Expanding Equitable Care in Gynecologic Oncology

Pharmacist Focus on Reducing Disparities for Patients with Ovarian and Endometrial Cancers

These slides are meant to be used as an accompaniment to the presentation for note taking purposes, they are not intended as a standalone reference.

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Disclosures

Dr Brown has disclosed that she has no actual or potential conflicts of interest in relation to this program.

Dr Solomon has disclosed that she has no actual or potential conflicts of interest in relation to this program.

The clinical reviewer, Megan May, PharmD, BCOP, has no actual or potential conflicts of interest in relation to this program.

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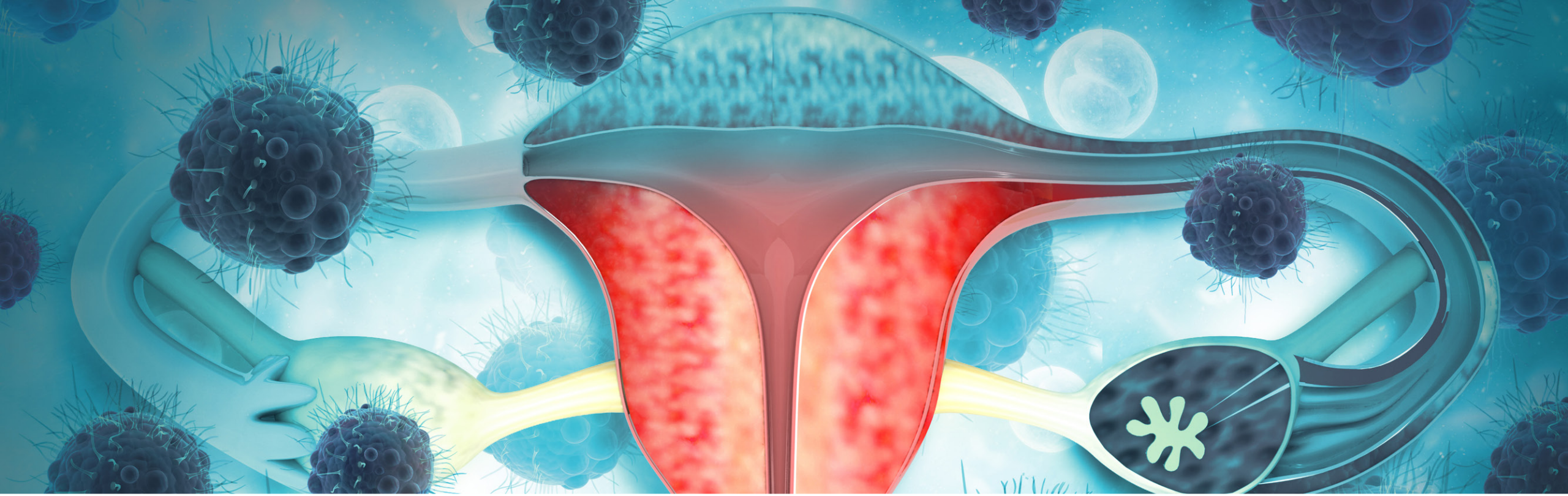
Type of Activity: Application

Learning Objectives

- **Identify** biologic, genetic, cultural, and socioeconomic factors underlying the ongoing problem of racial disparity in gynecologic cancer treatment and outcomes
- **Assess** policies, practices, and patient interaction patterns to identify potential disparities that may influence care of patients in the LGBTQ community and other marginalized groups
- **Develop** best practices in gynecologic cancer treatment across all patient groups, recognizing potential disparities that may affect access to care and patient outcomes



