UNDERGRADUATE RESEARCH IN NATURAL AND CLINICAL SCIENCE AND TECHNOLOGY (URNCST) JOURNAL
**Read more URNCST Journal articles and submit your own today at: https://www.urncst.com**

ENCYCLOPEDIA ENTRY OPEN ACCESS

# Endometrial Cancer

Sofia A. Ierullo, HBSc Student [1]*

[1] Department of Biology, University of Western Ontario, London, Ontario, Canada N6A 3K7

*Corresponding Author: sierull2@uwo.ca

**Abstract**

**Introduction and Definition:** Endometrial carcinoma, also referred to as endometrial cancer (EC), is a malignant tumor that arises from the epithelial lining of the uterus, known as the endometrium. EC is the most prevalent cancer of the female genital tract in developed countries, and its growing incidence driven by various risk factors is emerging as a significant public health concern. EC's precise etiology is uncertain, although known risk factors are correlated with estrogen-progesterone imbalances. Due to high morbidity and mortality associated with EC, reviewing recent research on its etiology, risk factors, and future directions is critical.

**Body:** ECs are classified as estrogen-dependent (type I) or estrogen independent otherwise (type II). Type 1 ECs are low-grade, endometrioid tumours often detected early and associated with better prognoses. Type II ECs exhibit non-endometroid histology, including carcinosarcomas, serous carcinomas, clear cell carcinomas, and other molecularly distinct tumours. Classification systems are evolving with new research to incorporate molecular, histological, and clinical factors, enhancing diagnosis and treatment protocols.

Major risk factors and treatments emphasize the critical role of estrogen signalling, such that estrogen receptor α (ER) acts as an oncogenic signal. Genomic and nongenomic estrogen signalling pathways both contribute to the development of EC. Type I and type II ECs exhibit distinct risk factors, although both are associated with estrogen-progesterone imbalances. Type I EC risk factors include diabetes, obesity, early-onset menarche, and late-onset menopause, all of which result in prolonged exposure to unopposed estrogen. Type II ECs are less understood, but specific mutations involving TP53, and BRCA1/2 genes are implicated in its risk. The standard approach is often primary debulking surgery (PDS); however, neoadjuvant chemotherapy (NACT) is explored if the disease is deemed surgically unresectable. Ongoing clinical trials are exploring optimal treatment strategies. Germline mutations in the Breast Cancer gene 1/2 (BRCA1/2) are suggested to increase EC risk, although further studies are required to determine if EC is a BRCA1/2-associated disease. Current research suggests BRCA1/2, specifically BRCA1 mutation carriers have increased risk for EC, particularly in those with serous-like histology and TP53 mutations. Specified research can permit targeted treatments from a genetic and oncologic perspective.

**Keywords:** cancer; endometrial; treatment; NACT; PDS; BRCA1/2; etiology; FIGO; risk factors; type I; type II; estrogen signalling

## Introduction and Definition

Endometrial carcinoma, otherwise known as endometrial cancer (EC), is a malignant condition that originates in the epithelial lining of the uterus, the endometrium.[1] "EC is the most common cancer in the female genital tract in developed countries, and with its increasing incidence due to risk factors, such as aging and obesity, it tends to become a public health issue [1]."

EC is a subtype of uterine cancer characterized by abnormal cell proliferation of endometrial cells, leading to a disruption of the estrogen-progesterone balance, contributing to its malignancy [1]. Although the precise etiology of EC remains unclear, research suggests that disruptions in estrogen and progesterone balance play a significant role. EC differs from other uterine cancers, such as uterine sarcomas, which arise from mesenchymal cells of the myometrium, exhibiting greater treatment resistance and poorer prognoses [2, 4]. The median age for EC diagnosis is 63 years, with over 75% of cases diagnosed after 55 years [2]. Understanding EC's molecular and genetic basis, including genes such as Breast Cancer Gene 1/2 (BRCA1/2) and TP53, is vital for targeted therapies. Given EC's high morbidity and mortality, reviewing recent research on its etiology, risk factors, and future directions is imperative.

