



ACOG

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# Role of Race in IVF

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Immediate Past President  
American College Ob/Gyn  
Iffath Hoskins



**Montefiore**

Science at the heart of medicine

Vice Chair, Recruitment  
Retention & Development  
Chief, Obstetric Safety Officer  
Montefiore Medical Center  
Albert Einstein College of  
Medicine, Bronx, NY





# Learning Objectives

- Demonstrate knowledge of the impact of race on IVF management
- Manage the burdens of race to ensure successful IVF outcomes
- Integrate evidence based guidelines into clinical practice to ensure equitable and inclusive care for all who seek IVF treatments

# The role of Race in IVF

- The discussion of race as a biological or social construct has become more complicated because of the evolving science of genetics and ancestry.

# role of Race in clinical medicine: Definition

What is the definition of race?

The categorization of different human beings using the arbitrary factor of skin color.

**race (noun)**

6. A group of sentient beings, particularly people, distinguished by common heritage or characteristics.

# Ethnicity

## Definition

- **ethnicity** (n) a term which represents social groups with a shared history, sense of identity, geography and cultural roots which may occur despite racial difference

**This is very different from race which is defined below:**

- **race** (n) a human population considered distinct based on physical characteristics.

# Race & Ethnicity

- In basic terms,
- **race:** physical traits, something you inherit
- **Ethnicity:** cultural identification, something you learn.



A dense crowd of people from various ethnicities and ages, looking in different directions. The image is used as a background for a text overlay.

**WHAT IS THE ORIGIN OF RACE?**

# World's most ancient **Race** traced in DNA study

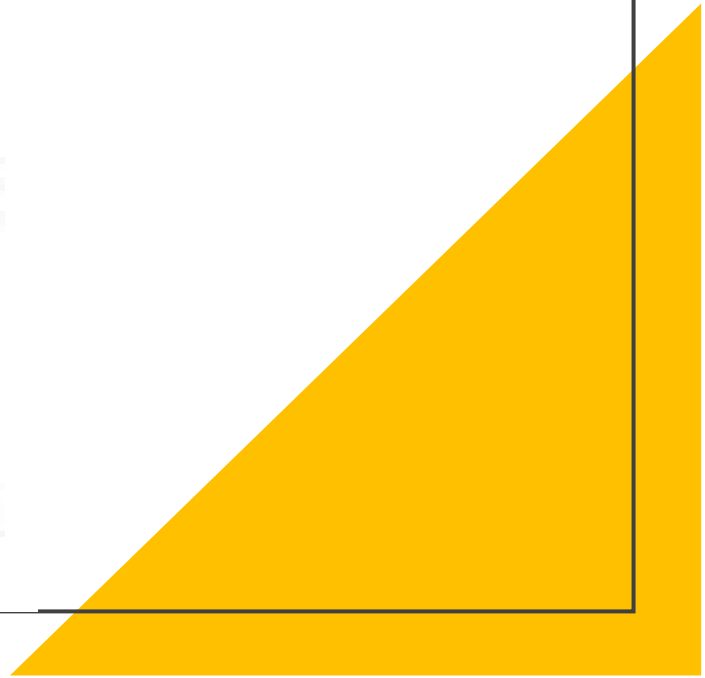
- African **Khoe-San** people - the world's most ancient race
- Scientists analyzed genetic variations within the DNA of more than 3,000 Africans and found that the Khoe-San had the most genetic diversity and were the oldest continuous population of humans on Earth.
- Out of Africa migrations (100,000 years ago)
- The study, reflected over 10 years of research using samples collected from diverse and distant parts of Earth.
- The project found that modern Africans had the most diverse DNA of all racial groups in the world, confirming the idea that Africa is the birthplace of humanity.
- Schlebusch CM et al. Mol Biol Evol 2020

# Correlation b/w race and IVF

- Our ability to capture race/ethnicity as a variable is inevitably imperfect because no consensus exists on the definitions of race and ethnicity or on how such data should be collected.
- There are **15 race categories** defined by the US Census Bureau (white; black or African American; American Indian or Alaska Native; Asian Indian; Chinese; Filipino; Japanese; Korean; Vietnamese; Native Hawaiian; Guamanian or Chamorro; Samoan; other Pacific Islander; other Asian; and some other race), as well as **2 ethnicity categories** (Hispanic or Latino, and not Hispanic or Latino).
- These, according to the bureau, reflect the social definition of race and ethnicity recognized in the United States.
- This list was augmented with PubMed Medical Subject Headings and other terms, such as “native,” “aboriginal,” and “of color.”
- Broad categories of White, Black, Asian, and Hispanic were used to simplify presentation of data.



