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# Eliminating HPV-Caused Cancers & Diseases in Europe

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# **Summary**

HPV (human papillomavirus) is a very common sexually transmitted infection that causes about 5% of all cancers in women and men worldwide. The virus is also responsible for genital warts.



 HPV-caused diseases can be prevented by vaccination, ideally before exposure to the virus.

- Vaccination is most effective if provided to both sexes. However, most countries in Europe do not yet vaccinate boys.
- Vaccination uptake remains low in some countries and needs to be improved.
- Cervical cancer screening is provided in most EU countries, but not all. Most countries do not yet offer HPV testing, now recognised to be the most effective screening method.
- The uptake of screening also varies widely across countries, as do cervical cancer treatment outcomes.
- The European CanCer Organisation (ECCO) is calling for urgent evidence-based action to eliminate cancers and diseases caused by HPV by the EU and all governments throughout the WHO European region.

# The impact of HPV



Up to **90%** of sexually active **women** and **men** will acquire **HPV** 

Human papillomavirus (HPV) is a very common sexually transmitted infection. **Up to 90% of sexually active women and men will acquire HPV** at some point in their lives.

HPV can cause a range of serious health problems in both sexes, including several cancers and genital warts. There are around 200 different types of HPV. About 13 types are considered 'high-risk' (ie. oncogenic, or cancer-causing), the most significant being types 16 and 18. Types 6 and 11 are considered 'low-risk' but can cause warts on or around the genital area. HPV is also implicated in recurrent respiratory papillomatosis (RRP), a relatively rare but very disabling condition that adversely affects breathing in children and adults of both sexes.

In some European countries, the prevalence of high-risk HPV infection exceeds 15% in women.¹ One study into the prevalence of HPV types 16 or 18 in men who have sex with men (MSM) found a rate as high as 20%.²

Most people exposed to HPV suffer no ill-effects. But some, particularly those who are repeatedly exposed to high-risk HPV types or who are already immunocompromised (e.g. because they are HIV+), may go on to be diagnosed with a disease caused by HPV.

Role of HPV in other Cancers

Oropharyngeal 70%

Anal 90%

Penile 60%

Vaginal 75%

Vulva 70%

Worldwide, **HPV** is believed to cause about 5% of all cancers and is implicated in almost all cervical cancers. Estimates vary concerning the role of HPV in other cancers but there is evidence that it causes 70% of oropharyngeal cancers, 90% of anal cancers, 60% of penile cancers, 75% of vaginal cancers and 70% of vulval cancers. HPV is also associated with several other cancers in the tissues of the head and neck.

HPV is thought to be responsible for about **53,000 new cases of cancer** annually across 31 European countries<sup>4</sup>, and **87,000 across the wider WHO European region.**<sup>5</sup> In both areas, about 20% of these cases occur in men, although one study has estimated the proportion could be closer to 30%.<sup>6</sup> In recent years, there has been a marked increase in the incidence of oropharyngeal cancers mainly caused by HPV type 16, particularly in men.<sup>7</sup>

Every case of genital warts is caused by HPV. There are between 379,000 and 510,000 new cases of genital warts in women and between 377,000 and 428,000 new cases in men annually in 31 European countries. There is no Europe-wide data on RRP but the prevalence in the United Kingdom has been estimated at about 1.5 per 100,000.8

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Almost **90%** reduction in the highest-risk cervical pre-cancers

# **HPV** prevention

HPV-related cancers and genital warts can be prevented by HPV vaccination. This is most effective when administered in adolescence, before exposure to the virus through sexual activity. There is, however, value in vaccinating older teenagers and young adults, at least up to the age of 26 because it can protect against a new infection or re-infection and block transmission to a new partner.9

The impact of HPV vaccination on cancer incidence is clear and significant. A large-scale study in Scotland found that, compared with unvaccinated women born in 1988, vaccinated women born in 1995 and 1996 had an almost 90% reduction in the highest-risk cervical pre-cancers (CIN grade 3 or worse), an almost equivalent reduction in CIN grade 2 or worse and a near-80% reduction in CIN grade 1.10 The incidence of genital warts has also been significantly reduced by HPV vaccination.11

# The case for universal HPV vaccination

The vaccination of females alone will not provide effective protection for men against HPV infection. Unvaccinated females – such as those too old to have been offered routine vaccination or women who, although eligible, did not receive it – remain at risk of infection and can pass the virus on. In Europe as a whole, only about 4% of all women are estimated to have been vaccinated; in northern Europe, the best-performing region, the figure rises to only 8%.<sup>2</sup> Although these statistics are expected to improve over time as more women receive the vaccine, they do indicate the extent of the HPV infection 'reservoir'.