Disparities in Gynecologic Cancers

Background

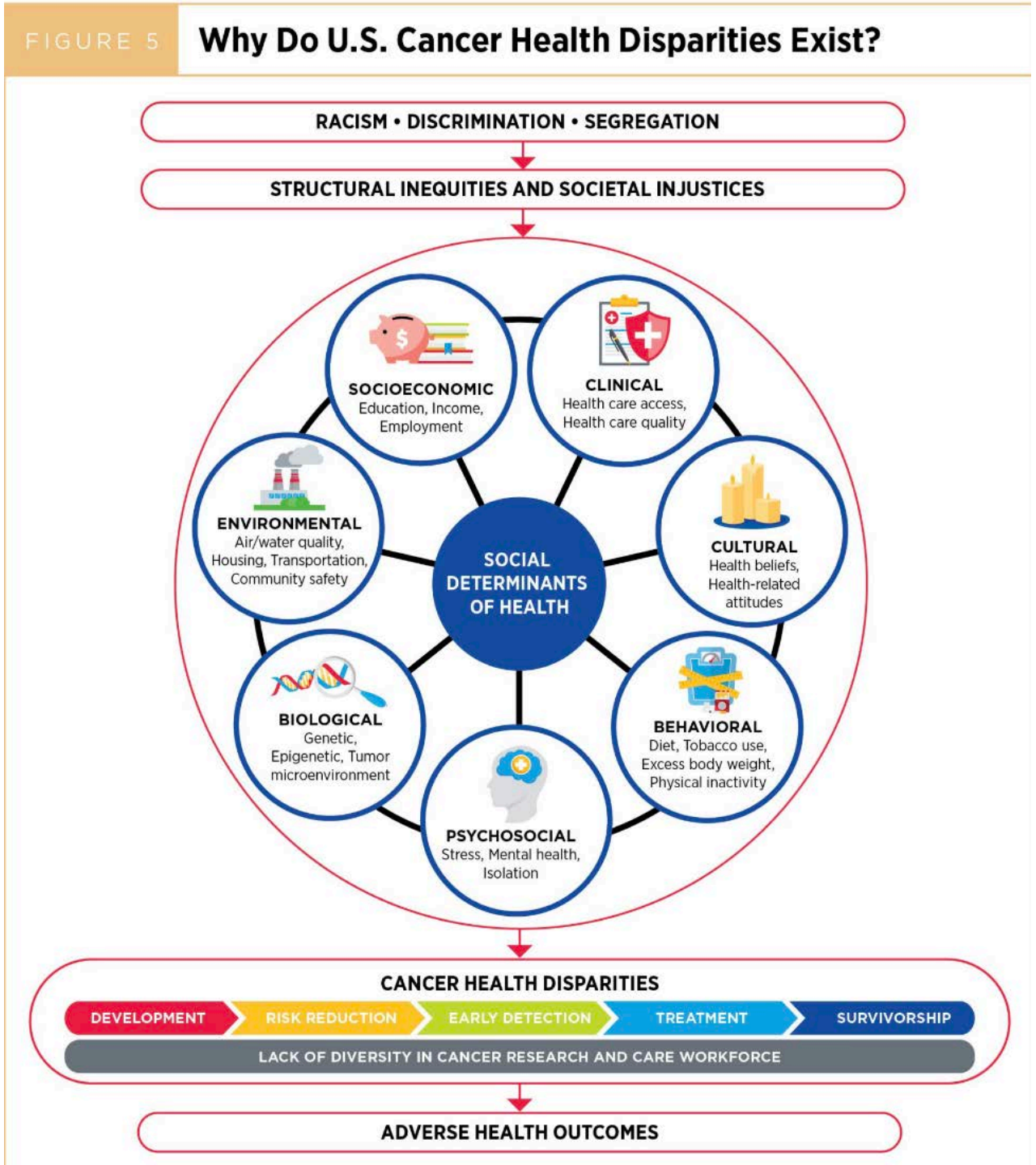
Background

- Historically marginalized groups, such as racially/ethnically minoritized persons as well as members of the LGBTQ+ community are at risk of worse outcomes in gynecologic oncology
- Cancer health disparities are a result of the complex intersection of race, ethnicity, gender identity, and socioeconomic status with the sociopolitical environment, behavior, social and cultural factors, and biology

Temkin SM, et al. *Gynecol Oncol*. 2018;149(1):70-77.

Sociopolitical factors drive health disparities

Cancer is no exception



Temkin SM, et al. *Gynecol Oncol*. 2018;149(1):70-77.
AACR Cancer Disparities Progress Report 2022.

Gynecologic Cancer Health Disparities: Background

- 2020 US Census: people living below the federal poverty level
  - 19.5% Black
  - 17% Hispanic
  - 8.2% non-Hispanic White
- Low socioeconomic status is associated with lower access to:


Healthy foods


Stable employment


Suitable housing


Quality education


Health care


Digital services

United States Census Bureau. Income and Poverty in the United States: 2020. AACR Cancer Disparities Progress Report 2022.

Disparities in Ovarian Cancer

Disclaimer: race and ethnicity are often reported as an aggregate and there is a recognized need for disaggregated data to better characterize health outcomes in subgroup populations

Survival:

- Black patients have an 18% increased risk of death vs White patients (RR 1.18, 95% CI 1.11–1.26)

Diagnosis:

- Black patients have a 20% increased odds of diagnosis at a later stage vs White patients (OR 1.20, 95% CI 1.07–1.35)
- Persists after adjusting for confounding variables such as health care availability and SES (OR 1.14, 95% CI 1.04–1.25)

Abbreviation: SES, socioeconomic status.

Mei S, et al. *Obstet Gynecol*. 2023;142(1):196-210.

Disparities in Ovarian Cancer

Genetic testing, precision testing

- Black and Asian patients are less likely to be referred to and complete genetic testing
- Medicare/Medicaid or uninsured patients were less likely to be referred to and complete genetic testing compared to patients with private insurance

Geographic and travel barriers

- Further distance from a high-volume hospital decreases potential for guideline-concordant care
- White (vs Black, Hispanic, and AAPI) patients are more likely to travel 20 miles or further to receive care at a high-volume hospital

Abbreviation: AAPI, Asian American and Pacific Islander.

Mei S, et al. *Obstet Gynecol*. 2023;142(1):196-210.

Disparities in Uterine (Endometrial) Cancer

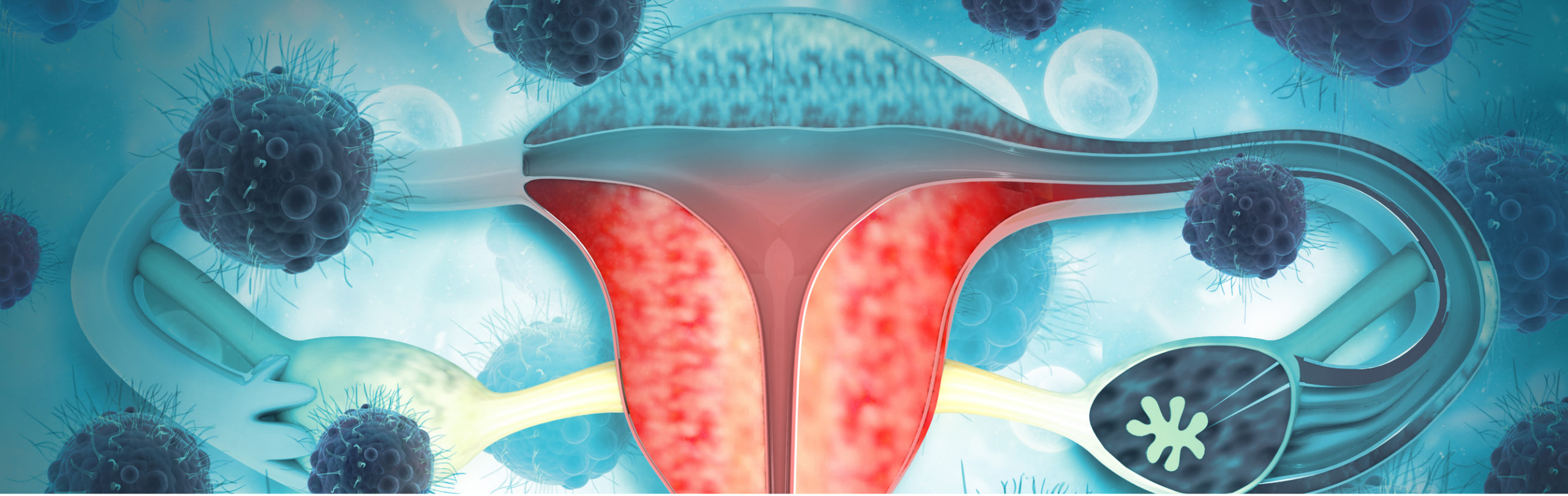
Survival:

- Worse outcomes among Black patients, with death rates nearly twice that of any other racial/ethnic group
- 5-year survival: 63% of Black patients vs 84% of White patients

Diagnosis:

- Greater incidence in Black patients than White patients
- Stage more advanced at diagnosis in Black and Hispanic patients

Whetstone S, et al. *Obstet Gynecol*. 2022;139(4):645-659.