**Infertility**



# Role of race in IVF

- Self-identified race is not a biologic category
- race and ethnicity may serve as a surrogate for known risk factors of IVF failure (age, obesity, smoking, medical conditions or uterine structural abnormalities, etc).
- Racial and ethnic minority groups may face social or societal barriers that are associated with worse outcomes, independent of other clinical risk factors.
- SDoH

# Role of Race in IVF

- Infertility is a global multi-ethnic problem.
- Blacks 7.2%\*
- Hispanics 6.1%\*
- White 5.5%\*
- Although ARTs are offered in clinics world-wide (162 out of total 195 countries), women who have a live birth using IVF are disproportionately White/Caucasian with high education and middle/high socioeconomic status.
- Reasons:
- Non-White women are less likely to use this option.
- Disparities occur due to cost and culture
- Higher likelihood of known risk factors for IVF failures
- Genetic or environmental predispositions, independent of clinical risk factors
  
- (SDOH)
  
- \*Grainger DA, Seifer DB, Frazier LM, et al Fertil Steril **2004**;82:S37-8
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# Navigating unequal paths (contd.)

- Black and Hispanic women face significant disparities in seeking care for infertility compared with White women.
  - Black women are half as likely to be evaluated for infertility
  - Black and Hispanic women spend 20 months longer in attempting to conceive before receiving care.
- 
- Siegel DR, Sheeder J, Polotsky AJ. Women's Health Rep. **2021**;2:347-54

# Racial & ethnic disparities in fertility awareness among reproductive age women

- A validated fertility-knowledge questionnaire
- non-Hispanic Black women scored significantly lower than non-Hispanic White women in overall fertility awareness, including areas such as natural fertility, infertility risk factors, and infertility treatment.
- Siegel DR, Sheeder J, Polotsky AJ. Women's Health Rep. **2021**;2:347-54



# Navigating unequal paths: racial disparities in the infertility journey

- Weiss MS, Marsh EE. Obstet Gynecol 142(4):940-7. Oct. **2023**

## Navigating unequal paths

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- The base of the pyramid represents the total population of people who wish to be pregnant, and each successive layer reflects attrition along the journey.
- Although clinical factors play an important role in determining a patient's outcome, for many, structural factors pose the greatest obstacles to reaching the top of the pyramid.



# Who engages in IVF?

IVF is the most successful treatment due to its high pregnancy rates relative to other treatment options.

IVF is the costliest form of fertility treatment and necessitates a substantial investment of time and effort, often requiring adjustments to daily routines and lifestyle choices.

The utilization of IVF among Black, Hispanic, and American Indian or Alaska Native women is below the national average.

CDC's National ART Surveillance System---In 2014, there were 1,434 IVF cycles performed per million Black women and only 997 per million among Hispanic women, compared with 2,888 cycles per million White women

Dieke AC, Zhang Y, Kissin DM, et al. J Women's Health 2017; 26:605-8

# Influence of race and ethnicity on IVF outcomes: systematic review

- Effect of IVF on clinical pregnancy and live birth outcomes
- 24 studies
- All 5 US Registry-based studies showed that Black, Hispanic, Asian women had lower clinical pregnancy rates and live birth rates after IVF versus White women.
- Most clinic specific studies showed similar disparities in these outcomes
- Studies varied with respect to definitions of race/ethnicity, clarification of first cycle vs multiple cycles
- 
- Humphries LA, Chang O, Humm K, et al AJOG 2016 vol 214 #2 p212-217

# Differences in IVF outcome between white and black women in an inner-city, university-based IVF program

- Retrospective
  - White: 95, 121 cycles
  - Black: 37, 47 cycles
  - Outcomes: implantation rate, pregnancy rate
- 
- Sharara FI, McClamrock HD. Fert Stert 2000 Jun;73(6):1170-3

# Differences in IVF outcome between white and black women in an inner-city, university-based IVF program (contd.)

- Black women
- 28.0% of the population
- 28.0% of the total cycles.
- No significant differences in age, basal FSH, number of ampules, duration of stimulation, endometrial thickness, P on the day of hCG, cancellation rate, number of oocytes, or embryos transferred.
- Significantly higher:
- Duration of infertility, body mass index (BMI), incidence of tubal-factor infertility, peak E<sub>2</sub> levels.
- Aggressive ovarian stimulation: needed in 70.2% vs 43.0% needed in White women
- Significantly lower
- Implantation rate: 9.8% vs 19.2% in White women
- Clinical pregnancy rate: 23.4% vs 42.2% in White women
- Sharara FI. 2000

