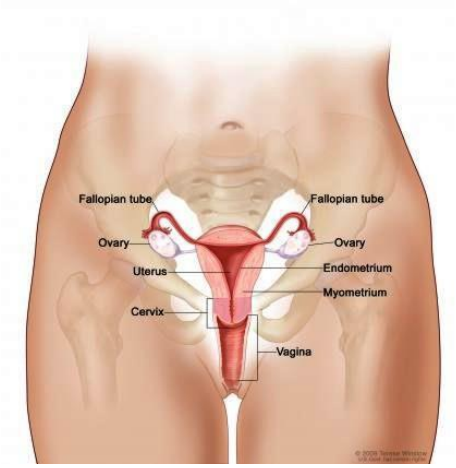
Cancer Association of South Africa (CANSA)

Fact Sheet
On
Ovarian Cancer

Introduction

The ovaries form part of the female reproductive organs that house the ova and are also responsible for the production of sex hormones. The ovaries are paired organs located on either side of the uterus within the broad ligament below the uterine (fallopian) tubes. Each ovary is within the ovarian fossa, a space that is bound by the external iliac vessels, obliterated umbilical artery, and the ureter. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. At birth, a female has approximately 1-2 million ova, but only about 300 of these eggs will ever become mature and be released for the purpose of fertilisation.



[Picture Credit – Ovarian Anatomy]

Ovarian Cancer

Ovarian cancer is cancer of the cells of one or both ovaries.

Cheasley, D., Wakefield, M.J., Ryland, G.L., Allan, P.E., Alsop, K., Amarasinghe, K.C., Ananda, S., Anglesio, M.S., Au-Yeung, G., Böhm, M., Bowtell, D.D.L., Brand, A., Chenevix-Trench, G., Christie, M., Chiew, Y.E., Churchman, M., DeFazio, A., Demeo, R., Dudley, R., Fairweather, N., Fedele, C.G., Fereday, S., Fox, S.B., Gilks, C.B., Gourley, C., Hacker, N.F., Hadley, A.M., Hendley, J., Ho, G.Y., Hughes, S., Hunstman, D.G., Hunter, S.M., Jobling, T.W., Kalli, K.R., Kaufmann, S.H., Kennedy, C.J., Köbel, M., Le Page, C., Li, J., Lupat, R., McNally, O.M., McAlpine, J.N., Mes-Masson, A.M., Mileshkin, L., Provencher, D.M., Pyman, J., Rahimi, K., Rowley, S.M., Salazar, C., Samimi, G., Saunders, H., Semple, T., Sharma, R., Sharpe, A.J., Stephens, A.N., Thio, N., Torres, M.C., Traficante, N., Xing, Z., Zethoven, M., Antill, Y.C., Scott, C.L., Campbell, I.G. & Gorringe, K.L. 2019. "Mucinous ovarian carcinoma (MOC) is a unique subtype of ovarian cancer with an uncertain etiology, including whether it genuinely arises at the ovary or is metastatic disease from other organs. In addition, the molecular drivers of invasive progression, high-grade and metastatic disease are poorly defined. We perform genetic analysis of MOC across all histological grades, including

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benign and borderline mucinous ovarian tumors, and compare these to tumors from other potential extra-ovarian sites of origin. Here we show that MOC is distinct from tumors from other sites and supports a progressive model of evolution from borderline precursors to high-grade invasive MOC. Key drivers of progression identified are TP53 mutation and copy number aberrations, including a notable amplicon on 9p13. High copy number aberration burden is associated with worse prognosis in MOC. Our data conclusively demonstrate that MOC arise from benign and borderline precursors at the ovary and are not extra-ovarian metastases."

Incidence of Ovarian Cancer in South Africa

According to the outdated National Cancer Registry (2017) the following number of ovarian cancer cases was histologically diagnosed in South Africa during 2017:

Group - Females 2017	No of Cases	Lifetime Risk	Percentage of All Cancer
All females	590	1:391	1,42%
Asian females	23	1:347	1,79%
Black females	203	1:804	1,07%
Coloured females	68	1:358	1,45%
White females	296	1:122	1,75%

The frequency of histologically diagnosed cases of ovarian cancer in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Females 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	19	18	42	90	139	165	94	23
Asian females	1	0	1	8	7	5	1	0
Black females	12	14	21	36	47	51	19	3
Coloured females	1	2	2	10	22	18	10	3
White females	5	2	18	36	63	91	64	17

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Causes of Ovarian Cancer

It is not clear what causes ovarian cancer. In general, cancer begins when healthy cells acquire a genetic mutation that turns normal cells into abnormal cells. Healthy cells grow and multiply at a set rate, eventually dying at a set time. Cancer cells grow and multiply out of control, and they do not die. The accumulating abnormal cells form a mass (tumour).