Do Biologic, Genetic, or Pharmacologic Factors Contribute to Disparities in Gynecologic Cancers?

Intracellular Biology in Cancer

- **Germline mutations**: inherited gene mutations (associated with approximately 10% of all cancers)
  - As demonstrated by EGFR mutations, ancestry (*not* race/ethnicity) contributes to the prevalence of genetic mutations
- **Somatic mutations** are acquired over the lifetime due to cell duplication errors or external factors
  - Environmental exposure
  - Lifestyle factors
  - Health conditions that fuel chronic inflammation
- **Epigenetic changes** can be aberrant and lead to cancer
  - How SDOH affects epigenetics is an area of current study
- **RNA splicing** may differ based on ancestry

Abbreviations: EGFR, epidermal growth factor receptor; SDOH, social determinants of health.

AACR Cancer Disparities Progress Report 2022.

Extracellular biology in Cancer

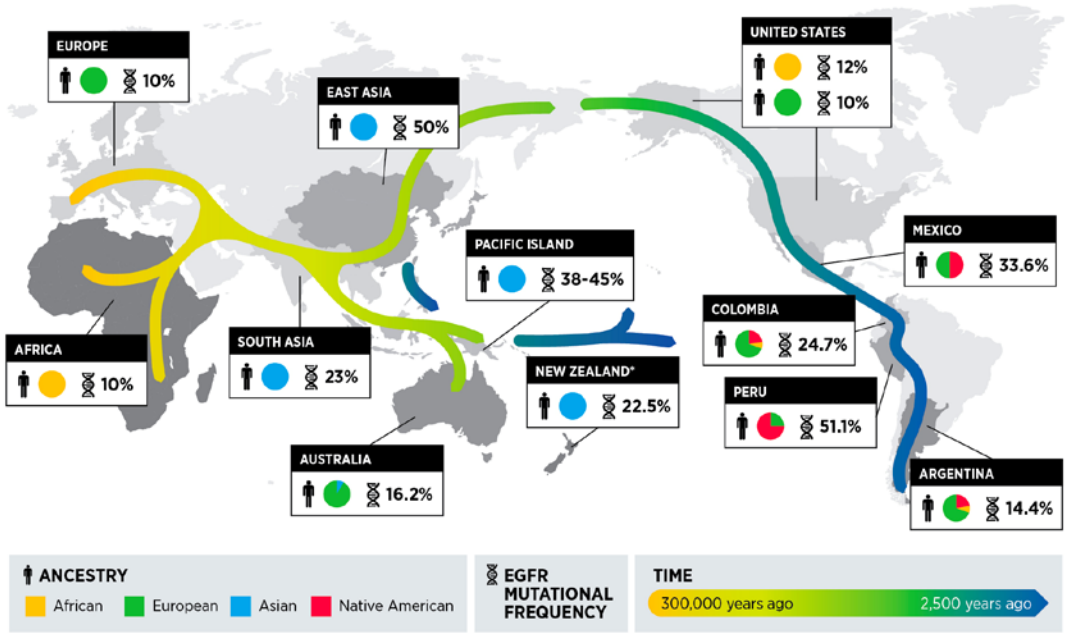
- **Vascularization** of tumors may vary based on ancestry
  - African American people with breast cancer have greater tumor vascularization compared to those of European ancestry
- **Hormones** may drive the development of cancers; however, how hormones affect cancer risk and outcomes is still an area of active study
- The **immune system** differs according to ancestry as well; however, people with diverse racial and ethnic backgrounds have historically been significantly underrepresented in immunotherapy clinical trials

AACR Cancer Disparities Progress Report 2022.

Ancestry is a predominant factor associated with genetic changes

FIGURE 6

Ancestry Contributes to the Prevalence of Cancer-associated Genetic Alterations

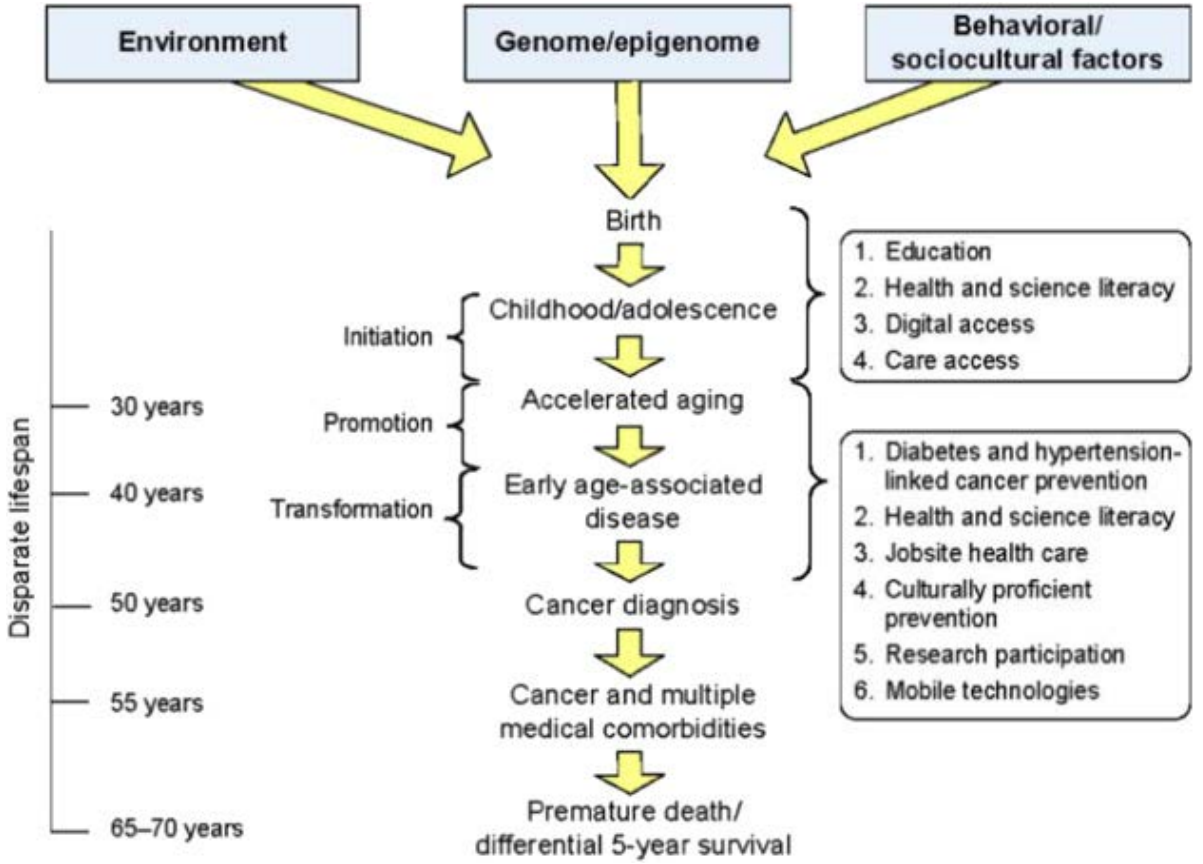


*This study exclusively profiled the EGFR mutational frequency in the native Māori population.