**Body**

Etiology

The etiology of EC is multifaceted, involving both biological and genetic factors. A crucial aspect of endometrial health is the estrogen-progesterone balance, which regulates the uterine lining's growth and shedding. Estrogen stimulates cell proliferation of endometrial cells of the uterine lining, while progesterone counters excess cell proliferation after ovulation. Estrogen can originate from internal sources, such as ovarian production, or external sources, including hormone replacement therapies [3]. Progestogens include natural progesterone and synthetic hormones that mimic its effects. Estrogen and progestogen act on target cells by binding to specific receptors, maintaining hormonal balance [3]. When estrogen levels are elevated relative to progestogen—either through high estrogen with normal progestogen or low progestogen with normal estrogen—estrogen receptors are overstimulated, leading to excess estrogen activity, known as unopposed estrogen [3]. Prolonged exposure to unopposed estrogen causes continuous endometrial proliferation and can lead to endometrial hyperplasia–the excessive thickening of the uterine lining–which is a precursor to EC.

EC classification has evolved with molecular research, enabling precise diagnoses and targeted treatment. In 1983, Bokhman's pathogenic classification system divided EC into two categories: estrogen-dependent (type I) and estrogen-independent (type II) [4]. In 2020, the World Health Organization (WHO) updated the classification system to include histological classifications and molecular markers, offering a more nuanced understanding of EC in clinical practice [5]. Generally, the WHO classification system histologically classifies endometrial carcinomas into "subgroups: endometrioid, serous, clear cell, mixed cell adenocarcinoma, and other relatively rare types, including mucinous adenocarcinoma, neuroendocrine tumours, dedifferentiated carcinoma, and undifferentiated carcinoma [5]."

EC is broadly classified into two main types, type I (endometroid) and II (non-endometroid). Type I ECs are typically low-grade endometrioid tumours, often referred to as endometroid endometrial cancer (EEC). Type I tumours have well-differentiated cells resembling normal endometrial tissue, with slow growth rates, low metastatic risk, and are often diagnosed early, resulting in a better prognosis. Type I ECs arise from unopposed estrogen-driven endometrial proliferation, fueled by internal or external sources of estrogen, unbalanced by progesterone [6]. Prolonged exposure to unopposed estrogen increases the activation of estrogen receptor α (ER) in type I EC, triggering oncogenic signalling pathways that drive tumour growth [7]. Approximately 80% of type I EC cases are confined to the uterus at diagnosis, which is associated with a favorable prognosis due to limited cancer spread [8].

Type II ECs are typically high-grade non-endometrioid tumours, including carcinosarcomas, serous carcinomas, clear cell carcinomas, and other molecularly distinct tumours [5, 9]. These aggressive tumors are poorly differentiated, treatment resistant, and often involve mutations to TP53, which regulates cell division and prevents the proliferation of damaged cells [10]. Tumour suppressor genes mutations, particularly TP53, disrupt DNA repair mechanisms, leading to uncontrolled cell growth and higher metastasis risk [10]. TP53 mutations are particularly prevalent in aggressive type II ECs, such as endometrial serous carcinomas (ESC), where over 90% of ESCs exhibit TP53 mutations [6, 10]. ESCs are a subtype of high-grade ECs, characterized by rapid growth, invasive behaviour, frequent metastasis, and resistance to treatment. Emerging research suggests BRCA1 gene mutations, commonly associated with ovarian and breast cancers, also indicate increased risk of EC by impairing DNA repair mechanisms. These mutations promote high-grade EC subtypes, particularly those with serous-like histology and TP53 mutations, associated with aggressive behaviour and poor prognosis [11]. Further research is needed to clarify how these mutations drive EC progression and to identify potential therapeutic targets.

The International Federation of Gynecology and Obstetrics (FIGO) staging system, published in 2009 and revised in 2023, enhances EC diagnosis by incorporating histological types, tumour patterns, and cancer spread [12]. FIGO staging accounts for the proportion of non-squamous solid areas, classifying EECs as "low grade = grade 1 (≤5%) and grade 2 (6%–50%); and high grade = grade 3 (>50%) [12]." This is crucial for clinical treatment decision-making, as a higher percentage indicates aggressive, high-grade tumour behaviour. Tumour size, cancer spread, and lymph node status are also considered to classify EC into stages I–IV, with stage IV being the most severe and extending beyond the uterus [12]. Stage III and IV ECs are considered high-grade, while stage I and II are typically low-grade. The FIGO, WHO, and EC type classification system collectively provide a comprehensive framework for enhancing EC diagnosis, prognosis, and treatment while clarifying biological mechanisms to improve patient outcomes.

Estrogen Signalling in EC

Estrogen signalling plays a critical role in the development and progression of type I EC, where prolonged exposure to estrogen, unopposed by progesterone, is one of the most significant contributors to drive oncogenesis [6]. Major risk factors and treatments for type I EC emphasize the critical role of estrogen signalling, where the steroid hormone receptor ER acts as an oncogenic signal [7]. ER signalling is divided into genomic and nongenomic signalling pathways, both of which are implicated in EC [7]. Understanding the distinction between ER signalling mechanisms reveals estrogen's role in shaping tumour behaviour.

