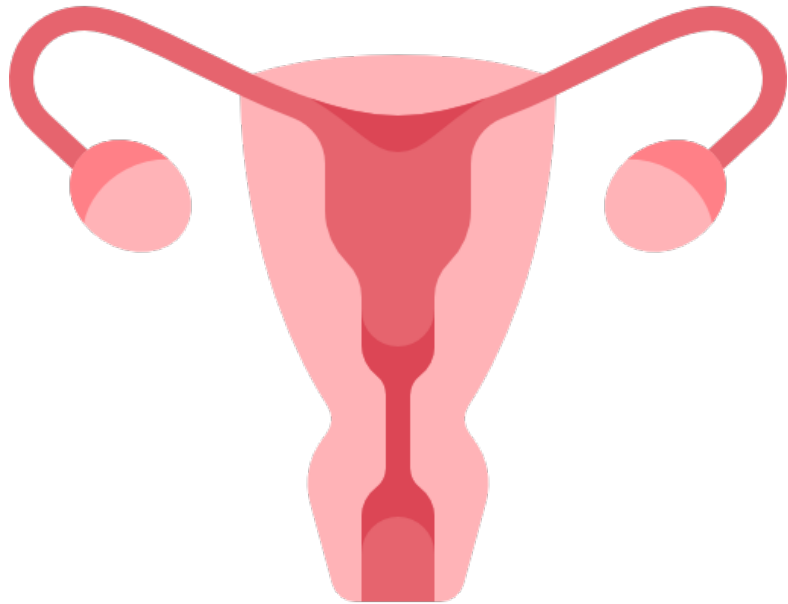


# HPV vaccination to prevent cervical cancer



## CASE OUTLINE

### I. Case for change

- *Situation*
- *Challenge*
- *Paradigm shift*
- *Patient population*

### II. Value to patients

### III. Value to the healthcare system

### IV. Value to society

### V. Annex

- *Key assumptions*
- *Reference list*

# Case summary | Cervical Cancer Vaccines

## HPV vaccination to prevent cervical cancer

### CASE FOR CHANGE



- **Situation** – Cervical cancer is a type of cancer that is found in the cervix, and primarily affects women of working age. Treatment for cervical cancer includes surgery, chemotherapy, radiotherapy and brachytherapy
- **Challenge** – Cervical cancer has a major impact on patients, the healthcare system, and society. Current estimates indicate that, in EU27, more than 30,000 women are diagnosed with cervical cancer and around 13,500 die from the disease every year
- **Paradigm shift** – Almost all ( $\geq 95\%$ ) cases of cervical cancer are caused by an infection from human papillomavirus (HPV). Since 2006, several vaccines against HPV have become available in the EU27, providing the opportunity to prevent most cases of cervical cancer
- **Population** – In the EU27, every year, over 2.2 M 12-year-old girls become eligible for HPV vaccination and can benefit from its protection throughout their lives

### VALUE FOR PATIENTS



- **Preventable cases and deaths** – More than 27,000 cervical cancer cases and 12,000 deaths can be prevented by HPV vaccination, each year
- **Preventable diagnostic wait time / events** – Each year, over 19M women are invited to be screened for HPV. Screening and testing can cause discomfort and stress. Screened women all wait 2-6 weeks in uncertainty for the results of a diagnostic test for cervical cancer. The burden of cervical cancer screening can be reduced by 57% with HPV vaccination, as vaccinated women require less screening

### VALUE TO THE HEALTHCARE SYSTEM



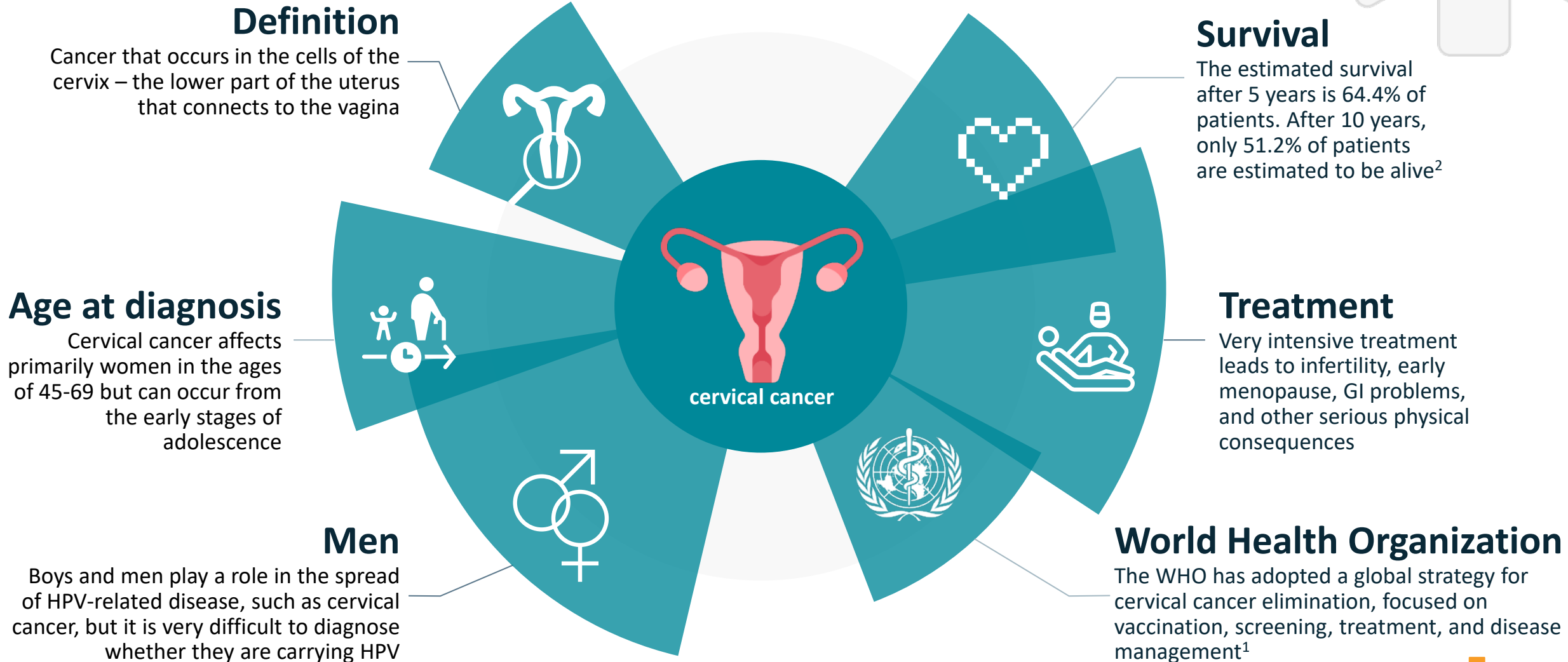
- **Preventable resource use (€)** – Treatment for cervical cancer requires a considerable amount of healthcare resources. On average, a course of treatment for cervical cancer costs over €26,000 (based on an Italian perspective). The total healthcare costs in Italy for the treatment of cervical cancer can be decreased by €74M due to HPV vaccination
- **Preventable resource use (Staff)** – With HPV vaccination, fewer patients require treatment, therefore a total of 493k working hours for nurses can be reallocated

