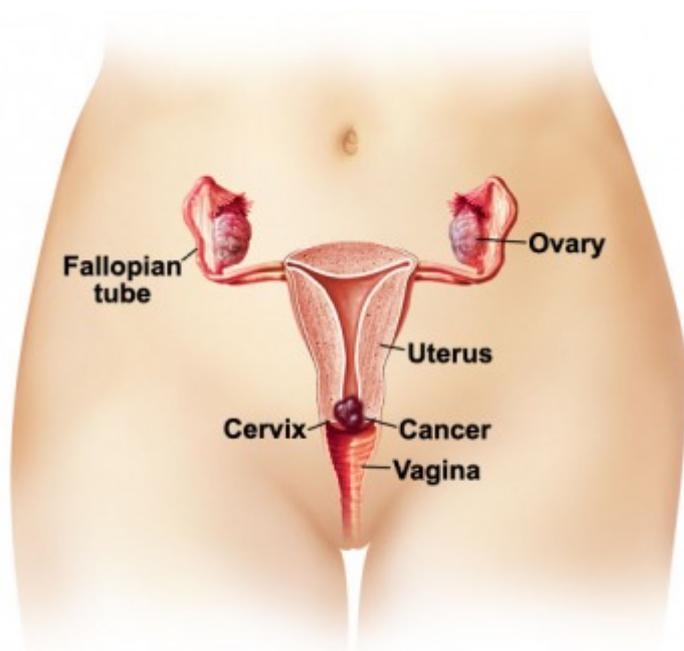


What is cervical cancer?

Cervical cancer is a term used for a tumour that starts in the cervix – where the uterus (womb) meets the vagina (birth canal). The cells of the cervix don't suddenly turn into cancer; they progress slowly through a series of changes that eventually leads to cancer. These precancerous changes in the cells can be detected during a cervical smear (sometimes called a Pap smear), which is why regular cervical smears are recommended and funded for all New Zealand women aged 20 to 70 years. Sometimes, the precancerous cells turn back into normal cells, but others will turn into cancer. Because it's impossible to tell which ones will turn into cancer and which ones won't, it is important for all abnormal smear results to be followed up.



Cervical cancer in New Zealand

Cervical cancer is less common than many other types of cancer affecting women.¹ It is estimated that approximately 165 women a year are diagnosed with cervical cancer, compared with almost 2900 diagnosed with breast cancer and around 450 diagnosed with uterine cancer.¹ This is because the national screening programme, which was introduced in 1991, has been very effective at finding early cases of cervical cancer in New Zealand women, resulting in a decrease in the number of cervical cancer cases by around 40%.² In recent years, 80% of the women who develop cervical cancer in New Zealand have not been having regular smears.³

Who is most at risk of getting cervical cancer?

Cervical cancer can develop in any woman, but tends to occur more often in women under the age of 50 years. Although there are several things that may increase the risk of cervical cancer, the most important is infection with the human papillomavirus (HPV). There are many types of HPV, some of which cause warts on the skin. HPV infection is very common, and most people don't develop any symptoms or warts when they have been infected. HPVs are spread by skin-to-skin contact, including during sex. Certain HPVs place people at high risk of developing cancer – this includes cancer of the

cervix, vulva or vagina in women, and of the penis in men. They can also cause cancers of the anus, mouth, and throat of both men and women. About two-thirds of cervical cancer cases are caused by HPV 16 and HPV 18. People who have had the vaccination against HPV (Gardasil) have a significantly lower risk of developing cervical cancer.

Your risk of cervical cancer may also be increased if your mother or sister has had cervical cancer, if you had your first full-term pregnancy when you were younger than 17 years old, you have had a Chlamydia infection, or are HIV-positive.

Several lifestyle factors also increase the risk of developing cervical cancer:

- Smoking
- A diet low in fruits and vegetables
- Obesity
- Long-term use of oral contraceptive pills.

What are the symptoms of cervical cancer?

The precancerous changes to the cells in the cervix do not generally cause any symptoms. Often, the symptoms of cervical cancer only appear when the cancer has started to grow into the tissues around the cervix.

