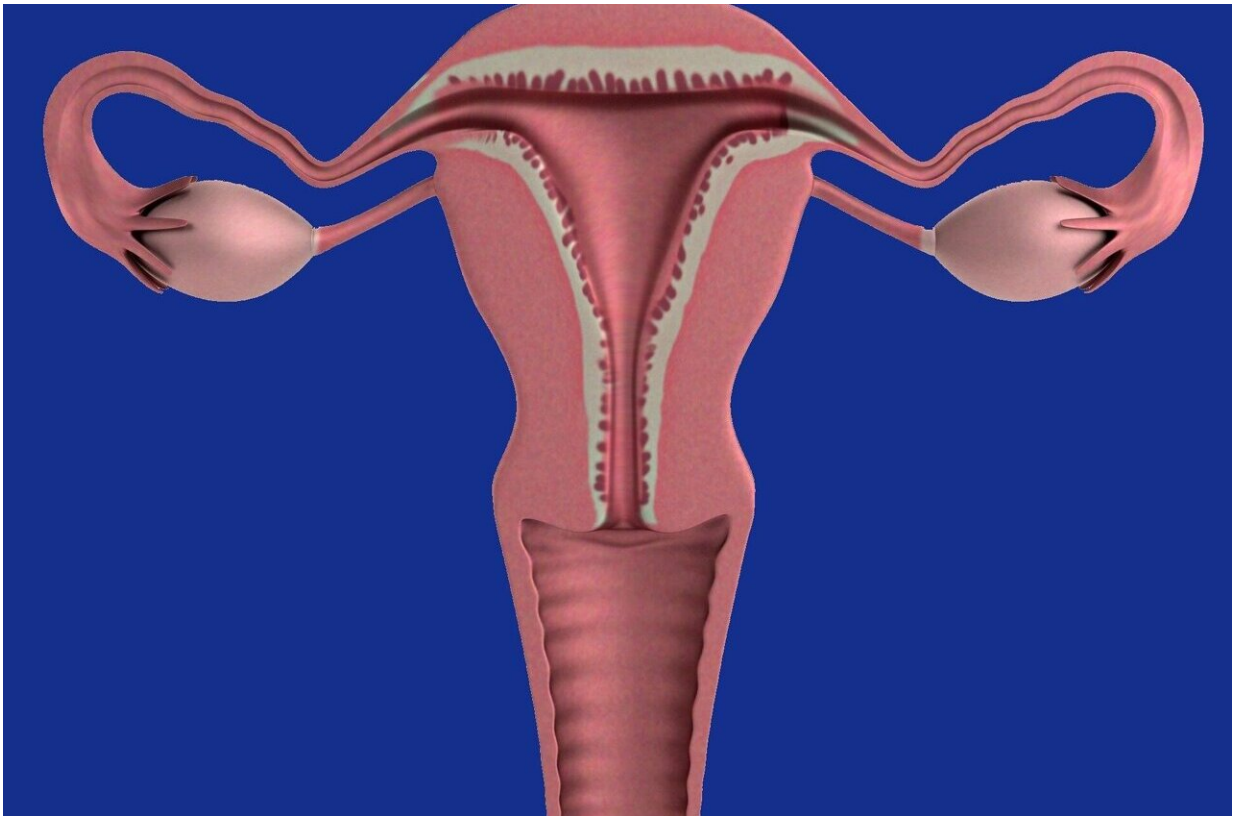


Endometrial cancer: New insights into a deadly disparity

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Endometrial cancer—which develops in the lining of the uterus (womb) and is sometimes called uterine cancer—is on the rise in the U.S. In 1987, there were 35,000 cases annually. That number has nearly doubled

in 2023 to more than 66,000 cases.

Deaths from the disease have also grown alarmingly in the same period, from less than 3,000 to more than 13,000 in the U.S. every year. And the trend line is not getting better.

"Endometrial [cancer](#) has been increasing at unprecedented levels over the past five years," says gynecologic surgeon Carol Brown, MD, Chief Health Equity Officer at Memorial Sloan Kettering Cancer Center (MSK). "It's becoming much more common in all [women](#) in the U.S., and it's occurring at much younger ages."

Against this backdrop, a particularly worrying situation is unfolding for Black women. Dr. Brown explains that the "incidence of endometrial cancer—and the death rate—are rising almost one and a half times more quickly in Black women than white women."

This disturbing trend mirrors a long-standing disparity involving endometrial cancer that finds Black women are almost twice as likely to die of the disease as white women.

"This is one of the few cancers where things are getting worse, not better," says Carol Aghajanian, MD, Chief of the Gynecologic Medical Oncology Service.

In 2023, researchers and clinicians at MSK played a leading role in addressing this cancer disparity. Their efforts stretch across the entire continuum of MSK, including groundbreaking research that provides insights at the molecular and genetic level, [clinical trials](#) that investigate new therapies, and hands-on work in communities most affected by endometrial cancer, where outreach and access to MSK treatment can be lifesaving.