### VALUE TO SOCIETY



- **Economic gains** – Vaccinating all women in EU27 against HPV would increase work productivity and labour income by 5.7M working hours and €387.0M respectively
- **Preventable family pain** – Cervical cancer has a significant impact on families and women who want to have children which can be prevented through HPV vaccination

# Cervical cancer primarily affects women of working age, who have a 1 in 2 chance of survival after 10 years



1. WHO, 2022.  
2. OECD STATLINE (2010-2014)

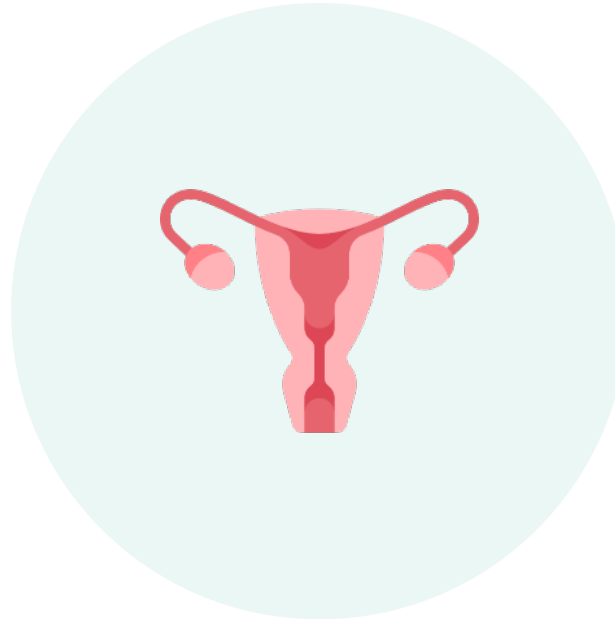
# Treatment for cervical cancer includes surgery, chemotherapy, radiotherapy and brachytherapy<sup>1</sup>

## Surgery

**Primary treatment for early stage CC**  
Radical surgery leads to pain, deformation and sometimes infertility

## Radiotherapy

**Treatment with curative or palliative intent**  
Often in combination with other treatment options. Side effects include fatigue, burns and excessive scarring of the radiated tissue



## **Chemotherapy**

**Primary treatment for advanced stage CC**  
Is often given for 6 cycles of 3 weeks during which diarrhoea, nausea, vomiting and infection are common. It can also lead to anaemia, kidney damage, hearing loss and pain.

## **Brachytherapy**

**Internal radiation used to increase success of treatment**  
Very painful for the patient, leading to irritation of the vagina and surrounding tissues. Also leads to fatigue, diarrhoea, nausea, irritation of the bladder, and anaemia.

*“At age 27, I was diagnosed with stage IVb cervical cancer. I received chemotherapy, radiotherapy, and brachytherapy. The treatment was very intensive and took a lot out of me physically. The emotional and social consequences have been even more challenging. My life will never be the same again.” -- Patient Expert*

# Cervical cancer has a major impact on patients, the healthcare system and society

2.5%

of all cancer cases in EU27 is cervical cancer<sup>1</sup>

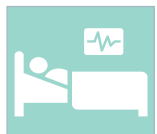
11<sup>th</sup>

in the EU27 among the most frequently occurring cancers in women<sup>1</sup>

12<sup>th</sup>

in EU27 among the most frequent causes of cancer death<sup>1</sup>

## Cervical cancer has a major impact on...



### Cervical cancer patients

Cervical cancer is a debilitating disease, treatment is intensive, has a prolonged effect on patients' health and wellbeing, and causes a lot of anxiety



### The healthcare system

The cost and resource use of cervical cancer treatment are significant

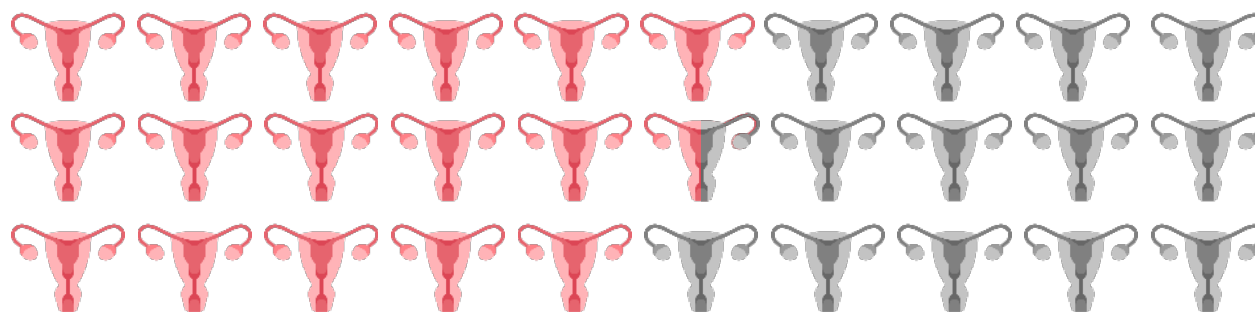


### Society as a whole

Cervical cancer patients may not be able to work or care for others, and they may require intensive treatment and care

