Enhancing the Diversity of Clinical Trial Populations- From FDA Guidance to Implementation

January 14, 2021

KHI KIDNEY HEALTH INITIATIVE

Disclaimer

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Welcome & Introductions

Melissa West
Senior Director,
ASN Research, Discovery and Innovation
Kidney Health Initiative

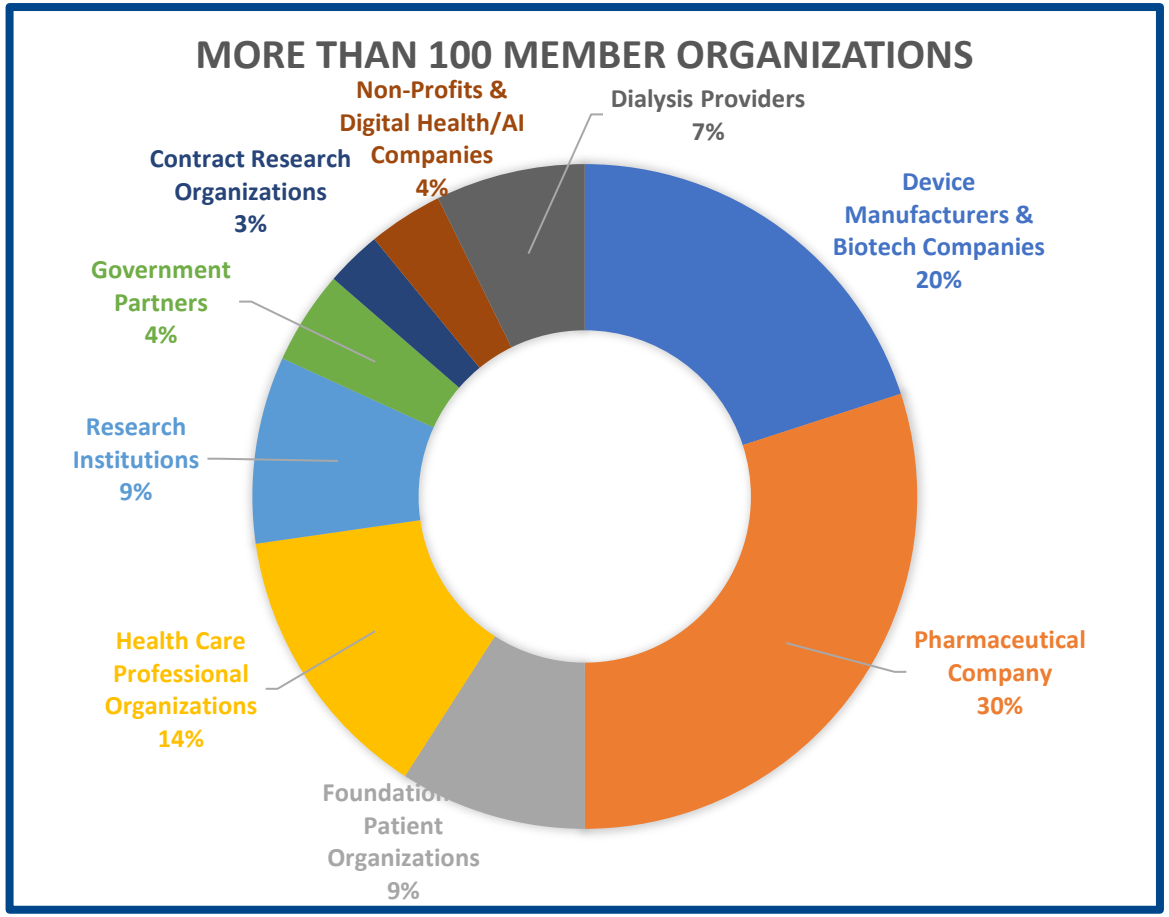
Today's Moderator

Barbara S. Gillespie, MD, FASN
KHI Board of Directors
Vice President, Therapeutic Head of Nephrology, Covance
and
Adjunct Professor, University of North Carolina

KIDNEY HEALTH INITIATIVE

A public-private partnership between the American Society of Nephrology, the U.S. Food and Drug Administration, and over 100 companies and organizations in kidney disease.

Established September 2012



KIDNEY HEALTH INITIATIVE

Mission

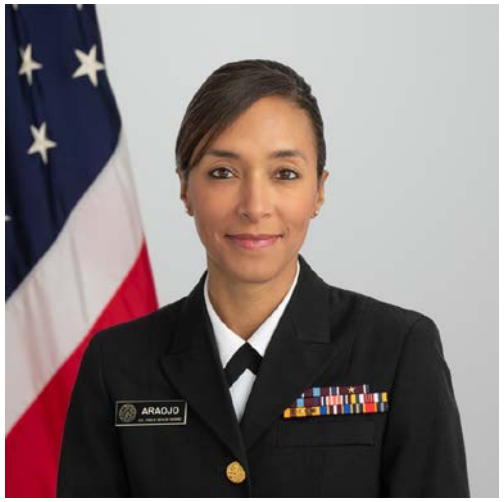
To catalyze innovation and the development of safe and effective patient-centered therapies for people living with kidney diseases.

KHI 2021
Board of Directors' Priority

Support efforts to address systemic racism in nephrology and address health disparities in kidney disease by ensuring the **Equity, Equality, Diversity and Inclusion of People with Kidney Disease in Clinical Trials.**

Specifically, we hope to cultivate patient engagement and partnerships to ensure participants in clinical trials reflect the community most impacted by the disease.

Today's Speakers



RADM Richardae Araojo, PharmD
FDA Office of Minority Health and Health Equity

Kirk N. Campbell, MD, FASN
Icahn School of Medicine at Mount Sinai

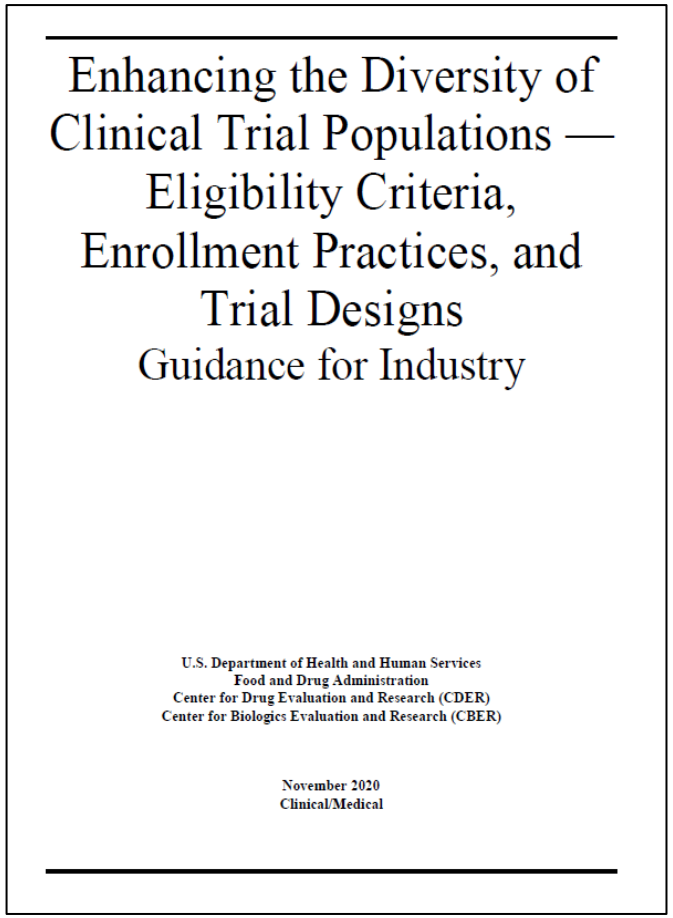
Owen Garrick, MD, MBA
Bridge Clinical Research

Lauren Lee
NephCure Kidney International

David M. White
KHI Patient and Family Partnership Council

TODAY'S OBJECTIVES

1. Review the background and elements of this FDA Guidance (finalized Nov 2020)
2. Outline key issues that are relevant to kidney diseases and associated trials.
3. Share past experiences, discuss future implementation strategies, and provide associated resources.



Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2020
Clinical/Medical

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial

Enhance the *Diversity*…to increase enrollment of *underrepresented* populations…this guidance considers:

Demographic characteristics	Non-Demographic Characteristics
Sex*	Patients with organ dysfunction
Race	Comorbid conditions
Ethnicity	Disabilities
Age	Extremes of weight range
Location of residency	Low prevalence diseases or conditions

These are the examples provided, but other characteristics should be considered

*women composed 45% of pivotal trials participants that led to FDA approvals from 2007-2017, short of the expected 49%

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial; and Tufts CSDD Impact Report, May/June 2020

Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity ("to be used in medical and clinical research")

Race

1. **American Indian or Alaska Native.** A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.

2. **Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

3. **Black or African American.** A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

4. **Native Hawaiian or Other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

5. **White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Ethnicity

1. **Hispanic or Latino.** A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

2. Not **Hispanic or Latino**

"its important to remember that race is a social construct and not just a biologic factor; we need to do a better job of tracking the social determinants that follow our arbitrary definitions of race"
—Dr. Keisha Gibson

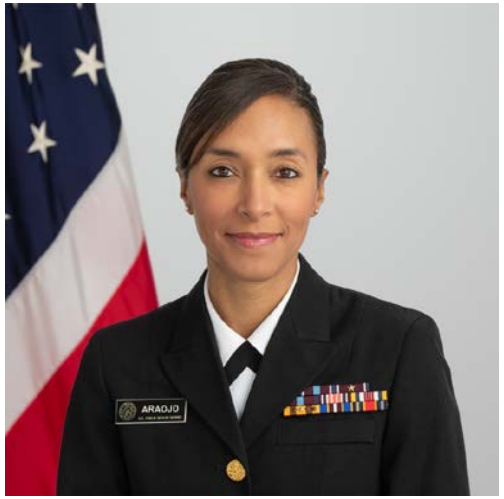
→ *"Are Arabs and Iranians white? Census says yes, but many disagree": Samira, of Iranian heritage, will have to choose white or other, and thinks that "erases a community"* (LA Times article, 2019)

→ *Race matters in CKD: understanding APOL1 genetic variants in CKD patients with African heritage can facilitate drug development in a personalized and precision medicine based manner if we study the right patients*

https://grants.nih.gov/grants/guide/notice-files/not-od-15-089.html; https://www.livescience.com/difference-between-race-ethnicity.html
Bryce, Whats the difference between race and ethnicity? Feb2020; https://open.lib.umn.edu/sociology/chapter/10-2-the-meaning-of-race-and-ethnicity/
https://www.census.gov/topics/population/race/about.html; https://www.latimes.com/projects/la-me-census-middle-east-north-africa-race/
Panico and Thompson in AJKD 2018 and Tuttle in CJASN 2018

KHI KIDNEY HEALTH INITIATIVE

FDA PERSPECTIVE



RADM Richardae Araojo, PharmD

U.S. FOOD & DRUG ADMINISTRATION

The FDA Office of Minority Health and Health Equity:

Working to Advance Clinical Trial Diversity

www.fda.gov/healthequity

Disclaimer

- This presentation represents the personal opinions of the speaker and does not necessarily represent the views or policies of FDA

- No conflicts of interest to declare

Objectives

- Provide an overview of the U.S. Food and Drug Administration's Office of Minority Health and Health Equity (OMHHE)
- Provide an update on FDA's efforts to advance clinical trial diversity
- Describe OMHHE's Diversity in Clinical Trials Initiative

Food and Drug Administration (FDA)

Mission

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

FDA also regulates the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

Consumer Protection Agency

Provide information on regulated products to ensure safe and effective use to consumers/patients/health care providers.

Regulatory Agency

Intersection of commerce, laws and public health

FDA Office of Minority Health and Health Equity (OMHHE)

Mission

To promote and protect the health of diverse populations through research and communication that addresses health disparities.

Vision

To create a world where health equity is a reality for all.

FDA OMHHE Goals

Goal 1: Improve regulatory science by increasing clinical trial data available on racial and ethnic minorities; improve data quality to determine how minorities react to medical products; and increase transparency and access to available data

Goal 2: Strengthen FDA's ability to respond to minority health concerns

Goal 3: Promote health and safety communication to minority populations who often experience low health literacy and/or speak English as a second language

What We Do

Research and Collaboration

- Intramural Research
- Extramural Research
- FDA Centers of Excellence in Regulatory Science and Innovation (CERSI) Projects
- Broad Agency Announcement (BAA)
- Other research opportunities
- Internships and Fellowships
- Academic Collaborations
- Stakeholder Input into Research Agenda

Outreach and Communication

- Programs/Initiatives/Campaigns
  - Diversity in Clinical Trials Initiative
  - Language Access Program
- Health Education Materials
- Social Media
- Newsletter & E-alerts
- Website
- Health Equity Lecture Series & Webinars
- Stakeholder Meetings/Symposiums/Exhibits
- Collaborations and Partnerships

The Need for Diverse Participation

- Racial and ethnic minorities have been historically under-represented in clinical trials
- Need representation to study the effects of medical products in the people who will ultimately use them
- Persons of different ages, races, and ethnicities could react differently to certain medical products
- To understand health disparities - diseases that occur more frequently or appear differently in diverse populations

Examples of Information Provided in FDA-Approved Product Labeling Directed at Specific Races/Ethnicities

Recommendation in FDA approved labeling	Example drug	Racial/ethnic information in the labeling	Rationale
Indicated for a specific racial population	Isosorbide dinitrate/ hydralazine	Indicated for self-identified blacks	Based on retrospective analyses, an effect on survival was reported in blacks, with little evidence to suggest an effect in the whites
Contraindicated in case of G6PD deficiency which is present in a higher frequency in specific racial populations	Rasburicase	Contraindicated in G6PD deficiency. Screen patients at a higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) prior to starting therapy	Recommendations to screen patients at a higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) prior to starting therapy because of the increased risk of hemolysis in patients with G6PD deficiency
Warnings and precautions directed at a specific racial population	Carbamazepine	Boxed warning for *HLA-B*1502* in Asian patients	Incidence of adverse event and prevalence of genetic factor are higher in Asian populations
Recommendations for considering alternative therapy for a specific racial population	ACE inhibitors or Angiotensin II antagonists, e.g., candesartan and losartan	A general statement for African-Americans/blacks in the labeling of a number of drugs belonging to this class because of the smaller effect size observed	Pathophysiologically, hypertension is driven less by the renin-angiotensin-aldosterone system in African-Americans/blacks
Different dosing recommendation for a specific racial population	Rosuvastatin	Lower initial starting dose in Asians	Based on clinical observation of ~2-fold higher exposure in Asians compared to Caucasians
	Tacrolimus	Higher dose in African-American transplant patients	Based on clinical observation; metabolized by CYP3A5 and African-American/black populations have low prevalence of reduced function variants compared to Caucasians

G6PD: glucose-6-phosphate dehydrogenase; HLA-B: human leukocyte antigen B; ACE: angiotensin-converting enzyme; CYP3A5: Cytochrome P450 3A5.

Ramamoorthy A, et al. Racial/ethnic differences in drug disposition and response: review of recently approved drugs. Clin Pharmacol Ther 2015;97:263–273.

