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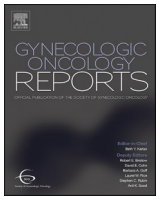

Editorial

# From knowledge to advocacy: Bridging the gap between research and action

Incidence and mortality rates of endometrial cancer have continued to increase over the past decade (Siegel et al., 2023).These rates have varied among racial groups with an increased incidence of 1 % per year in non-Hispanic White women and 2 – 3 % per year in women of all other racial/ethnic groups (Siegel et al., 2023; Facts and Figures, 2024). Findings from a Surveillance, Epidemiology, and End Results (SEER) database analysis demonstrated that the hysterectomy-adjusted incidence of endometrial cancer among Black women has exceeded that of non-Hispanic White women since the year 2000 (Clarke et al., 2019). Additionally, over the past 20 years, the mortality rate from endometrial cancer has risen by 1.7 % per year with the estimated overall mortality rate to be 5.1/100,000 women (Siegel et al., 2023). However, while the endometrial cancer mortality rate for non-Hispanic White women is 4.6/100,000, it is strikingly higher among non-Hispanic Black women with almost double the mortality rate at 9.1/100,000 (Giaquinto et al., 2022). In fact, endometrial cancer has the largest 5-year relative disparity in survival between Black and non-Hispanic White women of all cancers in the United States (Giaquinto et al., 2022).

Several factors have been shown to contribute to this disparity. The first symptom of endometrial cancer is often postmenopausal bleeding. Black women are less likely to undergo appropriate diagnostic evaluation of postmenopausal bleeding which places them at risk for delayed diagnosis and diagnosis at an advanced stage (Doll et al., 2018). Black women are also more likely to be diagnosed with aggressive tumors, less likely to receive standard of care treatment and less likely to participate in clinical trials (Fader et al., 2016; Maxwell et al., 2000; Maxwell et al., 2006; Scalici et al., 2015; Clifford et al., 1997; Fedewa et al., 2011; Santin et al., 2005; Cote et al., 2015). Taken together, these factors make Black women both at higher risk for developing endometrial cancer and experiencing worse cancer-related outcomes.

Seay et al. report on the disparate treatment of endometrial intraepithelial neoplasia (EIN), an endometrial cancer precursor, based on race (Seay et al., 2024). They observed that non-Hispanic Black women were 67 % less likely to undergo surgical intervention. The risk of non-Hispanic Black women not proceeding with surgical intervention persisted even after adjusting for clinical risk factors of age, cardiovascular disease, diabetes, and BMI. We applaud the authors for this study addressing racial disparities in the treatment of EIN (Seay et al., 2024). It should come as no surprise that racial disparities were observed in the treatment of EIN, just as with invasive disease. It has been established that compared to non-Hispanic White women, Black women are less likely to undergo definitive surgical treatment for endometrial cancer (Fader et al., 2016). This is true regardless of stage and grade and is true not only for surgery, but also in the settings of adjuvant chemotherapy and radiation therapy (Fader et al., 2016).

Disparities in incidence, treatment, and outcomes for endometrial cancer and now EIN are known. We continue to quantify and publish on disparities in endometrial cancer, yet the disparate incidence and mortality outcomes among racial groups only widen and worsen over time. We now recognize race as a social construct and surrogate marker for racism and its potential biological sequelae. A recent systematic review published in *Gynecologic Oncology* by Hicks et al. notes that one approach to attempting to determine the underlying cause(s) of disparate racial outcomes in endometrial cancer has been to categorize based on biology (Hicks et al., 2024). The review includes many examples. The authors note that when poor prognostic factors such as advanced stage, higher grade of endometrioid tumors, or aggressive histologic subtypes, are controlled for, then race ceases to be associated with survival gaps in endometrial cancer among most studies (Hicks et al., 2024). Another approach has been to categorize putative causal factors of disparate outcomes by social determinants of health. Lack of access to care, lack of insurance, lower socioeconomic status, and living in a rural location are social determinants of health variables that have been shown to be associated with poorer outcomes in endometrial cancer. In the setting of systemic racism, these social determinants of health variables often become a surrogate for Black race in epidemiologic studies. Hicks, et al astutely conclude that robust research is not enough to eliminate racial disparities in endometrial cancer, we are challenged to do more than just study and report on the problem. Recommendations for what we can and should be doing will require “coordination and cooperation of government agencies…, healthcare and medical education institutions…and medical and cancer societies” (Hicks et al., 2024). The National Academies of Sciences, Engineering and Medicine’s expert committee shares this sentiment in its recent consensus study reviewing health care inequities first reported in *Unequal Treatment* by the Institute of Medicine in 2003. The expert committee found that 20 years later, significant disparities still persist. The 2024 consensus report, *Ending Unequal Treatment*, outlines key goals and recommendations for advancing health care equity including enforcing existing laws, and building systems of accountability within healthcare and government agencies (National Academies of Sciences, 2024).