Genomic estrogen signalling involves the direct regulation of transcription by ER. When estrogen binds to ER, the receptor translocates to the nucleus and binds to estrogen response elements on the gene, directly influencing gene transcription [8]. The genomic pathway regulates genes involved in cell proliferation and survival that contribute to the growth of estrogen-dependent tumours in the endometrium.

Unlike genomic estrogen signalling, nongenomic signalling triggers a faster response and occurs outside the nucleus [7]. In the uterus, nongenomic signalling is initiated when estrogen binds to ER at the cell surface, rapidly activating a cascade of signalling pathways such as the mitogen-activated protein kinase (MAPK) pathway [13]. This leads to swift activation of the insulin-like growth factor 1 (IGF-1) receptor, promoting tumour growth and enhancing carcinogenesis [14]. In type I EC, estrogen-driven activation of IGF-1 abnormally accelerates endometrial cell proliferation and tumour growth [14]. Targeting both pathways in EC may offer new therapeutic options, highlighting the complexity of hormone-driven EC development.

## Risk Factors

### *Type I Risk Factors*

The development of EC is influenced by a combination of biological, lifestyle, and social factors, with distinct risk factors for type I and type II due to distinct etiology. Type I EC, being estrogen-dependent, is linked to risk factors that induce long-term exposure to unopposed estrogen. Type-I ECs have a higher incidence than type II and present several risk factors, including obesity, early-onset menarche, late-onset menopause, history of anovulatory cycles, polycystic ovarian syndrome (PCOS), diabetes mellitus (DM), and/or exposure to unopposed estrogens [15].

Obesity is a major risk factor for type I EC, with overweight women having twice the incidence and obese women having three times the incidence compared to women with a normal BMI [6]. Increased adipose tissue, commonly known as body fat, raises aromatase levels, an enzyme that converts androgens to estrogens. This leads to elevated circulating estrogen levels unopposed by progesterone, which stimulates the proliferation of the endometrial lining [16, 17]. Prolonged exposure to unopposed estrogen can result in endometrial hyperplasia, a precursor to EC [1]. Aromatase becomes the primary source of circulating estrogen in postmenopausal or late-onset menopausal women, further increasing the risk of EC [1]. Aromatase inhibitors such as letrozole and exemestane, used in breast cancer treatment, have also shown promise in addressing high estrogen levels in EC.

Obesity is also associated with type II DM and PCOS, which exacerbate estrogen-progesterone imbalances by reducing sex hormone-binding globulin and increasing levels of free estrogen in circulation [6]. Additionally, obesity and PCOS are linked to higher rates of anovulation, resulting in low progesterone levels and hormonal imbalances [7]. These connections highlight the need for targeted interventions, such as weight management and metabolic control, to mitigate type I EC risk factors.

### *Type II Risk Factors*

Type II EC is estrogen-independent and has a distinct set of risk factors, though its exact etiology is not fully understood due to its lower incidence and limited pathologic and epidemiologic data. Women with lower BMI, non-white race, TP53 mutations, a smoking history, an age older than 55 at diagnosis, post-menopausal status, and a history of breast cancer have an increased risk for type II EC [18, 19]. Women with low to normal BMI are at higher risk for type II EC, despite lower estrogen exposure compared to those with obesity. Type II ECs exhibit distinct, estrogen-independent molecular pathways, with notable genetic risks remaining poorly understood [18].

Cigarette smoking is a notable risk factor for type II EC, inducing early menopause by reducing estrogen levels and altering estrogen metabolism [19]. This contributes to increased progesterone receptor (PGR) and homeobox A10 (HOXA10) expression in endometrial cells, disrupting normal cell differentiation and potentially exacerbating disease progression in type II EC [18].

Type II tumours often harbour TP53 mutations, associated with elevated mortality rates, lower stage-adjusted 5-year survival rates, and higher recurrence rates compared to type I EC [20, 21, 22]. Disparities exist among Black patients with EC, who are more likely to possess TP53 mutations and poorer survival outcomes than their White counterparts [10]. Systemic health disparities, including limited healthcare access, contribute to later-stage diagnoses for Black patients. The high cost of genetic testing further exacerbates these disparities, highlighting the need for equitable healthcare access to enhance outcomes for marginalized populations.