# Factors Affecting IVF Success Rates



## Body mass index, not race, may be associated with an alteration in early embryo morphokinetics during IVF

- assessed the relationship b/w maternal BMI and embryo morphokinetics on time-lapse microscopy (TLM).
- Retrospective cohort study
- All IVF cycles between June 2015 and April 2017
- BMI prior to egg retrieval was collected through chart review.
- BMI ( $\text{kg}/\text{m}^2$ ) : underweight ( $< 18.5$ ), normal weight ( $18.5-25$ ), overweight ( $25-30$ ), and obese ( $\geq 30$ ).
- Embryos' morphokinetic parameters were assessed with TLM
- time to syngamy (fertilization), 2-cell, 3-cell, 4-cell, and 8-cell.
- Kassi LA, McQueen DB, Kimelman D, et al. J Assist Reprod Genet 2021 Dec 38 (12) 3091-3098



# BMI not race (contd)

## Results:

2150 embryos, 589 IVF cycles

BMI groups: underweight ( $N = 56$ ), normal weight ( $N = 1252$ ), overweight ( $N = 502$ ), and obese ( $N = 340$ ).

Adjusted for **race and use of ICSI**:

the mean time to the 8-cell stage in the underweight group was 4.3 (95% CI:  $-8.31, -0.21$ ) hrs less than in the normal weight group ( $P = 0.025$ ) and 4.6 (95% CI:  $-8.8, -0.21$ ) hrs less than in the obese group ( $p = 0.022$ ).

# BMI (not race) Conclusions.

Embryos from **underweight** women had a faster time to the 8-cell stage than normal weight or obese women.

- No significant difference was noted for race (after correcting for confounders).
- Weight (**not race**) can be a factor contributing to embryo development as observed with TLM.
- Kassi LA. 2021

## Racial disparities in frozen embryo transfer success

- Compare the pregnancy & birth outcomes after frozen embryo transfers (FET) in White, Black, Asian women
- Retrospective
- Autologous FET
- January 2013-March 2020
  
- Heyward Q, Walter JR, Alur-Gupta S et al J Assist Reprod Genet 2021 Dec;38(12):3069-3075

# Racial disparities in FET success

	White	Black	Asian
• Cycles completed	1181 (71.7%)	230 (14.0%)	235 (14.3%)
• Positive hCG level*	802 (67.9%)	132 (57.4%)	160 (68.1%)
• Clinical pregnancy	678 (57.4%)	110 (47.8%)	131 (55.7%)
• Live birth*	516 (45.1%)	76 (33.3%)	93 (41.5%)

• \*  $p < 0.05$

• Heywerd Q. 2021

# Racial disparities in frozen embryo transfer (contd.)

- Conclusion:
- Black race is associated with significantly worse pregnancy and live birth rates following FET when compared to White race.
- Additionally, significant differences in live birth rates among White, Black, and Asian women exist following natural cycle FET versus programmed FET.
- These disparities in success are not only important for patient counseling, but also when determining management strategies to improve fertility rates among minority women.
- Heywerd Q 2021

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- Heyward Q. 2021

# National egg freezing trends: cycle and patient characteristics with focus on race/ethnicity

- Assess trends and characteristics of oocyte cryopreservation (OC) cycles stratified by self-reported race/ethnicity in the US
- Retrospective cohort analysis using Society for Assisted Reproductive Technology Clinical Outcome Reporting System (SART-CORS)
- US fertility clinics
- All patients undergoing OC from 2012 through 2016
- Race/ethnicity groups: non-Hispanic white, non-Hispanic black, Asian/Pacific islander, Hispanic, and other (American Indian, Alaskan native, or mixed race).
- Katler QS, Shandley LM, Hipp HS, et al. Fertil Steril 116(2):528-537. 2021

# Egg freezing trends—race/ethnicity (contd.)

- Results:
- 2012 – 2016
- 29,631 OC cycles
- White patients using OC: 66.5%
- When compared with the demographics of the US, OC was underused by some minority patient groups.
- Total # of OC cycles increased annually among all the ethnic groups, most notably among Asian patients.
- Patients of **all** ethnic backgrounds: age <35 years of age
  - underwent 1 OC cycle
- Asian patients ages: 35 - 37 years
  - $\geq 2$  cycles
- After adjustment for cofounders, there were no clinically significant differences in oocyte yield and the percentage of maturation across the racial/ethnic groups.