Risk Factors for Ovarian Cancer

The risk for developing ovarian cancer appears to be affected by several factors:

- The more children a woman has and the earlier in life she gives birth, the lower her risk for ovarian cancer
- Certain genes defects (BRCA1 and BRCA2) are responsible for a small number of ovarian cancer cases. Women with a personal history of breast cancer or a family history of breast or ovarian cancer have an increased risk for ovarian cancer

- Women who take oestrogen replacement only (not with progesterone) for 5 years or more seem to have a higher risk of ovarian cancer
- Birth control pills decrease the risk of ovarian cancer.
- Being infertile or having fertility treatment
- Using a coil (intra-uterine device (IUD)
- Older women are at highest risk for developing ovarian cancer. Most deaths from ovarian cancer occur in women age 55 and older
- Research suggests that the risk of ovarian cancer is slightly higher for women who:
- have medical conditions such as endometriosis
    - smoke tobacco products
    - are obese
    - are tall

Caution Expressed Around Consumption of Foods High in Phytoestrogens by Individuals Diagnosed with a Hormone-Sensitive Cancer

The Cancer Association of South Africa (CANSA) has noted:

- A statement by Memorial Sloan Kettering Cancer Center saying that "… because compounds isolated from rooibos leaves demonstrated estrogenic activity, patients with hormone-sensitive cancers should use caution before taking rooibos." (Memorial Sloan Kettering Cancer Center).

- That phytoestrogens were successfully isolated from rooibos leaves by scientists from the School of Pharmaceutical Sciences, University of Shizuoka, Japan (Shimamura, *et al.*, 2006).

- That according to Deng, et al., (2010), "… there are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. Based on current evidence, we propose recommendations for advising breast cancer patients, …"

- That, according to Nelles, Hu & Prins (2011), "Early work on the hormonal basis of prostate cancer focused on the role of androgens, but more recently estrogens have been implicated as potential agents in the development and progression of prostate cancer."

- That, according to Reger, *et al*., (2016), "Experimental studies suggest that phytoestrogen intake alters cancer and cardiovascular risk. Some urinary phytoestrogens were associated with cardiovascular and all-cause mortality in a representative sample of 5 179 participants. This is one of the first studies that used urinary phytoestrogens as biomarkers of their dietary intake to evaluate the effect of these bioactive compounds on the risk of death from cancer and cardiovascular disease."

CANSA, therefore, wishes to advise individuals diagnosed with the following hormone-sensitive cancers, namely: Breast Cancer, Ovarian Cancer, Endometrial Cancer, and Prostate Cancer, to:

- use caution before taking Rooibos tea and to discuss the issue around Rooibos tea consumption with their treating Oncologist prior to consuming Rooibos tea
- also use caution before taking the following high phytoestrogen-containing foods: all soy foods (including soybeans, tofu, miso, and tempeh); legumes (especially lentils, peanuts and chickpeas) and flaxseed-containing foods. Patients are advised to discuss consumption of the listed high phytoestrogen-containing foods with their treating Oncologist prior to consuming them.

Research on Foods High in Phytoestrogens and Breast Cancer

Deng, G., Davatgarzadeh, A., Yeung, S. & Cassileth, B. 2010. Phytoestrogens: science, evidence, and advice for breast cancer patients. *Soc Integr Oncol*. 2010 Winter;8(1):20-30.
"There are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancerpatients with hormone-sensitive disease. However, no consensus has been reached concerning specific dietary items that should be avoided, and safe levels of potentially problematic foods have yet to be determined. Excellent qualitative reviews of phytoestrogens and breast cancerhave been published. These list agents that contain phytoestrogens and offer general cautions. Quantitative reviews, however, are needed but not yet available. Here we review quantitative data on phytoestrogens, their interaction with estrogen receptors, their bioavailability and pharmacokinetics, and their effects on breast cancer cells and animal models. We also note foods and botanicals with substances that interact with estrogen receptors and discuss the phytoestrogens they contain. Based on current evidence, we propose recommendations for advising breast cancer patients, which may also serve as a basis for the development of clinical practice guidelines."