# Current estimates indicate that in EU27, more than 30,000 women are diagnosed with cervical cancer and around 13,500 die from the disease every year<sup>1</sup>

## Every year, a significant number of women are diagnosed with, or even die from, cervical cancer



= 1,000 diagnosed cervical cancer patients, each year in EU27



= 1,000 patients who die from cervical cancer, each year in EU27

## There are clear differences between European countries...



**Mortality** rates are almost threefold higher in Central-Eastern Europe as compared with Western-Europe<sup>2</sup>



**Screening** rates vary from over 70% in some EU member states to around 30% in others<sup>2</sup>

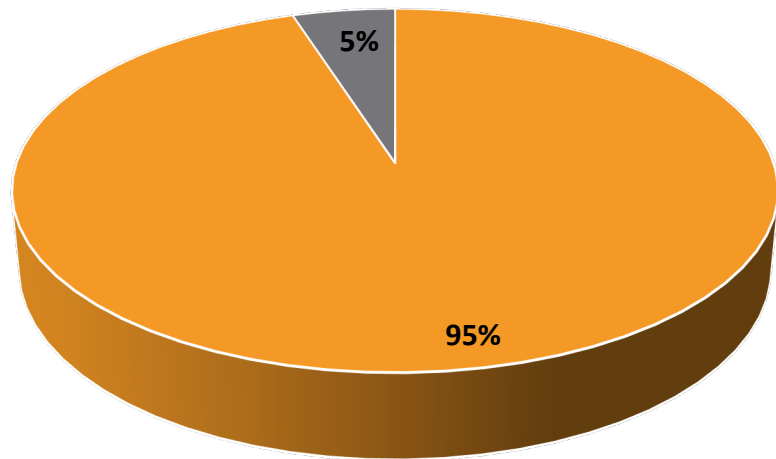


Not all countries cover the **costs** of follow up after a positive screening test or the treatment of precancerous lesions<sup>2</sup>

1. FACTSHEET BY THE EUROPEAN COMMISSION & EUROPEAN NETWORK OF CANCER REGISTRIES, 2021  
2. BAKER, 2020.

# Almost all ( $\geq 95\%$ ) cases of cervical cancer are caused by an infection from human papillomavirus (HPV)

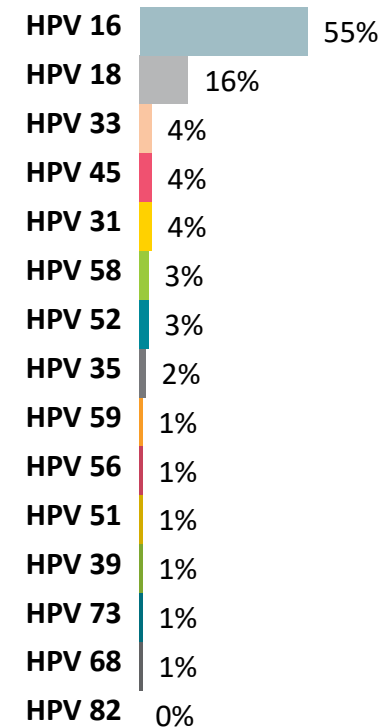
95% of all cervical cancer cases are caused by HPV<sup>1</sup>



■ Caused by HPV ■ Other causes

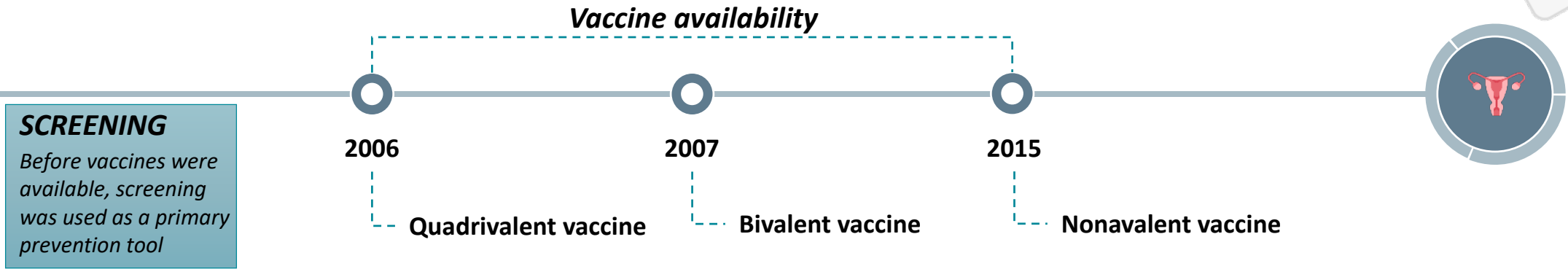
*“95%-100% of cervical cancer cases are caused by HPV. There may be a few cases where you cannot find signs of HPV, but this might also be because of the testing methodology.”*  
-- Oncologist & leading HPV researcher

A large proportion of cervical cancer cases is caused by HPV types 16 and 18<sup>2</sup>