The most common symptoms of cervical cancer include:

- Abnormal vaginal bleeding, including:
 - Bleeding after sexual intercourse
 - Bleeding after menopause
 - Spotting or bleeding between periods
 - Periods that are longer or heavier than they normally are.
- Vaginal discharge – may contain blood and occur between periods or after menopause
- Pain during sexual intercourse.

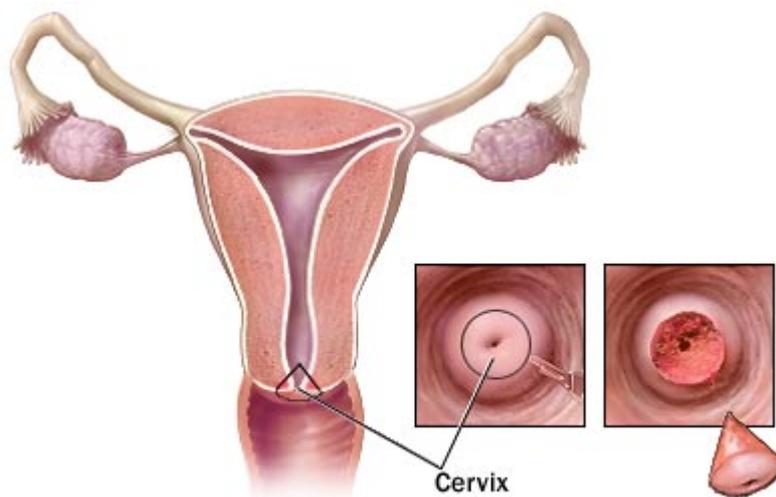
It is important to get any possible symptoms of cervical cancer checked by a doctor. Better still, ensure you are enrolled in the National Screening Programme and have regular cervical smears.

How is cervical cancer diagnosed?

Regular screening can find cervical cancer early before the onset of symptoms, when it is most likely to be curable. In many women, screening can prevent cervical cancer altogether by allowing precancerous changes to be found and removed before they turn into cancer.

If your smear shows the presence of abnormal cells, your doctor will recommend that you have a colposcopy. During this test, a doctor will examine your cervix using a colposcope inserted into the vagina. The colposcope allows the doctor to see a magnified image of the cervix, so they can closely examine the tissue, and identify any abnormal areas. If an abnormal area is found, the doctor will remove a small piece of tissue (a biopsy) and send it to a pathologist to examine under a microscope. Colposcopy is not usually painful, but some people find the removal of the tissue sample causes discomfort and pain.

Sometimes, the abnormal area may be difficult to see (possibly because it's on the inside surface of the cervix) so the doctor will use other techniques called endocervical curettage (scraping cells from the inside of the cervix) or conisation to obtain the biopsy sample. Conisation or cone biopsy involves removal of a cone-shaped piece of tissue from the cervix, and is often also used to treat pre-cancers.



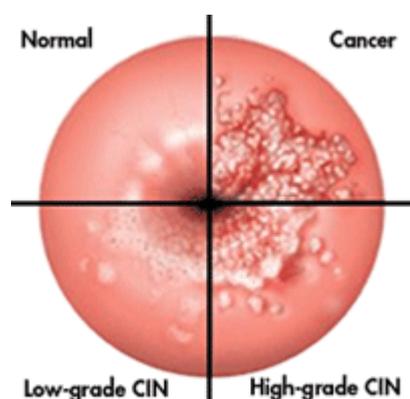
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For most people, cervical cancer is identified early, and no further tests are required. However, if it is not, you may need to undergo more thorough examination or have scans (like a computed tomography [CT] or magnetic resonance imaging [MRI] scan) to see if the cancer has spread to surrounding tissues, such as the uterus, bladder or bowel.

How is cervical cancer staged?

Precancerous changes to the cervix are called cervical intraepithelial neoplasia or CIN. Depending on how abnormal or widespread the cells are they may be classified as:

- CIN1 – a small amount of tissue looks abnormal; this is the least serious form of precancer
- CIN2 – a moderate amount of tissue looks abnormal
- CIN3 – most of the tissue looks abnormal; this is the most serious form of precancer and includes *carcinoma in situ*.



