected from highly-preventable HPV-related cancers and diseases.

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Executive summary

Purpose and scope

This white paper presents a practical plan for eliminating Human Papillomavirus (HPV)-related cancers and diseases in Belgium by 2030. This plan aligns with Sweden’s approach and centers on three main tactics: vaccination, early screening, and data collection.

Background and context

Human Papillomavirus (HPV) infection is responsible for approximately 5% of cancers across the globe [1]. Although more than two hundred types of HPV have been identified, persistent infections of twelve types are linked with cancer. Another seven genotypes were sporadically recovered from cancer tissues, but their oncogenic potential is uncertain [2]. HPV16 and HPV18 are known to be responsible for most HPV-related cancers [3].

HPV is largely linked to cervical cancer, which is the most common form of cancer caused by the virus. However, the virus also plays a role in cancers of the vagina, vulva, anus, penis, as well as some parts of the head and neck [4]. Additionally, HPV is related to non-cancerous diseases such as genital warts [5] and recurrent respiratory papillomatosis (RRP) [6]. It is estimated that over 1.000 people were diagnosed with cancer attributable to HPV in Belgium in 2021. Around 40% of these HPV-related cancers were not located in the cervix, underlining the importance of taking all HPV-related cancers into account when aiming for the elimination of the burden of cancers attributable to this virus [7] [8] [9].

Next to morbidity and mortality, HPV-related cancers are associated with a significant impact on quality of life. People living with HPV-related cancers have critical structures negatively impacted that are involved in breathing, eating, speaking, bodily waste elimination, and sexuality [10]. Cancer diagnoses in general are associated with a slightly decreased divorce rate, yet cervical cancer is linked to a higher divorce rate that may be due to the impact on intimacy and decreased sexual activity [11]. People who have survived head and neck cancers are twice as likely to die from suicide compared to people who have survived other types of cancer [12]. HPV-related cancers not only cause significant health burdens but also bring along substantial economic costs.

To tackle this widespread public health problem, the WHO and the European Commission have adopted strategies to eliminate cervical cancer, setting targets for vaccination, screening, and treatment. An overview of the most important targets is depicted in Table 1. These are further strengthened by the Council Recommendation on vaccine-preventable cancers to support Member States in increasing vaccination rates and improving monitoring of vaccination coverage, i.e. increasing efforts towards fully vaccinating at least 90% of girls against HPV at EU level by 2030, and aiming to significantly increase the vaccination of boys against HPV over the same period, so as to reduce the risk of transmission [13].

| | World Health Organization | | Europe’s Beating Cancer Plan | |
|-------------|---------------------------|---|------------------------------|---|
| Vaccination | 90% | Of girls fully vaccinated with HPV vaccine by 15 years old. | 90% | Of the EU target population of girls fully vaccinated with HPV vaccine and the vaccination of boys significantly increased by 2030. |
| Screening | 70% | Of women are screened using a high-performance test ¹ by 35 years of age and by 45 years of age. | 90% | Of the EU target population offered cervical cancer screening by 2025. |
| Treatment | 90% | Of women identified with cervical disease receive treatment. | 90% | Of eligible patients have access to tertiary specialized centers for treatment by 2030. |

Table 1. Global and European targets in cervical cancer elimination [1] [14]

Despite these goals and sharp deadlines, country strategies at national and regional levels remain underdeveloped. Progress in achieving these targets varies between countries.

¹ In the context of HPV early screening and detection, a high-performance test is considered a HPV test (explanation see further in this paper)

This report aims to assess the status, challenges, and opportunities in Belgium to contribute to the broader mission of reducing the burden of HPV-related cancers.

Current situation in Belgium

Vaccination

Vaccination data for Belgium show disparities in coverage between the first dose and full vaccination, and between the different federated entities. This holds opportunity for further improvements (see Table 2). It is important to emphasize that the latest figures for Flanders were recorded during the COVID-19 pandemic and are having an impact as a result.

| | Flemish Community 2020 | | | French Community 2022-2023 | | |
|------------|---------------------------|-------|-------|-------------------------------|-------|-------|
| | Boys | Girls | Total | Boys | Girls | Total |
| First dose | 86,7% | 92,3% | 89,4% | 55,8% | 63,6% | 59,7% |
| Final dose | 77,3% | 84,3% | 80,7% | 49,5% | 55,1% | 52,4% |

Table 2. HPV vaccination coverage for boys and girls by gender and geography in Flemish Community 2020 and French Community 2022-2023 [15] [16]

The vaccination rate for the French Community in 2022-2023 had a relative increase of ~10% compared to 2020 [16] [17] .

Suboptimal vaccination coverages in Belgium can be attributed to a complex interplay of factors. Firstly, a disconnect exists between the recommendations put forth by the Belgian Superior Health Council and the reimbursement policies of the National Institute for Health and Disability Insurance (NIHDI). There is currently no reimbursement for catch-up vaccinations after 19 years old, as well as for certain immunocompromised groups such as people living with HIV and pretransplant patients, and other populations with a greater likelihood to develop HPV-related cancers. This disparity hinders access and affordability, discouraging individuals from getting vaccinated.

Additionally, disparities in HPV vaccination coverage rates across Communities are primarily due to differences in the implementation of organized school vaccination programs between the Flemish and French Community. An analysis revealed that some services offer HPV vaccination while others do not [18]. It is observed that the eligible population of boys and girls for school-based HPV vaccination is unevenly distributed among these service types, with a substantial proportion overseen by services that do not offer vaccination (“non-vaccinating centers”) (30,6%) [18].

Gender disparities stem from the historical focus of vaccination programs on girls, perpetuating the misconception that HPV vaccination is exclusively for girls and solely related to cervical cancer prevention.

Parental consent requirements for underage students further complicate matters, as levels of education, awareness, and confidence regarding HPV vary among parents. Using a consistent and simple consent letter is a prerequisite in the engagement process for parents. While there were complexities in the French Community regarding the parental consent letter in the past, as compared to the Flemish Community, efforts have been made to create a clear, consistent, and simple template letter. However, this template letter is not systematically used by the extra-scholar health services. The lack of consistency can lead to less convincing parental advice, potentially resulting in suboptimal vaccine coverage rates for their children.

Screening

Specific for HPV-related cancers, organized screening of a target population for cervical and anal cancer is a second important pillar in the aim for eliminating HPV-related cancers in Belgium. In general, cancer screening can be conducted through two distinct approaches: opportunistic and organized screening. Opportunistic screening occurs when individuals decide to undergo screening at their own initiative or through a healthcare provider’s recommendation. Organized screening is a systematic and proactive approach where public authorities plan and implement screening programs targeting a predefined population with a high risk of developing a certain cancer.

Cervical screening

Similar to the HPV vaccination surveillance data, cervical cancer screening data also demonstrates disparities between the different regions, showing another opportunity to improve the screening coverage rates (Table 3). It is important to note that the figures for the Walloon and Brussels-Capital Region are underestimations due to the restriction to reimbursed Pap smear tests and the exclusion of non-reimbursed smears from the count.

| Flanders 2021 | Walloon 2017 | Brussels-Capital Region 2017 |
|------------------|-----------------|---------------------------------|
| 63,60% | 48,2% | 46,3% |

Table 3. Total cervical screening coverage rates for eligible women by geography in Belgium [19] [20].

Opportunistic screening prevails in Belgium due to low response rates in organized screening (14,6%) [20], resulting in a significant number of unscreened or irregularly screened women.

The Interministerial Conference for Public Health (IMC) announced in December 2022 that all women between 30 and 64 years old will be able to have an HPV test every five years, thereby replacing the current three-yearly cytology test [21]. KCE endorsed HPV-testing as primary screening test for cervical cancer in 2015 [22] and this evidence-based policy decision became effective on 1 January 2025 [23].

Suboptimal cervical cancer screening coverage in Belgium can be attributed to several drivers that contribute to disparities in screening rates. The discrepancy in cervical screening coverage rates between the Regions is most likely related to the presence of a structural, organized screening program in Flanders, which facilitates wider access to screening services and increased awareness among the population. The lack of a similar, well-established program in the French Community has likely contributed to lower screening rates in that area. As of January 2025, an invitation-based screening program was established for the Walloon Region [24].

Ongoing research efforts aiming to explore the most effective screening method for reaching specific population targets and underserved groups of women, including the use of self-sampling approach, add another layer of complexity to the suboptimal screening coverage. These research initiatives have yet to yield conclusive results, making it challenging to implement standardized and widely accepted screening protocols.

Anal screening

In Belgium, there is no organized screening program for anal cancer for high-incidence populations in place. As a result, coverage data about anal screening are lacking both at regional and at national level. As the burden of HPV-related cancers expands widely beyond the screening of cervical cancer alone, such screening program for people with a greater likelihood to develop HPV-related cancers and diseases should be implemented.

Data collection and quality assessment indicators

In the context of eliminating HPV-related cancers in Belgium, the goal is to support evidence-based decision making of academics, clinicians, and public health authorities. Enriched datasets have the potential to further direct research and public health measurements. This can be done by collecting the right datapoints, ensuring qualitative data and creating linkages between the different data repositories. Establishing effective data management for the epidemiology of HPV-related cancers, HPV vaccination coverage, and participation in cervical and anal screenings will enhance transparency regarding the progress made in Belgium towards achieving the various higher mentioned goals outlined by the WHO and the European Commission.

The management of HPV poses a multifaceted challenge in Belgium, primarily due to structural deficiencies and variations in data collection and linkage. One fundamental issue is the absence of the introduction of a systematic HPV test to detect high risk of any HPV-related oncogenic disease. This inability of the Belgian Cancer Registry to differentiate between HPV-related and non-HPV-related cancer, makes it difficult to gauge the actual impact of HPV on the cancer incidence in the country.

Also, completeness and accuracy of the collected data vary across different datasets. For instance, regional vaccination registers like Vaccinnet and e-vax are hindered by a lack of data collection for catch-up vaccinations and inconsistent participation by vaccinators, further complicating the assessment of vaccination coverage.

Furthermore, the lack of sustained linkage between vaccination registries and other data sources, such as screening and cancer registries, hampers the ability to conduct real-world evidence studies to evaluate the long-term effects of HPV vaccination.

Finally, the absence of a comprehensive report to monitor progress towards the elimination of HPV-related cancers, coupled with the quality of services and processes, leaves a critical gap in evaluating the effectiveness of public health measures in achieving international goals.

Conclusion and proposed actions

The well-defined targets set by the WHO, the European Commission, complemented with the European Council recommendations create a clear momentum to eliminate HPV-related cancers and diseases in Belgium by 2030. Despite that several measures for HPV prevention have already been implemented in Belgium, there is still room for improvement of the existing tools and the implementation of other targeted actions. Especially the disparities between Communities create opportunities to optimize the overall goal of eliminating all HPV-related cancers in Belgium by 2030.

To accelerate the elimination of HPV-related cancers and diseases, several practical and achievable steps can be taken to improve immunization rates and screening participation. In Table 4, a list of 14 actionable recommendations lumped to the following four major pillars are proposed: 1) HPV vaccination; 2) cervical and anal screening; 3) data and quality assessment indicators; and 4) multistakeholder commitment. Important progress has been made since the publication of the first edition of this whitepaper. However, there is still a large opportunity to take further steps towards making an important impact on public health.

Realizing the objectives necessitates a strategic and deliberate approach. Prioritizing actions based on their impact and effort required is obligatory to ensure effective channeling of resources and energies, in order to achieve a positive change.

