

Study tracks endometrial cancer in N.C.

UNC Lineberger researchers are launching a major initiative to track 1,000 women across North Carolina with endometrial cancer, cancer in the lining of the uterus, to understand why the cancer is increasing in incidence and mortality, and why the disease is more deadly for some women than others.

In the Carolina Endometrial Cancer Study, researchers will investigate factors contributing to these statistics, including patients' medical history or lifestyle. They will also evaluate the genetics of patients' tumors in order to potentially identify therapeutic strategies.

Not only do researchers want to understand why the disease is becoming more prevalent and mortality rates have increased, but also why mortality rates are higher in black women compared with white women.

"Despite being the fourth most common cancer in women, endometrial cancer has been a long under-studied cancer," said UNC Lineberger's **Victoria Bae-Jump, MD, PhD**, professor of gynecologic oncology in the UNC School of Medicine Department of Obstetrics & Gynecology. "We need to spend more time and research dollars trying to figure out this cancer."

Understanding cancer drivers

The National Cancer Institute has estimated there will be 65,620 new cases of uterine cancer diagnosed this year, representing about 4% of all new cancer cases.

And while 81% of women survive five years with this disease, endometrial cancer can be deadly once it has spread, and the statistics are trending the wrong way.

The NCI reported in the Annual Report to the Nation 2020 that between 2013 and 2017, uterine cancer mortality rates increased by an average annual rate of 2%, representing the largest increase for any cancer in women.

Researchers also found that black women have a higher risk of death from this disease, both nationally and in North Carolina.

Compared to other racial and ethnic groups, black women have a 93% higher five-year mortality rate. In North Carolina, black women have a more than two-fold risk of death.

"Endometrial cancer does harbor one of the worst disparities for African-American women," Bae-Jump said.

Already, Bae-Jump is entrenched in studies to try to identify potential new treatments for the disease, and to understand what may be contributing to rising mortality rates as well as racial disparities.

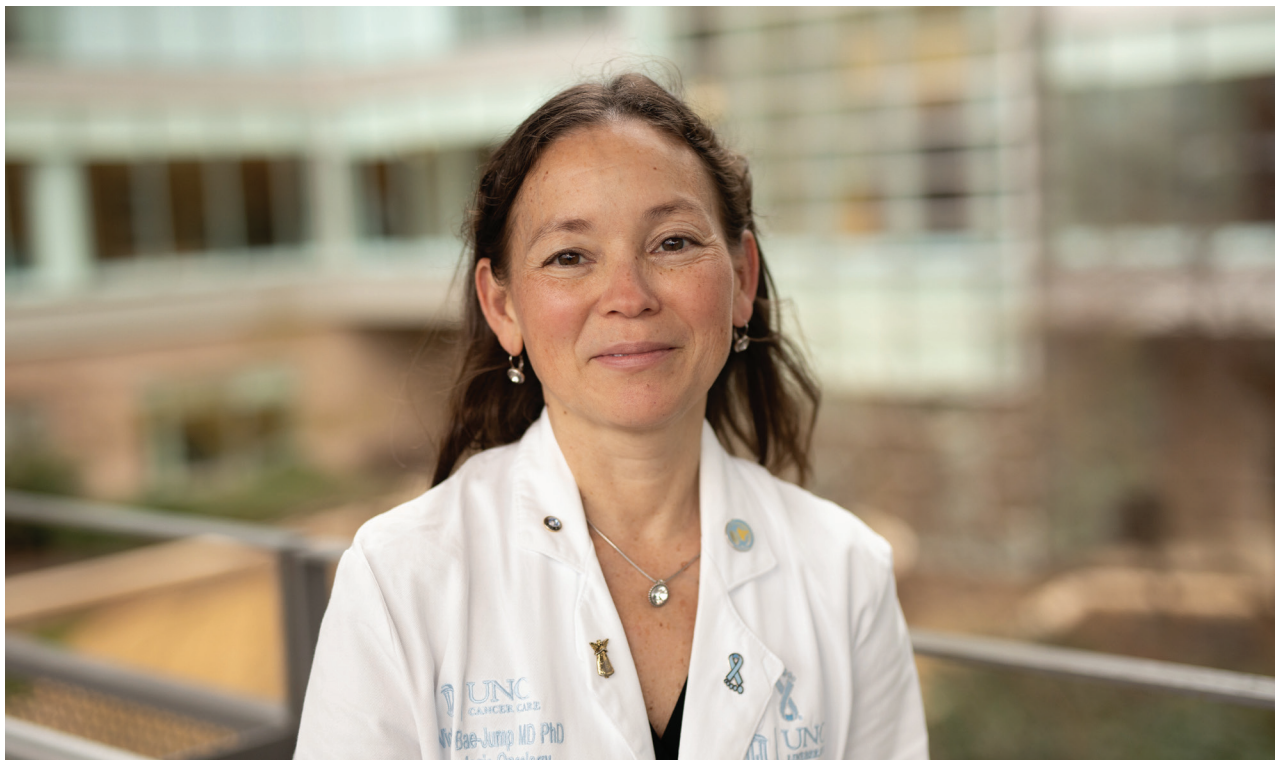
In her laboratory, Bae-Jump's working to develop mouse models of endometrial cancer using tumor tissue from patients in order to study genetic differences in the cancer of black and white women.