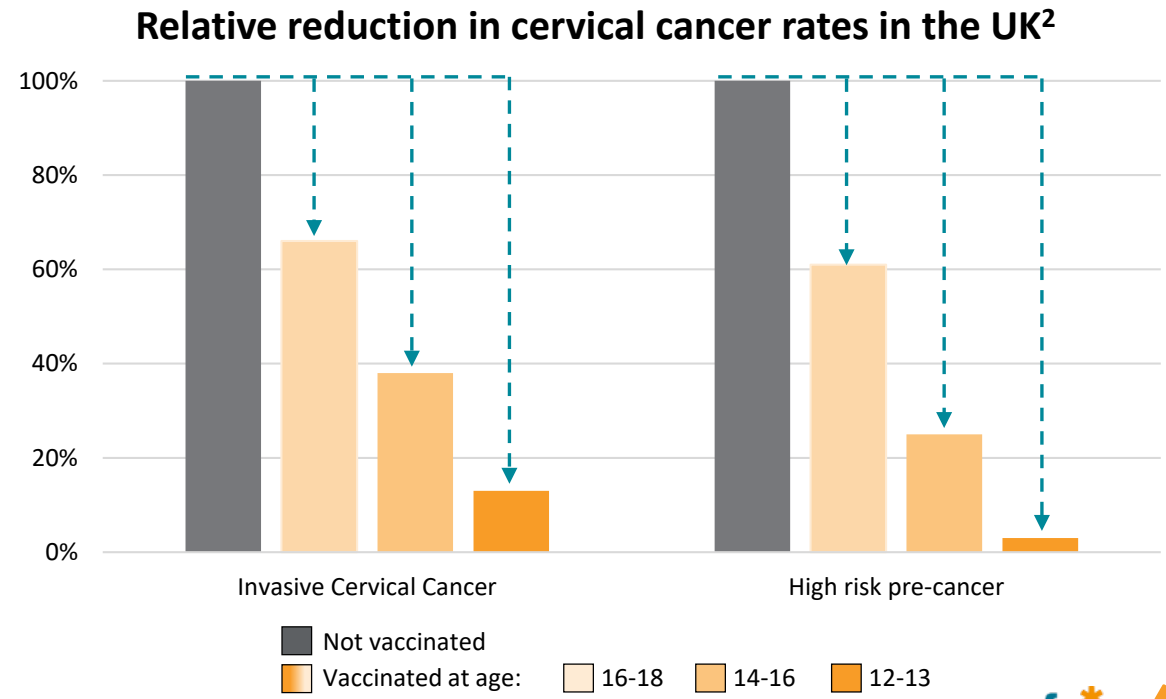
1. FERNANDES, 2022.  
2. CUZICK, 2021.

# Since 2006, several vaccines against HPV have become available in the EU27, providing the opportunity to prevent most cases of cervical cancer



100% vaccine effectiveness was demonstrated over 12 years in four Nordic countries: no cases of high-grade cervical dysplasia linked to HPV types 16 or 18 were found in a large sample of vaccinated women.<sup>1</sup>

*“HPV vaccination was a real change of paradigm. It is clearly a story of success: it is very effective, the safety is great, and uptake in lower developed countries is better than it is for screening because eligibility is at a younger age” – Oncologist & leading HPV researcher*



1. KJAER, 2020.  
2. HPV WORLD, 2022.



# In the EU27, every year over 2.2M 12-year-old girls become eligible for HPV vaccination and can benefit from its protection throughout their lives

## Eligibility for, and protection by HPV vaccination



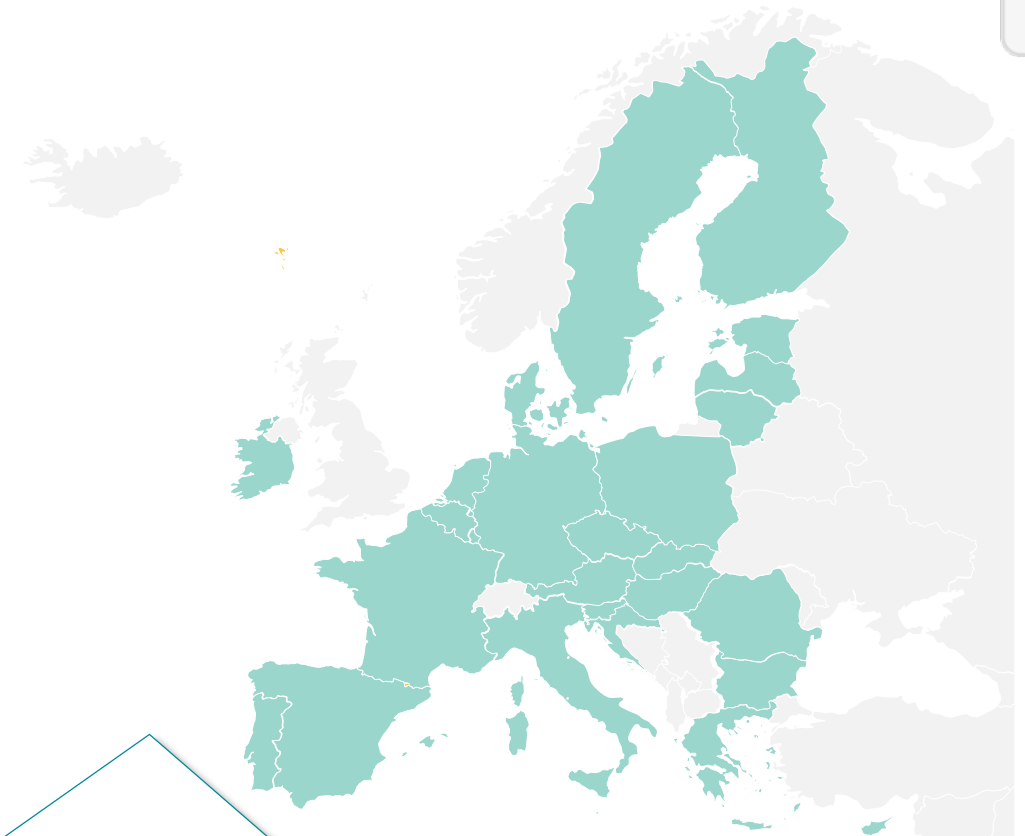
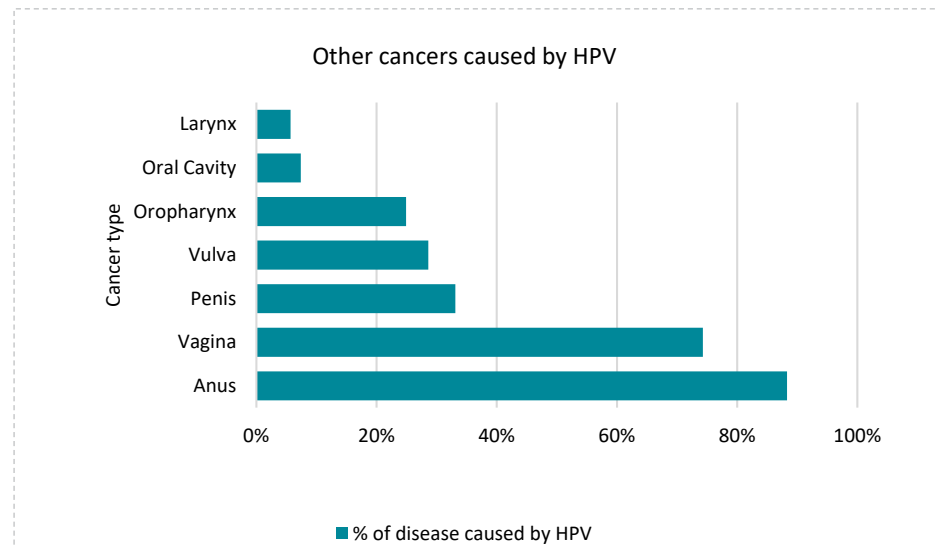
In general, HPV vaccines are available through national vaccination programmes **from 12 years of age**<sup>1</sup>