Acquired mutations of the *EGFR* gene are commonly observed in patients with lung cancer and represent a key target for molecularly targeted therapeutics. The frequency of overall somatic mutations in the *EGFR* gene differ based on ancestry of the patient, with the highest mutation rates observed in East Asian groups (50%) and the lowest rates observed in African (10%) and European (10%) populations. The frequency of this mutation follows patterns that are a result of the human diaspora out of Africa as well as more recent migration (forced or otherwise) of population groups to new geographic locations. For example, Peru has a high genetic admixture (i.e., inferring someone's geographical origins based on an analysis of their genetic ancestry) of Native American ancestry while Argentina has more admixture of European ancestry.

American Association for Cancer Research® (AACR) Cancer Disparities Progress Report 2022

The Intersection of Environmental, Genetic, and Behavioral/Sociocultural Factors



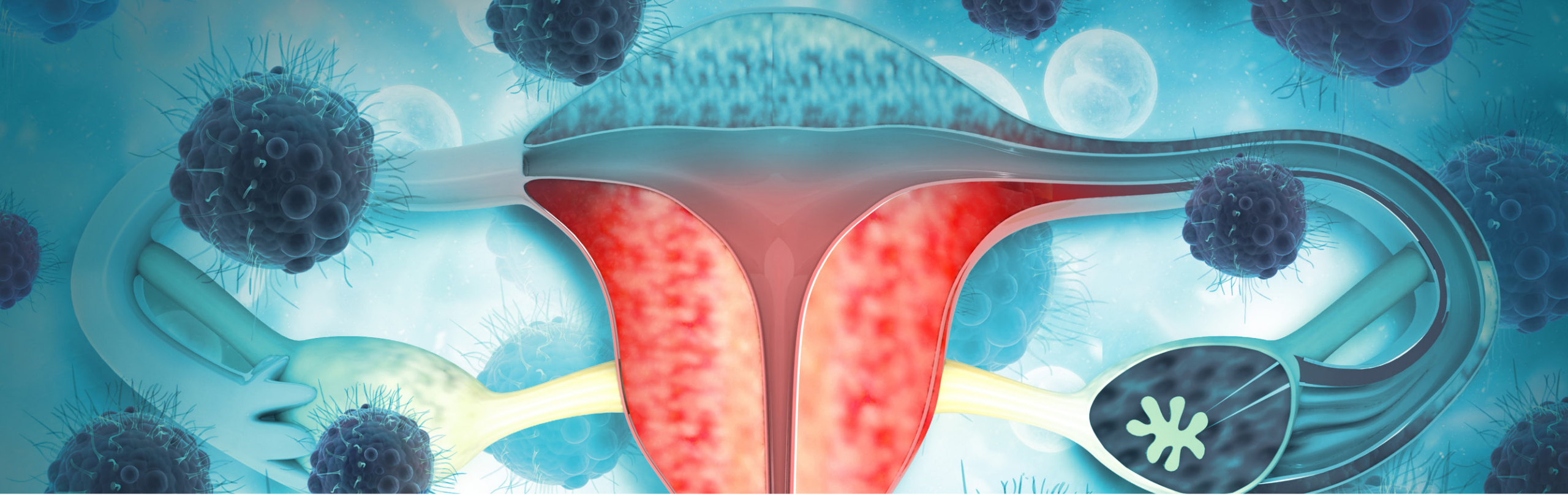
- Race is a social construct
- Centuries of systemic racism and discrimination have led to cancer health inequities
- There is underrepresentation of racial and ethnic minorities, even in genomic burden of cancer studies

Temkin SM, et al. *Gyn Oncol*. 2018;149(1):70-77; AACR Cancer Disparities Progress Report 2022.

Sexual and Gender Minority (SGM) Patients

- Gender dysphoria contributes to decreased screening for birth sex organs
- Gender affirming hormone therapy is not known to increase cancer risk although there remains a theoretical risk
- Those who retain birth sex organs should be screened according to the general population; transgender females have greater risk of breast cancer vs cisgender men
- Providers should seek and maintain education on caring for gender diverse populations
- SGM patients are at greater risk of certain cancers and delayed diagnosis due to the influence of bias and discrimination on health behaviors and access to care

Sterling J, et al. *Transl Androl Urol*. 2020;9(6):2771-2785; AACR Cancer Disparities Progress Report 2022.



How Discrimination and Bias Affect Health Outcomes

Disparities in Endometrial Cancer: Diagnosis

2023 landmark series on disparities

- Transvaginal ultrasounds missed 5 times more cases among Black patients compared to White patients
- **Black patients are less likely to report or receive care** for post-menopausal bleeding

2023 report of the Black Medicaid population

- More likely to:
  - Have an abnormal uterine bleed first reported in an ER visit
  - Require multiple visits for uterine bleeds before referrals are made
  - Have their cancer incidentally diagnosed

Corey L, et al. *Am J Obstet Gynecol.* 2023;226(4):541.e1-541.313; Xu X, et al. *J Natl Cancer Inst.* 2023;115(6):636-643.

Fear of Bias or Discrimination Delays Treatment

Barriers among Black patients

- Noninclusive environment
  - Medical mistrust (and untrustworthiness of medical system)
  - Negative treatment experiences of family/friends and in the media
- SDOH:
  - Transportation issues
  - Absence of a support system
  - Inadequate health care resources
  - Education
  - Neighborhood and built environment
- Implicit racial bias

Prediagnostic Experiences of Black Women with Endometrial Cancer in the United States: Themes

- Stigma, silence, and shame around bleeding
- Lack of education on normal menopausal symptoms and appropriate time point to wait before reporting symptoms
- Vaginal bleeding commonly misconstrued as a resumed menstrual cycle or continued menopause
- Decades of provider mismanagement of abnormal uterine bleeding (AUB)
- Inappropriate provider response to AUB patient report

Doll KM, et al. *JAMA Netw Open*. 2020;3(5):e204954.