Barriers to Clinical Trial Participation

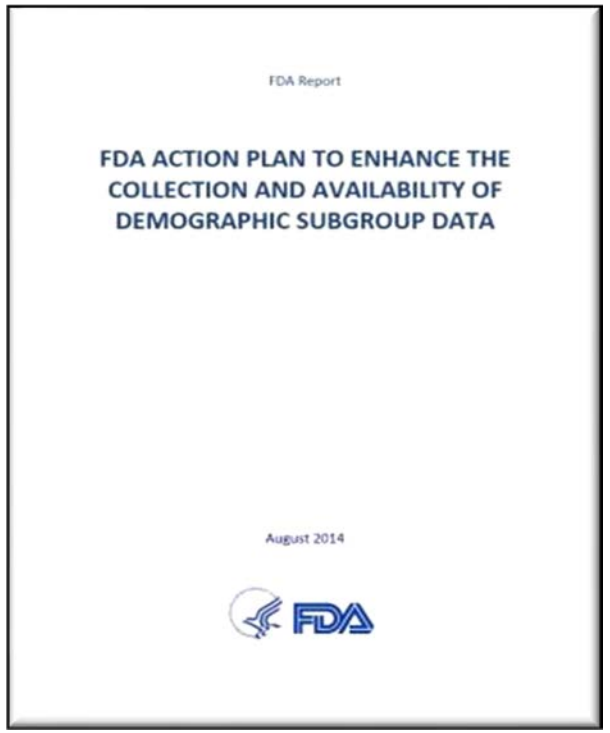
- Mistrust and distrust of the medical system due to historical abuses
- Lack of awareness of what a clinical trial is and what it means to participate
- Inadequate recruitment and retention efforts
- Lack of minority physicians, researchers, and clinical investigators
- Misunderstanding of racial/ethnic minorities' beliefs and values that contribute to their decision making process
- Lack of culturally and linguistically appropriate communication
- Perception that racial/ethnic minorities do not want to participate
- Physicians/providers may not talk to their patients about clinical trials
- Enrollment criteria
- Return of Results
- Privacy concerns
- Lack of access
- Time and resource constraints for patients

2012 FDA Safety and Innovation Act (FDASIA)

- **Section 907** - Reporting of Inclusion of Demographic Subgroups in Clinical Trials and Data Analysis in Applications for Drugs, Biologics, and Devices

  – Report to determine the extent of demographic subgroups in applications, in FDA reviews for safety and efficacy; if information is publicly available on FDA website or in labeling; **report posted August 2013**

  – Publish and provide to Congress an action plan outlining recommendations for improving the completeness, quality and availability of demographic subgroup data; **action plan posted August 2014**



2012 FDA Safety and Innovation Act (FDASIA) Section 907 Action Plan Priorities & Strategies

Priority One

Improve the completeness and quality of demographic subgroup data collection, reporting and analysis

(Quality)

FDA Guidance Documents

Collection of Race and Ethnicity Data in Clinical Trials

Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies

Priority Two

Identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation

(Participation)

Public Meetings

Tools to support diverse clinical trial participation

Priority Three

Make demographic subgroup data more available and transparent

(Transparency)

Drug Trials Snapshots

(Center for Drug Evaluation and Research)

Drug Trials Snapshots: Summaries (2017-2019)

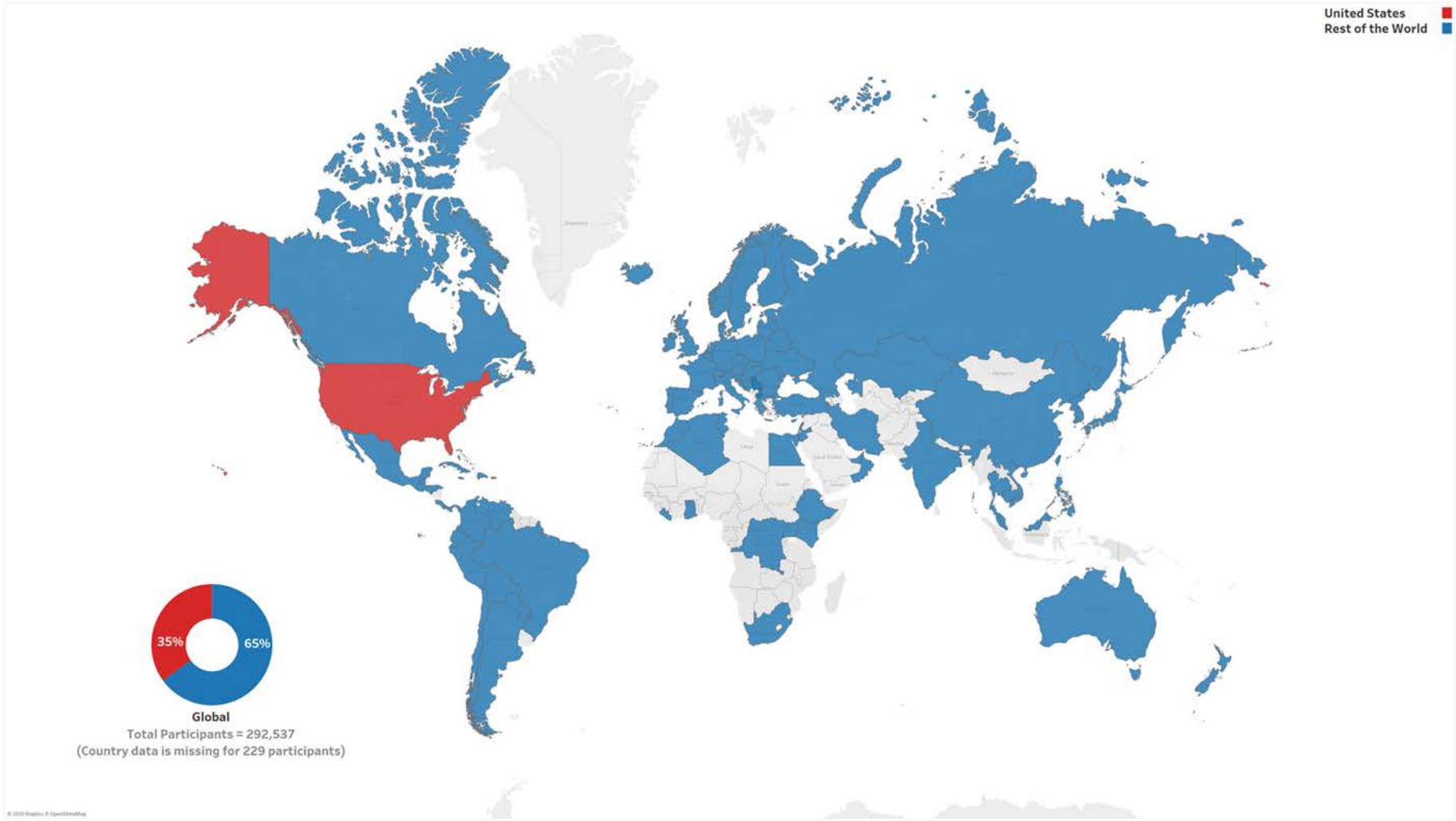
	WOMEN	BLACK or AFRICAN AMERICAN	ASIAN	WHITE	HISPANIC	AGE 65 AND OLDER	UNITED STATES
2017	55%	7%	11%	77%	14%	32%	34%

	WOMEN	BLACK or AFRICAN AMERICAN	ASIAN	WHITE	HISPANIC	AGE 65 AND OLDER	UNITED STATES
2018	56%	11%	10%	69%	14%	15%	47%

	WOMEN	BLACK or AFRICAN AMERICAN	ASIAN	WHITE	HISPANIC	AGE 65 AND OLDER	UNITED STATES
2019	72%	9%	9%	72%	18%	36%	40%

https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots

2015-2019: FDA DRUG TRIALS SNAPSHOTS
Five-Year Summary and Analysis of Clinical Trial Participation and Demographics