In our view, the generalized administration of the HPV vaccination is a top priority (see actions 1-4, dark green). The rationale behind this is two-fold: firstly, the initial vaccination establishes long-term protection against HPV, thereby reducing the risk of any HPV-associated cancer. Secondly, it is important to administer catch-up vaccination up to the age of 30 years and to vaccinate immunocompromised groups. The former is crucial for reducing the transmission of HPV infection and the latter for altering the burden of developing HPV-related cancers eventually. This approach aligns with the EVEN FASTER concept for cervical cancer elimination in Sweden.

Subsequently, optimal screening for anal and cervical cancer is the next priority (see actions 5-8, grass green), as early detection leads to efficient interventions that prevent progression to invasive disease and ultimately increase survival rates.

Additionally, collecting and analyzing data on vaccination coverage, screening participation and disease prevalence helps in assessing the program's impact and making informed decisions (See actions 9-11; light green). As these actions require deep-technical knowhow, it will take more effort and must be seen as part of a larger project, but for which the first steps should be set as of today.

Finally, stakeholder commitment by multiple partners is pivotal in sustaining and expanding HPV management efforts (see actions 12-14; gray). Therefore, collaborative engagement from healthcare professionals, experts, as well as from policymakers and the wider public is essential for ensuring the success and longevity of these initiatives.

| Domain | Proposed actions | | |
|-----------------------------|------------------|---|---|
| Vaccination | 1 | Improve the implementation of regional school-based programs | <p>Included in election programs MR, Les Engagés, PS</p> <p>Parliamentary resolutions have been submitted by N-VA [25], Les Engagés [26], and Open Vld [27]</p> <p>Coalition agreement of the French Community 2024-2029 [28]</p> <p>New vaccination rate study of ONE shows already slight increase in HPV vaccination rate [16]</p> |
| | 2 | Implement HPV catch-up vaccination for boys and girls until 30 years | Parliamentary resolutions have been submitted by N-VA, Les Engagés, and Open Vld |
| | 3 | Enhance access to HPV vaccination for immunocompromised individuals: people living with HIV and pretransplant recipients | Parliamentary resolutions have been submitted by N-VA, Les Engagés, and Open Vld |
| | 4 | Change the framing of the message around HPV and HPV-related cancers | |
| Screening | 5 | Implement HPV testing as primary screening test | Achieved January 2025 |
| | 6 | Further increase cervical screening coverage rates in all regions | Invitation-based program initiated in the Walloon Region in January 2025 |
| | 7 | Integrate cervical screening into routine care for immunocompromised people: people living with HIV and transplant recipients | |
| | 8 | Start organized anal cancer screening for high-incidence populations | |
| Data | 9 | Invest in qualitative and complete vaccination registries | |
| | 10 | Create linkage of vaccination and cancer registries | |
| | 11 | Track and monitor progress in the elimination of HPV-related cancers in Belgium | |
| Multistakeholder commitment | 12 | Prioritize HPV within national and regional cancer policies in the future | The coalition agreement of the Federal Government 2025-2029 indicates a new cancer plan should be developed [29] |
| | 13 | Establish a task force to monitor and address disparities in HPV vaccination and screening | |
| | 14 | Further invest in research for HPV-related cancers | |

Table 4. Overview of proposed actions in the context of HPV vaccination, screening, data collection and multistakeholder commitment.

1. Why are HPV-related cancers and diseases a public health problem?

1.1. Context

Human Papillomavirus (HPV) infection is responsible for approximately 5% of cancers across the globe [1]. Although more than 200 types of HPV have been identified, persistent infections of twelve types are linked with cancer. Another seven genotypes were sporadically recovered from cancer tissues, but their oncogenic potential is uncertain [2]. Of these, HPV16 and HPV18 are known to be responsible for most HPV-related cancers [3].

HPV is most closely linked to cervical cancer, which is the most common form of cancer. However, the virus also plays a role in cancers of the vagina, vulva, anus, penis, as well as some parts of the head and neck region [4]. Additionally, HPV is related to non-cancerous diseases such as genital warts [5] and recurrent respiratory papillomatosis (RRP) [6]. An overview of the total number of cancers by primary site in Belgium in 2021, the relative number of cancers associated with HPV infections globally and the estimated number of cancers attributable to HPV in Belgium in 2021 are shown in Table 5.

| Site | Number of primary tumors | % of primary tumors attributable to HPV | Estimated number of primary tumors attributable to HPV |
|--------------|--------------------------|---|--|
| Cervix | 641 | ~100 ² | ~641 |
| Penis | 122 | 47 | 57 |
| Vulva | 246 | 40 | 98 |
| Vagina | 49 | 70 | 34 |
| Anus | 167 (female) /101 (male) | 84 (female) /84 (male) | 140 (female) /85 (male) |
| Oropharynx | 60 (female) /130 (male) | 19 (female) /19 (male) | 11 (female) /25 (male) |
| <i>Total</i> | <i>1.516</i> | - | <i>1.091</i> |

Table 5. Number of invasive tumors by primary site in Belgium in 2021, % of invasive tumors associated with HPV infections globally and the estimated number of invasive tumors attributable to HPV in Belgium in 2021 [7] [8].

It is estimated that more than 1.000 people were diagnosed with cancer attributable to HPV in Belgium in 2021. Around 40% of these HPV-related cancers are not located in the cervix, underlining the importance of taking all HPV-related cancers into account when aiming for the elimination of the burden of cancers attributable to this virus.

² HPV is detectable in virtually 100% of cervical cancer cases, although individual studies may show lower estimates which generally explained by technical issues [9]

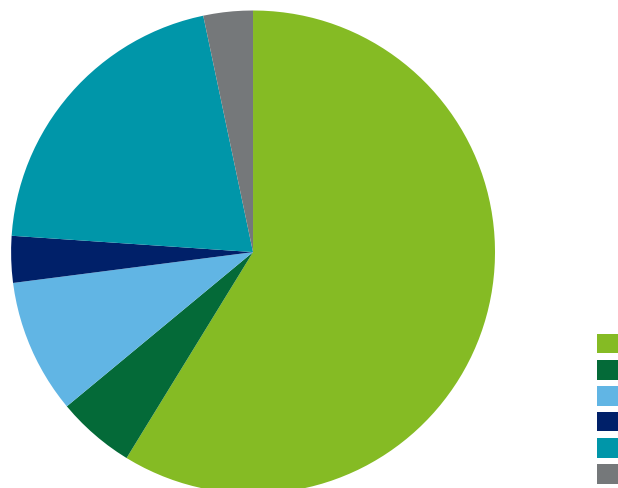


Figure 1. Estimation of primary tumors attributable to HPV based on actual numbers of primary tumors in 2021 in Belgium [7] [8].

The burden of HPV-related cancers is substantial. These cancers cause significant long-term disabilities and morbidities and are linked to a significant economic burden. Next to mortality, HPV-related cancers are associated with a negative effect on quality of life. People living with HPV-related cancers have critical structures impacted that are involved in breathing, eating, speaking, bodily waste elimination, and sexuality [10]. Cancer diagnoses in general are associated with a slightly decreased divorce rate, yet cervical cancer is an exception as it is linked to a higher divorce rate that may be due to the impact on intimacy and decreased sexual activity [11]. People that are survivors of head and neck cancers are twice as likely to die from suicide compared to people who have survived other types of cancer [12].

Research in Sweden shows that the total annual cost of all HPV-attributable precancers and cancers runs up to 94 million euros in that country with roughly the same amount of inhabitants as Belgium (10.5 million) [19]. Remarkably, an analysis dating back to 2006 already estimated the total yearly societal cost of cervical cancer in Belgium at the same amount of 94,4 million euro [30] [31].

Numerous stakeholders, including researchers, healthcare practitioners, patients, and policymakers, have voiced the goal of eliminating HPV-related cancers. In August 2020, the World Health Organization (WHO) adopted a comprehensive strategy aimed at eliminating cervical cancer. The objective is to reduce the occurrence of cervical cancer to less than 4 cases per 100.000 people per year. This strategy setting 90-70-90 targets by 2030: achieving a minimal vaccination rate of 90% for girls by age 15, screening at least 70% of women between 35 and 45 of age with a high-precision test (namely the HPV test) and ensuring that 90% of women diagnosed with cervical disease receive adequate treatment and care [1]. In 2021, the European Commission issued the 'Europe's Beating Cancer Plan (EBCP)', outlining specific objectives to eliminate HPV-related and other cancers. One of 10 flagship initiatives in the Europe's Beating Cancer Plan is to support member state efforts to extend routine vaccination against viruses that can cause cancers later in life. It aims to vaccinate minimum 90% of girls, while also significantly increase vaccination rates of boys by 2030. The plan also strives to offer cancer screening to 90% of eligible people in the EU by 2025 and provide access to Comprehensive Cancer Centers for treatment to 90% of affected patients by 2030 [14]. This is further strengthened by the Council Recommendation on vaccine-preventable cancers to support member states in increasing vaccination rates and improving monitoring of vaccination coverage. These include increasing efforts towards fully vaccinating at least 90% of girls against HPV at EU level by 2030, and aiming to significantly increase the vaccination of boys against HPV over the same period, so as to reduce the risk of transmission [13].

| | World Health Organization | | Europe’s Beating Cancer Plan | |
|-------------|---------------------------|---|------------------------------|---|
| Vaccination | 90% | Of girls fully vaccinated with HPV vaccine by 15 years old. | 90% | Of the EU target population of girls fully vaccinated with HPV vaccine and the vaccination of boys significantly increased by 2030. |
| Screening | 70% | Of women are screened using a high-performance test ³ by 35 years of age and by 45 years of age. | 90% | Of the EU target population offered cervical cancer screening by 2025. |
| Treatment | 90% | Of women identified with cervical disease receive treatment. | 90% | Of eligible patients have access to tertiary specialized centers for treatment by 2030. |

Table 6. Global and European targets in cervical cancer elimination [1] [14].

While these ambitions and deadlines are well-defined, concrete strategies to attain these goals are often missing, especially at the level of individual member states or regions. Progress in achieving the WHO’s and the European Commission’s targets for eliminating HPV-related cancers is highly variable between countries. Based on predictive models, Australia is likely to be the first country in the world to achieve the targets, estimated by 2028 [32]. In Europe, Sweden is seen as a leading example. It has set an ambitious target and plan to eliminate cervical cancer within the next 5 years. The plan’s main pillars consist of the introduction of reliable, compulsory registries, generalized public health strategies to execute population wide gender-neutral vaccination, maximal HPV screening and, not unimportant, a solid political commitment in their country. Their “HPV-FASTER” elimination strategy also includes the combination of catch-up HPV vaccination and screening in the age groups between 23 and 28 years of age [33] [34]. It is predicted that cervical cancer will be completely eliminated in the coming years in Sweden [35].

1.2. Goal of the position paper

This white paper provides an evidence-based call to action for Belgian stakeholders on how to eliminate HPV-related cancers in Belgium by 2030, focusing on three pillars in line with the Swedish elimination plan:

1. Generalized vaccination actions to prevent the circulation of HPV infections in the population.
2. Optimized screening to enable early detection of precancerous lesions of anal en cervical cancer.
3. Comprehensive data collection and quality assessment indicators to facilitate the monitoring and evaluation of HPV-related trends and interventions.

The first section of the report elaborates on the current situation in Belgium and its geographical areas. The remainder of the report proposes a practical approach for eliminating HPV-related cancers in Belgium, including a set of evidence-based actions endorsed by experts in the field to speed up the progress in achieving the WHO’s and the European Commission’s targets for eliminating HPV-related cancers.

Important to note is that the WHO and Europe’s Beating Cancer Plan also include objectives on treatment. Although treatment forms an important pillar within the management of HPV, this paper is focusing on vaccination, screening, and early detection.