Implicit Bias

- Unconscious bias
- Influences the degree of care received by patients
- Has been reported by sexual and gender minority patients
- A 2016 survey regarding implicit bias in oncology showed:
  - Oncologists with higher implicit racial bias had shorter patient interactions
  - Patients had negative views of these experiences
  - Patients had less confidence in treatment plans

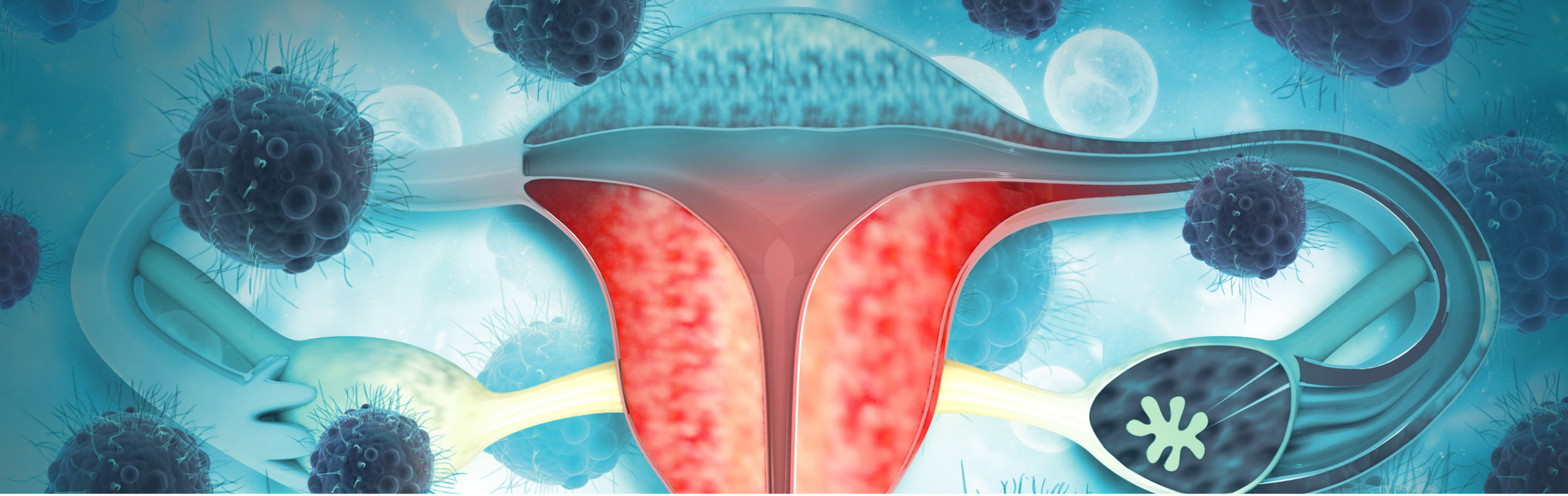
Penner LA, et al. *J Clin Oncol*. 2016;34(24):2874-2880.

Fear of Bias or Discrimination Delays Treatment

Barriers among sexual and gender minority patients

- Lack of provider competency and/or services
- Fear of disclosing personal information
- Noninclusive environment
  - Example: use of the term “women’s cancers”
  - Past experiences of discrimination
- Gynecologic cancers involve the organs centered around sexuality
- Effect of cancer treatment on gender transitioning
- Lack of health care resources
- Absence of a support system

Frecher H, et al. *Obstet Gynecol.* 2018;131:81S. Kano M, et al. *Front Oncol.* 2022;12:833195. Kamen C, et al. *Curr Sex Health Rep.* 2020;12(4):320-328. Stenzel AE, et al. *Gynecol Oncol.* 2020;159(3):899-905.



Disparities in Treatment Access

Overall Disparities That Limit Guideline Adherence

- Historically marginalized communities (ie, racially/ethnically diverse and sexual and gender minority)
- Young age
- Comorbidities
- Uninsured/lack of private insurance
- Distance from treatment center
- Low socioeconomic status
- Treatment center lacking a robust oncology program
- Absence of a support system

Bandera EV, et al. *Clin Cancer Res*. 2016;22(23):5909-5914. Barrington DA, et al. *Am J Obstet Gynecol.* 2022;227:244e1-17. Collins Y, et al. *Gynecol Oncol.* 2014;133(2):353-361. Fader AN, et al. *Gynecol Oncol.* 2016;143(1):98-104. Kaspers M, et al. *Am J Obstet Gynecol.* 2020;223(3):398.e1-398.e18. Long B, et al. *Gynecol Oncol.* 2013;130(3):652-659.

Health Disparities in Ovarian Cancer (2023 Report)

- Black patients are more likely to be diagnosed with later-stage cancer
- Lack of guideline-concordant care in ethnic minority groups
- Limited knowledge of genetic-based testing in Black population
- Low socioeconomic status
- Geographic barriers
- Language barriers
- Underrepresentation in clinical trials
- Lack of quality studies focusing on gender identity or sexual orientation

Mei S, et al. *Obstet Gynecol.* 2023;142(1):196-210.

Adherence to Guidelines in Ovarian Cancer

- 2018 report based on the National Cancer Database
  - Lymphadenectomy
    - Lower rates among Black and Hispanic patients
    - Higher rates among Asian patients
  - Odds of receiving chemotherapy compared to White patients
    - 22% lower (Asian)
    - 25% lower (Black)
    - 19% lower (Hispanic)
  - 5-year survival
    - 62.5% (Asian)
    - 55.2% (Hispanic)
    - 50.8% (White)
    - 40.1% (Black)

Rauh-Hain JA, et al. *Gynecol Oncol*. 2018;149:4-11.

Adherence to Guidelines in Ovarian Cancer

- 2021 analysis of Black patients noted:
  - Lower adherence to treatment guidelines compared to White patients (60.8% vs 70.4%)
  - Risk factors identified
    - Insurance status, treatment facility type, highest education level, age, and comorbidities
  - Percentage of contributors to racial disparities in survival
    - 36.4%: nonadherence to guidelines
    - 22.7%: access to care
    - 18.2%: comorbidities

Chen F, et al. *Gynecol Oncol.* 2021;160(1):10-15.