Patisaul, H. & Jefferson, W. 2010. The pros and cons of phytoestrogens. *Front Neuroendocrinol*.. Author manuscript; available in PMC 2011 Apr 12.
Phytoestrogens are plant derived compounds found in a wide variety of foods, most notably soy. A litany of health benefits including a lowered risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, are frequently attributed to phytoestrogens but many are also considered endocrine disruptors, indicating that they have the potential to cause adverse health effects as well. Consequently, the question of whether or not phytoestrogens are beneficial or harmful to human health remains unresolved. The answer is likely complex and may depend on age, health status, and even the presence or absence of specific gut microflora. Clarity on this issue is needed because global consumption is rapidly increasing. Phytoestrogens are present in numerous dietary supplements and widely marketed as a natural alternative to estrogen replacement therapy. Soy infant formula now constitutes up to a third of the US market, and soy protein is now added to many processed foods. As weak estrogen agonists/antagonists with molecular and cellular properties similar to synthetic endocrine disruptors such as Bisphenol A (BPA), the phytoestrogens provide a useful model to comprehensively investigate the biological impact of endocrine disruptors in general. This review weighs the evidence for and against the purported health benefits and adverse effects of phytoestrogens.

Rodriquez-Garcia, C., Sánchez-Quesada, C., Toledo, E., Delgado-Rodriquez, M. & Gaforio, J.J. 2019.
"Dietary guidelines universally advise adherence to plant-based diets. Plant-based foods confer considerable health benefits, partly attributable to their abundant micronutrient (e.g., polyphenol) content. Interest in polyphenols is largely focused on the contribution of their antioxidant activity to the prevention of various disorders, including cardiovascular disease and cancer. Polyphenols are

classified into groups, such as stilbenes, flavonoids, phenolic acids, lignans and others. Lignans, which possess a steroid-like chemical structure and are defined as phytoestrogens, are of particular interest to researchers. Traditionally, health benefits attributed to lignans have included a lowered risk of heart disease, menopausal symptoms, osteoporosis and breast cancer. However, the intake of naturally lignan-rich foods varies with the type of diet. Consequently, based on the latest humans' findings and gathered information on lignan-rich foods collected from Phenol Explorer database this review focuses on the potential health benefits attributable to the consumption of different diets containing naturally lignan-rich foods. Current evidence highlight the bioactive properties of lignans as human health-promoting molecules. Thus, dietary intake of lignan-rich foods could be a useful way to bolster the prevention of chronic illness, such as certain types of cancers and cardiovascular disease."

Ovarian Cancer and Use of Talc

There have been several lawsuits in the United States of America against the manufacturer of a popular brand of baby powder which contains talc. Retrospective research was conducted by Cramer, *et al*. (2016). They concluded that multiple studies of ovarian cancer and genital talc use have led only to consensus about possible carcinogenicity. Risks for epithelial ovarian cancer from genital talc use vary by histologic subtype, menopausal status at diagnosis, hormone therapy use, weight, and smoking. These observations suggest that oestrogen and/or prolactin may play a role via macrophage activity and inflammatory response to talc.

Kadry Taher, M., Farhat, N., Karyakina, N.A., Shilnikova, N., Ramoju, S., Gravel, C.A., Krishnan, K., Mattison, D., Wen, S.W. & Krewski, D. 2019.

Over the past four decades, there has been increasing concern that perineal use of talc powder, a commonly used personal care product, might be associated with an increased risk of ovarian cancer.
OBJECTIVES: To critically review all available human epidemiological data on the relationship between perineal use of talc powder and ovarian cancer, with consideration of other relevant experimental evidence.
METHODOLOGY: We identified 30 human studies for qualitative assessment of evidence, including 27 that were retained for further quantitative analysis.
RESULTS: A positive association between perineal use of talc powder and ovarian cancer was found [OR: 1.28 (95% CI: 1.20 - 1.37)]. A significant risk was noted in Hispanics and Whites, in women applying talc to underwear, in pre-menopausal women and in post-menopausal women receiving hormonal therapy. A negative association was noted with tubal ligation.
CONCLUSION: Perineal use of talc powder is a possible cause of human ovarian cancer.