2. Opportunities to eliminate HPV-related cancers in Belgium by 2030

Despite implementation of several measures for HPV prevention in Belgium, there is a need for improvement of the existing tools and to introduce new targeted actions to achieve the goals defined by the WHO and the European Commission by 2030. Especially the disparities between communities create opportunities in optimizing the overall goal of eliminating HPV-related cancers in Belgium. The incidence rate of cervical cancer in 2021 was almost twice as high as the WHO target (7,6/100.000/year vs. 4,0/100.000/year) [8]. A comparison between the current situation in Belgium and international targets for HPV vaccination and screening is listed in Table 7. The communities (Flemish, French and German-speaking) are responsible for the organization of vaccination programs and the regions (Flemish, Walloon and Brussels-Capital) for the

³ In the context of HPV early screening and detection, a high-performance test is considered a HPV test (explanation see further in this paper)

screening programs. Hence, there are different approaches and various levels of immunization and screening participation observed in the country.

| | Description | International targets | Belgium |
|-------------|---|--|---|
| Vaccination | Percentage of girls fully vaccinated at the age of 15 years old | 90% (WHO + EU) | 84,3% (Fl, 2020) ^{4,4} ; 55,1% (Fr, 2022-2023) ⁵ |
| | Percentage of boys fully vaccinated at the age of 15 years old | Significant increase (EU) | 77,3% (Fl., 2020) ⁶ ; 49,5% (Fr., 2022-2023) ⁷ |
| Screening | Percentage of women screened with HPV test by 35 years of age and by 45 years of age | 70% (WHO) | HPV test implemented in organized screening as of January 2025 |
| | Percentage of women screened with HPV test by 45 years of age | 70% (WHO) | HPV test implemented in organized screening as of 2025 |
| | Percentage of the EU target population offered cervical cancer screening by 2025 | 90% (EU) | 63,6% (Fl., 2021); 48,2% (W., 2017); 46,3% (BCR., 2017) |
| Data | Population-based surveillance consisting of a continuous system of data collection, storage, validation and analysis of reliable and linked cancer registries, vaccination registries and population data | Only guidelines were published by EU and WHO | Not easily publicly accessible datasets + Immature linkage of datasets |
| | Program monitoring: assessment of the quality and coverage of the different preventive interventions | Only guidelines were published by EU and WHO | HPV program monitoring not yet in place |

Table 7. Comparison between international targets and the situation in Belgium for HPV [1] [14] [16] [15] [19] [20] [23]

⁴ Numbers in the Flemish Community are measured among first-year secondary school students (12-13 years old).

⁵ Numbers in the French Community are measured among second-year secondary school students (13-14 years old).

2.1. Vaccination

Drivers for suboptimal HPV vaccination coverage rates

- There is a gap between recommendations of the Belgian Superior Health Council and the current reimbursement regimens implemented by the National Institute for Health and Disability Insurance (NIHDI). There is currently no reimbursement for catch-up vaccination for people older than 18 years, nor for populations with greater likelihood to develop HPV-related cancers, including people living with HIV, pre-transplant patients, immunocompromised people (due to autoimmune diseases, immune disorders, or immunomodulating medication), women treated for CIN, sex workers, people that were confronted with sexual assault, transgenders, and HIV-PrEP users. This lack of reimbursement for vaccination for certain groups hinders access, thereby impeding health equity. This unequal access may have an impact on the vaccination coverage rates for Belgium.
- Disparities in HPV vaccination coverage rates between the communities can largely be explained by the difference in the roll-out of the organized vaccination school programs between the Flemish and the French Community. In the French Community, the variation in HPV vaccination practices among different extra-scholar health services and the fact that HPV vaccination is not consistently offered by all services have contributed to these differences. In certain cases, general practitioners failed to inform the parents about the possibility of HPV vaccination.
- The gender disparities in HPV vaccination coverage rates are primarily attributed to historically school-based vaccination programs that in the first campaign only targeted girls. Also, the wider public is mainly aware about the link between HPV and cervical cancers but is less aware about the other HPV-related cancers and diseases occurring in men and women.
- HPV vaccination of students under 16 years old requires parental consent. The level of education, awareness, and confidence regarding HPV of parents can further explain suboptimal levels of vaccine coverage rates. While there were complexities in the French Community regarding the parental consent letter in the past, as compared to the Flemish Community, efforts have been made to create a clear, consistent, and simple template letter. However, this template letter is not systematically used by the extra-scholar health services.

In their scientific report of 2017, the Belgian Superior Health Council provides three distinct recommendations on vaccination against human papillomavirus [36]:

- General vaccination for boys and girls⁶ (9-14 years): The Belgian Superior Health Council advises the annual vaccination of both girls and boys aged 9 to 14 years. While it is preferred that school health services manage this, any qualified healthcare provider can perform the vaccination.
- Catch-up vaccination for adolescents (15-26 years): For individuals within the 15-26 age range who missed the initial prophylactic vaccination, catch-up HPV vaccination is recommended. Effectiveness is greatest in those not yet engaged in sexual activity, while sexually active individuals may gain protection against HPV types they are not yet infected with. Indeed, currently available prophylactic vaccines do not improve the outcome of an infection with HPV vaccine types that are present in the cervix at the time of administration [37]. However, clinical trials have shown that the efficacy of the vaccines against other types remains intact [38]. Furthermore, the vaccines offer protection against HPV-types to which women were previously exposed but are no longer present at the time of first vaccination [39] [40].
- Immunocompromised individuals' vaccination: Patients who have undergone transplants or live with HIV face increased risks associated with persistent HPV infections and related complications. The final dose should be administered two weeks before a transplant procedure for optimal results [36] [41].

To assure equitable access to vaccination, NIHDI⁷ provides national reimbursement schemes for boys and girls between 12 and 18 years old via co-payment. No reimbursement schemes are in place for catch-up vaccination for young adults older

⁶ Throughout this paper, we use the terms 'boys' and 'girls' to refer to individuals typically assigned male (people with penis) and female (people with vagina) at birth. However, we acknowledge and respect a diverse range of gender identities and expressions beyond the binary, and we encourage inclusivity and sensitivity when addressing all individuals, regardless of their gender identity.

⁷ NIHDI equals Rijksdienst voor Ziekte- en Invaliditeitsverzekering (RIZIV) or Institut National d'Assurance Maladie-Invalidité (INAMI)

than 18 years, nor for people with greater likelihood to develop HPV-related cancers such as people living with HIV, and pre-transplant patients. Other affected communities include people that are immunocompromised (due to autoimmune diseases, immune disorders, or immunomodulating medication), women treated for CIN, sex workers, people that were confronted with sexual assault, transgenders, and HIV-PrEP users.

Following the Belgian Superior Health Council’s advice, public authorities from the different regions made it possible for boys and girls between 12 and 14 years to get vaccinated free of charge via regional school programs. In the Flemish Community, the vaccine is offered in the first year of secondary education (12-13 years old) via a school-based program organized by the Student Guidance Centers (NL: Centra voor Leerlingen Begeleiding). In the French Community⁸, girls and boys attending the second year of secondary education (13-14 years old) are offered vaccination via a school-based program organized by two distinct types of extra-scholar health services, Services de Promotions de la Santé à l’école (SPSE) and Centres Psycho-Médico-Sociaux (CPMS). A parental consent is required for vaccination of boys and girls under the age of 16 [42]. Parents can also choose in both regions that children are vaccinated via their physician of choice⁹. This is done by 6,0% of the adolescents in Flemish Community¹⁰ and 8,2% (14,2% of girls and 2,8% of boys) in the French Community [14], [15].

Vaccination data show disparities in coverage between the first dose and full vaccination, between boys and girls and between the different regions (see Table 8). It is important to emphasize that the latest figures were recorded during the COVID-19 pandemic and are having an impact as a result.

| | Flemish Community 2020 | | | French Community 2022-2023 | | |
|------------|---------------------------|-------|-------|-------------------------------|-------|-------|
| | Boys | Girls | Total | Boys | Girls | Total |
| First dose | 86,7% | 92,3% | 89,4% | 55,8% | 63,6% | 59,7% |
| Final dose | 77,3% | 84,3% | 80,7% | 49,5% | 55,1% | 52,4% |

Table 8. HPV vaccination coverage for boys and girls by gender and geographical area in Belgium in 2020 [15] [16].

HPV-vaccination rate is one of the cancer risk factors on which Belgium could further improve.

⁸ Throughout this paper, the term “French Community” is used interchangeably with “Fédération Wallonie-Bruxelles” for the sake of simplicity.

⁹ Parents choosing vaccination via a physician of choice are charged a consultation fee.

¹⁰ Note that only the administration of the first dose was reported in the analysis based on a questionnaire.

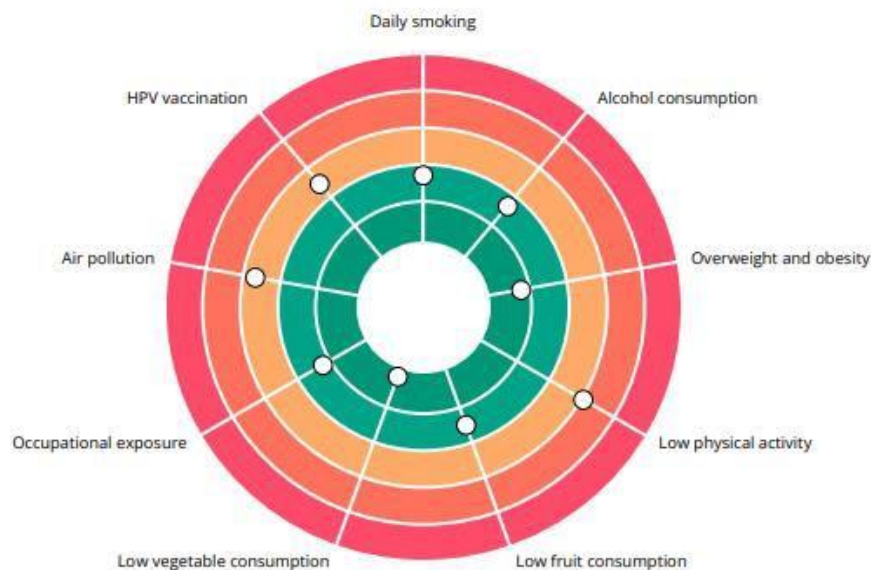


Figure 2. Belgium’s ranking on risk factors for developing cancer. The closer the dot is to the centre, the better the country performs compared to other EU countries. OECD calculations based on the 2022 EU-SILC Survey for overweight, obesity, physical activity, fruit and vegetable consumption (in adults); Eurofound Survey for occupational exposure; OECD Health Statistics for smoking, alcohol consumption (in adults) and air pollution; and WHO for human papillomavirus (HPV) vaccination (15-year-old girls). [43]

Disparities in immunization coverage across regions can be attributed to several factors. In the French Community, the major contributor is the variation in HPV vaccination practices among different extra-scholar health services, coupled with disparities in their budgets. An analysis revealed that some services offer HPV vaccination while others do not [18]. As depicted in Figure 3, the eligible population of children for school-based HPV vaccination is unevenly distributed among these service types, with a substantial proportion taken care by non-vaccinating centers (30,6%). Furthermore, there is a notable imbalance in the distribution of children under the supervision of extra-scholar health services that offer vaccination, resulting in varying vaccination coverage across geographic areas, as indicated in Table 9. An analysis demonstrates that in 2017, the HPV vaccination coverage for young girls under the supervision of vaccinator services/centers was significantly higher (51,2%) compared to those taken care by centers that do not routinely advocate or provide HPV vaccination (3,9%) [18].