"If we know what the differences are, we could target those with therapy," she said.

In addition, she has sought to understand the link between endometrial cancer and obesity, which is a known risk factor for multiple cancer types. Her goal is to find ways to treat these molecular drivers linked to obesity to stop the cancerous growth.

"Obesity is a huge driver of endometrial cancer," Bae-Jump said. "My initial work looking in mouse models and gene expression profiles found that endometrial cancers that arise in the setting of obesity actually behave much more aggressively in that they grow faster, and are metabolically quite different."

An ongoing study is evaluating whether researchers can change some of the obesity-linked molecular drivers of endometrial cancer using weight loss surgery in mice.



UNC Lineberger's Victoria Bae-Jump, MD, PhD, said despite being the fourth most common cancer in women, endometrial cancer has been a long under-studied cancer.

While they've already begun working on understanding the relationship between obesity and endometrial cancer, researchers reported there's only a limited understanding of the impact of obesity and its link to the development of endometrial cancer and treatment outcomes, particularly in black women, who are more likely to meet criteria for obesity in the United States.

In addition to these factors, Bae-Jump said there are other questions that remain. Researchers in her lab are also looking at other factors that could be contributing to the disparity for black women, including the presence of other diseases such as diabetes, and a lack of information on molecular subtypes of disease.

When she reviewed existing studies that analyzed tumors to find what may be contributing to the disparity at the level of the gene or protein, she found black women were under-represented in those studies.

"When you go to the big genomic studies to find out why African-American women are doing so poorly, their cancers are under-represented," she said.

That's where the Carolina Endometrial Cancer Study, which is funded with about \$1.7 million from UNC Lineberger, will come in. Researchers plan to evaluate the genetic patterns in the tumors of women who participate in the study. By investigating the molecular alterations in endometrial tumors, they intend to uncover what may be driving more aggressive behavior, or lead to worse outcomes as well as into how treatment, access to care and follow-up are all delivered.

"We are going to look at the genomic differences on a greater scale than has ever been done before," she said.

In addition, they will evaluate the microbiome – or the naturally occurring micro-organisms present – that might play a role in disease outcomes.

And ultimately, they believe their approach will uncover new ways for drug targets to improve treatment.

Making a difference in North Carolina

Growing up, Bae-Jump always wanted to be a doctor. She used to do pretend operations on her brother and had a role model of a happy doctor in her dad, a pediatrician.

She did her undergraduate studies at Duke University before attending Virginia Commonwealth University in Richmond to receive her doctoral and medical degrees. She completed her residency training and her fellowship at UNC School of Medicine.

The drive to uncover the reasons behind the disparity and potential new therapies is personal for Bae-Jump, who is both a researcher at UNC Lineberger and a gynecologic oncologist at the North Carolina Cancer Hospital. She treats women with all types of gynecologic cancers, including ovarian, cervical, vulva, vaginal and endometrial.

"Many patients with endometrial cancer have stage I disease, and they do quite well, but for women with advanced and recurrent disease, we need more therapeutic options for them," she said. "It makes me sad when I have a short list of options for women with advanced and recurrent endometrial cancer. And on top of that, there are terrible disparities. I just think it's time we spend time and money trying to figure out why, and how to make outcomes better."

She is working with a multidisciplinary team to launch the Carolina Endometrial Cancer Study, including UNC Lineberger cancer epidemiologists and co-leaders **Andy Olshan, PhD**, and **Hazel Nichols, PhD**; microbiome researcher **Temitope O. Keku, PhD**; molecular pathologist **Jason Merker, MD, PhD**, molecular pathologist **Russell Broaddus, MD, PhD**, chair of the Department of Pathology and Laboratory Medicine, and **Wendy Brewster, MD, PhD**, director of the UNC Center for Women's Health Research and professor of gynecologic oncology at the UNC School of Medicine, among others.

They're actively working to find additional grants to fund multiple projects, all with the same goal of improving the statistics for women with endometrial cancer in North Carolina, and beyond.

"We believe that we can make a real difference in a disease that's important to North Carolina," said UNC Lineberger Director **Shelton Earp, MD**. "That's a very purposeful strategic direction that we've taken."