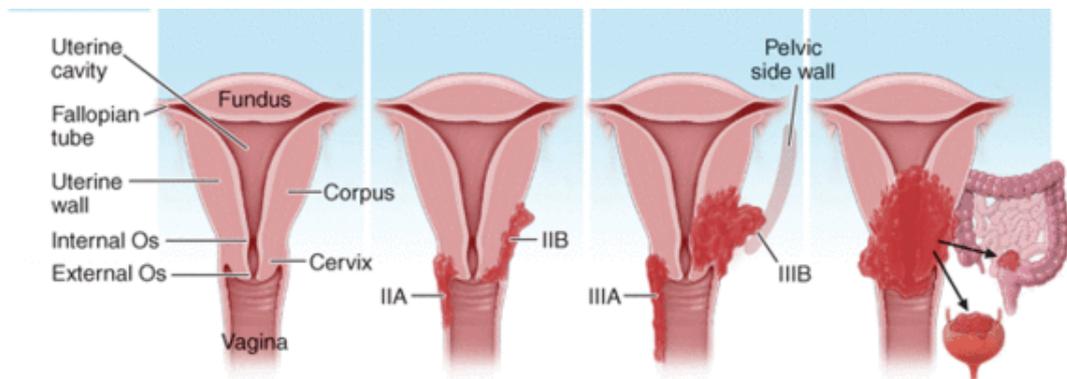
If the biopsy finds a cancer, the pathologist will determine whether it is a squamous cell carcinoma or adenocarcinoma. Based on information from the tests, the cancer is then staged which helps the doctors to decide which form of treatment is most appropriate for you.

The stages of cervical cancer are:

- Stage 0 – the cancer is only affecting cells on the surface of the cervix, and is not growing any deeper. This stage is also called *carcinoma in situ* (CIS), which is a form of CIN3.
- Stage I – the cancer has grown into the tissues of the cervix, but hasn't spread beyond the uterus or into nearby lymph nodes
- Stage II – the cancer has grown beyond the cervix and uterus, but hasn't spread into the walls of the pelvis or the lower part of the vagina
- Stage III – the cancer has spread to the walls of the pelvis and the lower part of the vagina, and may be blocking the ureters (tubes that carry urine to the bladder from the kidneys), but has not spread to nearby lymph nodes or other parts of the body yet
- Stage IV – the cancer has spread to nearby organs or other parts of the body.

Staging of cervix cancer

Stage	0	I	II	III	IV
Extent of tumor	Carcinoma in-situ	Confined to cervix	Disease beyond cervix but not to pelvic wall or lower 1/3 of vagina	Disease to pelvic wall or lower 1/3 vagina	Invades bladder, rectum or metastasis



How is cervical cancer treated?

The type of treatment your doctor recommends will depend largely on the stage of your cancer. The main types of treatment that can be used for cervical cancer are:

- Surgery
- Radiation therapy
- Chemotherapy
- Biologic therapies

For cervical cancer that has not spread, conisation or surgery to remove the cancer is usually the main treatment. In some women, surgery may involve removal of the uterus (hysterectomy). Radiation therapy, with or without chemotherapy, can also be given to kill any cancer cells that were not removed by the surgery. This may involve external beam radiation, where the x-rays are aimed at the tumour from outside the body, or internal radiation (brachytherapy) where the device that emits the radiation is placed inside the vagina.

Sometimes, the recommended treatment for cervical cancer is a combination of radiation therapy and chemotherapy. The two treatments are used together because the chemotherapy makes the radiation more effective. Chemotherapy can also be given without radiotherapy, either before or after the chemoradiation, or if the cancer has come back after treatment or has spread to other organs and tissues.

Standard chemotherapy kills cells that are dividing. Because cancer cells divide more quickly than healthy cells, chemotherapy has most effect on these cells, but this form of treatment also kills some healthy cells, causing side effects. Biologic drugs work differently to standard chemotherapy, because they are able to target cancer cells specifically, and mostly leave healthy cells alone. Biologic drugs are often used with chemotherapy, but they can also be used by themselves if chemotherapy is no longer working.

