# WOMEN AND CERVICAL CANCER IN THE EU

**European Institute of Women's Health Policy Brief** *2017*

## Overview

Cervical cancer was estimated to be responsible for the deaths of 279,311 women around the world in 2015.[1] According to the World Health Organization's (WHO) World Cancer Report 2014, cervical cancer was the fifteenth most common cancer globally in 2012,[2] while for women it is currently the fourth most common cancer.[3] The vast majority of cases (estimated to be approximately 70%) are located in countries with low or medium levels of development.[4]

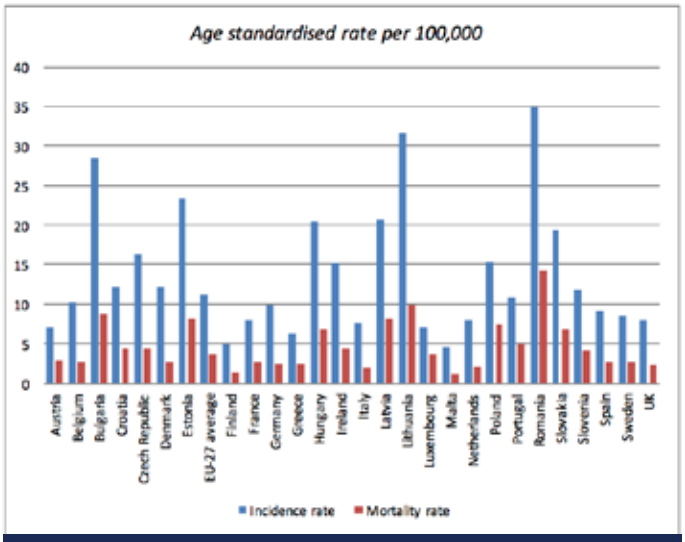


*Fig 1. EU-27 incidence and mortality from cervical cancer (2012)*
*Source: WHO. International Agency for Research on Cancer. 2012. Cervical Cancer: estimated incidence, mortality & prevalence, 2012.*

*In 2012, the most recent year for which complete data is available, 58,348 women across Europe were estimated to suffer from cervical cancer.*[5] In that same year, the disease was the cause of death of approximately 24,397 women. Figure 1 presents the mortality and incidence rates (age standardized rates per 100,000 women) for that period across the EU-27. We can see that there is substantial variation across the Member States in terms of both the incidence of the disease and mortality rates. Malta has the lowest incidence rate of cervical cancer in the EU-27 at 4.6 women per 100,000, below the EU-27 average of 11.3. However, this rate rises to more than 30 cases per 100,000 for Lithuania and Romania. Indeed, Eastern and Central European countries have the highest incidence rates, while most Western European countries fall below the EU-27 average.

There is similar variation in terms of the mortality rates. Again, Malta has the lowest mortality rate in the European Union; 1.1 women per 100,000 in that Member State were estimated to have died as a result of cervical cancer in 2012. Romania has the highest mortality rate across these countries at 14.2, more than 3.8 times the EU-27 average. Again, we can see a split between Western Europe and Eastern and Central Europe in terms of cervical cancer mortality rates. This split is most likely due to the intensity of organized screening programs in Western Europe, while countries with high incidence rates of the disease have yet to implement extensive vaccination programs.[6]

Most cases of cervical cancer are preventable since almost all of them are caused by human papillomavirus (HPV), of which there are more than 100 types and roughly 40% of which can be sexually transmitted.[7] At least 13 types if HPV are considered to be cancer-causing,[8] and two high-risk types alone (HPV-16 and HPV-18) are responsible for about 70% of all cervical cancers worldwide. Vaccines that protect against these high-risk strains of HPV have been developed and used to great effect in national vaccination programmes. Vaccination programmes and national cervical cancer screening programmes represent substantial costs to national healthcare systems. However, they represent the best strategy to tackle incidence of and mortality from this largely preventable disease.