All three vaccines provide great protection, if the required **2 doses** are given.<sup>2</sup> Vaccination effectiveness is at least 94.7%<sup>3</sup>



The vaccines also offer “cross”-protection for other HPV-related disease such as genital warts and other types of cancer<sup>4</sup>



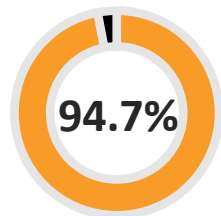
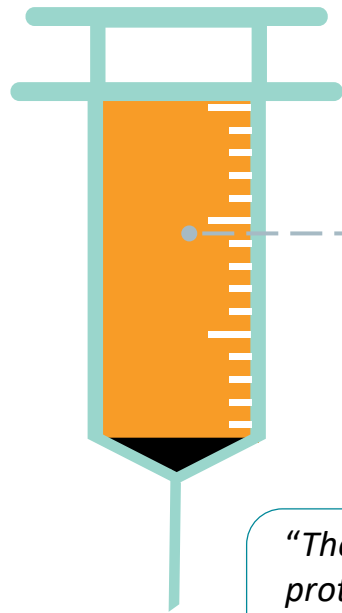
*“HPV vaccination provides cross-protection for other diseases as well. This effect is not negligible, especially when it comes to genital warts.”*

*-- Oncologist & leading HPV researcher*

1. BONNANI, 2020.  
2. MISHRA, 2015.  
3. KJAER, 2020.  
4. DE SANJOSÉ, 2016.

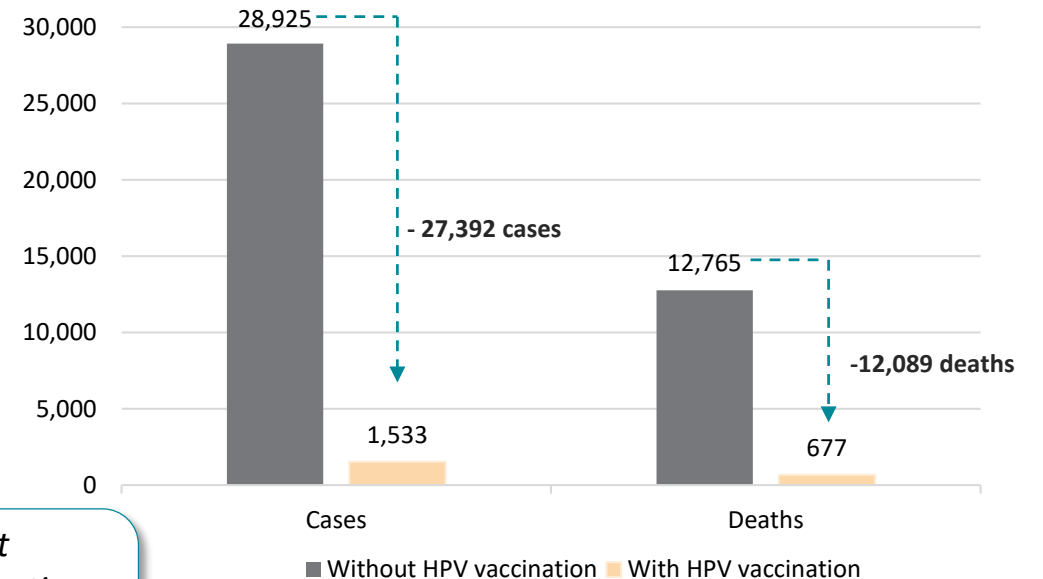
# More than 27,000 cervical cancer cases and 12,000 deaths can be prevented by HPV vaccination, each year

HPV vaccines are at least 94.7% effective in preventing HPV infections<sup>1</sup>



*“The impact of massive vaccination is larger than the direct protection of vaccinated girls. It reduces the risk of HPV infection per sexual contact. So we achieve protection of the non-vaccinated as well.” – Oncologist & leading HPV researcher*

This means that, every year, over 27,000 cases and 12,000 cervical cancer-related deaths can be prevented by HPV vaccines