# Egg freezing trends

- Nationally, OC cycles are increasing in number
  - Most often seen in patients < 35 years
  - Similar proportions of patients of all minority groups pursue OC.
  - The oocyte yield is comparable across the ethnic groups.
- 
- Katler QS. 2021

# Race, ovarian responsiveness & live births after IVF

- To determine if ovarian responsiveness to gonadotropin stimulation differs by race/ethnicity
- Determine whether this predicts live birth rates (LBRs) in non-White patients undergoing IVF.
- Retrospective cohort study.
- White, Asian, Black, and Hispanic patients undergoing ovarian stimulation for IVF.
- Self reported race/ethnicity
  
- Lee IT, Berger DS, Koelper N, et al. Fertil Steril 120(5),1023-32. 2023

# Race, ovarian responsiveness & live birth (contd)

- Primary outcome: ovarian sensitivity index (OSI)
- # of oocytes retrieved  $\div$  total gonadotropin dose)  $\times$  1,000
- (to measure of ovarian responsiveness)
- adjusting for age, body mass index, infertility diagnosis, and cycle number.
- Secondary outcome: live birth and clinical pregnancy after first retrievals
- adjusting for age, infertility diagnosis, and history, body mass index, dx and duration of infertility.
- Lee IT. 2023

# Race, ovarian responsiveness & live birth (contd.)

- Primary analysis of OSI
- 3,360 (70.2%) retrievals from White patients, 704 (14.7%) retrievals from Asian patients, 553 (11.6%) retrievals from Black patients, and 168 (3.5%) retrievals from Hispanic patients.
- Black and Hispanic patients had higher OSIs than White patients (after accounting for those with multiple retrievals and adjusting for confounders)
- 6.08 in Black, 6.27 in Hispanic, 5.25 in White.
- There was no difference in OSI between Asian and White patients.
- Lee IT. 2023

# Race, ovarian responsiveness & live births (contd.)

- Pregnancy outcomes analyses:
- 2,299 retrievals.
- Greater ovarian responsiveness in Black and Hispanic patients
- Lower live births
- (not significant after adjusting for confounders)(adjusted odds ratio, 0.83; 95% confidence interval [CI], 0.63–1.09, for Black; adjusted odds ratio, 0.93; 95% CI, 0.61–1.43, for Hispanic).
- Ovarian sensitivity index was modestly predictive of live birth in White and Asian patients but not in Black (area under the curve, 0.51; 95% CI, 0.38–0.64) and Hispanic (area under the curve, 0.50; 95% CI, 0.37–0.63) patients.
- Lee IT 2023

# Race, ovarian responsiveness & live births (contd.)

- Conclusions:
- Black and Hispanic patients have higher ovarian responsiveness to stimulation during IVF but do not experience a consequent increase in live births.
- Factors beyond differences in responsiveness to ovarian stimulation need to be explored to address the racial/ethnic disparities previously described.
  
- SDoH

# Influence of Paternal Race on Characteristics and Outcomes of Assisted Reproductive Technologies

- Association between paternal race and reproductive outcomes (pregnancy, miscarriage, live birth) following IVF.
- Stratified by male and female partner race
- 2014-2019
- 1878 IVF cycles; 1069 couples.
- 86.5% shared a common self reported race
  
- |            | <u>Males</u>   |
|------------|--|
| • White    | 50.1% younger (37.0 yrs), lower BMI (28.0), lower rate of male factor (33.5%)  |
| • Black    | 28.5% older (39.6 yrs) , higher BMI (30.4), higher rate of male factor (91.8%) |
| • Asian    | 15.1%  |
| • Hispanic | 2.3%   |
  
- Vest AN, Kipling LM, Patil D, et al Urology 2022 May:163:56-63

# Influence of Paternal Race on Characteristics and Outcomes of Assisted Reproductive Technologies (contd.)

- Female partners

	<u>Black male</u>	<u>White male</u>
• age	older (35.6 yrs )	younger (33.8 yrs)
• BMI	29.6	25.2
• Rate of female factor	91.8%	83.9%

- Vest AN et al 2022



# Influence of paternal race--IVF cycle characteristics

- Paternal race did impact variability in IVF cycle characteristics
- Rates of oocyte banking were low in the overall cohort