Why endometrial cancer is so deadly for Black women

It has long been known that Black people in America suffer disproportionately from a host of cancer types. The American Cancer Society puts it bluntly: "For most types of cancer, Black people have the highest death rate and shortest survival rate of any racial or ethnic group [in America]."

Dr. Brown, who has devoted her career to helping end these disparities, says, "The theory has been that some of the disparity with endometrial cancer might be related to lower access to adequate health care, which can mean cancers are diagnosed at more advanced stages when they are harder to treat."

Now, more pieces of the puzzle are coming into focus, thanks to new research by Dr. Brown and MSK colleagues, including Dr. Aghajanian; molecular geneticist Britta Weigelt, Ph.D.; the MSK gynecologic pathology team, directed by Lora Hedrick Ellenson, MD; and medical oncologist and clinical geneticist Ying Liu, MD, MPH.

"In the past decade," says Dr. Brown, "we're learning that most of the disparity in endometrial cancer outcomes has to do with the more aggressive types of cancer that Black women get."

Take the endometrial cancers called [serous carcinoma and carcinosarcoma](#). MSK research shows these types of cancer are more likely to be diagnosed in Black women and are also more aggressive than the type more commonly found in white women.

Reasons for disparity discovered at the molecular level

In November 2023, MSK researchers published first-of-its-kind work that provided important new answers for this disparity.

Drs. Brown, Aghajanian, Weigelt, Ellenson, and Liu, along with colleagues from MSK, published findings in [Cancer Discovery](#) that showed Black women not only had more aggressive tumor types but also had other key factors that made their cancers both higher risk and more difficult to treat.

One such factor is a molecular subtype of endometrial cancer called copy number-high or TP53 abnormal (CN-H/TP53abn). People whose endometrial tumors are CN-H/TP53abn generally have worse outcomes, notes Dr. Weigelt.

"The difference between Black and white patients is really striking," she says.

Almost 70% of Black patients had this high-risk molecular subtype of endometrial cancer, as opposed to only 35% of [white patients](#).

The team also found that the tumors of Black women are less likely to be of a molecular subtype called microsatellite instability-high (MSI-H), a subtype that benefits from some forms of immunotherapy.

Checkpoint inhibitors and endometrial cancer

One of the most common forms of immunotherapy is known as a [checkpoint inhibitor](#). This therapy works by unleashing the patient's own immune cells so they recognize and attack cancer cells, which can camouflage themselves to appear normal.

"Checkpoint inhibitors have been a game-changer," says Dr. Liu. "They have completely transformed how we treat advanced and recurrent

endometrial cancer."

This form of immunotherapy works best when an endometrial tumor displays many mutations. That makes it easier for the immune system to recognize that the tumor cells are not normal and attack them.

Here's where MSK researchers found a key difference in Black women: Their endometrial tumors had relatively few mutations. "That means," explains Dr. Weigelt, "that these patients benefit much less from checkpoint inhibitors than white women."

To begin to address this challenge, Dr. Aghajanian has also published early research in [*The New England Journal of Medicine*](#) about efforts to explore if immunotherapy could be made more effective against endometrial tumors that do not have lots of mutations. She stresses that it is very early days for this research but says, "This is just one approach we are taking to end this disparity."

How MSK leads the field in endometrial cancer

"No institution is better suited to making these kinds of discoveries than MSK," says Dr. Brown. "We have incredible resources and data on a very large group of women of African ancestry—that's really unique."

She also credits the leadership of the Gynecology Disease Management Team; Dr. Aghajanian and surgeon Nadeem Abu-Rustum, MD, Chief of the Gynecology Service; as well as the Marie-Josée and Henry R. Kravis Center for Molecular Oncology. "Their determination to make a difference for endometrial cancer patients allowed us to offer genetic and molecular testing for every patient with endometrial cancer who walked through the door."

Unfortunately, outside of these types of efforts, access to genetic testing

lags far behind for Black women, according to Dr. Liu's recent research. And endometrial cancer has been a low priority for federal cancer research funds, despite the growing incidence and death rate from the disease.

Reaching out to people who need it most

Dr. Brown stresses that all these approaches rely on efforts to teach people—patients and providers as well as the wider community—about the grim realities of endometrial cancer and its disproportionate effect on Black women.

"We've made a lot of changes here at MSK over the past decade," she says, "in educating people and making them aware of cancer disparities in general, and particularly endometrial cancer."

Improving equity in endometrial cancer care

MSK's Endometrial Cancer Equity Program is a community outreach, clinical, and research program that helps people of color at high-risk of developing [endometrial cancer](#) understand their risk, get the right diagnosis, and receive the appropriate care.

More information: Britta Weigelt et al, Molecular Characterization of Endometrial Carcinomas in Black and White Patients Reveals Disparate Drivers with Therapeutic Implications, *Cancer Discovery* (2023). [DOI: 10.1158/2159-8290.CD-23-0546](https://doi.org/10.1158/2159-8290.CD-23-0546)

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