1. KJAER, 2020.  
2. FERNANDES, 2020.

# The burden of cervical cancer screening can be reduced by 57% with HPV vaccination, as vaccinated women require less screening

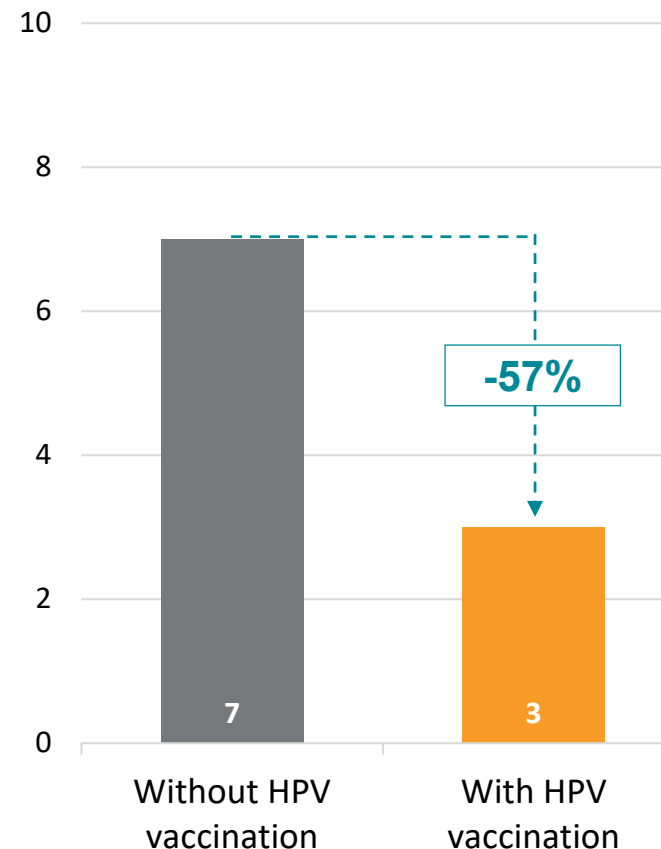
## The burden of cervical cancer screening is high

- Each year, 19.3 M women require cervical cancer screening in the EU27
- After each screening, women wait on average 2-6 weeks for the results
- Screening and testing for cervical cancer can cause a lot of stress, as screening is uncomfortable and is associated with long waiting times for the results

*“After being cured from cervical cancer, every check up is very stressful. The waiting time between the examination and the results is nerve-racking”* -- Patient Expert

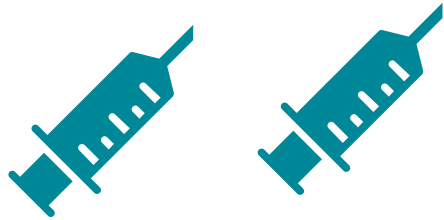
## HPV vaccination significantly decreases the burden of cervical cancer screening<sup>1</sup>

Number of lifetime cervical cancer screenings with and without HPV vaccination



*“The generalized use of vaccines may have a counterbalance in reducing the needs for screening. Vaccinated women have to come in for screening much less, and the funds could be moved to vaccination.”*  
-- Oncologist & leading HPV researcher

# Treatment for cervical cancer requires a considerable amount of healthcare resources



The total cost<sup>1</sup> for two courses of vaccination are estimated at

**€132.71**



Unvaccinated women need 7 screens during their lifetime. Pap smear cost<sup>1</sup> is estimated at

**€18.05**



The cost of treatment<sup>2</sup> is country dependent, and could increase over the next decade

**>€20,000**

 *Deep dive into Italy* 

1. HAEUSSLER, 2015.  
2. MENNINI, 2017.

# On average, a course of treatment for cervical cancer costs over €26,000 (based on an Italian perspective)

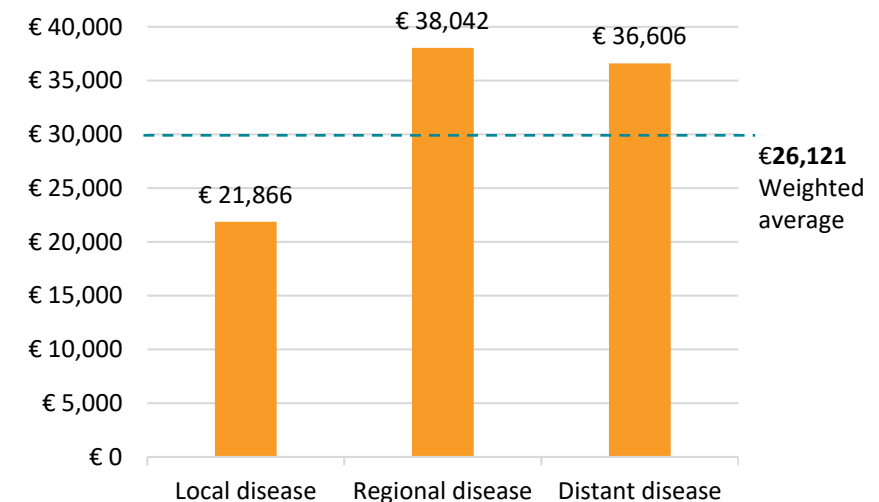
## Per-patient cervical cancer treatment costs are significant

### *Deep dive into Italy*

Based on an Italian cost estimate, cervical cancer treatment costs are:

- **Locally spread disease**  
Costs for treating locally spread cervical cancer are €21,866 on average<sup>1</sup>
- **Regionally spread disease**  
Costs for treating cervical cancer which has spread to the surrounding tissue are €38,042 on average<sup>1</sup>
- **Distant disease**  
Costs for treating metastasized cervical cancer are €36,606 on average<sup>1</sup>

Average (weighted) costs per patient are €26,121<sup>1,2</sup>



# A €74M decrease in the total healthcare costs for the treatment of cervical cancer in Italy can be achieved through HPV vaccination