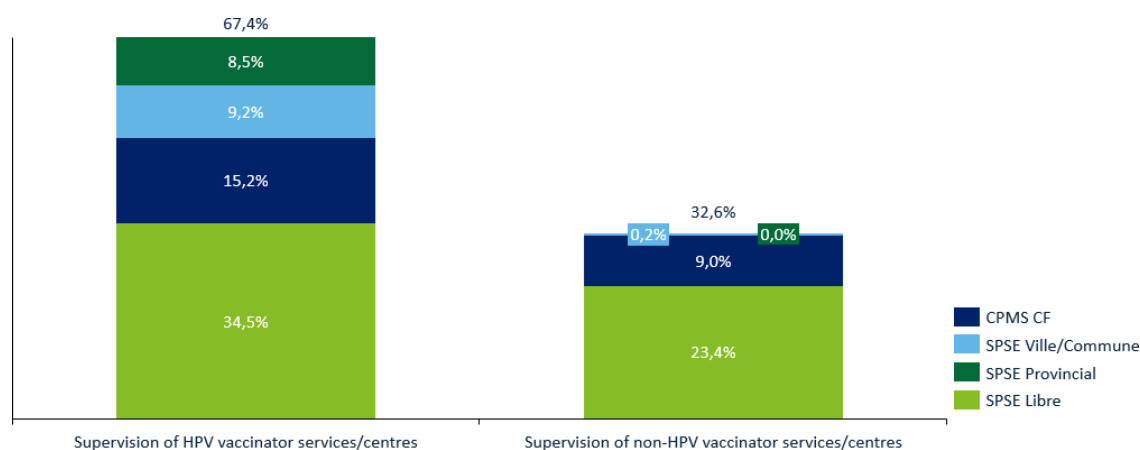


Figure 3. Distribution of total target population under supervision of HPV vaccinator services/centers and non-HPV vaccinator services/centers in 2016-2017 [18].

Since 2016-2017, as illustrated in Figure 3, the regulatory framework for extra-scholar health services (PSE) has evolved. This development can be attributed to the decree of the Government of the French Community dated August 25, 2022, which aimed to ensure that PSE services offer all vaccinations outlined in the program [44]. However, in practice, despite the provision of additional funding, there are still extra-scholar health services (SPSE or CPMS) that do not endorse, nor provide vaccinations at schools. This is evident from a more recent vaccination coverage study conducted by ONE [16]. As a result, this remains a significant obstacle to achieving a higher vaccination rate in the French Community.

| | Brussels-Capital | Brabant-Walloon | Hainaut | Liège | Luxembourg | Namur | Total |
|----------------|------------------|-----------------|---------|-------|------------|-------|-------|
| Girls | 42,9% | 58,4% | 42,5% | 51,3% | 65,6% | 65,5% | 55,1% |
| Boys | 39,7% | 57,5% | 39,3% | 47,3% | 57,9% | 53,8% | 49,5% |
| Total | 41,3% | 57,9% | 40,9% | 49,3% | 61,9% | 59,8% | 52,4% |
| <i>Refused</i> | 12% | 19,6% | 7% | 7% | 8,9% | 6,8% | 9,4% |

Table 9. Vaccination status (%) for the second HPV dose of the target population based on geography in 2022-2023 [16]

Vaccine hesitancy appears to be increasing. The percentage of parents refusing HPV vaccination for their children was 6,2% in 2019-2020 and is currently at 9,4% [16] [45]. Vaccine hesitancy for HPV is higher compared to the vaccine against measles, mumps, and rubella (MMR) which was 0,1% [16]. The use of complex letters to parents may have contributed to this hesitancy including the lack of consistency between different extra-scholar health services. Although ONE took efforts in creating a simple and validated template letter, the letter is not systematically used by the extra-scholar health services. In case of the healthcare workers, it was observed in research dating back to 2017 (Provac¹¹) that even a core group of professionals remains hesitant to recommend HPV vaccination for both boys and girls. This hesitancy is linked to beliefs such as promoting early sexual activity, the difficulty of discussing sexuality with young people, perceived uncertainties around long-term efficacy of vaccination and the risk of promoting a false sense of security among vaccinated people. The results of this study were further followed up in the meantime with additional communication and education efforts to health workers.

¹¹ A project in the French Community with the mission to promote the vaccination program among the general public and vaccinators.

2.2. Screening

Specific for HPV-related cancers, organized screening of a target population for cervical and anal cancer is a second significant pillar in the aim for eliminating HPV-related cancers in Belgium. Cancer screening can be conducted through two distinct approaches: opportunistic and organized screening. Opportunistic screening occurs when individuals decide to undergo screening at their own initiative or through a healthcare provider's recommendation. Organized screening is a systematic and proactive approach where public authorities plan and implement screening programs targeting a predefined population with a high risk of developing a certain HPV-related cancer.

2.2.1. Cervical cancer screening

Drivers for suboptimal cervical cancer screening coverage rates

- There are disparities in cervical cancer screening coverage rates across Regions, that can be explained by the non-existence of a structural organized screening program in the Brussels-Capital Region compared to the Flanders. The Walloon Region introduced an invitation-based screening program in January 2025.
- Further research on determining the best screening method for different population targets is currently ongoing at different research institutions, including the use of self-sampling.

With respect to cervical cancer, a research report published in 2015 by the Belgian Health Care Knowledge Centre (KCE) recommended the HPV test as the primary screening method for cervical cancer replacing the Pap Smear test using cytology only [22]. The HPV test is more sensitive than cytology in detecting precancerous lesions, reducing the likelihood of false-negative results. Because of its ability to detect the presence of the virus years before oncologic changes begin to occur, it enables timely intervention [22]. Another advantage of the HPV test is that it is eligible for self-sampling approaches which offers unseen opportunities to reach under screened women.

The Interministerial Conference for Public Health (IMC) announced in December 2022 that all women between 30 and 64 years old will be able to have an HPV test every five years, thereby replacing the current three-yearly cytology test. This evidence-based policy decision became effective on 1 January 2025 [23].

For women between 25 and 30 years, the current screening management remains applicable. Although screening programs for breast and colorectal cancer are being organized in all regions, a dedicated program for organized screening for cervical cancer is operational in Flanders, developed and managed by the Center for Cancer Detection (NL: Centrum voor Kankeropsparing). Women that have not participated to the program within the three-year period receive a letter of invitation for screening and an informative folder. To participate, you must make an appointment with a general practitioner or gynecologist [46]. The Walloon Region, held a pilot for organized screening with a consortium of three hospitals (CHU Liège, CHU de Charleroi, and Grand Hôpital de Charleroi) [47]. The Walloon Region introduced an invitation-based screening program as of January 2025.

Cervical cancer screening data demonstrates disparities between the different regions, showing an opportunity to improve the screening coverage rates. It is important to note that the figures for Walloon and the Brussels-Capital Region are underestimations due to the restriction to reimbursed Pap smear tests and the exclusion of non-reimbursed smears from the count.

| Flanders 2021 | Walloon Region 2017 | Brussels-Capital Region 2017 |
|------------------|------------------------|---------------------------------|
| 63,60% | 48,2% | 46,3% |

Table 10. Total cervical screening coverage rates for eligible women by geography [19] [20].

The screening coverage rates for cervical cancer in Belgium are predominantly driven by opportunistic screening, as organized screening is only implemented in Flanders with a rather low response rate (14,6%) compared to organized screening for breast cancer (53,2%) or colon cancer (52,5%) [18]. The rather low response rate must be seen in the light of the fact that this concerns only a group of women who were already not responding to opportunistic screening or for some reason may have no indication for cervix screening (such as post-hysterectomy). Still, a significant number of women do not adhere to the screening regimen or were not screened at all. In 2021, 24,1% of women in Flanders were not up to date with screening, i.e., their last participation more than three years ago. Moreover, the proportion of age-eligible women in Flanders who were never screened was 12,2% in 2021 [19]. Since non-response to screening is one of the major risk factors for the development of cervical cancer, other ways to reach and convince non-compliant women need to be explored. Research shows that offering self-sampling kits is generally more effective in reaching under screened women than sending regular invitations for a visit at their physicians' office [48]. These self-samples were as accurate as samples collected by a clinician [48]. Key advantages of this method are the assurance of privacy and bypassing certain barriers such as shame, fear, cultural or religious considerations [49]. Several studies are ongoing in Belgium to determine the most effective screening method for different patient cohorts (e.g., ScreenUrSelf study¹², ESSAG study¹³). Similar to the existing screening services, a clear follow-up management of the screening tests results is vital to maximize the effect of screening and early detection and the broader HPV-management plan.

2.2.2. Anal cancer screening

Drivers for suboptimal anal cancer screening coverage rates

- There is a gap between the international guidelines calling for organized anal screening for specific high-incidence populations (namely persons living with HIV, gay and bisexual men, transwomen women diagnosed with HPV-related gynecological precancerous lesions or cancer, solid organ transplant recipients and patients with autoimmune disease) and the non-existence of organized screening programs in Belgium for these targeted population.
- There is a lack of specific reimbursement regimens for techniques used in anal cancer screening: digital anorectal examination (DARE), cytology analysis and high resolution anoscopy (HRA). This financial barrier can further hamper a well-organized roll-out of screening programs for patients at risk.

Anal cancer is a are cancer with an increasing incidence. The Belgian Cancer Registry recorded 268 new diagnoses in 2022 of which 63% in women (Figure 4).

¹² [ScreenUrSelf | ScreenUrSelf | University of Antwerp \(uantwerpen.be\)](#)

¹³ [ESSAG studie - English \(testhpv.be\)](#)

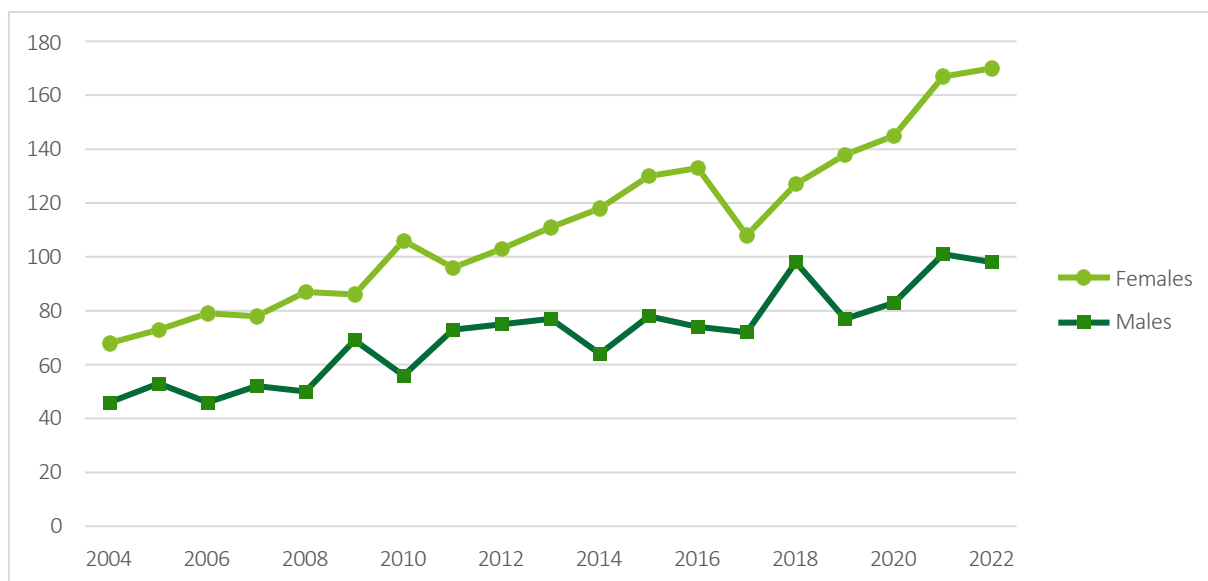


Figure 4. Anus and anal canal cancer incidence in Belgium by sex, 2004-2022 [50]

Like cervical cancer, HPV is responsible for the majority of anal cancers [51]. Since HPV infections remain frequent and high-incidence populations are growing steadily, organized screening in Belgium should be implemented as soon as possible starting with patients at risk [52]. Based on evidence from the anal cancer risk scale, the target patients for screening having a significant increased risk of anal cancer are persons living with HIV, gay and bisexual men and transwomen, women diagnosed with HPV-related gynecological precancerous lesions or cancer, solid organ transplant recipients (SOTR) and patients with autoimmune disease [53].