Endometrial Cancer Treatment Delay by Race

2022 report of the Medicare population noted:

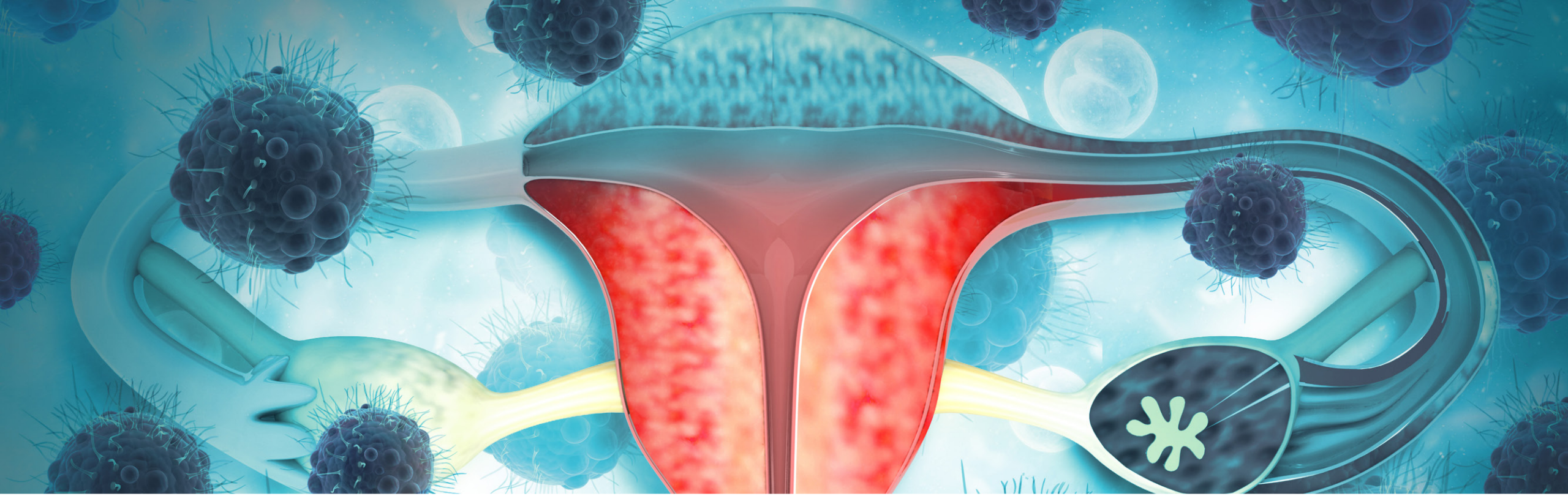
- Hispanic patients
  - 71% increased risk of delay for all stages
- Black patients
  - Twice as likely not to be recommended surgery
  - More likely to experience perioperative complications
  - 39% did not receive adjuvant treatment
    - Those who received treatment had delays

Corey L, et al. *Am J Obstet Gynecol*. 2022;226(4):541.e1-541.e13.

Endometrial Cancer Treatment Disparities

- A 2021 study noted:
  - 40% of the patients included did not receive appropriate care
  - Nonadherence was significantly associated with decreased survival
  - Worse survival noted among Black and native Hawaiian/Pacific Islander patients
- A 2020 study noted:
  - Adherence to treatment guidelines led to improved survival among Black patients
  - Survival was still less compared to White patients

Rodriguez VE, et al. *Cancer*. 2021. Huang AB, et al. *Am J Obstet Gynecol.* 2020;223:396.e1-1.



Latest in NCCN Guideline Recommendations

Ovarian Cancer

First-Line Treatment

- Standard-of-care
  - Carboplatin and paclitaxel
  - Role for bevacizumab
- Other considerations
  - Intraperitoneal chemotherapy
  - Treatment options for older population and/or poor performance status

NCCN Clinical Practice Guidelines in Oncology Ovarian Cancer. Version 2.2023. National Comprehensive Cancer Network.

Maintenance Therapy

- Poly ADP-Ribose Polymerase Inhibitors (PARPi)
  - Niraparib (Zejula)
  - Olaparib (Lynparza)
  - Rucaparib (Rubraca)
- Use in the primary setting
  - Following complete or partial response to platinum-based therapy
  - Based on mutation testing
  - Finite period of therapy
- Use in the recurrent setting
  - Indefinite period of therapy

NCCN Clinical Practice Guidelines in Oncology Ovarian Cancer. Version 2.2023. National Comprehensive Cancer Network.

Platinum-Sensitive Recurrence

- Time from end of treatment to recurrence is at least 6 months
- Treat with combination platinum-based therapy
  - May add bevacizumab
  - Can replace the taxane with liposomal doxorubicin or gemcitabine
- Options for low-grade serous cancer*
  - Trametinib
  - Fulvestrant

*Not FDA-approved but are NCCN-guideline concordant

NCCN Clinical Practice Guidelines in Oncology Ovarian Cancer. Version 2.2023. National Comprehensive Cancer Network.