This call to coordinate with government agencies, in particular, brings to mind a current and relevant example of how research alone is insufficient in effecting change and that coordination with our federal agencies *could* lead to action. Recent analyses of both the Sister Study and the Black Women’s Health Study have shown an association between chemical hair straightening products and endometrial cancer (Bertrand et al., 2023; Chang et al., 2022). In brief, the Sister Study enrolled over 50,000 women from all US states and Puerto Rico between the ages of 35 and 74 who had a sister with breast cancer. Participants

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answered survey questions about their personal and family history of cancer and of lifestyle behaviors. Among the 33,947 women who had a uterus at the time of enrollment in this study, 378 cases of endometrial cancer were identified. A reanalysis of these data, published in 2022 demonstrated that women who used chemical hair straightening products frequently (defined as more than 4 times within the previous year) were more than twice as likely to develop uterine cancer compared to women who had never used them, HR 2.55 (95 % CI = 1.46 to 4.45. (Chang et al., 2022). While the findings and limitations of this study have been debated (Chang et al., 2023; Etminan, 2023), comparable results were seen in another longitudinal cohort study of Black women. The Black Women's Health Study included 44,798 US Black women with an intact uterus who were between the ages of 21 and 69 at the time of enrollment. An analysis of these data regarding the risk of endometrial cancer and hair straightening use was published in 2023. There were 347 cases of endometrial cancer in this population. Hair relaxer use was associated with increased risk of endometrial cancer among postmenopausal but not premenopausal women. A 50 % increased risk of endometrial cancer was seen in women who used hair straightening products more than twice a year or for more than 5 years. Elevated risks were most apparent for postmenopausal women who reported at least 10 years of use (Bertrand et al., 2023).

While association does not prove causality, these data suggest that chemical hair straightening products may cause harm. Personal care products and chemical hair straightening products marketed specifically to Black women have been investigated for their potential to contain endocrine disrupting chemicals (James-Todd et al., 2012; Helm et al., 2018; Mallozzi et al., 2017). These chemicals can theoretically provide a link between excess hormonal exposure and conditions like EIN and endometrial cancer. Since at least 2009, formaldehyde (FA) (a main ingredient in chemical hair straightening products) has been categorized as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), an entity of the World Health Organization. This Group 1 classification signifies that there is sufficient evidence in human beings that the chemical can increase the risk of cancer in people exposed to it over time (Baan et al., 2009). In 2011, the Cosmetic Ingredient Review Panel tentatively concluded that formaldehyde (FA) and methylene glycol were unsafe at any level in hair straightening products in which FA or methylene glycol vapor or gas will be produced. The Food and Drug Administration (FDA) has been urged to ban hair straightening products that include FA and formaldehyde-releasing chemicals (such as methylene glycol) since 2011. Following renewed pressure from members of Congress, an FDA ban was proposed in 2023 with a published timeline for the ban to take effect in April 2024 (Rep Ayanna Pressley, 2023; FDA, 2023). As of this publication, the proposed ban has yet to be implemented. Now that the FDA seems to be delaying this important measure, perhaps this is an opportunity for action from our gynecologic oncology cancer societies. Further guidance and even pressure on the FDA from our cancer societies and organizations may be required for the FDA to proceed with the ban. We need to put evidence and research into action.

The authors do realize that the FDA ban on FA and formaldehyde-releasing products will eliminate one associated risk and it will not be enough to eradicate disparate outcomes from endometrial cancer among Black women. However, this ban would provide a small step in the right direction to build trust within a community that has long-standing mistrust of healthcare and government entities. We now have two decades of evidence that mortality from endometrial cancer is higher for Black women than any other group. When we diagnose EIN or endometrial cancer we need to ensure that we are offering guideline concordant care to all of our patients. Surgical management of EIN, an endometrial cancer precursor, should be prioritized when appropriate. We also desperately need to ensure Black women are adequately represented in clinical trials that determine our clinical treatment guidelines. The National Academies of Science, Engineering and Medicine concluded that from their report in 2003 to the report this year, the US has "made little progress in advancing health care equity". The committee asserts that "greater accountability is necessary to ensure that progress is made in achieving equitable outcomes in health care." (National Academies of Sciences, 2024). Without holding ourselves accountable, and answering these calls to action, we risk continued widening of these disparate outcomes over the next two decades.

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