Protective Factors for Ovarian Cancer

There's currently nothing that can be done to prevent ovarian cancer. However, there are some things that are thought to protect against ovarian cancer. These are called protective factors. Women with protective factors may still develop ovarian cancer.

Getting enough vitamin D may reduce your risk of developing a number of cancers, including ovarian cancer – although more research needs to be done to be certain.

Research has shown that the following may be associated with a reduced risk of certain types of ovarian cancer:

- Women who have never given birth are more likely to develop ovarian cancer than those who have biological children. The risk seems to decrease with every pregnancy. Breastfeeding may also decrease risk.
- Women who have taken birth control pills have a lower risk of ovarian cancer. Taking the pill for at least five years reduces a women's risk by about 50%. Birth control pills and pregnancy both stop ovulation, and some researchers think that less frequent ovulation lowers the risk of ovarian cancer.
- Tubal ligation (having one's tubes tied) or having a hysterectomy while leaving the ovaries intact may both offer some protection against ovarian cancer.
- Removal of the ovaries is an option for women with genetic mutations that increase their cancer risk. This option can also be considered for women over 40 who are undergoing a hysterectomy.
- No definitive dietary changes have been shown to prevent ovarian cancer. Nevertheless, a study showed that women who consumed a low-fat diet for at least 4 years had a lower risk of ovarian cancer. Other studies showed that ovarian cancer may be less common in women who consume a lot of vegetables. More studies, however, are needed to clarify any relationship between diet and ovarian cancer.

Prophylactic Oophorectomy

Prophylactic oophorectomy may significantly reduce one's odds of developing breast cancer and ovarian cancer if one is at high risk. One should weigh the pros and cons of this cancer-prevention option in collaboration with an oncology geneticist and a medical practitioner.

Who can consider prophylactic oophorectomy?

Prophylactic oophorectomy is usually reserved for women with a significantly increased risk of breast cancer and ovarian cancer due to an inherited mutation in the BRCA1 or BRCA2 gene - two genes linked to breast cancer, ovarian cancer and other cancers. Women who have inherited mutations and have completed childbearing are the best candidates for this surgery.

Prophylactic oophorectomy may also be recommended if one has a strong family history of breast cancer and ovarian cancer but no known genetic alteration. It might also be recommended if one has a strong likelihood of carrying the gene mutation based on one's family history but choose not to proceed with genetic testing.

Women who are at risk, could consider this procedure as follows:

- Having a BRCA1 gene mutation: age 35 to 40
- Having a BRCA2 gene mutation: age 45 and older

Types of Ovarian Cancer

The type of cell where the cancer begins determines the type of ovarian cancer you have. Ovarian cancer types include:

- Cancer that begins in the cells on the outside of the ovaries. Called epithelial tumours, these cancers begin in the thin layer of tissue that covers the outside of the ovaries. Most ovarian cancers are epithelial tumours
- Cancer that begins in the egg-producing cells. Called germ cell tumours, these ovarian cancers tend to occur in younger women
- Cancer that begins in the hormone-producing cells. These cancers, called stromal tumours, begin in the ovarian tissue that produces the hormones oestrogen, progesterone and testosterone
- The type of ovarian cancer you have helps determine your prognosis and treatment options

Symptoms of Ovarian Cancer

Many ovarian cancer symptoms mimic those of less life-threatening conditions such as irritable bowel syndrome. These symptoms may include:

- Bloating
- Pelvic or abdominal pain
- Urinary urgency or frequency
- Difficulty eating or feeling full quickly

Further Late Stage Symptoms of Ovarian Cancer

- Spread of the cancer to other organs
- Loss of organ function
- Fluid in the abdomen (ascites)
- Blockage of the intestines

Early Detection of Ovarian Cancer

Early detection of ovarian cancer saves women's lives. No screening test exists that can test all women for ovarian cancer. The Pap test does not test for ovarian cancer; it screens for cervical cancer.

Nash, Z. & Menon, U. 2020.