Platinum-Resistant/Refractory Recurrence

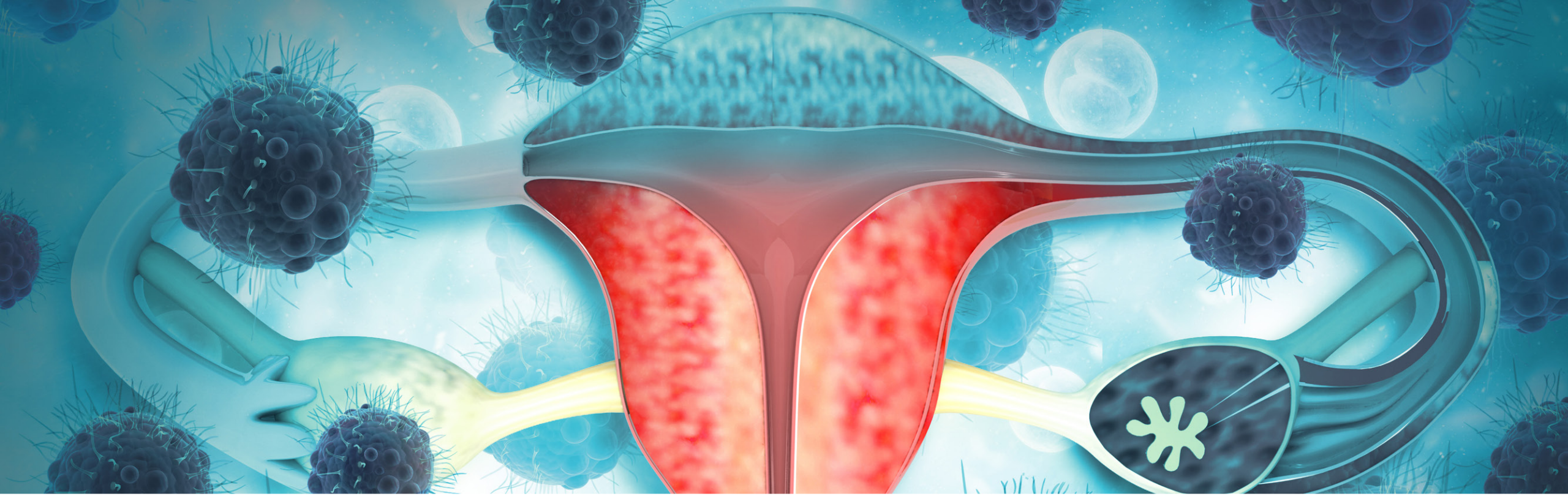
- Cytotoxic treatment options have response rates of 19%-27%
- Tumor molecular testing can guide treatment
  - Neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion
    - Entrectinib and larotrectinib
  - Deficient mismatch repair (dMMR) or microsatellite instability-high (MSI-H)
    - Pembrolizumab and dostarlimab
  - BRAF V600E
    - Dabrafenib and trametinib
  - BRCA mutation
    - Olaparib and rucaparib

NCCN Clinical Practice Guidelines in Oncology Ovarian Cancer. Version 2.2023. National Comprehensive Cancer Network.

Newest Targeted Therapy Approval

- Mirvetuximab Soravtansine
  - Antibody-drug conjugate targeting folate receptor-α (FRα)
  - Approved in November 2022
    - For patients with FRα-positive disease
    - Status-post receipt of 1-3 systemic regimens
  - Approval based on the SORAYA trial
    - 31.7% overall response rate
    - Median duration of response was 6.9 months

NCCN Clinical Practice Guidelines in Oncology Ovarian Cancer. Version 2.2023. National Comprehensive Cancer Network.



Latest in NCCN Guideline Recommendations

Endometrial Cancer

First-Line Therapy

- Historic standard-of-care (SOC)
  - Carboplatin and paclitaxel
- Addition of trastuzumab if HER2-positive
- New NCCN-preferred upfront options
  - Dostarlimab with SOC
    - FDA-approval received end of July
    - Based on RUBY trial
  - Pembrolizumab with SOC
    - Not FDA-approved
    - Based on NRG-GY018 trial

NCCN Clinical Practice Guidelines in Oncology Uterine Neoplasms. Version 1.2024. National Comprehensive Cancer Network.

First-Line Therapy in the Recurrent Setting

- Options listed in previous slide if no previous systemic therapy
- Biomarker-directed therapy
  - Mismatch repair proficient (pMMR) or MSI-stable
    - Pembrolizumab and lenvatinib
  - Tumor mutational burden (TMB)-high
    - Pembrolizumab monotherapy
  - MSI-H/dMMR
    - Pembrolizumab
    - Dostarlimab

NCCN Clinical Practice Guidelines in Oncology Uterine Neoplasms. Version 1.2024. National Comprehensive Cancer Network.

Second-Line or Subsequent Therapy

- Choice of cytotoxic agents
  - Not limited to cisplatin/doxorubicin, liposomal doxorubicin, paclitaxel, topotecan, temsirolimus, etc
- Biomarker-directed therapy
  - Mismatch repair proficient (pMMR) or MSI-stable
  - Tumor mutational burden (TMB)-high
  - MSI-H/dMMR
  - HER2-positive tumors (IHC 3+ or 2+)
    - Fam-trastuzumab deruxtecan (new addition to NCCN guidelines)
  - *NTRK* gene fusion-positive

NCCN Clinical Practice Guidelines in Oncology Uterine Neoplasms. Version 1.2024. National Comprehensive Cancer Network.

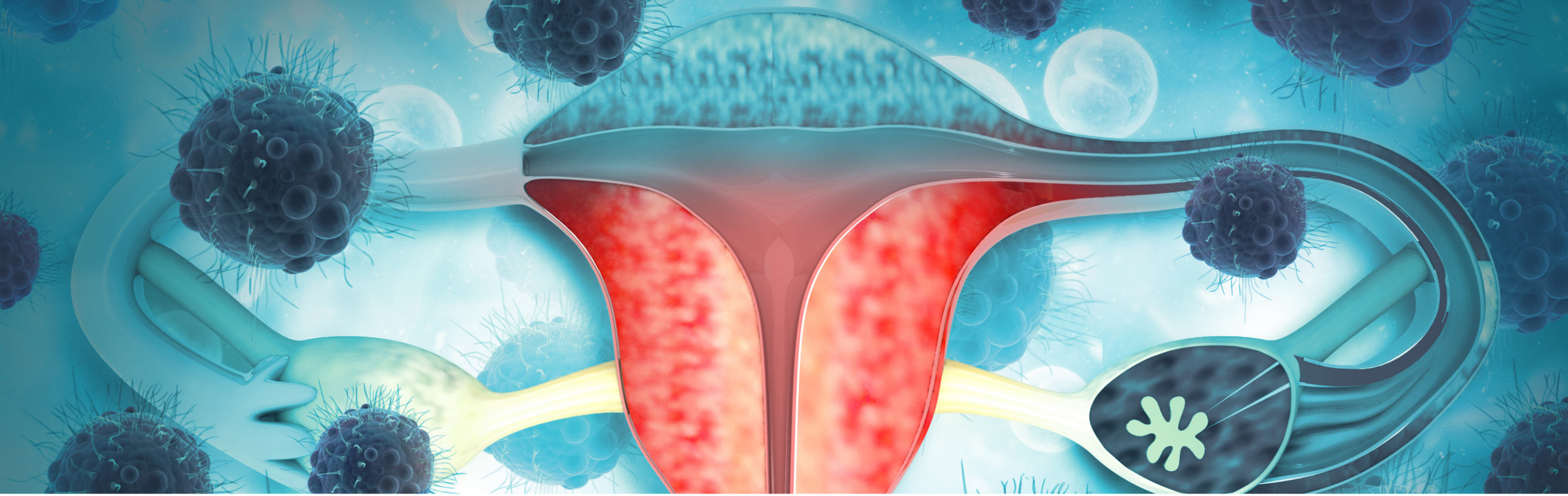
Hormonal Therapy for Recurrent or Metastatic Disease