## Current Treatment

Treatment of EC is highly tailored to the tumour's histological subtype and FIGO stage at diagnosis. Primary debulking surgery (PDS) is the standard of care for most EC cases, aiming to surgically remove as much tumour mass as possible. This typically includes a total abdominal hysterectomy (TAH), which removes the uterus and cervix, and a bilateral salpingo-oophorectomy (BSO), which entails the removal of both ovaries and fallopian tubes [23] After PDS, adjuvant therapy, including chemotherapy, radiation, and/or brachytherapy, is typically employed to eliminate remaining cancer cells and reduce recurrence risk [23, 24]. Advanced-stage EC patients (FIGO stages III-IV) may require more extensive surgical procedures as disease may have spread to lymph nodes in the pelvis, groin, or chest, tissues of the upper abdomen and omentum, or distant organs such as the lungs or liver [6, 25]. These may include omentectomy, lymphadenectomy, and extensive tumour

debulking with tumour resections of affected organs. Residual disease post-surgery largely contributes to adjuvant therapy approaches, which aim to eliminate any targeting remaining cancer cells and reduce recurrence.

In cases where PDS is not feasible due to disease extent, neoadjuvant chemotherapy (NACT) is often used to reduce tumour size and cancer cell count before surgical intervention [22]. Personalized treatment approaches have led to a risk-based strategy, tailoring treatment to cancer stage, molecular characteristics, and lymph node status. A phase III study indicates low-risk patients with early-stage disease (FIGO I-II) do not need adjuvant treatment due to the low recurrence rate recorded; however, data is inconclusive for advanced stages [23, 25] Treatment for intermediate- to high-risk EC patients varies significantly based on lymph node status and other clinical factors. Common treatment modalities include brachytherapy, external beam radiation therapy (EBRT), NACT, or combination approaches based on tumour histology and response [26, 27]. Ongoing clinical trials investigate novel adjuvant therapies and combination treatments to improve outcomes and optimize future protocols. There is an urgent need to identify effective treatments for EC patients with positive malignant lymph nodes and low-volume disease, with the goal of enhancing patient outcome and quality of life.

Future Directions

Research suggests that germline mutations in the BRCA1/2 may increase the risk of EC, warranting further investigation to determine if EC is a BRCA1/2-associated disease [11, 28]. BRCA1 and BRCA2, located on chromosome 17 and 13, respectively, are autosomal dominant tumour suppressor genes involved in DNA damage repair [12]. BRCA mutation (BRCAm) carriers, specifically BRCA1m carriers, may have an increased risk of EC [29]. Somatic testing for BRCA1/2 along with other genes in tumour tissue is of more common practice, particularly when next-generation sequencing (NGS) has not been conducted or when germline mutations are not detected. FDA-approved for ovarian, pancreatic, and prostate cancer, poly-ADP ribose polymerase (PARP) inhibitors show promise for EC treatment, but benefit appears to vary by disease, gene, and mutation type (germline or somatic) [29]. Targeted research on risk associated with germline and somatic variants is crucial for optimizing treatment and improving outcomes in BRCAm EC patients.

**List of Abbreviations**

BRCA1/2: breast Cancer gene 1/2
BRCA1: breast cancer gene 1
BRCA2: breast cancer gene 2
BRCAm: bRCA mutation
BSO: bilateral salpingo-oophorectomy
DM: diabetes mellitus
EBRT: external beam radiation therapy
EC: endometrial Cancer
EEC: endometroid endometrial cancer
ER: estrogen receptor α
ESC: endometrial Serous Carcinomas
FIGO: International Federation of Gynecology and Obstetrics
IFG-1: insulin-like growth factor 1
MAPK: mitogen-activated protein kinase
NACT: neoadjuvant chemotherapy
NGS: next-generation sequencing
PARP: poly-ADP ribosome polymerase
PCOS: polycystic pvarian syndrome
PDS: primary debulking surgery
TAH: total abdominal hysterectomy
WHO: World Health Organization

**Conflicts of Interest**

The author, Sofia Ierullo declares that she has no conflict of interests.

**Authors' Contributions**

SAI**:** Made full contribution to the writing of the manuscript, collection of sources, revised the manuscript critically and gave final approval of the version to be published.

**Acknowledgements**

This encyclopedia entry was assisted using artificial intelligence chatbot, Scholar GPT where contributions were carefully assessed and verified with scholarly sources to ensure accuracy.

**Funding**

The development of this encyclopedia entry was not funded.