"Ovarian cancer is the third most common gynaecological malignancy and the most lethal worldwide. Most patients are diagnosed with advanced disease which carries significant mortality. Improvements in treatment have only resulted in modest increases in survival. This has driven efforts to reduce mortality through screening. Multimodal ovarian cancer screening using a longitudinal CA125 algorithm has resulted in diagnosis at an earlier stage, both in average and high risk women in two large UK trials. However, no randomised controlled trial has demonstrated a definitive mortality benefit. Extended follow up is underway in the largest trial to date, UKCTOCS, to explore the delayed reduction in mortality that was noted. Meanwhile, screening is not currently recommended in the general population Some countries offer surveillance of high risk women. Novel screening modalities and longitudinal biomarker algorithms offer potential improvements to future screening strategies as does the development of better risk stratification tools."

Amin, N., Chaabouni, N. & George, A. 2020.
"As the treatment of epithelial ovarian cancer (OC) moves further into personalised medicine, the importance of determining the presence or absence of inherited mutations in cancer susceptibility genes has grown. It is now becoming routine to test for germline mutations in the BRCA1 and BRCA2 genes, which are responsible for a significant proportion of hereditary epithelial OC and are established predictive biomarkers of potential benefit from poly ADP ribose polymerase (PARP) inhibitors. The identification of patients with hereditary OC allows the patient to benefit from personalised treatment, while allowing family members to undergo cascade testing, where identification of unaffected carriers can allow early detection, risk-reduction or prevention for both breast and OC, and ultimately improve long-term outcomes. Other susceptibility genes, include the Lynch Syndrome (mismatch repair) genes and several other genes involved in the homologous recombination pathway (HRD genes), are implicated in OC genesis, and are also becoming of increasing interest as therapeutic options grow for these patients. This review will highlight the importance of the early detection of a germline gene pathogenic variant, which informs on the clinical course of disease in a particular patient, and therefore, guides therapeutic management including risk reducing and personalised treatment."

Diagnosis of Ovarian Cancer
In someone showing the symptoms mentioned above, the doctor may order one or more of the following tests:

Ultrasound - Ultrasound (ultrasonography) is the use of sound waves to create an image on a video screen. Sound waves are released from a small probe placed in the woman's vagina or on the surface of her abdomen. The sound waves create echoes as they enter the ovaries and other organs. The same probe detects the echoes that bounce back, and a computer translates the pattern of echoes into a picture.

Computed Tomography - The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied.

Barium Enema X-ray - This is a test to see whether the cancer has invaded the colon (large intestine) or rectum (it is also used to look for colorectal cancer). After taking laxatives the day before, the radiology technician puts barium sulphate, a chalky substance, into the rectum and colon. Because barium is impermeable to x-rays (impossible for x-rays to go through), it outlines the colon and rectum on x-rays of the abdomen.

Magnetic Resonance Imaging - MRI scans use radio waves and strong magnets instead of X-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body.

Chest X-ray - This procedure may be done to determine whether ovarian cancer has spread (metastasized) to the lungs.

Positron Emission Tomography (PET scan) - In this test, radioactive glucose (sugar) is given to look for the cancer. Because cancers use glucose (sugar) at a higher rate than normal tissues, the radioactivity will tend to concentrate in the cancer. A scanner can spot the radioactive deposits.

Baranim M,, Bilalm M,, Sabirm F,, Rahdarm A, & Kyzas, G.Z. 2021.
"To overcome the drawbacks of conventional delivery, this review spotlights a number of nanoscale drug delivery systems, including nanoparticles, liposomes, nano micelles, branched dendrimers, nanocapsules, and nanostructured lipid formulations for the targeted therapy of ovarian cancer. These nanoformulations offer numerous advantages to promote therapeutic drug delivery such as nontoxicity, biocompatibility, good biodegradability, increased therapeutic impact than free drugs, and non-inflammatory effects. Importantly, the development of specific ligands functionalized nanoformulations enable preferential targeting of ovarian tumors and eventually amplify the therapeutic potential compared to nonfunctionalized counterparts. Ovarian cancer is typically identified by biomarker assessment such as CA125, HE4, Mucin 1, and prostatic. There is, nevertheless, a tremendous demand for less costly, faster, and compact medical tools, both for timely detection and ovarian cancer control. This paper explored multiple types of tumor marker-based on nanomaterial biosensors. Initially, we mention different forms of ovarian cancer biomarkers involving CA125, human epididymis protein 4 (HE4), mucin 1 (MUC1), and prostate. It is accompanied by a brief description of new nanotechnology methods for diagnosis. Nanobiosensors for evaluating ovarian cancer biomarkers can be categorized based on electrochemical, optical, paper-based, giant magnetoresistive, and lab-on-a-chip devices."