Heterosexual men living in countries with relatively high female vaccination rates still remain at risk of infection from unvaccinated women locally, as well as from women from countries with low, or no, vaccination programmes. **MSM** are at particular risk as they are completely unprotected by female-only vaccination programmes, even in countries with very high levels of uptake by girls. It should be noted that HPV can also be transmitted between unvaccinated female sex partners.<sup>12</sup>

The case for vaccinating boys is reinforced by the fact that **men have a poorer immune response to HPV infection than women**. HPV infection rates appear to stay constant in men, independent of age, whereas HPV prevalence in women is highest during 18–24 years of age and then decreases until middle age. This means that, unless they are vaccinated, men are more likely to acquire a new infection thereby creating a potential risk to their own health and the health of their sexual partners.

Vaccinating both sexes (known as 'universal' or 'gender-neutral' vaccination) provides much greater levels of protection for everyone. Its efficacy lies in preventing the transmission of HPV between the sexes and in same-sex couples, reducing the circulation of the virus overall and creating

what is termed 'herd protection'. Universal vaccination is an especially important public health strategy in countries where vaccination uptake in girls is relatively low.

Universal vaccination is consistent with the **fundamental human right** to the highest attainable standard of health. Excluding men is unfair as it makes a potentially life-saving intervention unavailable solely on the grounds of sex. Universal vaccination would also lead to greater equity between the sexes, between countries, and between income groups (in the absence of national programmes, wealthier families are already choosing to purchase vaccines for their sons or daughters).

Universal programmes also remove from females the sole responsibility for preventing HPV infection and help to **overcome stigma** about female vaccination based on unfounded concerns that it might encourage 'promiscuity'. Universal programmes are also more resilient to unexpected falls in uptake as a result of unfounded scares spread by 'fake news'.<sup>14</sup>

All EU countries, with the exception of Poland, now provide HPV vaccination programmes for girls. \*\* Most countries in the EU do not, or do not plan to, also offer HPV vaccination to boys. However, the number that do vaccinate boys, or have made a commitment to do so, has recently increased to 11 (Austria, Croatia, Czech Republic, Denmark, Germany, Ireland, Italy, Liechtenstein, The Netherlands, Sweden and the United Kingdom).\*\*

Several European countries outside of the EU, including Albania, Belarus and the Ukraine, do not have yet have HPV vaccination programmes for girls. Only three non-EU countries, Norway, Serbia and Switzerland, already vaccinate both sexes.

Vaccinating both sexes provides a **cost-effective** and **faster approach** to preventing or **reducing the incidence of cancers and other HPV-related diseases**. The European Centre for Disease Prevention and Control (ECDC) has suggested that if the objective of HPV vaccination is to prevent all HPV-caused disease, rather than cervical cancer alone, then universal vaccination may be a cost-effective option. In 2018, the highly-influential Joint Committee on Vaccination and Immunisation (JCVI), the UK government's vaccination advisory committee, concluded that vaccinating both boys and girls is cost-effective, even when over 80% of girls are vaccinated, if the impact of HPV-related diseases in the long-term is taken into account. In 17

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<sup>\*</sup>Information about vaccination policies in specific countries may not be complete as up-to-date information for every state in the WHO European Region is not readily available. The same caveat applies to the section on cancer screening.

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# **Vaccination uptake**

Vaccination uptake in females varies significantly across EU countries – few meet the widely-accepted target of achieving at least 80% coverage. In some countries, such as Bulgaria, France and Greece, vaccination rates are particularly low.

In Western and Southern Europe, about one-third of females in the targeted populations is estimated to have completed the full course of vaccination. In Eastern Europe, the proportion is only one-fifth. **However, in Northern Europe, the best-performing region, about two-thirds of eligible females have already been vaccinated.** 

Vaccination rates can also **vary widely within countries themselves**. The UK, for example, has a high overall vaccination rate (just over 80%) but, at the local level, uptake varies between **50% and 95%**.<sup>19</sup>

Low uptake has a range of causes, including cost, restricted access to health services and concerns about vaccine safety, which need to be better understood for each country. But **action is now needed to improve vaccine delivery systems** (school-based systems generally have the highest uptake) and to reassure the public, using **robust scientific evidence**, **about vaccine safety**.

# **Cancer screening**

**Cervical cancer screening programmes** are likely to remain an essential element of the management of HPV-related disease for the foreseeable future. Currently there are no screening programmes available for any other HPV-caused cancers, including those affecting men.

A survey conducted in 2016 found that 22 EU states were implementing, piloting, or planning a population-based cervical cancer screening programme; however, at the time, programmes had been **rolled-out in only 9 out of 28 EU member states**: Denmark, Estonia, Finland, Latvia, Poland, Slovenia, Sweden, The Netherlands and the United Kingdom.<sup>20</sup> However, other countries without an organised population-based programme did have schemes in place with at least some elements of organised screening.