Male Partner	non-H White%	Black%	Hispanic%
all oocytes/embryos frozen	8.4	5.1	0
Pre-implantation genetic testing	18.5*	14%*	8.5*
Donor oocyte	7.4	6.1	4.3
Gestational carrier	1.7	0.7	0
ICSI	53.5	51.3	46.8
Cancelled cycles	8.2	10.0	10.6

- \*P <0.05
- Vest AN 2022

# Influence of Paternal Race on Characteristics and Outcomes of Assisted Reproductive Technologies (contd.)

	non-H White%	Black%	Hispanic%
• Singleton pregnancy	82.2	79.6	80.6
• biochemical pregnancy	57	25	18
• clinical intrauterine pregnancy	59.7	53.9	52.5
• ectopic pregnancy	0.3	0.7	1.0
• No significant differences			
• Vest AN et al 2022			

# Public perspectives on the use of preimplantation genetic diagnosis

- To study the perspectives of the US population towards the use of preimplantation genetic diagnosis (PGD) in various clinical scenarios.
- Online cross-sectional population based questionnaire of a nationally representative sample
- age, gender, [race/ethnicity](#), income, education and religion.
- Winkleman WD, Missmer SA, Myers D, et al. J Assist Reprod Genet. 2015 May; 32(5): 665–675.

## Public perspectives (contd.)

- 1006 completed the questionnaire
- overall response rate of 94 %.
- A majority supported PGD for diseases fatal early in life or those causing lifelong disability (72.9 and 66.7 %, respectively)
- 48.0 % supported PGD for diseases that manifest late in life.
- Respondents were more supportive of PGD for genetic diseases if they were aware of PGD prior to the survey (OR = 1.64; CI = 1.13–2.39).
- However, a small proportion were in favor of genetically-based trait selection:
- 21.1 % supported PGD for sex selection
- 14.6 % for physical traits
- 18.9 % for personality traits.

# Public perspectives (contd)

- Compared to women, men were nearly two- to three-fold more supportive of PGD for:
  - sex selection (OR = 1.65; CI = 1.20–2.78),
  - physical traits (OR = 2.38; CI = 1.60–3.48)
  - personality traits (OR = 2.31; CI = 1.64–3.26).
- Compared to Caucasians, Asians (OR = 3.87; CI = 1.71–8.78) and African Americans (OR = 1.61; CI = 1.04–2.74) were more supportive of PGD for sex selection.
- Winkleman WD. 2015

# Social Determinants of Health



# Social determinants of health (SDoH) affecting IVF outcomes

- SDoH also determine healthcare utilization and adherence to treatment
- **WHO defines social determinants of health as “*non-medical factors that influence health outcomes.*”**
- *They are the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies and political systems”*
- This broad definition can include numerous non-clinical factors of health such as age, gender, ethnicity, education, income and social security, social support, food security, housing, job security, harmful alcohol consumption or tobacco addiction, etc.

# Social Determinants of Health

- There is relatively low minority representation in IVF clinics.
- Therefore, literature on ART predominantly reflects the experiences of white women.
- This is problematic because racial and ethnic groups differ in fertility characteristics and incidence of adverse perinatal outcomes.
- Disparities found in the outcomes of spontaneously conceived pregnancies are known to persist after adjustment for socioeconomic status and demographic characteristics, suggesting that other biological, environmental, or behavioral factors are at play.



# Social determinants of health (contd)

- These same factors may affect IVF outcomes as well.
- Black and Hispanic women are more likely to have preterm birth after IVF, compared with White women
- Infants born to Black, Hispanic, and Asian women after IVF are more likely to have moderate and severe growth restriction.
- A recent study of ART in the United States reported that, of all the patient characteristics thought to influence ART success, non-Hispanic black race had the strongest negative association with a good perinatal outcome after ART.
- Ebeh DN, Jahanfar S. SN Compr Clin Med 2021;3(5):1106-1114

## SDoH (contd)

- Analysis of National ART Surveillance System data, 2014
- ART utilization was higher among Black women in states with IVF mandates vs in states without mandates.
- However, utilization rates for Black and Hispanic women were still lower than the overall utilization rate for those states.
- Analysis using SARTCORS (Society of Assisted Reproductive Technologies Clinical Outcomes Reporting System) data found no evidence that state mandates mitigate racial and ethnic disparities in IVF utilization.
- Although utilization was higher across all racial groups in states with mandates, the increase was greatest for White women.

## Conclusions

The burdens of race remain as long term factors affecting the success of IVF

These burdens are confounded by social determinants of health affecting people of colour

Knowledge of these burdens may help to mitigate the adverse impacts and assist in ensuring IVF successes