Similar to cervical cancer, anal cancer is preceded by high-grade squamous intraepithelial lesions. The ANCHOR trial investigated whether there was a difference in outcome for people with biopsy-proven anal HSIL when they were treated versus active monitoring without treatment. The rate of progression to anal cancer was lower in the treatment group than in the active-monitoring group by 57% [54]. The trial was stopped earlier than foreseen because it was no longer considered ethical not to treat patients. There is consensus that high-grade lesions should be treated and to detect these, screening is required.

International guidelines propose that the above targeted patients at risk should undergo annual clinical evaluations that include digital anorectal examination (DARE), cytology analysis, and high resolution anoscopy (HRA) [55]. For individuals at lower risk, specifically those with normal cytology and a negative HPV16 status at their initial assessment, it can extend the screening interval to every three years. However, it is important to note that there is currently limited high-quality evidence available to provide clear guidance on the most appropriate follow-up protocols.

Even though there is the advice of Belgian experts and current international guidelines, there is no official countrywide organized screening program implemented in the different regions. Patients are only opportunistically screened when they are referred to certain doctors who are trained in high resolution anoscopy (HRA). This referral is based on what the doctors find during colonoscopy or observed in specimens [52]. Local screening initiatives also include referring asymptomatic HIV-positive patients for high resolution anoscopy (HRA) based on yearly digital anorectal examination (DARE) and/or anal cytology.

Therefore, there is also a lack of anal screening coverage data at regional or national level.

2.3. Data collection and quality assessment indicators

Drivers for suboptimal data collection and quality assessment indicators

- Structurally, there is no HPV test conducted on all tumors that carry a risk of being attributable to HPV. Consequently, the Belgian Cancer Registry reports general statistics for invasive tumors without being able to distinguish HPV-related from other tumors.
- Completeness and accurateness of data differs from one dataset to another. Vaccinnet (Flemish Community) and e-vax (French Community), are mainly used in the context of the community-based vaccination programs with limited data collection for catch-up vaccination via federal reimbursement. Additionally, it is observed that the vaccination registry in the French Community is less consistently completed by vaccinators than in Flanders.
- Linkage of vaccination registries and other data (e.g., screening registries, cancer registries,) is not routinely done in Belgium. Without sustained linkage of registries, real world evidence (RWE) studies cannot be conducted to evaluate the long-term impact of HPV vaccination on HPV-related cancers.
- Measuring progress towards the elimination of HPV-related cancers, including the evaluation of the quality of services and processes in place, is not being comprehensively monitored. While multiple stakeholders collect and publish various data, there is no comprehensive report available to assess the effectiveness of public health measures and the quality of services in achieving the established international goals.

In the context of eliminating HPV-related cancers in Belgium, the ultimate goal is to support evidence-based decision making of academics, clinicians and public health authorities. By collecting the right datapoints, ensuring qualitative data and creating linkages between the different data repositories, enriched datasets have the potential to further direct research as well as public health measurements. Establishing effective data management for the epidemiology of HPV-related cancers, HPV vaccination coverage, and participation in cervical and anal screenings will enhance transparency regarding the progress made in Belgium towards achieving the various goals outlined by the WHO and the European Commission.

A prerequisite in creating enriched datasets is collecting the right datapoints. Structurally, there is no HPV test conducted on all tumors that carry a risk of being attributable to HPV. Consequently, the Belgian Cancer Registry reports general statistics for invasive tumors without distinguishing HPV-related from other tumors. Structurally performing HPV testing of all tumors that carry a risk of being attributable to HPV should further enrich insights about the burden of HPV-related cancers in Belgium that can be used to further track the progress to eliminate HPV-related cancers in the country.

Next to that, the completeness of vaccination registries can be optimized. Vaccinnet (Flemish Community) and e-vax (French Community) were created by the respective health authorities in the context of the community-based vaccination programs linked to a registration system for vaccinations. One barrier is the consistent and proper use of the digital platforms by vaccinators. It is observed that the registry is completed less consistently by vaccinators in the French Community than in the Flemish Community. This was confirmed by an analysis of ONE, stating that one third of the targeted boys' and girls' cohort were labeled with an unknown vaccination status in the French Community [45] [56]. As a result, health care workers have no accurate view on the vaccination status of boys and girls. Another barrier with the vaccination registries is that only vaccination data is registered that is part of the organized programs. As a result, there is a lack of data on HPV catch-up vaccination or vaccination among immunocompromised groups in the registries, leading to an absence of a comprehensive view on the HPV vaccination status of the population in Belgium.

A third step is providing linkage between diverse data sources. When datasets are linked, it becomes easier to identify patterns, trends and correlations that might not be apparent when examining individual datasets. Additional benefits of linking data are reduced redundancy, broader general overview, and improved data accuracy. Linking data decreases the risk that the same information is duplicated across multiple datasets, helping to improve data management (storage saving) and reduced risk for inconsistencies [57]. An overview of registers that can be linked in Belgium in the context of vaccination and screening is displayed in Table 11 [58]. In Belgium, sustained data linkages are not yet in place and some datasets might have overlapping data.

| Registry | Description |
|-------------------------------|---|
| Belgian Cancer Registry (BCR) | The Belgian Cancer Registry monitors the burden of cancer and all (cyto-histo-pathological) samples relating to cancer types within organized screening programs. Additionally, BCR contributes to the evaluation of the screening programs through linkage of population health data, epidemiological data and screening data. |
| Screening registries | Belgium's regional screening registries are instrumental in tracking screening performance indicators: Centrum voor Kankeropsporing (CvKO) in Flanders, Centre Communautaire de Référence pour le dépistage des cancers (CCR) in the Walloon Region, and BruPrev in the Brussels-Capital Region. |
| Vaccination registries | Vaccinnet in the Flemish Community and the Platform e-vax in the French Community serve as ordering and distribution systems for vaccines in the context of the organized vaccination policy. Due to the voluntary nature of registration, the quality of data varies between regional registries. |
| Intermutualistic Agency | The IMA-AIM manages a robust health administrative database, housing a wealth of information concerning reimbursed vaccinations, trends in screening indicators, the economic burden of cancer, and longitudinal health consumption. This registry holds key datasets eligible for the development of population-based health programs. |
| IFSTAT database | The IFSTAT database is a source for the evaluation of pharmacotherapeutic practices and for contributions to pharmaco-epidemiological studies. |
| Farmaflux | FarmaFlux was established as an umbrella NPO on the initiative of Vlaams Apothekers Netwerk (VAN), Association des Unions de Pharmaciens (AUP), Algemene Pharmaceutische Bond (APB) and Vereniging der Coöperatieve Apotheken van België (OPHACO) to manage data exchange to and from pharmacies in a secure and uniform manner |

Table 11. Overview of most important health registries in Belgium relevant for HPV [58].

While working on the completeness of datasets and the linkage between datasets, it is also important to capture the right data including the measurement of the quality of services and processes that are in place in the context of vaccination and screening. Currently, comprehensive reports about the monitoring of elimination of HPV-related cancers in Belgium are missing.

3. We need to act now if we want to eliminate HPV-related cancers in Belgium by 2030

The well-defined targets set by the WHO and the European Commission create a clear momentum in the process of eliminating HPV-related cancers in Belgium. Despite several measures for HPV prevention already been implemented in Belgium, there is much room to improve the existing tools and implement other targeted actions. Especially the disparities between communities create opportunities in optimizing the overall goal of eliminating HPV-related cancers in Belgium by 2030.

To further accelerate the elimination of HPV-related cancers, several practical and achievable steps can be taken to improve immunization rates and screening participation to reduce the burden of HPV and prevent cancers. In Table 12, an overarching goal is defined for the four key dimensions that are driving HPV-elimination: 1) HPV vaccination, 2) cervical and anal screening, 3) data and quality assessment indicators and 4) multistakeholder commitment. The following section proposes fourteen actionable recommendations around these four key dimensions. Throughout these actions, collaboration among diverse stakeholders will be of utmost importance.

| Dimension | Overarching goal by 2030 |
|--|--|
| HPV vaccination | Reach 90% vaccination of boys and girls at the age of 15 years old |
| Cervical and anal screening | <i>Cervical screening</i> : Screen at least 90% of women |
| | <i>Anal screening</i> : Screen at least 90% of targeted population group for anal cancer |
| Data and quality assessment indicators | <i>Population-based surveillance</i> : Create enriched datasets to further orient research and public health measurements |
| | <i>Program monitoring</i> : Install a holistic program monitoring process for HPV-elimination in Belgium |
| Multistakeholder commitment | Create a synergetic approach in eliminate HPV-cancers in Belgium supported by the different stakeholders involved in the topic |

Table 12. Overview of overarching goals for eliminating HPV-related cancers in Belgium.

4. Proposed actions

4.1. HPV Vaccination

4.1.1. Improve the implementation of regional school-based programs

Specific actions involved

- Ensure that every child in Belgium gets HPV vaccination offered through the regional school program and is aware on the possibility to get vaccinated free of charge which will result in equitable access for all. Although significant progress has been made, the largest opportunities are observed in the French Community, with the potential to implement measures aimed at increasing vaccination rates and enhancing the capacity of extra-scholar health services.
- Rephrase the message around HPV vaccination for both healthcare workers and parents to cancer prevention (More suggestions on communication are given in section 4.1.4).
- Streamline the informed consent letter for parents across various extracurricular health services, using the template letter created by ONE as a best-practice example. (More suggestions on communication are given in section 4.1.4).
- Investigate the possibility to lower the vaccination age.
- Create a dashboard with HPV vaccination coverage data to establish transparency and to be able to take targeted actions in under vaccinated geographical areas (More suggestions on data are given in section 4.3).

Research shows that a well-organized school-based vaccination program tends to be associated with the highest HPV vaccination coverage rates [59]. This is in line with the advice of the Belgian Superior Health Council to recommend general HPV vaccination for boys and girls between 9 and 14 years old preferably managed by the school health services (see page 13).

Taking into account the numbers of HPV vaccine coverage in different regions (see Table 8), the most promising opportunities and improvements can be created within the school-based programs of the French Community. Putting numbers further into perspective, we can already see results of previous efforts causing a relative increase in coverage of ~10% for boys and girls between school year 2019-2020 and 2022-2023 (see Error! Reference source not found.) [16] [45]. The Coalition Agreement 2024-2029 of the Walloon Region foresees a focus on prevention through vaccination and investigating the opportunity to

increase participation rate to preventive measures through automated appointments [60]. The Coalition Agreement 2024-2029 for the French Community also recognizes the importance of prevention through the following elements [28]:

- Enhance prevention by increasing vaccination rates, particularly improving the HPV vaccination strategy based on Superior Health Council recommendations and evaluating the potential benefits of lowering the vaccination age.
- Establish an action and communication plan on vaccination issues.
- Improving coordination between CPMS and PSE and considering a unified student health structure, focusing on harmonizing practices, strengthening teams, reestablishing mobile vaccination units, and advancing digitalization and IT tools.
- Continue implementing the child's computerized medical-social file, integrating it with the overall medical file and the PSE file.
- Expand the neonatal screening program for congenital anomalies in line with advancements in scientific knowledge.
- Support the development of ONE prenatal and child consultations.