Avastin® (bevacizumab) is a biologic anti-cancer agent that is registered in New Zealand for use in combination with chemotherapy to treat persistent, recurrent, or metastatic cervical cancer.⁴ It works by blocking the development of new blood vessels in the tumour; limiting the cancer's blood supply helps to stop it from growing. Avastin is not currently funded, so you must pay for this treatment yourself. You can ask your oncologist whether you might benefit from Avastin, and how much you can expect to pay for treatment.

References

1. Ministry of Health. 2014. Cancer: New registrations and deaths 2011. Wellington: Ministry of Health. Available from: <http://www.health.govt.nz/system/files/documents/publications/cancer-new-registrations-deaths-2011-v4sept14.pdf> . Accessed April 2015.
2. Ministry of Health 2007. High grade squamous intra-epithelial lesions (HSIL) in New Zealand. Wellington: Ministry of Health, National Cervical Screening Programme, National Screening Unit. March 2007.

3. Lewis H, Yeh L-C, Almendral B, Neal H. Monitoring the performance of New Zealand's National Cervical Screening Programme through data linkage. *NZ Med J* 2009;122(1305):
4. Avastin (bevacizumab) Data Sheet. 13 April 2015. Available from: <http://www.medsafe.govt.nz/profs/datasheet/a/Avastininf.pdf>

Avastin[®] (bevacizumab), 100 mg/4mL and 400 mg/16 mL vials, is a **Prescription Medicine** used to treat metastatic (spreading) colorectal, kidney, breast, brain, lung, ovarian and cervical cancers. **Do not use Avastin if:** you have had an allergic reaction to Avastin, any of its ingredients or other antibodies, or if you have been coughing or spitting up blood. **Tell your doctor if:** you are pregnant or breast-feeding, or plan to become pregnant or breast-feed; you have any other health problems, especially the following: inflammation of the bowel or stomach ulcers, high blood pressure, a history of blood clots or stroke, bleeding problems, bleeding in the lungs or coughing or spitting up blood, low white blood cell counts, you have/ had a fistula, or have a history of diabetes; you have had major surgery in the last 28 days or a wound that has not healed properly; you have had a blocked lung artery (pulmonary embolism); you have heart disease; you have received anthracyclines (e.g. doxorubicin) for cancer, or radiotherapy to your chest; you are 65 years of age or older, or you are taking any other medicines.

Tell your doctor immediately or go to your nearest Accident and Emergency Centre if you notice any of the following: severe body or stomach pain or cramps; severe headache; severe diarrhoea, nausea and vomiting; loss of control of your bladder or bowels; passage of wind or bowel motions through the vagina; coughing or spitting up blood; pain, redness, swelling and warmth over a vein which may suggest blood clots; pain and/or swelling in the lower legs, feet or hands; severe bleeding or problems with your wounds healing after surgery; seizures; confusion; sleepiness/drowsiness or fainting; abscesses (pus-filled sores); severe infection with high fever, chills, headache, confusion and rapid breathing; feeling of numbness or tingling in feet or hands; dry mouth with thirst and/or darkened urine; increased heart rate; shortness of breath; symptoms of an allergic reaction which may include shortness of breath, wheezing or difficulty breathing, swelling of the face, lips, tongue or other parts of the body, or rash, itching or hives on the skin. **Possible common side-effects may also include:** high blood pressure (symptoms include, headache, dizziness, ringing in the ears, tiredness, blurred vision); body pain, tiredness/ weakness; diarrhoea, constipation or rectal bleeding; sore mouth or mouth ulcers; loss of appetite, being thirsty; shortness of breath; runny, blocked or bleeding nose; dry, scaling or inflamed skin, change in skin colour; taste changes; blurred vision or other eye problems; dizziness; headache; frequent infections with symptoms such as fever, chills or sore throat; changes in your voice or difficulty speaking; loss of body weight; abdominal, pelvic, rectal or back pain.

Avastin has risks and benefits. Ask your oncologist if Avastin is right for you. Use strictly as directed. If symptoms continue or you have side effects, see your healthcare professional. For further information on Avastin, please talk to your health professional or visit www.medsafe.govt.nz for Avastin Consumer Medicine Information.

Avastin is not funded by PHARMAC. You will need to pay the full cost of this medicine. A prescription charge and normal oncologist fees may apply.

Consumer panel dated 23/04/2015 based on CMI dated 13/04/2015.

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