## Cervical cancer: the basics

Cervical cancer occurs when the cells lining the cervix (the entrance to the womb from the vagina) mutate and grow uncontrollably.[9] This disease tends to develop slowly, over a number of years. Initially, abnormal changes take place, which are called precancerous, and if left untreated they may develop into cervical cancer.[10] There are several types of cervical cancer:[11,12]

- Squamous cell cancer: this type of cancer develops in the squamous cells that cover the outer surface of the cervix. This is the most common type, accounting for between approximately 70 and 80% of all cases of cervical cancer.
- Adenocarcinoma: this type of cancer emerges in the glandular cells that are located in the passage connecting the cervix to the womb (the endocervical canal). This type of cervical cancer is responsible for a little more than 10% of all cases.
- Adenosquamous carcinoma: this form of the disease produces tumours with both the squamous and glandular cancer cells. It is rare, however, making up between 5 and 6% of all diagnoses of cervical cancer.
- Small cell cancer: this type of cancer is rare but it is particularly aggressive.
- Other types of cervical cancer: these include sarcomas and lymphomas. They are extremely rare and are treated very differently to other types.

Treatment for cervical cancer varies depending on the type of cervical cancer and how far it has spread.[13] Chemotherapy, radiation therapy, and surgery are all commonly used treatments.[14] As well as the type of cancer, the stage of the cancer will also impact on treatment.

Like other cancers, cervical cancer can be divided into various stages using the tumour, node, and metastasis (TNM) categorisation, a coding system for cancer staging. Stages describe the size of the cancer and whether or not it has spread to other parts of the body. The staging is used for treatment decisions:[15,16]

- **Tumour (T):** T describes the size of the tumour
- **Node (N):** N indicates whether (or not) and to what extent the tumour has spread to the lymph nodes (small, ball-shaped organs of the immune systems, distributed throughout the body)
- **Metastasis (M):** M specifies whether or not the tumour has spread to other areas of the body.

## Symptoms of cervical cancer

Symptoms of cervical cancer are easy to miss and early on in the disease there are often no symptoms. As the disease becomes more advanced, some of the following symptoms may be present:[17,18,19,20,21,22,23]

- Vaginal bleeding after or during sex
- Vaginal bleeding after the menopause
- Vaginal bleeding between periods
- Vaginal bleeding after a pelvic exam
- Vaginal bleeding after douching
- Pelvic pain or discomfort
- Discomfort or pain during sex
- Blood-stained or unpleasant-smelling vaginal discharge

**Where cervical cancer has spread beyond the cervix to surrounding tissue and other organs, a range of other symptoms can be triggered. Some of these include: the following**[24]

- Constipation
- Blood in urine
- Loss of bladder control
- Loss of appetite
- Unexplained weight loss
- Tiredness and exhaustion
- Changes to bladder and bowl habits
- Severe pain in the side or back due to swelling in the kidneys

## Risk factors for cervical cancer

Some risk factors for developing cervical cancer have been identified as the following:[25,26,27,28,29,30]

- Smoking[31]
- Family history of cervical cancer
- Human Papilloma Virus (HPV) infection[32]
- Age (cervical cancer is more common in women under the age of 60)
- HIV positive status[33]
- Having a sexually transmitted infection (STI) such as chlamydia[34]
- Long-term use of oral contraceptives[35,36]
- Having a diet that is low in fruits and vegetables
- Being overweight or obese[37,38]
- Having had children
- Having had other forms of cancer (e.g. cancer of the vulva, kidney, urinary tract etc.)
- Becoming sexually active at a young age[39,40]
- Race/ethnicity (in the US, for example, Hispanic and Black women are more likely to suffer from cervical cancer[41])

### Cervical cancer and Human Papillomavirus (HPV)

Most cases of cervical cancer are caused by human papillomavirus (HPV). HPV is a group of more than 170 related viruses, each one of which is identified by a number which represents its HPV type.[42] It is the most common viral infection of the reproductive tract, so common that most sexually active people will at some point become infected with it over the course of their lives.[43] Many strains of HPV are sexually transmitted and as such the use of condoms and dental dams offer some protection against infection.[44] However, skin-to-skin genital contact is also a common mode of transmission. HPV can be passed from person-to-person even when symptoms are not in evidence, and such symptoms may take years to develop, making it difficult to determine when infection first occurred.[45] Different types of HPV cause various types of warts, cysts, as well as certain forms of cancer. Most types of HPV infection clear up by themselves within two years, and most women who are infected with the HPV virus will not develop cervical cancer.[46]