**References**

[1] Paleari L, Pesce S, Rutigliani M, Greppi M, Obino V, Gorlero F, et al. New Insights into Endometrial Cancer. Cancers. 2021 Mar;13 (7):1496. https://doi.org/10.3390/cancers13071496
[2] Sorouri K, Lynce F, Feltmate CM, Davis MR, Muto MG, Konstantinopoulos PA, et al. Endometrial Cancer Risk Among Germline BRCA1/2Pathogenic Variant Carriers: Review of Our Current Understanding and Next Steps. JCO Precision Oncology 2023 Dec;(7). https://ascopubs.org/doi/10.1200/PO.23.00290
[3] Oliva MM, Gambioli R, Forte G, Porcaro G, Aragona C, Unfer V. Unopposed estrogens: current and future perspectives. European Review Medical and Pharmacological Sciences. 2022 Apr;26(8):2975-2989. https://doi.org/10.26355/eurrev_202204_28629
[4] Bokhman, JV. Two pathologic types of endometrial carcinoma. Gynecologic Oncology. 1983 Feb;15(1):10-7. https://doi.org/10.1016/0090-8258(83)90111-7

[5] Yen TT, Wang TL, Fader AN, Shih IM, Gaillard S. Molecular Classification and Emerging Targeted Therapy in Endometrial Cancer. International Journal Gynecological Pathology. 2020 Jan;39(1):26-35. https://doi.org/10.1097/PGP.0000000000000585
[6] Mahdy H, Casey MJ, Crotzer D. Endometrial Cancer. StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing. [cited 2024 May 12]. Available from https://www.ncbi.nlm.nih.gov/books/NBK525981/
[7] Rodriguez AC, Blanchard Z, Maurer KA, Gertz J. Estrogen Signaling in Endometrial Cancer: a Key Oncogenic Pathway with Several Open Questions. Hormonal Cancer. 2019 Jun;10(2-3):51-63. https://doi.org/10.1007/s12672-019-0358-9
[8] Chelmow D, Brooks R, Cavens A, Huber-Keener K, Scott D, Sheth S, Whetstone S, et al. Executive Summary of the Uterine Cancer Evidence Review Conference. Obstetrics & Gynecology. 2022 Apr;139(4)626-43. https://doi.org/10.1097/AOG.0000000000004711
[9] Buhtoiarova TN, Brenner CA, Singh M. Endometrial carcinoma: Role of current and emerging biomarkers in resolving persistent clinical dilemmas. American Journal of Clinical Pathology. 2016 Jan;145(1):8–21. https://doi.org/10.1093/ajcp/aqv014
[10] Whelan K, Dillon M, Strickland KC, Pothuri B, Bae-Jump V, Borden LE, et al. TP53 mutation and abnormal p53 expression in endometrial cancer: Associations with race and outcomes. Gynecologic Oncology. 2023 Nov;178:44-53. https://doi.org/10.1016/j.ygyno.2023.09.009
[11] Gasparri ML, Bellaminutti S, Farooqi AA, Cuccu I, Di Donato V, Papadia A. Endometrial Cancer and BRCA Mutations: A Systematic Review. Journal of Clinical Medicine. 2022 Jun;11(11):3114. https://doi.org/10.3390/jcm11113114
[12] Berek JS, Matias-Guiu M, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. International Journal of Gynecology & Obstetrics. 2023 Jun;162(2):383-94. https://doi.org/10.1002/ijgo.14923
[13] Losel R, Wehling M. Nongenomic actions of steroid hormones. Nature Reviews Molecular Cell Biology. 2003 Jan;4(1):46–56. https://doi.org/10.1038/nrm1009
[14] Kahlert S, Nuedling S, van Eickels M, Vetter H, Meyer R, Grohe C. Estrogen receptor alpha rapidly activates the IGF-1 receptor pathway. Journal of Biological Chemistry. 2000 Jun;275(24):18447–18453. https://doi.org/10.1074/jbc.M910345199
[15] Bassette E, Ducie JA. Endometrial Cancer in Reproductive-Aged Females: Etiology and Pathogenesis. Biomedicines. 2024 Apr;12(4):886. https://doi.org/10.3390/biomedicines12040886
[16] Cleland WH, Mendelson CR, Simpson ER. Aromatase activity of membrane fractions of human adipose tissue stromal cells and adipocytes. Endocrinology. 1983 Dec;113(6):2155–2160. https://doi.org/10.1210/endo-113-6-2155
[17] Santen RJ, Brodie H, Simpson ER, Siiteri PK, Brodie A. History of aromatase: saga of an important biological mediator and therapeutic target. Endocrine Review. 2009 Jun;30(4):343–375. https://doi.org/10.1210/er.2008-0016
[18] Feinberg J, Albright B, Black J, Lu L, Passarelli R, Gysler S, et al. Ten-Year Comparison Study of Type 1 and 2 Endometrial Cancers: Risk Factors and Outcomes. Gynecologic and Obstetrics Investigation. 2019 May;84(3):290-7. https://doi.org/10.1159/000493132
[19] Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II Endometrial Cancers: Have they Different Risk Factors? Journal of Clinical Oncology. 2013 Jun;31 (20). https://doi.org/10.1200/JCO.2012.48.259
[20] HP Yang, LA Brinton, EA Platz, etal: Active and passive cigarette smoking and the risk of endometrial cancer in Poland. European Journal of Cancer. 2010 Mar;46(4):690– 696. https://doi.org/10.1016/j.ejca.2009.11.015
[21] Felix AS, Weissfeld JL, Stone RA, Bowser R, Chivukula M, Edwards RP, Linkov F. Factors associated with Type I and Type II endometrial cancer. Cancer Causes & Control. 2010 Jul;21(11):1851-6. https://doi.org/10.1007/s10552-010-9612-8
[22] Lobo FD, Thomas E. Type II endometrial cancers: A case series. Journal of Midlife Health. 2016 Apr-Jun;7(2):69-72. https://doi.org/10.4103/0976-7800.185335
[23] Cuccu I, D'Oria O, Sgamba L, De Angelis E, Golia D'Augè T, Turetta C, et al. Role of Genomic and Molecular Biology in the Modulation of the Treatment of Endometrial Cancer: Narrative Review and Perspectives. Healthcare. 2023 Feb;11(4):571. https://doi.org/10.3390/healthcare11040571
[24] Cummings M, Nicolais O, Banks J, Keith SW, Burton E, Shahin MS, et al. Neoadjuvant chemotherapy versus primary surgery in patients with stage III/IV endometrial cancer: A National Cancer Database study. Journal of Clinical Oncology. 2024 Mar;42(16)5603. https://doi.org/10.1200/JCO.2024.42.16_suppl.5603
[25] Endometrial Cancer Stages: Uterine Cancer Staging [Internet]. American Cancer Society. [cited 2024 Sep 2]. Available from: https://www.cancer.org/cancer/types/endometrial-cancer/detection-diagnosis-staging/staging.html