A key driver that will further improve the HPV vaccination coverage in the French Community is strengthening the vaccination mission of the different extra-scholar health services offering vaccination (“vaccinator centers”). As mentioned above, the regulatory framework has evolved since 2017 with the aim to ensure that services offer all vaccinations outlined in the program (See 0, page 13). However, in practice, there are still extra-scholar health services (SPSE or CPMS) that do not provide, nor promote vaccinations at schools. Additionally, enhancing the use of the previously mentioned template letter by the extra-scholar health services that offer vaccination will further contribute to the improvement of the vaccination coverage rates. The goal would be to ensure that every child in Belgium gets HPV vaccination offered through the regional school program and that parents are aware that this is free of charge, which will result in equitable access for all.

Next to the organizational aspect, vaccine hesitance by health care workers needs to be avoided as much as possible. As mentioned in the Vaccine Confidence Project, a core group of professionals in Belgium (10%) remains hesitant to recommend HPV vaccination for both boys and girls [61]. Proper education of healthcare workers whether actively administering the HPV vaccination themselves, and consequently strengthening this topic in the academic curriculum, will positively contribute to the vaccination coverage rates. Vaccinators should also be supported in their communication in a tailored way. The Vaccination Barometer is a survey to identify how confident vaccinators are in recommending a vaccine. Information such as ‘have you recently received a question on vaccination that you could not address’ allows to identify areas for support [62]. Additionally rephrasing the message for both healthcare workers and parents will contribute to confidence in HPV vaccination and improve the HPV vaccine coverage rates. More advice on how to rephrase the message about HPV is given in section 4.1.4.

Important to note in achieving the mentioned targets for HPV vaccination is that it is also important to further strengthen the HPV vaccine uptake in boys for reaching the gender-neutral vaccination (“Universal vaccination”) in all Communities. Vaccinating all sexes against HPV provides an effective and faster approach preventing or reducing the incidence of cancers and other HPV-related diseases by reducing the circulation of the virus within the entire population, especially between sexes [63].

It should also be investigated whether lowering the age of vaccination could further improve public health goals and vaccination coverage rates, as mentioned in the Coalition Agreement of the French Community. Research suggests that moving routine vaccination against HPV to ages 9 to 10 may improve coverage rates in early and mid-adolescence [64] [65]. Primary schools also have better resources to organize vaccination programs as they already do so for other diseases. With the lowering of the age of the MMR vaccine, a vaccination slot becomes available in the 6th year of primary school. This could help integrating the HPV vaccine into routine childhood immunization schedules, thereby potentially increasing the coverage rate, as the coverage rate for MMR in 2021-2022 for the French Community was above 70 [66] . As of 1 July 2024, Austria provides HPV vaccination free of charge to people aged 9 to 30 years old.

4.1.2. Implement HPV catch-up vaccination for boys and girls until 30 years

Specific actions involved

- Extend catch-up vaccination reimbursement till 30 years for both boys and girls to create consistency with the new screening method and align with the potential spreading of the infection by age group.
- Provide reminders to adolescents about the HPV vaccination status and potentially missed doses. (More suggestions on communication are given in section 4.1.4).
- Organize a onetime community-based campaign for catch-up vaccination till 30 years old, similar to the existing school-based immunization programs during the first or second year of high secondary education (More suggestions on communication are given in section 4.1.4).
- Increase access by allowing other health care professionals such as pharmacists to administer the HPV-vaccine.

Research showed a benefit to immunize young adults, even if they are already sexually active. Currently available prophylactic vaccines do not improve the outcome of an infection with HPV vaccine types that are present in the cervix at the time of administration [27]. However, clinical trials have shown that the efficacy of the vaccines against other types remains intact [28]. Furthermore, the vaccines appear to offer protection against HPV-types to which women were exposed previously but are no longer present at the time of first vaccination [29].

The extension of reimbursement schemes for catch-up vaccination till 30 years old for boys and girls instead of 18 years old would improve equitable access to vaccination resulting in potential enhanced HPV vaccination coverage rates in the population and an acceleration of HPV elimination and would create consistency with the new screening method of HPV-testing as of the age of 30. Verifying vaccination status at time of screening and offering the opportunity to vaccinate as an opportunity to further increase the vaccination rate and contribute to the public health goal of eliminating HPV-related cancers in Belgium by 2030. This also aligns with the Swedish concept 'EVEN FASTER', based on using the HPV reproductive rate to determine the optimal age groups for vaccination and screening [67] [33].

To further improve initiating HPV vaccination in this specific age cohort, research showed higher vaccination uptake when giving a brief educational intervention on HPV knowledge [68]. Organizing a onetime community-based campaign for catch-up vaccination until 30 years old, similar to the existing school-based immunization programs during the first or second year of high secondary education could further facilitate the uptake. Research in Sweden showed that involving catch-up vaccination of girls and boys up to the age of 30 years will speed up the reduction of HPV prevalence, when compared to the school-based programs only.

As a result, several European countries created already publicly funded programs that include catch-up vaccination until 26 years old or more. A non-exhaustive overview is given in Table 13.

| Country | Current situation |
|-----------------|---|
| Sweden | Catch-up cohort women vaccination up to 28 years old* |
| Switzerland | Catch-up cohort vaccination up to 26 years old* |
| The Netherlands | One-off catch-up vaccination 18-27 years old in 2023 |
| Croatia | Catch-up cohort vaccination up to 26 years old* |
| Romania | Catch-up vaccination for women 18 to 45 years old reimbursed at 50% |
| Austria | Free of charge between 9 and 30 years old as part of the free childhood vaccination program |

Table 13. Non-exhaustive overview of countries with publicly funded programs including catch-up until 26 years or older (*Note: situation for 2023).

Expanding HPV vaccination administration to community pharmacists, analogue as for COVID-19 and influenza, could improve vaccine accessibility and coverage, particularly amongst adolescents and young adults. Exploring this option is

foreseen in the Federal Coalition Agreement 2025-2029 [29]. Pharmacists are highly accessible healthcare professionals, often serving as a first point of contact for people seeking medical advice. Allowing them to administer the HPV-vaccine could reduce barriers such as the need for a doctor's appointment.

4.1.3. Enhance access to HPV vaccination for people with greater likelihood of HPV-related cancers and diseases: people living with HIV , pretransplant recipients and other affected communities

Specific actions involved

- Extend the vaccination reimbursement for people living with HIV and pretransplant recipients in line with the advice of the Belgian Superior Health Council.
- Increase access of HPV for other affected communities, such as people that are immunocompromised (due to autoimmune diseases, immune disorders, or immunomodulating medication), women treated for CIN, sex workers, people that were confronted with sexual assault, transgenders, and HIV-PrEP users.
- Add HPV vaccination structurally to care pathways for people living with HIV and pretransplant recipients.

Immunocompromised people demand extra attention because of their increased likelihood to develop HPV-related cancers. The life expectancy of transplant recipients and people living with HIV has increased tremendously over the past decades due to significant improvements in treatment options. Yet, these people now face heightened risks associated with persistent HPV infections and related complications. For example, research shows that women living with HIV are six times more likely to develop cervical cancer than women living without HIV [69] and that the incidence of anal cancer is 40 to 80 times higher in the population living with HIV, especially in males [70]. Another example is given by a study addressing patients selected for solid kidney transplantation. Kidney transplant recipients have a 14-fold increased risk of cervical cancer, a 50-fold increased risk of vulvar cancer and a 100-fold increased risk of anal cancer [71] [72]. This is in line with the recommendation of the Belgian Superior Health Council to endorse HPV vaccination of these immunocompromised individuals: People living with HIV and transplant patients preferably with a final dose administered two weeks before the transplant procedure (see page 13).

Taken the Belgian Superior Health Council's recommendation into account, the extension of reimbursement schemes for vaccination of this targeted, relatively small population would assure equitable access for these people with an increased likelihood to develop HPV-related cancers, and could potentially prevent the development of HPV-related cancers and the increase of extra healthcare spendings. In Belgium, 1.055 kidney transplants were reported in 2022 [73] and 781 people were newly diagnosed with HIV in 2021 [74]. Systematic vaccination of these affected communities would therefore have a dramatic effect of disease prevention and reduction of HPV transmission, at a marginal expense only.

Next to people living with HIV and pretransplant recipients, there are other communities disproportionately affected by HPV-related cancers that warrant further investigation into the benefits of vaccination. Immunocompromised individuals, including those with autoimmune diseases, immune disorders, or on immune-modulating medications, face an increased risk of persistent HPV infections and malignancies. Similarly, women treated for cervical intraepithelial neoplasia (CIN) remain vulnerable to reinfection and disease recurrence [75]. Sex workers, people that were confronted with sexual assault, transgenders individuals, and HIV PrEP users also experience elevated HPV exposure risks. Evidence on the effectiveness of including these groups as additional priority groups for vaccination should be further investigated by the High Health Council to allow for targeted public health policy measures. HPV-vaccination is already recommended and reimbursed for women with cervical precancer in Austria [76].

4.1.4. Change the framing of the message around HPV and HPV-related cancers

Specific actions involved

- Create targeted communication campaigns on HPV importance by all governments toward the general public.
- Implement the education of HPV in schools and curricula of health care workers.
- Further educate healthcare workers and parents about HPV with a focus on cancer, supported by healthcare professional organizations.

Today, HPV vaccine messaging still predominantly focuses on its role in preventing cervical cancer in women and its transmissibility through sexual contact. This is partly due to the historical context in which school-based vaccine programs were initially designed exclusively for young girls to prevent cervical cancer.

Literature [77] suggests the following actions to enhance a justified communication about HPV and HPV-related cancers:

- Focus on cancer instead of the sexual transmission. By changing the message to preventing cancer instead of focusing on the sexual part, it would resonate more with all styles of parenting, especially around the age of the school-based programs.
- Appeal to moral responsibility to prevent cancer. The HPV vaccine is the only vaccine available for preventing cancer. It would be unethical not to vaccinate boys and girls.
- Broaden the message about cancer beyond cervical cancer. Bring the message that around 40% of all HPV-related cancers are not attributable to cervical cancer, but to oropharyngeal cancer, anal cancer, penile cancer, vulvar cancer and vaginal cancer. Stress the occurrence of HPV-related cancers in men. In Belgium, we can leverage awareness days for different cancers as well as specific campaigns such as 'Make Sense' for oropharyngeal cancer.
- Normalize HPV as part of the vaccination routine. Present the HPV vaccine in the generally implemented vaccination schemes together with already well-accepted immunization schemes raising confidence about the HPV vaccine.
- Emphasize vaccine uptake among males. It is important to emphasize and convey the message about the significance of vaccinating boys. This can be explained together with the broader message of HPV-related cancers beyond cervical cancer.

Several actions can be taken to rephrase the message around HPV and HPV-related cancers. As mentioned earlier, organizing a community-based communication campaign for catch-up vaccination until 30 years old for all sexes can support the facilitation of catch-up vaccination rates in Belgium resulting in faster elimination of HPV-cancer in the country. Another example is using a simplified and coherent informed consent letter in the organized vaccination programs with a message predominantly focusing on HPV as a cancer-causing virus instead of focusing on the sexual transmission. Further education of vaccinators as part of their curriculum in the safety and efficacy of HPV vaccination and the prescribed usage for boys and girls is another best practice that can be implemented.