Konstantinopoulos, P.A., Norquist, B., Lacchetti, C., Armstrong, D., Grisham, R.N., Goodfellow, P.J., Kohn, E.C., Levine, D.A., Liu, J.F., Lu, K.H., Sparacio, D. & Annunziata, C.M. 2020.
PURPOSE: To provide recommendations on genetic and tumor testing for women diagnosed with epithelial ovarian cancer based on available evidence and expert consensus.
METHODS: A literature search and prospectively defined study selection criteria sought systematic reviews, meta-analyses, randomized controlled trials (RCTs), and comparative observational studies published from 2007 through 2019. Guideline recommendations were based on the review of the evidence.
RESULTS: The systematic review identified 19 eligible studies. The evidence consisted of systematic reviews of observational data, consensus guidelines, and RCTs.
RECOMMENDATIONS: All women diagnosed with epithelial ovarian cancer should have germline genetic testing for *BRCA1/2* and other ovarian cancer susceptibility genes. In women who do not carry a germline pathogenic or likely pathogenic *BRCA1/2* variant, somatic tumor testing for *BRCA1/2* pathogenic or likely pathogenic variants should be performed. Women with identified germline or somatic pathogenic or likely pathogenic variants in *BRCA1/2* genes should be offered treatments that are US Food and Drug Administration (FDA) approved in the upfront and the recurrent setting. Women diagnosed with clear cell, endometrioid, or mucinous ovarian cancer should be offered somatic tumor testing for mismatch repair deficiency (dMMR). Women with identified dMMR should be offered FDA-approved treatment based on these results. Genetic evaluations should be conducted in conjunction with health care providers familiar with the diagnosis and management of hereditary cancer. First- or second-degree blood relatives of a patient with ovarian cancer with a known germline pathogenic cancer susceptibility gene variant should be offered individualized genetic risk evaluation, counseling, and genetic testing. Clinical decision making should not be made based on a variant of uncertain significance. Women with epithelial ovarian cancer should have testing at the time of diagnosis.

Staging of Ovarian Cancer
Staging of ovarian cancer is done as it assists the oncologist in deciding treatment.

Where Ovarian Cancer May Spread to in the Body
Should ovarian cancer spread (metastasise) in the body, it would most probably spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

Treatment of Ovarian Cancer
Treatment for ovarian cancer usually involves a combination of surgery and chemotherapy. Less often, treatment may include radiotherapy. The type of treatment women receive depends on the type and stage of their ovarian cancer and their general health. Treatment is best managed by a gynaecological oncologist.

Surgery
Nearly all women who have ovarian cancer will require surgery. Sometimes, it is not possible to confirm the stage of the cancer until the surgery.

Chemotherapy
Chemotherapy involves using anti-cancer (cytotoxic) drugs to kill cancer cells. It is often given after surgery for ovarian cancer. In some cases, it can be given before surgery as it may help to shrink the tumour and make it easier to remove. This is called neo-adjuvant chemotherapy.

Radiotherapy
Radiotherapy uses high energy X-rays. Like chemotherapy, it works by targeting rapidly growing cancer cells. Radiotherapy is not often used to treat ovarian cancer. But occasionally, the multidisciplinary team may recommend it for ovarian cancer treatment under very specific circumstances, such as treating pain and bleeding from a localised tumour mass.

Mirza, M.R., Coleman, R.L., González-Martín, A., Moore, K.N., Colombo, N., Ray-Coquard, I. & Pignata, S. 2020.