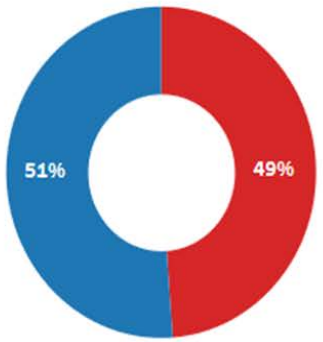
2015-2019: FDA DRUG TRIALS SNAPSHOTS
Five-Year Summary and Analysis of Clinical Trial Participation and Demographics

Demographics of Trial Participation

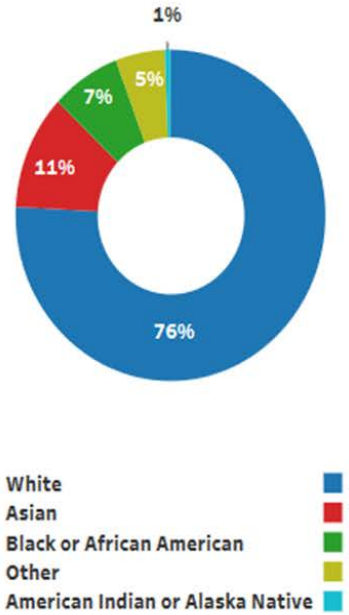
Demographic Categories

Clinical trial participation is broken down into four categories: sex, race, age, and ethnicity. *

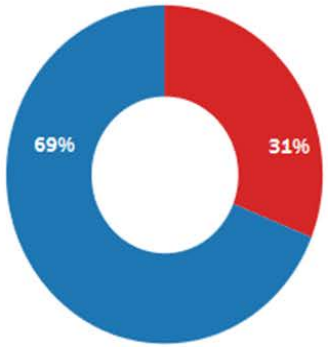
Sex Distribution



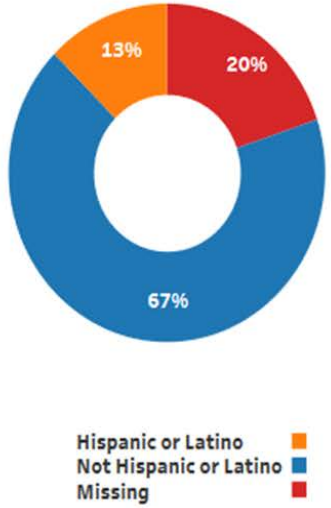
Race Distribution



Age Distribution



Ethnicity Distribution



*Definitions for race and ethnicity used in the document can be found in the Terminology section.

2015-2019: FDA DRUG TRIALS SNAPSHOTS
Five-Year Summary and Analysis of Clinical Trial Participation and Demographics

Ethnicity Composition

How Does Participation by Ethnicity Differ by Geographic Location?

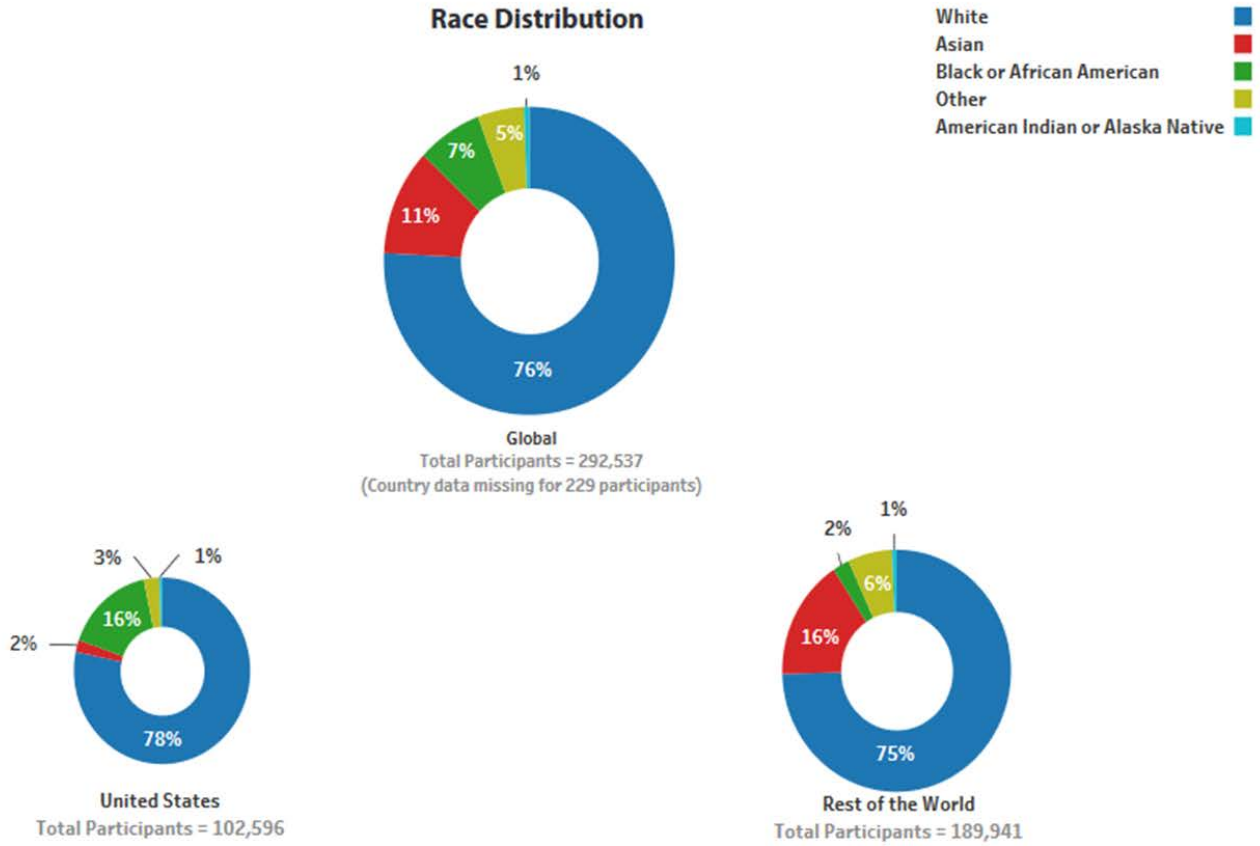
The highest proportion of Hispanics (15%) was reported by participants from the U.S.

2015-2019: FDA DRUG TRIALS SNAPSHOTS
Five-Year Summary and Analysis of Clinical Trial Participation and Demographics