There are two particularly high-risk strains of HPV, HPV-16 and HPV-18, which are estimated to be responsible for about 70% of all cervical cancers worldwide.[47,48] Not only is HPV a cause of cervical cancer, but there is increasing evidence linking it other cancer of the vagina, vulva, penis, and anus, as well as cancers of the neck and head.[49]

Vaccines that protect against the two highest-risk types of HPV have been developed and are licensed for use in many countries around the world. The HPV vaccine is almost 100% effective in preventing cervical cancer-causing HPV infections.[50] This vaccination is most effective prior to exposure to HPV (that is, when women become sexually active).[51] HPV vaccination cannot treat an existing HPV infection.

Vaccination against HPV is typically recommended for girls aged 9 to 13 years by international organisation like the World Health Organization (WHO), and the International Federation of Obstetricians and Gynaecologists, in addition to national medical organisations.[52] While some countries have decided to vaccinate boys too, it is thought that the vaccination of young girls is the most cost-effective means of reducing incidence of cervical cancer.[53]

### Screening for cervical cancer

While HPV vaccination is considered by many developed nations to be a key component of strategies to tackle cervical cancer, the current vaccinations that are in use only offer protection against the HPV-16 and HPV-18 strains of the virus, the causes of approximately 70% of all cases of cervical cancer worldwide. As a result, screening for the disease is recommended not only for women who are unvaccinated, but also for those who have been vaccinated in order to target the 30% of cervical cancers that the HPV vaccine does not offer protection.[54]

Cancer screening generally involves testing for the presence of cancer before a person presents symptoms. This enables cancer to be detected at an early stage, when it is typically easier to treat, leading to improved outcomes for patients.[55] Screening for cervical cancer can involve two tests (co-testing),[56] though they are not always performed together and national screening programmes may only perform the test for the presence of cancerous cells.

Firstly, a Pap smear, which involved a collection of a sample of cells from the cervix, is performed. The sample is tested for pre-cancers, cell changes in the cervix that have the potential to develop into cancer if left untreated. The CDC recommends that women receive regular Pap smears from age 21 at three-year intervals, if the results from the smear do not detect any abnormalities.[57] Women 45 years and older are recommended to reduce the frequency of testing, from 3- to 5-year intervals.[58] Women who are 65 or older, or who have had several normal tests over a period of years, may be advised by their doctors to reduce the frequency of testing or that testing is no longer necessary.[59] In such cases, women should still seek medical advice as soon as possible if they notice any of the symptoms listed above.

A second test, a HPV test, can be performed as part of a cervical cancer screening programmed in order to detect the virus that is often responsible for the changes in the cells of the cervix that can lead to cancer. There are several different HPV tests that are approved for use in screening programmes; most detect the DNA of high-risk HPV types in general, though some other tests detect infection with HPV-16 or HPV-18 in particular.[60] Where cervical cancer screening results are abnormal, follow-up tests and perhaps treatment will be necessary.

For women aged 30 and older, co-testing (performing a Pap smear with a HPV test) means that an abnormality is much less likely to be missed than when a Pap smear is performed alone. In 2012, U.S. Preventive Services Task Force indicated that co-testing would enable women aged 30 to 65 years to lengthen the screening interval for cervical cancer from every 3 years to every 5 years, where both tests fail to detect any abnormalities.[61]

### European and national strategies for cervical cancer prevention

The European Council acknowledges that screening for cancer facilitates early detection which has the potential to avoid many thousands of deaths if properly implemented. The Council's 2003 R*ecommendation on Cancer Screening,*[62] adopted unanimously by EU Ministers of Health, issued a call for Member States to implement national screening programmes for the detection of cancer of the colon, cervix, and breast. In addition, it presented what it concluded were best-practice guidelines with respect to the implementation of such programmes. It recommended that Pap smear screening be

implemented, starting no earlier than age 20 and no later than age 30. A follow-up report, published in 2008, assessed the extent to which the EU-27 had made progress on the Council recommendations from 2003; while 6 Member States had completed the roll-out of population-based screening programmes, others had regional programmes only, were running pilot schemes, or were still in the planning phase.[63] A second follow-up report on the 2003 Council recommendations, published in 2017, finds that population-based cervical cancer screening programmes exist in 22 Member States either at national or at regional level.[64] The report indicates that substantial progress has been made in the roll-out of the recommended screening programme for cervical cancer across Member States.