- Preferred:
  - Megestrol acetate with tamoxifen
  - Letrozole with everolimus
- Other recommended regimens:
  - Medroxyprogesterone, aromatase inhibitors, tamoxifen, fulvestrant
- Newest update for ER-positive tumors
  - Letrozole/ribociclib
  - Letrozole/abemaciclib

NCCN Clinical Practice Guidelines in Oncology Uterine Neoplasms. Version 1.2024. National Comprehensive Cancer Network.

Applying Treatment Guidelines to All Patients

- Use strategies that overcome implicit racial bias and disparities (ie, utilizing a treatment pathway; outreach to patients lost to follow-up)
- Engage patients in treatment planning
- Offer support system
  - Connect patients to current/previous patient(s) with similar backgrounds
  - Support groups
  - Appropriate material/resources to review at home
  - Race-concordant care



Addressing, Reducing, and Removing Disparities

Call to Action

Direct Pharmacy Interventions

Chemotherapy dosing

Example: calculating creatinine clearance

Chemotherapy education

Addressing patient(s)

Sexual Orientation And Gender Identity (SOGI)

Support person(s)/caregivers

Intercourse

Identification of medication-specific risk factors

Tamoxifen and risk of endometrial cancer: counseling

Patients looking to manage symptoms of gynecologic cancers: asking about duration, details of symptoms

Research

ENCOURAGE CLINICAL TRIALS TO ALL PATIENTS WITH AN EQUITY APPROACH

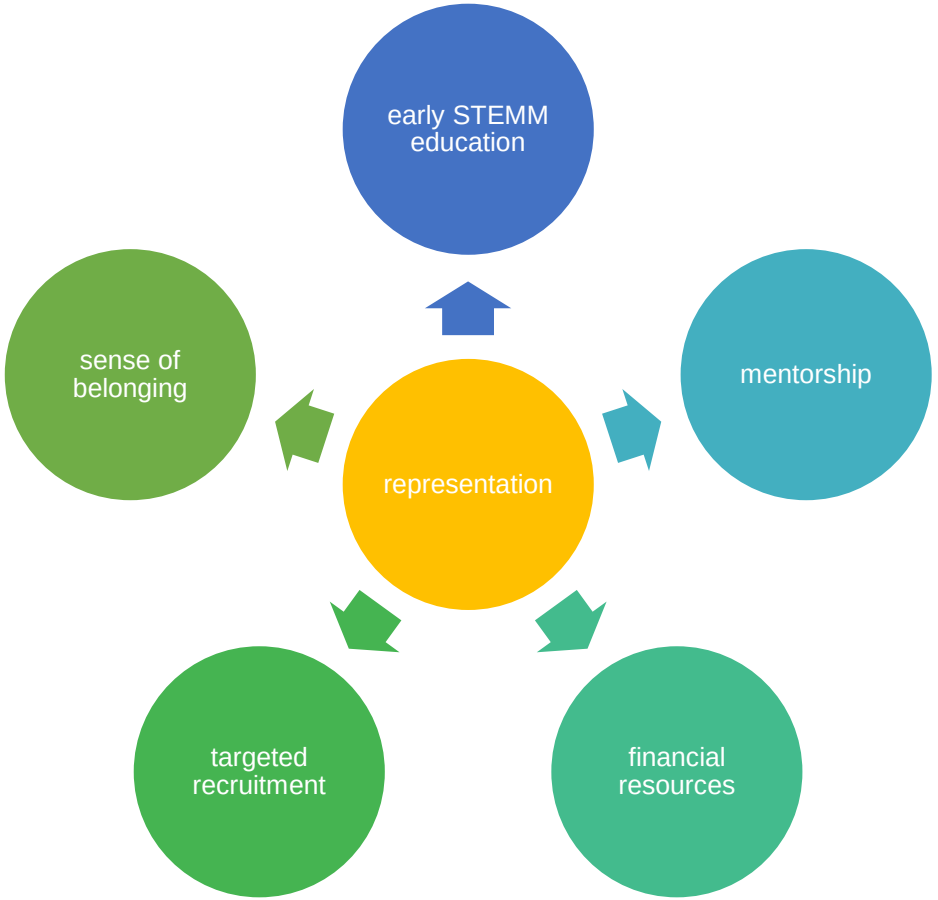
PREPARE EDUCATIONAL MATERIALS IN MULTIPLE LANGUAGES

ENGAGE WITH AND HIRE COMMUNITY PARTNERS INTO YOUR RECRUITMENT TEAMS TO INCREASE RACIAL-CONCORDANCE AND TRUST

IDENTIFY BASELINE BARRIERS TO ENROLLMENT AND LEVERAGE YOUR NETWORK/ COLLEAGUES TO ASSIST

AIM FOR ENROLLMENT THAT MATCHES YOUR PATIENT POPULATION

Cultivating a Diverse Workforce



Abbreviation: STEMM, science, technology, engineering, math, medicine.

Integration With Your Health Care Team

- Encourage Diverse, Equitable, and Inclusion (DEI) training as a group
- Identify stakeholders and meet to create goals to track your progress
- Inclusivity
  - Use of “women’s cancer”
  - Update medical records and paperwork
  - Advertisements
  - Support services
- Patient advocacy
- Helping patients with barriers to care

Patient Education and Referral

- Pharmacists are the most accessible health care provider
- Recognize signs of gynecologic malignancies and refer when necessary
  - Ovarian cancer: bloating, early satiety, pelvic/abdominal pain, frequent urination
  - Endometrial cancer: abnormal uterine/vaginal bleeding, watery/bloody discharge, painful intercourse, pelvic pain/cramps
- Familiarize yourself with community resources for at-risk populations (ie, low English proficiency, uninsured/underinsured, food insecure, low health literacy)
  - Planned Parenthood
  - Open enrollment
  - Local free clinics
  - 211 (health care, housing and utilities, food)

Questions and Answers