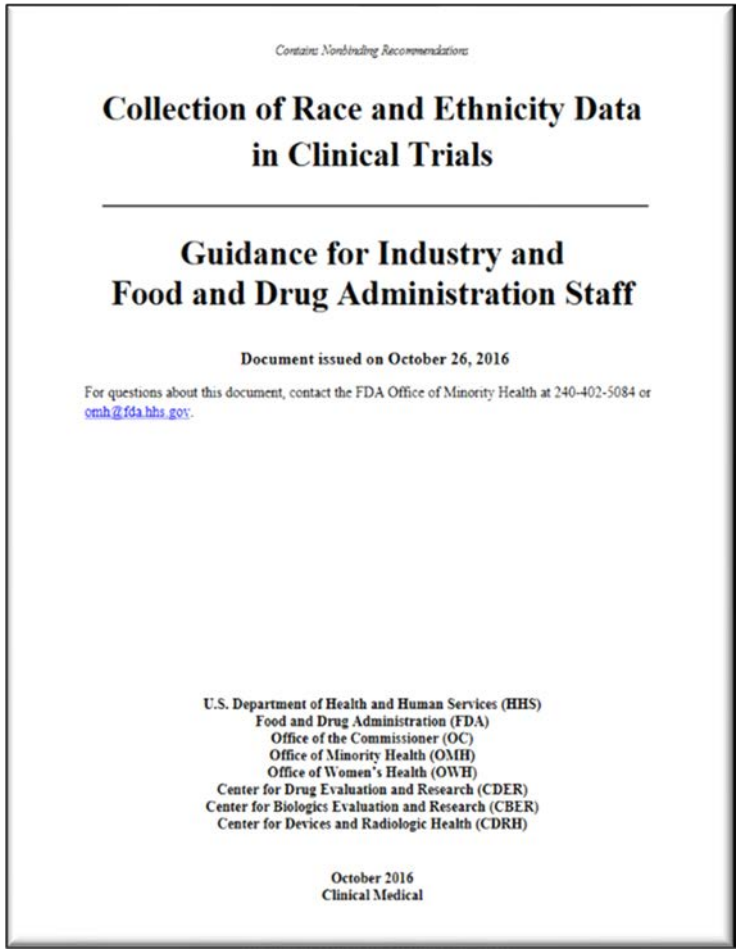
Race Composition

How Does Participation by Race Differ by Geographic Location?

Most Asian trial participants were enrolled at non-U.S. sites; in contrast, most Black or African Americans were from U.S. sites.



Guidance Documents for Industry



Contains Nonbinding Recommendations

Collection of Race and Ethnicity Data in Clinical Trials

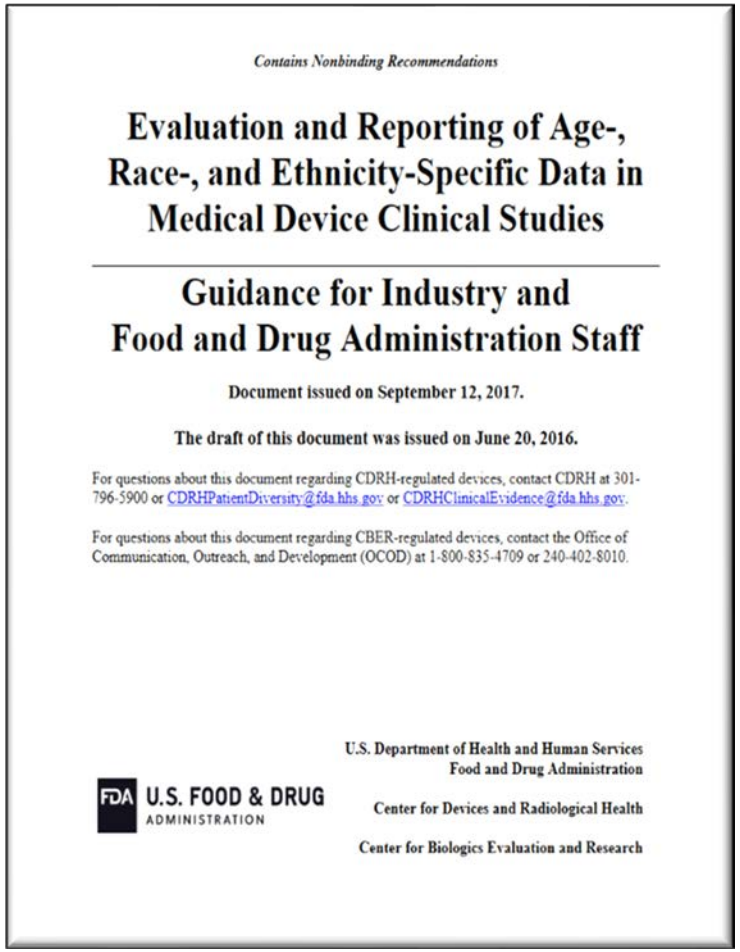
Guidance for Industry and Food and Drug Administration Staff

Document issued on October 26, 2016

For questions about this document, contact the FDA Office of Minority Health at 240-402-5084 or omh@fda.hhs.gov.

U.S. Department of Health and Human Services (HHS)
Food and Drug Administration (FDA)
Office of the Commissioner (OC)
Office of Minority Health (OMH)
Office of Women's Health (OWH)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiologic Health (CDRH)

October 2016
Clinical Medical



Contains Nonbinding Recommendations

Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 12, 2017.

The draft of this document was issued on June 20, 2016.

For questions about this document regarding CDRH-regulated devices, contact CDRH at 301-796-5900 or CDRHPatientDiversity@fda.hhs.gov or CDRHClinicalEvidence@fda.hhs.gov.

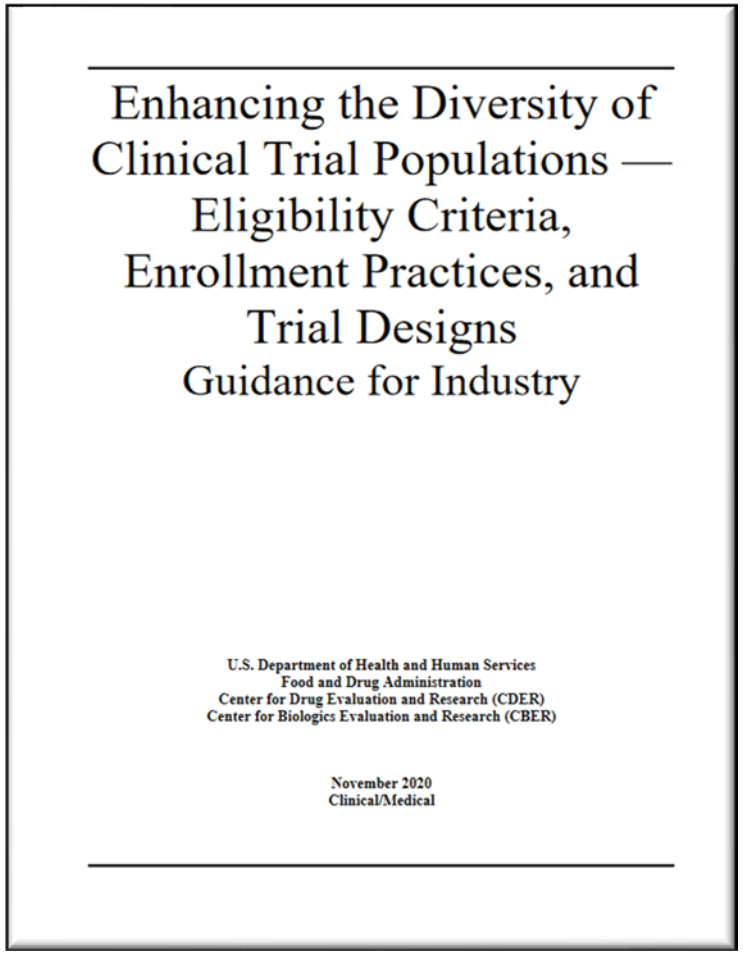
For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research



Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs

Guidance for Industry

U.S. Department of Health and Human Services
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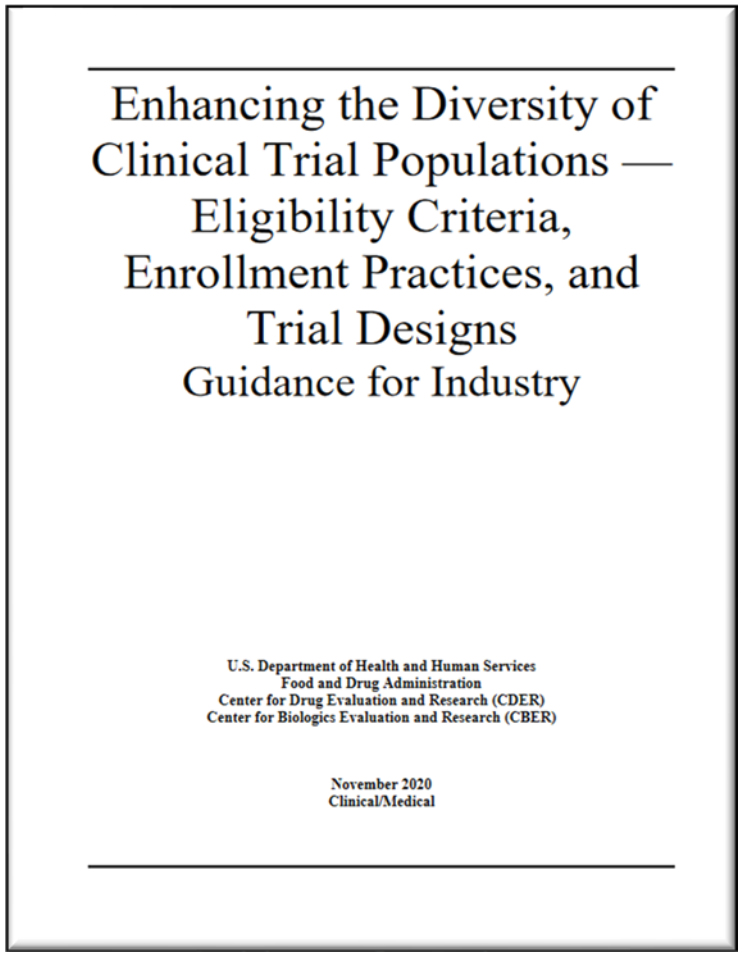
November 2020
Clinical/Medical

Guidance Documents for Industry



- Provides the agency's current thinking on steps to broaden eligibility criteria in clinical trials through inclusive trial practices, trial designs, and methodological approaches.
- Provides recommendations for how sponsors can increase enrollment of underrepresented populations in their clinical trials and improve trial recruitment so that the participants enrolled in trials will better reflect the population most likely to use the drug, if the drug is approved, while maintaining safety and effectiveness standards.
- Provides recommendations for broadening eligibility criteria and encouraging recruitment for clinical trials of investigational drugs intended to treat rare diseases or conditions.

Other Regulations and Guidance

- IND regulations, at 21 CFR 312.33(a)(2), require that IND data regarding subjects' participation in clinical trials be presented in annual reports by gender, age, and race.

- NDA regulations, at 21 CFR 314.50(d)(5)(v) and (vi)(a), require sponsors of NDAs to include summaries of effectiveness and safety data presented by gender, age, and race.

- Other guidance documents

COVID-19
Inclusion of Diverse Populations

- FDA Guidance for Industry on Development and Licensure of Vaccines to Prevent COVID-19; June 2020
  - "FDA encourages the inclusion of diverse populations in all phases of vaccine clinical development. This inclusion helps to ensure that vaccines are safe and effective for everyone in the indicated populations."
  - "FDA strongly encourages the enrollment of populations most affected by COVID-19, specifically racial and ethnic minorities."
- FDA Guidance for Industry on COVID-19: Developing Drugs and Biological Products for Treatment or Prevention; May 2020
  - "Racial and ethnic minority persons should be represented in clinical trials. Sponsors should ensure that clinical trial sites include geographic locations with a higher concentration of racial and ethnic minorities to recruit a diverse study population."

Strategies to Support Diverse Participation

- There is not a one size fits all approach
- All actions should begin and end with the patient in mind
- A plan to address inclusion should be developed early on
- Consistent and continued community engagement
- Engage patients in trial design, logistics, and recruitment and retention practices
- Site locations where there are more racial and ethnic minorities
- Workforce diversity
- Engage providers
- Cultural sensitivity, competency, and awareness
- Eliminate language barriers
- Organizational goals that support diversity

Diversity in Clinical Trials Initiative

Developed an ongoing multi-media public education and outreach campaign to raise awareness around the importance of diverse participation in clinical trials.

Motivators for Campaign

- Reinforce the importance of diverse participation
- Educate consumers about key issues
- Help stimulate dialogue among peers and patient-provider

Diversity in Clinical Trials Campaign

- Videos
- Newsletters & E-alerts
- Webpage
- Stakeholder Collaboration
- Podcasts
- Social Media
- Communications Toolkit
- Culturally & Linguistically Tailored

Diverse Participation in Clinical Trials
Videos I Podcast I Social Media

Shirley's Story: Diversity is Critical to Making Better Medical Products

Veterans in Clinical Trials

Veterans Health Administration
Office of Health Equity

Diversity in Medical Device Clinical Trials Video

Clinical Trial Diversity Resources

Clinical Trial Diversity

FACT SHEET

Clinical trials are research studies that determine whether medical products like medicines, vaccines, or devices are safe and effective. These studies may show which medical approaches work best for certain illnesses or groups of people.

Office of Minority Health and Health Equity

4 things you should know about clinical trials

1. Clinical trials are research studies conducted with people—they are designed to answer specific research questions about medical products or procedures. Researchers must follow detailed protocols and the FDA's safety guidelines to make each trial as safe as possible.

2. Participation is always voluntary—and you can leave a study whenever you want.

3. Clinical trials often need **healthy volunteers** to help answer research questions.

4. FDA does not conduct clinical trials—FDA works with companies that develop medical products to protect participants and review the results to ensure that the medical product is safe and effective.

The importance of diverse participation in clinical trials

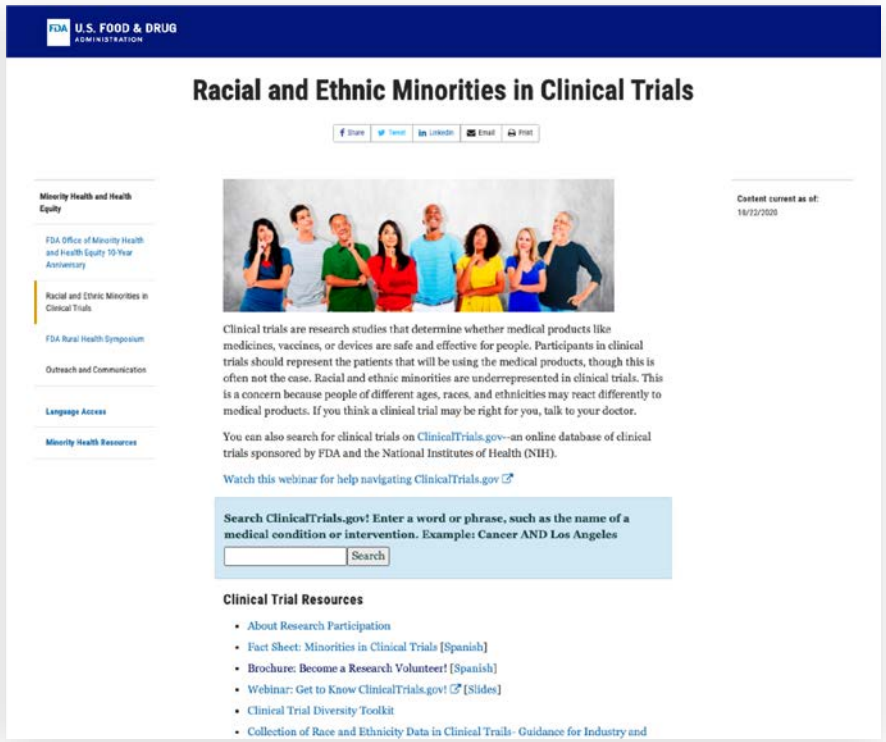
Participants in clinical trials should represent the patients that will use the medical products. This is often not the case–racial and ethnic minorities are underrepresented in clinical research. This is a concern because people of different ages, races, and ethnicities, may react differently to medical products. We are committed to working with companies to change this. Joining a clinical trial might be a good choice for you if:

- You and your doctor believe current treatments aren't good options and a clinical trial offers additional alternatives.
- You want to help ensure that the benefits and risks of new medical products are studied in the diverse patients likely to need them.
- You want to help researchers find better ways to fight diseases.