HPV testing is the most effective, and accurate, method of cervical cancer screening and is now being adopted by an increasing number of countries. However, it is not yet universal. Finland, Germany, Italy, the Netherlands, Sweden and the United Kingdom, as well as Norway and Turkey outside of the EU, have either started to implement HPV screening on a regional or national level or plan to do so. It has also been piloted in several other countries, including France, Poland and Portugal.



Uptake of screening is highly variable between and within countries. Rates vary from over 70% in some EU member states to around 30% in others. In countries with historically high screening rates, uptake has been falling in recent years. In the United Kingdom, for example, around 71% of women are now screened despite an 80% target. Overall, in 2014, about 14% of EU women aged 20-60 had never had a PAP smear test. In each nation state, women with lower educational attainment are least likely to have been screened

There are also wide variations in survival from HPV-caused cancers across Europe. In Bulgaria, about 50% of women with cervical cancer survive for five years compared to 71% in Norway.<sup>23</sup> Women with CIN 3 (high grade or severe dysplasia), or invasive cancers, require equitable and prompt access to the best available treatment and care.

Action is needed now to improve the secondary prevention of cervical cancer through universally accessible, **high-uptake**, **high-precision HPV testing across the European region**.





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Eliminating HPV-Caused Cancers & Diseases in Europe

# **Public awareness of HPV**

Efforts to eliminate HPV-caused diseases risk being undermined by a lack of public awareness about HPV and the risks it poses and about the safety and efficacy of prevention technologies. The impact of 'fake news' about vaccination safety generally and HPV vaccination specifically is often generated by mainstream media reports and amplified by social media, and has recently been associated with the rapid falls in uptake in Denmark, Ireland and Japan. In Denmark specifically, the uptake of the first HPV vaccine dose was around 90% for girls born in the period 1998 to 2000 but dropped to 54% for girls born in 2003.<sup>24</sup>



Recent research suggests that only 73% of people in Northern Europe believe that vaccines, in a general sense, are safe. In Western Europe, this figure is even lower, at 59%; and in Eastern Europe this stands at 40%. Across Europe, the main causes of HPV vaccine hesitancy' specifically are related to: insufficient and inadequate information about HPV vaccination; misinformation about the potential side effects of the vaccine; issues around trust in health authorities, doctors and in new vaccines; and a perception of low vaccine effectiveness. There are differences between countries: in Italy, for example, there are greater concerns about the vaccine impacting negatively on sexual activity in younger women.

Many people currently lack basic knowledge about HPV and the associated risks. One study of men and women in the United Kingdom, where HPV vaccination for girls began in 2008 and systematic cervical cancer screening in 1988, found that just over one third (37%) had even heard of HPV.<sup>27</sup> Of these, 70% were aware that HPV could be transmitted during sex, and about 40% recognised that HPV could cause oropharyngeal cancer but only two thirds (64%) knew that a preventive vaccine existed.

There is a clear need to improve public knowledge about HPV-related health risks, to raise awareness of HPV in general, including the value of HPV screening and the safety of vaccination.

# Conclusion

The time has come to **take action** to eliminate HPV-related cancers by introducing **gender-neutral vaccination across the European region** and improving the uptake of vaccination and screening using the most effective technologies. People with cancers caused by HPV should also receive the best possible treatments wherever they live.

Cancer prevention is already an EU priority. The European Parliament, in its resolution on vaccine hesitancy adopted in 2018, welcomed 'the encouraging progress made in the fight against HPV diseases and cancers thanks to vaccination programmes against the HPV virus' and called on member states 'to further develop these programmes and explore ways to increase coverage rates and prevent other forms of cancer, for example by including boys in vaccination programmes.'28





Global targets of 90%

The World Health Organization (WHO) has recently drafted a global strategy to accelerate cervical cancer elimination, with clear goals and targets for the period 2020–2030. This calls for global targets of 90% of girls to be vaccinated by the age of 15, 70% of women to be screened with a high-precision test at 35 and 45 years of age, and 90% of women with cervical disease to receive treatment and care.<sup>29</sup>

WHO Europe's men's health strategy, adopted in 2018, contains a recommendation that its 53 member states should now consider a wide range of measures to improve the health and wellbeing of men and boys including 'promoting the role of adolescent boys and men in policies, programmes and services related to ... sexually transmitted infections.'30

As a result, at the ECCO 2019 European Cancer Summit, a consensus resolution was passed by over 300 cancer stakeholders urging: «By 2030, effective strategies to eliminate cancers caused by HPV as a public health problem should be implemented in all European countries. It is complemented by the following recommended actions:

# **ACTIONS ON HPV VACCINATION**

- **By 2025**, all European country cancer plans should include actions towards achieving population-based and gender-neutral HPV vaccination, if not already in place.
- **By 2030**, gender-neutral vaccination programmes against the HPV infection should be in place in all European countries.
- The **target vaccination rate by 2030** in all European countries should be **at least 90%** of adolescents for both genders.
- In support of vaccination goals, EU guidelines on integrated HPV vaccination and cervical cancer screening should be regularly updated. A third edition of **evidence-based guidelines** should be developed by 2022.
- Supplementary to gender-neutral vaccination programmes, consideration should be given to the needs of high risk groups that may otherwise fall outside of the age parameters of the universal vaccination programme.
- In support of vaccination goals, global cooperation should be fostered, through WHO or other agents, to resolve vaccine supply chain issues to ensure no country's HPV vaccination programmes are impacted because of shortage.

#### **ACTIONS ON SCREENING & EARLY DIAGNOSIS**

- **By 2030**, at least 70% of women in Europe should have been screened for cervical cancer with an appropriate high precision HPV test within the last 5 years. This coverage should be reached, at minimum, at 35 and 45 years of age, as part of an organised programme. HPV screening programmes should take into consideration innovations such as self-sampling in respect to their potential for achieving higher rates of screening.
- **By 2025**, all European country cancer plans should include actions towards achieving the 70% screening target, if not already achieved.
- In support of screening goals, EU guidelines on integrated HPV vaccination and cervical cancer screening should be regularly updated. A third edition of evidence-based guidelines should be developed by 2022.

#### **ACTIONS ON TREATMENT**

- **By 2030**, across all European countries, 90% of women with Grade 3 cervical intraepitheal neoplasia should be treated within 3 months; and 90% of all invasive cancer cases should have been detected and managed.
- **By 2025**, all European country cancer plans should include actions towards achieving these treatment goals if not already achieved.













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# FURTHER ACTIONS TO SUPPORT THE ACHIEVEMENT OF THE SUMMIT HPV RESOLUTION

#### **HPV** Awareness

- **By 2025** all European country cancer plans should include actions towards increasing public, patient and healthcare professional understanding and awareness about HPV. This awareness should include the range of related cancers and diseases, their symptoms and forms of prevention. Furthermore, this communication effort should elaborate to the public, patients and healthcare professionals the potential and need for HPV elimination, the strategies being pursued to achieve that goal, and the role of the public, patients and healthcare professionals to achieve the elimination goal. Awareness levels of the public, patients and healthcare professionals on HPV should be thereafter be monitored and reported on.
- These awareness raising actions should encompass the dental workforce in respect to oropharyngeal cancer, and the schooling system.

# Combating the impact of Fake News on Vaccination

- **By 2021**, cancer societies, patient and healthcare professional associations, and other stakeholders, should publish a core list of consensus recommendations for European member states to implement in order to combat the impacts on HPV vaccination uptake posed by fake news.
- **By 2021**, all major social media platforms operating in Europe should have developed and implemented strategies to reduce the spread of fake news on vaccination.
- **By the end of 2022**, all national cancer plans in Europe should include actions to combat the deterrence effects of fake news upon HPV vaccination rates, as part of a broader campaign to reduce the negative impact of fake news on all vaccination programmes.

#### Improving data and monitoring

**By 2025**, all European countries should have population based registries in place to accountably track and report upon HPV vaccination, HPV screening and HPV related (and other) cancer incidence and mortality data.

# **EU Cancer Mission**

- **By 2021** the EU Cancer Mission should have clear elements within its programme that are supportive to the WHO global strategy for the elimination of cervical cancer as a public health problem, and the ECCO 2019 European Cancer Summit resolutions on elimination of HPV.
- This should include supporting research priorities such as new vaccine and screening technologies as well as care and treatment techniques.

# Complementing the EU Cancer Mission with an EU Cancer Masterplan

**EU Cancer Mission goals**, such as on HPV, should be complemented by an EU Cancer Masterplan that supports achievement in respect to non research related matters. This might include facilitating greater use of EU Structural Funds to achieve EU and WHO wide HPV vaccination, cervical cancer screening, and treatment goals for HPV related cancers.

# Monitoring of Member State Cancer Plans

As part of the coordination role that the EU should play in assisting member states to combat cancer by 2025 a public **monitoring and reporting** exercise should be established in respect to EU member state cancer plan items, similar to 'the State of Health in the EU' exercise. This should **include monitoring of actions towards international goals on HPV related cancer elimination**.

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