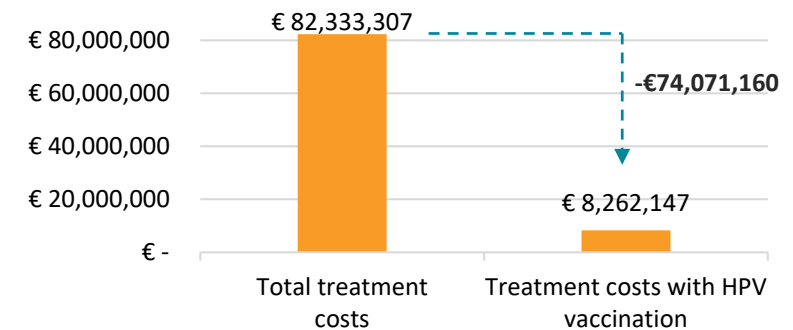
A significant amount of costs spent on cervical cancer treatments can be prevented through HPV vaccination

## *Deep dive into Italy*

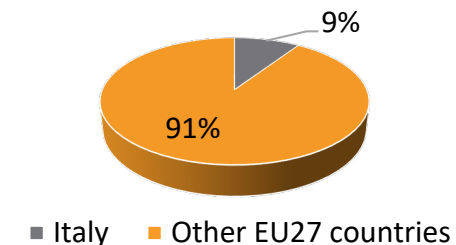
- The average (weighted) cost per patient in Italy is €26,121
- The number of potentially prevented cervical cancer cases due to HPV vaccination is 2,836
- This means that ~€74M spent on cervical cancer treatment can be prevented by HPV vaccination
- Italy has only 9% of the potentially prevented cervical cancer cases in EU27



Cervical cancer treatment costs in Italy



Potentially prevented cervical cancer cases



# With HPV vaccination, a total of 493k working hours for nurses can be reallocated in the healthcare system, as fewer patients require treatment

## Cervical cancer treatment is labour intensive

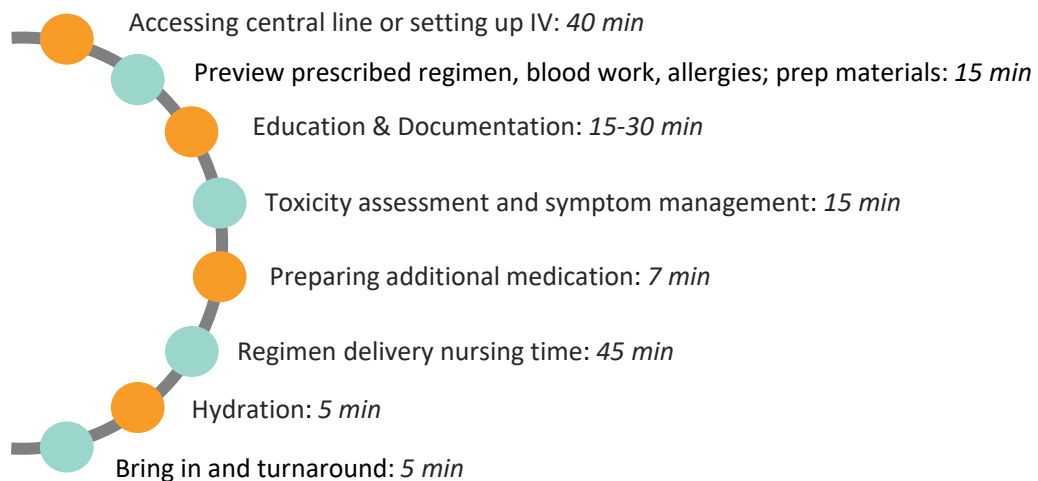


**Chemotherapy** – Patients require 6 courses, each taking a nurse ~2 hours to complete. This equates to 12 hours per patient<sup>1</sup>



**Radiotherapy** – Patients require at least 24 sessions, each taking a nurse ~15 minutes to complete. This equates to 6 hours per patient<sup>2</sup>

### Nurse time break-down for course of Chemotherapy<sup>1</sup>



## HPV vaccination could save many nurse hours spent on cervical cancer treatment

Assuming that all cervical cancer patients require chemotherapy and radiotherapy; preventing the cancer by vaccinating all women in EU27 against HPV would save:

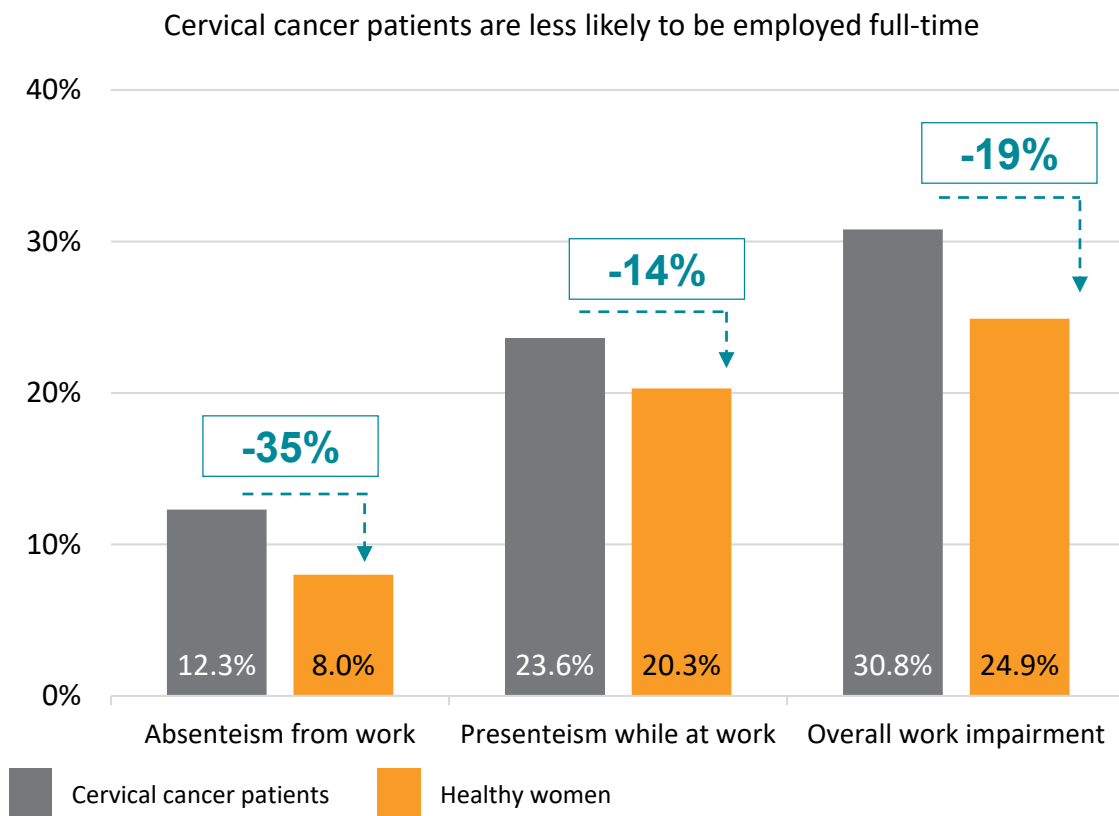


**493,050 nurse working hours per annum**

*“In addition to savings on treatment, we can also save on screening costs. There was a full industry around screening, this was a gigantic piece of work that involved a high cost.” – Oncologist & leading HPV researcher*

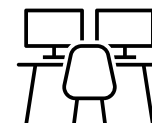
# Vaccinating all eligible women in EU27 against HPV would increase work productivity and labour income by 5.7M working hours and €386M, respectively

**Cervical cancer patients are less likely to be full-time employed and are more impaired at work, resulting in productivity loss<sup>1</sup>**



**Preventing cervical cancer through HPV vaccination results in significant economic benefits<sup>2</sup>**

Preventing cervical cancers by vaccinating all women in EU27 against HPV would increase:



Annual productivity in EU27 by **5.6M working hours**



Annual labour income in EU27 **€386M**

*"I lost my job because I had a chemo brain, making it impossible to focus. I had very low energy levels and my work capacity was severely affected. I was unable to function professionally" -- Patient Expert*

1. DOANE, 2019.  
 2. EUROSTAT, 2022.



# Cervical cancer has a significant impact on families and women who want to have children – this can be prevented through HPV vaccination

## Cervical cancer burden for families<sup>1</sup>



On average in the EU27, each year:

**3,039** mothers with children ( $\leq 18$  years old) living at home die of cervical cancer

**5,167** children living at home ( $\leq 18$  years old) lose their mother due to cervical cancer

## Cervical cancer burden for adolescent women

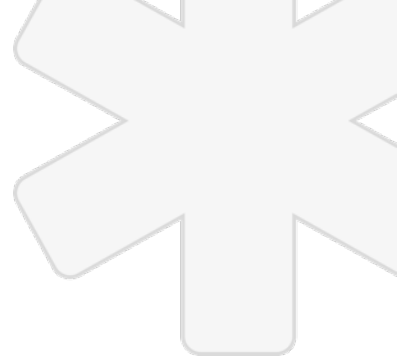


Burden of cervical cancer persists after treatment:

- Unfortunately, after most treatment for cervical cancer, women will not be able to get pregnant
- This can result in stress and psychosocial burden for women surviving cervical cancer

*"I had to accept that my life will be completely different than what I had always envisioned. I will never be who I was before. I entered menopause at the age of 27 and will not be able to conceive a child" -- Patient Expert*

# Looking towards the future...



## Education

People have the right to make an informed decision about HPV vaccination, so education is key

## Expanding the use of vaccination

Globally, In 2006–2017, 100 million adolescent girls received at  $\leq 1$  dose of the HPV vaccine – 95% were in high income countries

## Gender-neutral vaccination

26 countries in the European region are currently, or will be, including boys in their vaccination programmes

## HPV diagnosis in men

HPV-related disease is well studied in women, but until recently the natural history of HPV among males was relatively unknown

## Improved access and new treatment options for cervical cancer patients

Currently the five-year survival rate for early-stage cancer is more than 80% in countries where timely diagnosis and high-quality treatment are available

# Assumptions for Cervical Cancer case study



Parameter	Value	Rationale
Proportion of cervical cancer cases caused by HPV	95%	Conservative assumption based on multiple sources
Estimated effectiveness of vaccine	94.7%	Kjaer et al. (2020) estimate 100% effectiveness with a lower 95%-confidence interval of 94.7%
Age of vaccination eligibility	12 years	Seems to be a good assumption looking at the spread between countries in EU27 (more information in calculations file)
Target vaccination coverage	90%	European Cancer Organisation (2020) & WHO target
Current number of lifetime screens advised	7 screens	Every 5 years from age 35 to age 65. Based on the European guidelines for quality assurance in cervical cancer screening. This is dependent on policy per country, but most countries are relatively close to this; some start earlier or have more frequent screens, which makes this a conservative assumption.
Lifetime screens required after vaccination	3	Landy et al. (2018) estimate that HPV16/18-vaccinated women require three lifetime screens, HPV16/18/31/33/45/52/58-vaccinated women require two lifetime screens
Cervical cancer stage at diagnosis	Local disease: 72.6% Regional disease: 14.9% Distant disease: 12.5%	Landy et al. (2016)
Reduction in workload for cervical cancer patients	19%	Conservative assumption based on interviews
Scope	EU27 countries	EU27 includes Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovenia, Slovakia, Spain, Sweden.

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## Interviews

Interviews conducted in July and August 2022 with 1 Patient Expert and 1 Healthcare Professionals (KOLs).