4.2. Cervical and anal screening

4.2.1. Further increase cervical screening coverage in all regions

Specific actions involved

- Establish an organized screening program for cervical cancer in all Regions and enhance efforts to reach more responders to attend screening.
- Take an evidence-based decision to determine the most effective screening method for different patients cohorts, based on the results of ongoing studies.

For women currently having precancer lesions, the only option to avoid a cervical cancer is being tested and treated. Therefore the immediate goal should be to increase cervical screening coverage to detect and treat cervical abnormalities. However, eventually, as HPV infections are reduced through vaccination, the need for frequent and widespread cervical screening may decrease because the risk of cervical cancer will also decrease.

Taking into account the cervical screening coverage rates in the regions (See Table 10), opportunities for improving cervical screening coverage are seen in all regions with the most opportunities identified in the French Community. First, establishing an organized screening program for cervical cancer in Brussels including enhancing efforts to reach more responders could help facilitating the screening coverage ratio. Next to that, as these patients carry the highest risk of undetected cancer, exploring strategies for reaching persistent non-responders in all communities is needed. As explained in section 2.2.1, several studies are ongoing in Belgium to determine the most effective screening method for such different populations with increased likelihood to develop HPV-related cancers.

Lessons can be learnt from Sweden. First, it is predicted that HPV-self sampling is leading to faster elimination of cervical cancer in Sweden [35]. Moreover, optimizing prevention strategies including vaccination and screening using the HPV-EVEN FASTER strategy have the potential of accelerating the elimination of HPV-related cancers in Belgium. In the HPV-EVEN FASTER strategy, the HPV reproductive rate is used to determine optimal age groups for vaccination and screening campaigns. It was shown that the reproductive rate of HPV-infection up to the age of 30 was higher than 1, meaning that the infection is spreading exponentially. Swedish data suggests that HPV-infection would be rapidly eliminated from the population if the age groups below 30 years of age could not transmit the HPV infections [33] [67].

4.2.2. Integrate cervical screening into routine care for immunocompromised people: people living with HIV and transplant recipients

Specific actions involved

- Add cervical screening structurally to care pathways for people living with HIV and transplant recipients.

As described above, people with HIV and solid organ transplant (SOT) recipients are having an increased risk for cancers in general including HPV-related cancers due to immune deficiency.

For immunocompromised patients, no local guidelines are published in Belgium yet. Clinicians should perform cervical screening for people with HIV and solid organ transplant recipients according to the recommendations of the American Society for Colposcopy & Cervical pathology (ASCCP), the European Federation For Colposcopy (EFC). Clinicians should establish a scheme for routine cervical screening based on a patient's medical history, anatomical inventory, age, and risk profile [78].

4.2.3. Start organized anal cancer screening for patients with an increased likelihood to develop HPV-related cancers

Specific actions involved

- Start organized anal cancer screening for persons living with HIV, **gay and bisexual men and transwomen**, women diagnosed with HPV-related gynecological precancerous lesions or cancer, solid organ transplant recipients and patients with autoimmune disease.

Since HPV infections remain frequent and populations at risk are growing steadily, organized screening in Belgium should be implemented as soon as possible starting with patients at risk [52].

Taken into account the experts' opinion, using the anal cancer risk scale, organized screening should be implemented for persons living with HIV, **gay and bisexual men, transwomen**, women diagnosed with HPV-related gynecological precancerous lesions or cancer, solid organ transplant recipients and patients with autoimmune disease [53], in line with the international guidelines for anal cancer screening [55].

It is apparent that the highest risk for anal cancer is observed in individuals living with HIV (both gay and bisexual men, heterosexual men, as well as (trans)women), and in solid organ transplant recipients who have surpassed more than 10 years since their transplantation, as indicated by reference [53]. Consequently, the initial priority for launching screening programs should be on these two specific population groups. In a subsequent phase, the screening initiative can be extended to encompass HIV-negative gay and bisexual men, transwomen, and women with a history of HPV-related anogenital conditions [52].

4.3. Data and quality assessment indicators

4.3.1. Invest in qualitative and complete vaccination registries

Specific actions involved

- Make the registration of HPV vaccination (organized programs, catch-up and immunocompromised groups) obligatory for all vaccinators in e-vax (French Community) and Vaccinnet (Flemish community).
- Further link vaccination registration with the electronic patient reports enhancing the transparency for healthcare workers in daily practice.

As described in 2.3, the vaccination registries Vaccinnet and e-vax are not comprehensive enough to facilitate data-driven decision making. As a result, investing in vaccination registries with the right goal could enhance the completeness and quality of the dataset. As the goal is to identify the individual's vaccination status, it is important to capture both the information about the organized vaccination programs, the catch-up vaccination data and the vaccination status of immunocompromised groups. Furthermore, ensuring that all vaccinators register vaccines in e-vax is one easy solution that will help improving the completeness of the registry, hence the quality of the data set. Additionally, further linking vaccination registries with electronic patient reports ensuring that healthcare workers have a good view on the vaccination status of patients to take targeted actions needs to be a priority.

4.3.2. Create linkage of vaccination and cancer registries to be able to perform studies on the development of HPV-related cancers in vaccinated and unvaccinated population

Specific actions involved

- Link different sources of data to be able to establish real-life effects at population level using real-world evidence (RWE) similar to the example of Sweden.

Belgium has already existing databases that can be used for creating enriching datasets aiming for better exploitation of real-world data (see Table 11). In light of the current landscape, it is imperative that Belgium takes effective steps to link existing registries. This endeavor should encompass the establishment of standardized and simplified data linkage procedures, further research of unique identifiers, the promotion of mandatory registration and easily accessibility for both healthcare workers, researchers, and patients, especially in the context of vaccination records and cancer screening.

Especially the linkage of HPV vaccination registries and cancer registries will allow long-term follow-up about the efficacy of HPV vaccines and the vaccination strategies. In this context, Sweden is a leading example, creating universal registries where different data sources are linked include HPV vaccination status and epidemiological cancer data. The Swedish HPV vaccine studies consist of three key pillars. Firstly, studies focus on a Complete Ascertainment Protocol (CAP) where comprehensive registries allow research for any cervical tests taken by trial participants, even out of scope of the study sample. Secondly, studies are well known for their long-term follow-up. Trial participants are further followed-up for 15 years after closing study sites with registry linkage allowing to assess effects on very late endpoints. A third component of these HPV vaccine studies is the research of vaccine impact on population-level by linking real-life HPV vaccination and follow-up with the existing registry. As a result, Swedish researchers were able to establish a real-life effect on invasive cervical cancer at population level using real-world evidence (RWE) [40]. This breakthrough stresses the importance of data-linkages and the urgency for Belgium to start population-based research.

4.3.3. Track and monitor progress in the elimination of HPV-related cancers in Belgium

Specific actions involved

- Measure the progress in HPV-elimination in Belgium by tracking a set of quality assessment indicators.
- Publish an HPV program status update for Belgium regularly will further support the elimination of HPV-related cancers in Belgium.
- Register the HPV-status as a mandatory field in the Belgian Cancer Registry

In order to reduce the burden of HPV-related cancers, monitoring the progress towards achievement of HPV-elimination targets is essential. A set of quality assessment indicators can measure how successful the HPV management plan is and will bring transparency and accountability for all involved stakeholders.

Inspired by the Australian Program Update that publishes the progress in achieving the stated WHO-targets regularly [79], the Vaccine Confidence Project that tracks the confidence of people and healthcare workers in vaccines [80] and interviews with academics and clinicians, a non-exhaustive list of quality indicators concerning epidemiology, vaccination and screening are listed in the Table 14. Publishing an HPV program status update for Belgium regularly will further support the elimination of HPV-related cancers in Belgium as a public health problem as it will create more awareness and transparency on the current state regarding the predefined goals.

| # | Indicator | Description | Current state |
|------------------------------------|--|---|-------------------------|
| <i>Disease outcome indicator</i> | | | |
| 1 | Cervical cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of cervical cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to cervical cancer divided by the total population | Belgian Cancer Registry |
| 2 | Anal cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of anal cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to anal cancer divided by the total population | Belgian Cancer Registry |
| 3 | Penile cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of penile cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to penile cancer divided by the total population | Belgian Cancer Registry |
| 4 | Vulvar cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of vulvar cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to vulvar cancer divided by the total population | Belgian Cancer Registry |
| 5 | Oropharyngeal cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of oropharyngeal cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to oropharyngeal cancer divided by the total population | Belgian Cancer Registry |
| 6 | Vaginal cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the number of new cases of vaginal cancer divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to vaginal cancer divided by the total population | Belgian Cancer Registry |
| 7 | HPV-related cancer incidence and mortality | <ul style="list-style-type: none"> Incidence: the total number of new cancers attributable to HPV divided by the number of persons at risk for the disease over one year Mortality: the number of deaths due to cancers attributable to HPV divided by the total population | Not routinely measured |
| <i>Vaccine coverage indicators</i> | | | |
| 8 | HPV vaccine initiation by age 15 years | <ul style="list-style-type: none"> The HPV vaccination coverage ratio first dose at the age of 15 years for boys and girls | Vaccinnet, e-vax |

| | | | |
|---|--|--|--|
| 9 | HPV vaccine completion by age 15 years | <ul style="list-style-type: none"> The HPV vaccination coverage ratio second dose at the age of 15 years for boys and girls | Vaccinnet, e-vax |
| 10 | HPV vaccine completion by age 26 years | <ul style="list-style-type: none"> The HPV vaccination coverage ratio second dose at the age of 26 years for boys and girls with split via school-based program or catch-up | Not routinely measured |
| <i>HPV Vaccine confidence indicators</i> | | | |
| 11 | HPV vaccine confidence general public | <ul style="list-style-type: none"> Survey about the importance, safety, effectivity and compatibility with beliefs. Each item is answered on a four-point scale that ranges from “strongly disagree” to “strongly agree. Respondents may also indicate that they “do not know” or provide no response. | Vaccine Confidence Project |
| 12 | HPV vaccine confidence healthcare professionals | <ul style="list-style-type: none"> Survey about the likelihood of recommending HPV vaccination to patients | Vaccine Confidence Project |
| <i>Screening participation indicators</i> | | | |
| 13 | Cervical screening participation by age 35 years and age 45 years | <ul style="list-style-type: none"> % participation to cervical screening with HPV test by age of 35 years and 45 years (See Table 6, page 11) | CvKO, CCR, BruPrev in collaboration with Belgian Cancer Registry |
| 14 | Colposcopy attendance | <ul style="list-style-type: none"> % colposcopy attendance for women eligible for colposcopy | Belgian Cancer Registry |
| 15 | Anal screening participation by patients at risk | <ul style="list-style-type: none"> % participation to anal screening for patients at risk: persons living with HIV, gay and bisexual men, transwomen, women diagnosed with HPV-related gynecological precancerous lesions or cancer, solid organ transplant recipients and patients with autoimmune disease | Not routinely measured |
| <i>Quality assurance of HPV management¹⁴</i> | | | |
| 16 | % unknown HPV vaccine status at 15 years old | <ul style="list-style-type: none"> % of boys and girls at 15 years old with an unknown HPV vaccination status | Not routinely measured |
| 17 | Cytology | <ul style="list-style-type: none"> Sensitivity of primary screening with respect to final report after rapid review of all negative and inadequate smears | Not quality indicators in place (?) |
| 18 | Fail-safe protocols for colposcopy procedure | <ul style="list-style-type: none"> % of women that were followed up after abnormal primary screening test | Partly reported by CvKO ¹⁵ |
| 19 | Quality of cytohistopathology registry | <ul style="list-style-type: none"> % of complete datapoints within the cytohistopathology registry | CvKO |
| 20 | Survival rates per tertiary treatment centra for HPV-related cancers | <ul style="list-style-type: none"> The percentage of people who will be alive at a certain time after diagnosed with cervical, penile, vulvar, vaginal or oropharyngeal cancer | Not routinely measured (?) |

¹⁴ This is a first guidance of key quality indicators needed to assure the quality of management for vaccination and screening. A proposed task force for HPV-management (see further) can evaluate the efficacy of indicators over time and adapt these accordingly.