The European Partnership for Action Against Cancer (EPAAC), launched in 2009, was a joint action between the European Commission, Member States, and relevant stakeholders.[65] It advocated for the adoption of integrated national cancer plans by all Member States by 2013; plans which included screening initiatives for diseases like cervical cancer.

As part of the EU's strategy on cervical cancer prevention, guidelines have also been issued on the use of HPV vaccines for young girls. The European Centre for Prevention and Disease Control (ECDC) issued a guidance document in 2008, promoting the use of the vaccine and laying out the optimal strategy for its delivery in Member States.[66] It stated that school-based delivery for the HPV vaccine represented the most cost-effective and feasible strategy. In addition, this strategy was recommended as it would facilitate the monitoring of vaccine uptake. It was not recommended that vaccination replace national cervical cancer screening programmes; such screening is required even where vaccination has taken place. The ECDC subsequently conducted the Venice 2 Survey to evaluate the status of HPV and rotavirus (RV) vaccination across Member States;[67] identifying points of similarity among the programmes implemented across countries.

Today, all 31 EEA countries recommend HPV vaccination to some extent, though some (Bulgaria, Czech Republic, Romania) recommend it for specific groups only.[68] Every country, with the exception of Bulgaria, funds the vaccine through their national health service, though the ages for which the vaccines are recommended and funded vary across country.

With many demands on national healthcare systems, the biggest barrier to the implementation of population-based cervical cancer screening programmes remains cost. Many Member States still suffer from budgetary constraints which were occasioned or exacerbated by the recession which began in Europe in 2007. Putting in place a comprehensive cervical cancer prevention strategy therefore requires that Member States make the elimination of preventable cervical cancer a national priority. As always, mustering the political will for action and for sustained financial resources will be necessary.

## Steps for policy action

1. **Improve existing EU data collection to track incidence and mortality of cervical cancer.**
   Annually collect data on the prevalence and incidence of cervical cancer, disaggregating by age in order to fully understand trends. Existing comparable data for all Member States that is freely available is not up-to-date. A robust comparable monitoring system to track cervical cancer incidence and mortality across the EU Member States should be set up at the EU-level.

2. **Increase awareness among women of the necessity of being screened for cervical cancer.**
   Women suffering from cervical cancer often do not experience symptoms in the early stages of the disease. Like other cancers, catching cervical cancer early leads to better outcomes for sufferers of the disease. It is important then that women not wait until they experience symptoms to be tested for the disease. Even in Member States with population-based screening programmes, coverage is not 100%. Member States must do more to persuade women that it is necessary to enter screening programmes.

3. **Efforts must be taken in order to reduce health inequities with regard to cervical cancer within and across Member States.**
   The EU together with the Member States and key stakeholders—including health organisations, patient organisations, and other relevant stakeholders—must encourage and support improved education, research, prevention, screening, and treatment guidelines. Europe must also provide guidance and support in to order to reduce health inequalities across Member States.

4. **Strategies must be developed so that HPV vaccination programmes will reach vulnerable and marginalized young girls, and that vulnerable women are included in cervical cancer screening programmes.**
   While school-based HPV vaccination programmes have many benefits associated with them (not least with respect to cost), Member States must ensure that additional strategies are put in place to reach vulnerable young girls whose irregular attendance may mean that they are excluded from any vaccination programme delivered at school. Similarly, vulnerable women who have irregular contact with medical professionals may fail to be captured by cervical cancer screening programmes. Strategies to reach these women who may also form part of the high-risk population for cervical cancer should be investigated and deployed.

5. **The benefits of co-testing (performing a Pap smear and a HPV test) in a European context as the basis of a national screening programme for cervical cancer should be investigated.**
   Existing research in an American context indicates that co-testing enables the frequency of screening to be reduced (from 3 to 5 years), as well as representing a more robust test of cervical health. In particular, the impact of co-testing on the cost of population-based national screening programmes should be investigated.

**A warm thank you to our expert reviewers:**

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*December 2017*

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