[26] Stelloo E, Nout, RA, Osse EM, Jürgenliemk-Schulz IJ, Jobsen JJ, Lutgens LC, et al. Improved risk assessment by integrating molecular and clinicopathological factors in early-stage endometrial cancer-combined analysis of the PORTEC cohorts Running title Molecular risk assessment in endometrial cancer. Clinical Cancer Research. 2016 Aug;22(16):4215–24. https://doi.org/10.1158/1078-0432.CCR-15-2878

[27] Church D, Stelloo E, Nout RA, Valtcheva N, Depreeuw J, Haar N, Noske A, et al. Prognostic Significance of POLE Proofreading Mutations in Endometrial Cancer. Journal of the National Cancer Institute. 2014 Dec;107(1). https://doi.org/10.1093/jnci/dju402

[28] de Jonge MM, de Kroon CD, Jenner DJ, Oosting J, de Hullu JA, Mourits MJ, et al. Endometrial Cancer Risk in Women With Germline BRCA1 or BRCA2 Mutations: Multicenter Cohort Study. Journal of the National Cancer Institute. 2021 Sep;113(9): 1203-11. https://doi.org/10.1093/jnci/djab036

[29] Yap TA, Stadler ZK, Stout LA, Schneider BP. Aligning Germline Cancer Predisposition With Tumor-Based Next-Generation Sequencing for Modern Oncology Diagnosis, Interception, and Therapeutic Development. American Society of Clinical Oncology Educational Book. 2023 Jun;(43). https://doi.org/10.1200/edbk_390738

**Article Information**
Managing Editor: Jeremy Y. Ng
Peer Reviewers: Ella Guo, Chun Ju Liang
Article Dates: Received Jul 08 24; Accepted Nov 26 24; Published Feb 06 25

**Citation**
Please cite this article as follows:
Ierullo SA. Endometrial cancer. URNCST Journal. 2025 Feb 06: 9(2). https://urncst.com/index.php/urncst/article/view/681
DOI Link: https://doi.org/10.26685/urncst.681