Background: In recurrent ovarian cancer, poly(ADP-ribose) polymerase (PARP)-inhibiting agents have transformed the treatment of platinum-sensitive disease. New data support use of PARP inhibitors earlier in the treatment algorithm.
Design: We review results from recent phase III trials evaluating PARP inhibitors as treatment and/or maintenance therapy for patients with newly diagnosed ovarian cancer. We discuss the efficacy and safety of these agents in the all-comer and biomarker-selected populations studied in clinical trials, and compare the strengths and limitations of the various trial designs. We also consider priorities for future research, with a particular focus on patient selection and future regimens for populations with high unmet need.
Results: Four phase III trials (SOLO-1, PAOLA-1/ENGOT-OV25, PRIMA/ENGOT-OV26 and VELIA/GOG-3005) demonstrated remarkable improvements in progression-free survival with PARP inhibitor therapy (olaparib, niraparib or veliparib) for newly diagnosed ovarian cancer. Differences in trial design (treatment and/or maintenance setting; single agent or combination; bevacizumab or no bevacizumab), patient selection (surgical outcome, biomarker eligibility, prognosis) and primary analysis population (intention-to-treat, BRCA mutated or homologous recombination deficiency positive) affect the conclusions that can be drawn from these trials. Overall survival data are pending and there is limited experience regarding long-term safety.
Conclusions: PARP inhibitors play a pivotal role in the management of newly diagnosed ovarian cancer, which will affect subsequent treatment choices. Refinement of testing for patient selection and identification of regimens to treat populations that appear to benefit less from PARP inhibitors are a priority.

Boussios, S., Karihtala, P., Moschetta, M., Abson, C., Karathanasi, A., Zakynthinakis-Kyriakou, N., Ryan, J.E., Sheriff, M., Rassy, E. & Pavlidis, N. 2020.
"Epithelial ovarian cancer (EOC) accounts for nearly 90% of all ovarian malignancies. The standard therapeutic strategy includes cytoreductive surgery and neo (adjuvant) platinum-based chemotherapy. Relapse of advanced high grade serous ovarian cancer (HGSOC) is related to the development of drug resistance. A defective DNA damage response is a defining hallmark of HGSOC. Poly (ADP-ribose) polymerase (PARP) inhibitors exploit this deficiency through synthetic lethality and have emerged as promising anticancer therapies, especially in breast cancer gene (BRCA1 or BRCA2) mutation carriers. Apart from inducing synthetic lethality, PARP inhibitors have also been shown to trap PARP1 and PARP2 on DNA, leading to PARP-DNA complexes. This "PARP trapping" potentiates synergism between PARP inhibition and both alkylating agents and platinum-based chemotherapy. However, there are remarkable differences in the ability of PARP inhibitors to trap PARP, based on the size and structure of each separate molecule. Since monotherapy with PARP inhibitors is unlikely to induce cancer cell death in BRCA-proficient tumors, the efficacy of PARP inhibitors could be potentially optimized when combined with DNA-damaging agents, or with molecular targeted agents that also impair mechanisms of DNA repair. Olaparib, rucaparib, and niraparib have all obtained US Food and Drug Administration (FDA) and/or European Medicines Agency (EMA) approval in ovarian cancer in different settings. Veliparib does not yet have an approved label; nevertheless, there are currently promising results available in preclinical and early clinical settings. This comprehensive review summarizes the mechanism of action of veliparib and provides an overview of its early and ongoing clinical investigations."

Kuroki, L. & Guntupalli, S.R. 2020.
"Ovarian cancer is the third most common gynecologic malignancy worldwide but accounts for the highest mortality rate among these cancers. A stepwise approach to assessment, diagnosis, and treatment is vital to appropriate management of this disease process. An integrated approach with gynecologic oncologists as well as medical oncologists, pathologists, and radiologists is of paramount

importance to improving outcomes. Surgical cytoreduction to R0 is the mainstay of treatment, followed by adjuvant chemotherapy. Genetic testing for gene mutations that affect treatment is the standard of care for all women with epithelial ovarian cancer. Nearly all women will have a recurrence, and the treatment of recurrent ovarian cancer continues to be nuanced and requires extensive review of up to date modalities that balance efficacy with the patient's quality of life. Maintenance therapy with poly ADP-ribose polymerase inhibitors, bevacizumab, and/or drugs targeting homologous recombination deficiency is becoming more widely used in the treatment of ovarian cancer, and the advancement of immunotherapy is further revolutionizing treatment targets."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.
Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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