If you think a clinical trial may be right for you, talk to your doctor. You can also search for clinical trials through an online database, **www.ClinicalTrials.gov**.

If you want to know more about a recently approved drug you may be taking, visit the **Drug Trials Snapshots**—a database that gives you information on who participated in a trial for drug approvals. You can find more information at **www.FDA.gov/DrugTrialsSnapshot.**

For more information on minority health go to **www.fda.gov/healthequity.** To watch videos and view a list of questions to ask researchers go to **www.hhs.gov/about-research-participation**.



Examples of Stakeholder Engagement Activities

- **FDA CDER Small Business and Industry Assistance webinar on *Diversity in Clinical Trials: Learn about Enrollment Trends and Resources from FDA***
  - December 16, 2020 from 1:00 - 2:30 p.m. Eastern (link to recording)

Examples of Stakeholder Engagement Activities

KIDNEYTODAY
The American Kidney Fund Blog

Home > Kidney Today > Minorities and Clinical Trials: Why it Matters

Minorities and Clinical Trials: Why it Matters

Author(s): Cariny Nunez and Jovonni Spinner
Topics: News , Living with kidney disease , Healthy living

Clinical trials are "voluntary human research studies designed to answer specific questions about the safety and effectiveness of medical products, which include drugs/medications, vaccines, devices, diagnostic tests, and other therapies, or to study new ways of using existing treatments" [1]. Before the Food and Drug Administration (FDA) can approve new medical products, experimental medications and therapies are tested in controlled environments on the people most likely to use them. This process enables FDA and medical product developers to ensure that medical products are safe and that they work for their intended uses.

Clinical Trials and Kidney Disease
American Kidney Fund Webinar
Speaker: Jovonni R. Spinner, FDA OMHHE
Estudios clínicos y enfermedad renal
Speaker: Cariny Nuñez, FDA OMHHE

Upcoming FDA UMD-CERSI Workshop

COLLABORATING TO ADVANCE HEALTH EQUITY FOR DIABETES AND CHRONIC KIDNEY DISEASE

February 10, 2021

Workshop Objectives:

- Leveraging patient experience data and community/system approaches to inform care, drug development and overall research agenda to improve patient outcomes and reduce health inequities for diverse communities with diabetes and chronic kidney disease (CKD).
- Explore barriers to diversity in clinical trials for CKD and diabetes and strategies to improve diversity in clinical trials.
- Utilization of real-world data to inform strategies and decision making on the management of diabetes and CKD.

Examples of Stakeholder Engagement Activities

- The Alliance of Multicultural Physicians and FDA OMHHE Memorandum of Understanding
  - Collective of the Association of American Indian Physicians (AAIP), Association of Black Cardiologists (ABC), National Council of Asian Pacific Islander Physicians (NCAPIP), National Hispanic Medical Association (NHMA), and National Medical Association (NMA). Opportunities to collaborate on developing educational, outreach, and training initiatives for physicians and the patients they serve to advance health equity.

- Yale and FDA OMHHE Memorandum of Understanding
  - To advance the Yale Cultural Ambassadors Program, an engagement of community partners to increase diverse participation in clinical research

Examples of Stakeholder Engagement Activities

- The Multi-Regional Clinical Trials Center and Harvard, “Achieving Diversity, Inclusion, and Equity in Clinical Research” Workgroup and Diversity Framework
  - Heterogeneity of Treatment Effects in Clinical Trials: Methods and Innovations; November 30 - December 1, 2020.

- Clinical Trials Transformation Initiative (CTTI) Diversity Project
    - CTTI is a Public-Private Partnership Co-founded by Duke University and FDA

- Society for Clinical Research Sites (SCRS) Diversity Awareness Program

Thank You!

Follow us at: @FDAHealthEquity

Email us at: OMHHE@fda.hhs.gov

Visit us at: FDA.gov/HealthEquity

Join webinars and stakeholder calls

CULTURE SHIFT IN NEPHROLOGY: TRIAL PARTICIPATION IS AN OPTION FOR CARE

Barbara S. Gillespie, MD, FASN

KDIGO CLINICAL PRACTICE GUIDELINE ON GLOMERULAR DISEASES

PUBLIC REVIEW DRAFT
JUNE 2020

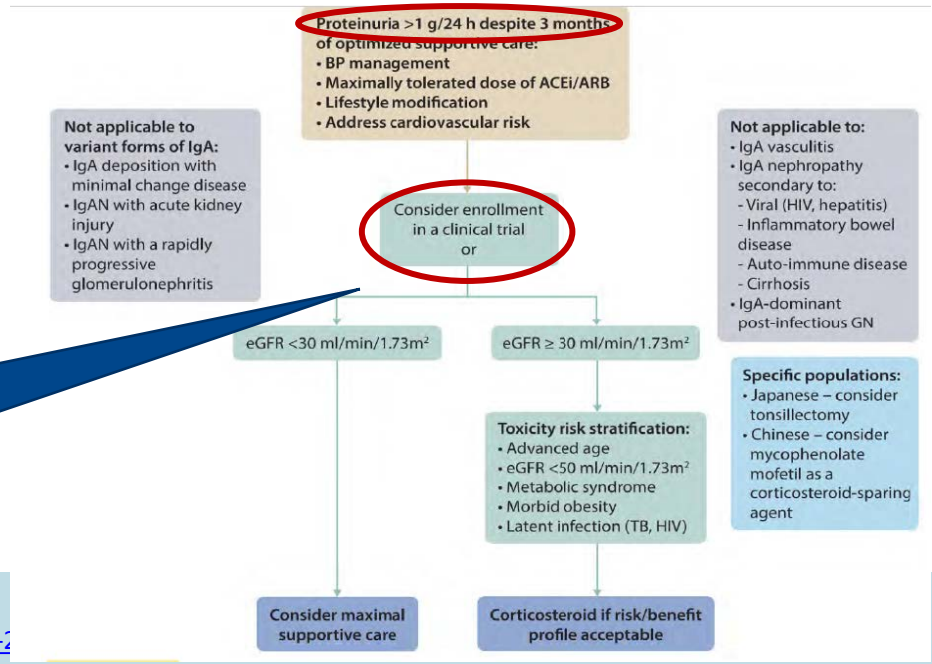
Trial participation is an option for clinical care…and now recommended in clinical practice guidelines!

Chapter 1: General Principles in Glomerular Disease Management

Practice Point 1.16.1. Patients with GN should be offered participation in a disease registry and clinical trials, whenever available.

Chapter 2: IgAN

All patients who remain at high risk of progressive CKD despite maximal supportive care should be offered the opportunity to take part in a clinical trial.



Offer trial participation to patients in which IgAN is most prevalent and more likely to cause kidney failure: ***East Asian*** > Caucasians >> African descent (rare)

"Asian Americans are the fastest growing minority group in the US, yet the least represented in [US] clinical trials"[1]

per communications with Dr. Jon Barratt;
https://kdigo.org/wp-content/uploads/2017/02/KDIGO-GN-GL-Public-Review-Draft_1-June-2
https://cebp.aacrjournals.org/content/26/2_Supplement/A16;
[1]2017 Lam et al abstract A16, Cancer Epidemiology, Biomarkers & Prevention (a publication of American Association for Cancer Research)

KHI KIDNEY HEALTH INITIATIVE

PATIENT PERSPECTIVE

David M. White

KHI Patient and Family Partnership Council (KHI PFPC)

The KHI PFPC is charged with driving patient-centered innovation in every stage of the development of devices, drugs, and biologics by:

- Assisting with the development of strategic priorities and goals that can help FDA, KHI members and patients partner to drive patient-centered innovation;
- Empowering patients and care partners to have equal and fair representation in product development conversations by developing and leveraging current educational and training tools;
- Advising KHI members on project proposals and identifying patients and care partners to serve on KHI or FDA related projects and initiatives; and
- Developing patient-centered project(s) to submit for KHI endorsement.