¹⁵ In the annual report of CvKO, some indicators to assure the quality of the screening results are already implemented mostly focusing on type of abnormal cells that were detected [17].

Table 14. Non-exhaustive overview of quality assessment indicators that can be used for monitoring and tracking HPV-elimination in Belgium [61], [79].

4.4. Multistakeholder commitment

4.4.1. Prioritize HPV within national and regional cancer policies in the future

Specific actions involved

- Implement the prioritization to eliminate HPV-related cancers as a public health problem in Belgium in national and regional policy statements in the future.
- Provide sufficient budgets and targeted actions to execute the strategy and commitments.

The Federal Government and the Regional Governments express in their policy statements the intent to work around vaccination, screening and treatment of cancer. The federal policy statement Public Health of 2023 cites the aim for dedicated investments improving the treatment and quality of life for people with cancer [81]. The Flemish coalition agreement 2024-2029 declares the willingness to continue to focus on vaccination programs for children and adults based on scientific evidence and to stimulate participation to existing screening programs, making them more efficient and targeted with new technologies and artificial intelligence [82]. Next to that, it highlights the importance of health literacy so that each citizen can make informed decisions on their health and healthy living [82]. The French Community also expresses a strong focus on prevention, see p. 23 [28].

Although policymakers are investing in vaccination, screening and treatment of cancers, elimination of HPV-related cancers is not defined as a priority. As opposed to frontrunners such as Australia and Sweden, Belgium has not yet a comprehensive HPV-related cancer elimination plan, although that many building blocks are already in place (~90% HPV vaccination coverage in Flanders) or planned in the near future (switch to HPV testing). HPV elimination in Belgium can be envisaged in the national cancer plan mentioned in the Federal Coalition Agreement 2025-2029.

As we have the right knowledge and tools such as vaccination and screening, elimination of cervical cancer and other HPV-related cancers is at our fingertips. Furthermore, investing in cervical cancer prevention and control also economically makes sense. It is estimated by the WHO that every euro invested in cervical cancer prevention and treatment will return at least 3 EUR to the economy globally through 2050 [83].

4.4.2. Establish a task force to monitor and address disparities in HPV vaccination and screening

Specific actions involved

- Ensure stakeholder commitment and collaboration by establish a task force to monitor and address disparities in HPV vaccination and screening in Belgium.

To maximize effects and drive results, it is a prerequisite to establish a task force for future HPV-management in Belgium. A task force is a technique that can be used to further develop solutions for specific identified problems and needs.

One of the key advantages of forming a task force for HPV-management in Belgium is the pooling of expertise from various disciplines, which can lead to more comprehensive and innovative solutions to this public health challenge. Task forces allow for better coordination among healthcare professionals, researchers, policymakers, and community leaders, fostering a collaborative approach to eliminate HPV-related cancers as a public health problem in Belgium. This group could further develop and publish an HPV-management status report on a regularly basis and drive new policy guidelines and studies (e.g. around QALYs) based on identified needs in society.

Ultimately, the establishment of a task force not only enhances the overall effectiveness of public health initiatives but also strengthens the community's resilience and preparedness.

4.4.3. Further invest in research for HPV-related cancers

Specific actions involved

- Make further research around HPV-related cancers possible in Belgium in order to further optimize the HPV-management consequently resulting in speeding up the elimination of HPV-related cancers in Belgium and optimizing treatment care after developing HPV-related cancers.

Although prevention and early detection of HPV-related cancers is the ultimately goal for solving this public health problem in Belgium, further research is needed especially for optimizing treatment after screening. In Figure 5, we can see that the peak incidence of cervical cancer is earlier (around 45 years) compared to the other HPV-related cancers. This leads to the phenomenon that the effect of HPV vaccination in HPV-related cancers will be seen much later instead of cervical cancer resulting in the need of more research of optimizing treatment options for this patient population.

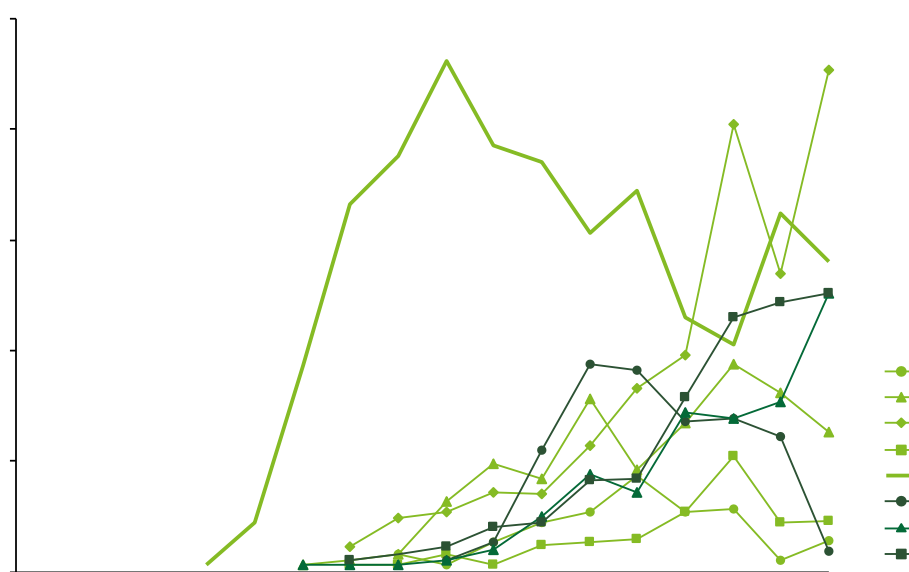


Figure 5. Age-specific and age-standardized incidence rates of cancer by primary site in 2021 (n/100.000 person years) [84].

For each cancer attributable to HPV, specific needs in research can be identified. A non-exhaustive list of research topics per HPV-related cancer is displayed in Table 15.

| Primary site cancer | Research topics that require further investigation (non-exhaustive) |
|---------------------|--|
| Cervix | <ul style="list-style-type: none"> • Identification of non-invasive treatment opportunities after HPV dysplasia for cervical cancer • Efficacy of the use of prophylactic vaccination after treatment |
| Anus | <ul style="list-style-type: none"> • Standardization of screening protocol, used materials and techniques [52] • Local guidelines about screening and follow-up in anal cancer [52] |
| Penis | <ul style="list-style-type: none"> • The investigation of optimal sequencing of treatments within the multimodal management and accurate patient selection [85]. • The development of more effective and less toxic therapeutic options [85] • Future knowledge of the penile microbiota composition and its correlation with HPV infection and the development of penile cancer could potentially pave the way for novel strategies in the prevention and treatment of penile squamous cell carcinoma (PSCC) [86]. |

| | |
|------------|---|
| Oropharynx | <ul style="list-style-type: none">• The investigation of optimal sequencing of treatments and accurate patient selection given the strong evidence that HPV-positive oropharyngeal squamous-cell carcinomas have a superior prognosis compared to HPV-negative tumors [87].• The impact of deintensified treatment approaches for medium-risk HPV-positive oropharyngeal cancers. Research shows already outstanding oncologic outcomes and favorable functional outcomes when using a less toxic treatment strategy in a selection of subpopulation [88]. |
|------------|---|

Table 15. Non-exhaustive list of research topics that require further investigation in the near future.

5. Roadmap

In the previous chapter, we have listed some practical steps to make progress in the elimination of HPV-related cancers in Belgium outlining tangible actions on vaccination, screening, data and multistakeholder commitment.

However, realizing the objectives necessitates a strategic and deliberate approach. To navigate this path effectively, prioritizing actions based on their impact and subsequent effort is needed to ensure that resources and energies are channeled most efficiently, ultimately maximizing the ability to effect positive change. In Table 16, actions are ranked, unveiling the most impactful and feasible paths that will drive us closer to the international goals in eliminating HPV-related cancers in Belgium.

| Domain | Proposed actions | | |
|-----------------------------|------------------|---|--|
| Vaccination | 1 | Improve the implementation of regional school-based programs | Included in election programs MR, Les Engagés, PS Parliamentary resolutions have been submitted by NV-A, Les Engagés, and Open Vld Coalition agreement of the French Community 2024-2029 [28] New vaccination rate study of ONE shows already slight increase in HPV vaccination rate |
| | 2 | Implement HPV catch-up vaccination for boys and girls until 30 years | Parliamentary resolutions have been submitted by NV-A, Les Engagés, and Open Vld |
| | 3 | Enhance access to HPV vaccination for immunocompromised individuals: people living with HIV and pretransplant recipients | Parliamentary resolutions have been submitted by NV-A, Les Engagés, and Open Vld |
| | 4 | Change the framing of the message around HPV and HPV-related cancers | |
| Screening | 5 | Implement HPV testing as primary screening test | Achieved January 2025 |
| | 6 | Further increase cervical screening coverage rates in all regions | Invitation-based program initiated in the Walloon Region in January 2025 |
| | 7 | Integrate cervical screening into routine care for immunocompromised people: people living with HIV and transplant recipients | |
| | 8 | Start organized anal cancer screening for high-incidence populations | |
| Data | 9 | Invest in qualitative and complete vaccination registries | |
| | 10 | Create linkage of vaccination and cancer registries | |
| | 11 | Track and monitor progress in the elimination of HPV-related cancers in Belgium | |
| Multistakeholder commitment | 12 | Prioritize HPV within national and regional cancer policies in the future | The coalition agreement of the Federal Government 2025-2029 indicates a new cancer plan should be developed [29] |
| | 13 | Establish a task force to monitor and address disparities in HPV vaccination and screening | |

14 Further invest in research for HPV-related cancers

Table 16. Overview of proposed actions in the context of HPV vaccination, screening, data collection and multistakeholder commitment.

In our view, the generalized administration of the HPV vaccination is a top priority (see actions 1-4, dark green). The rationale behind this is two-fold: firstly, the initial vaccination establishes long-term protection against HPV, thereby reducing the risk of any HPV associated cancer. Secondly, it is important to administer catch-up vaccination up to the age of 30 years and to vaccinate immunocompromised groups. The former is crucial for reducing the transmission of HPV infection and the latter for altering the burden of developing HPV-related cancers eventually.

Subsequently, optimal screening for anal and cervical cancer is the next priority (see actions 5-8, grass green), as early detection leads to efficient interventions that prevent progression to invasive disease and ultimately increase survival rates.

Additionally, collecting and analyzing data on vaccination coverage, screening participation and disease prevalence helps in assessing the program's impact and making informed decisions (See actions 9-11; light green). As these actions require deep-technical knowhow, it will take more effort and must be seen as part of a larger project, but for which the first steps should be set as of today.

Finally, stakeholder commitment by multiple partners is pivotal in sustaining and expanding HPV management efforts (see actions 12-14; gray). Therefore, collaborative engagement from healthcare professionals, experts, as well as from policymakers and the wider public is essential for ensuring the success and longevity of these initiatives.

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