The KHI PFPC is not a decision making group. KHI PFPC's ideas and recommendations will be made to the KHI Board of Directors for review and approval.

Celeste Castillo Lee

KHI Patient and Family Partnership Council

Founding Chair

July 26, 1965 - February 9, 2017

2021 KHI PFPC Membership

- Mary Baliker
- Vanessa Evans (Incoming)
- Derek Forfang
- Patrick O. Gee, Sr., PhD, JLC
- Amanda Grandinetti, *KHI PFPC Vice Chair*
- Nichole Jefferson
- Jack Lennon
- Glenda Roberts
- David M. White, *KHI PFPC Chair*
- Leigh-Ann Williams (Incoming)

Photo Credit: 2019 &2020 KHI PFPC, ASN Kidney Week 2019, Washington, DC

KHI KIDNEY HEALTH INITIATIVE

NEPHROLOGIST'S PERSPECTIVE

Kirk N. Campbell, MD, FASN

Kidney Disease Underrepresentation in Clinical Trials

Underrepresentation of Renal Disease in Randomized Controlled Trials of Cardiovascular Disease

Table 2. Inclusion and Exclusion of Patients With Renal Disease in Cardiovascular Trials

	No. (%)
No. of trials	153
Trials excluding renal disease	86 (56)
Reported as excluded in original article or methods article	73 (48)
Reported as excluded via personal communication	13 (8)
Threshold for exclusion	
Serum creatinine >1.5-2.0 mg/dL (133-177 µmol/L)	19 (12)
Serum creatinine ≥2.1-2.9 mg/dL (186-256 µmol/L)	24 (16)
Serum creatinine ≥3.0 mg/dL (265 µmol/L)	16 (10)
eGFR ≤30 mL/min per 1.73 m²	3 (2)
No creatinine given (nonspecific exclusion)	24 (16)
Trials reporting proportion of patients with renal disease allocated to each arm	22 (14)
Reported in original article	8 (5)
Reported in subsequent article	14 (9)
Trials reporting baseline creatinine or eGFR given for each group	19 (12)
Reported in original article	15 (10)
Reported in subsequent article	4 (3)
Trials performing at least 1 subgroup analyses by baseline characteristics in original article	81 (53)
Average number of nonrenal subgroup analyses performed in original article, mean (SD)	5.8 (4.6)
Subgroup analysis performed on patients with renal disease	10 (7)
Reported in original article	4 (3)
Reported in subsequent article	6 (4)
Report on renal adverse effects (RAAS trials only)*	18/31 (58)

Coca et al JAMA 2006

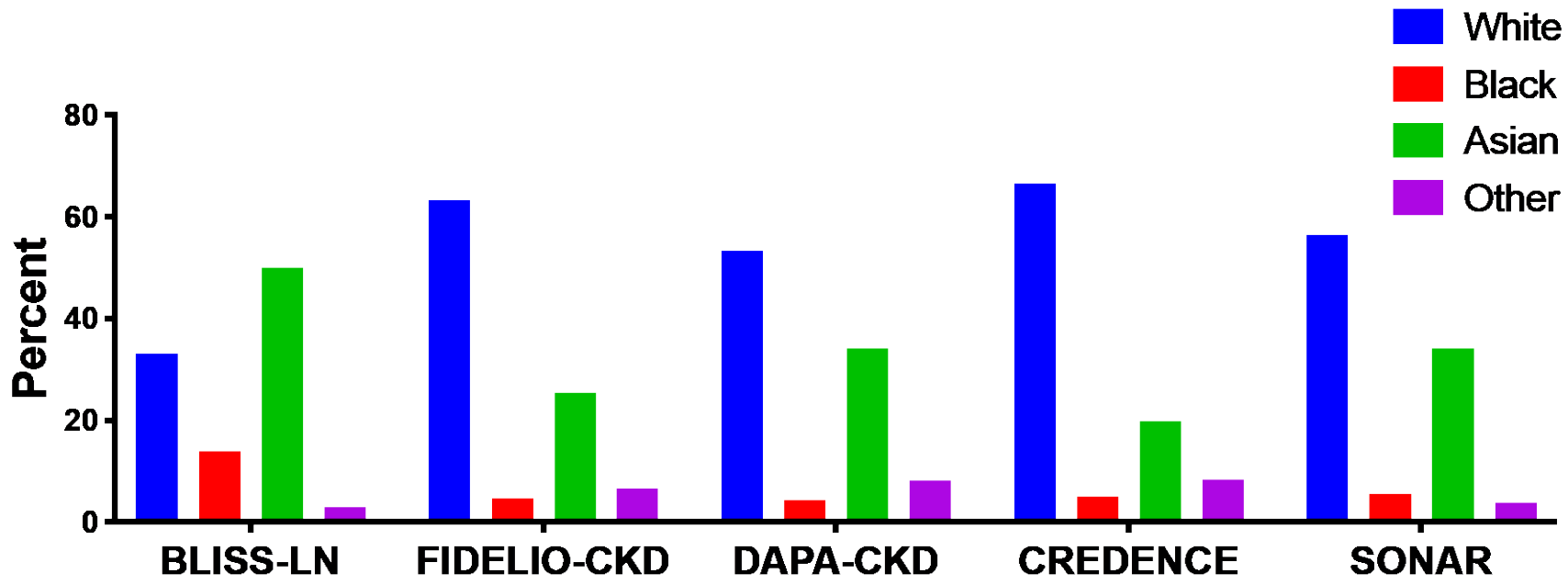
Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

	BNT162b2 (30 µg) (N[a]=18860)	Placebo (N[a]=18846)	Total (N[a]=37706)
Charlson Comorbidity Index Category	**n[b] (%)**	**n[b] (%)**	**n[b] (%)**
Participants with any Charlson comorbidity	3934 (20.9)	3809 (20.2)	7743 (20.5)
AIDS/HIV	59 (0.3)	62 (0.3)	121 (0.3)
Any malignancy	733 (3.9)	662 (3.5)	1395 (3.7)
Cerebrovascular disease	195 (1.0)	166 (0.9)	361 (1.0)
Chronic pulmonary disease	1478 (7.8)	1453 (7.7)	2931 (7.8)
Congestive heart failure	88 (0.5)	83 (0.4)	171 (0.5)
Dementia	7 (0.0)	11 (0.1)	18 (0.0)
Diabetes with chronic complication	99 (0.5)	113 (0.6)	212 (0.6)
Diabetes without chronic complication	1473 (7.8)	1478 (7.8)	2951 (7.8)
Hemiplegia or paraplegia	13 (0.1)	21 (0.1)	34 (0.1)
Leukemia	12 (0.1)	10 (0.1)	22 (0.1)
Lymphoma	22 (0.1)	32 (0.2)	54 (0.1)
Metastatic solid tumor	4 (0.0)	3 (0.0)	7 (0.0)
Mild liver disease	125 (0.7)	89 (0.5)	214 (0.6)
Moderate or severe liver disease	1 (0.0)	2 (0.0)	3 (0.0)
Myocardial infarction	194 (1.0)	188 (1.0)	382 (1.0)
Peptic ulcer disease	52 (0.3)	71 (0.4)	123 (0.3)
Renal disease	123 (0.7)	133 (0.7)	256 (0.7)
Rheumatic disease	62 (0.3)	56 (0.3)	118 (0.3)

Polack et al. NEJM 2020

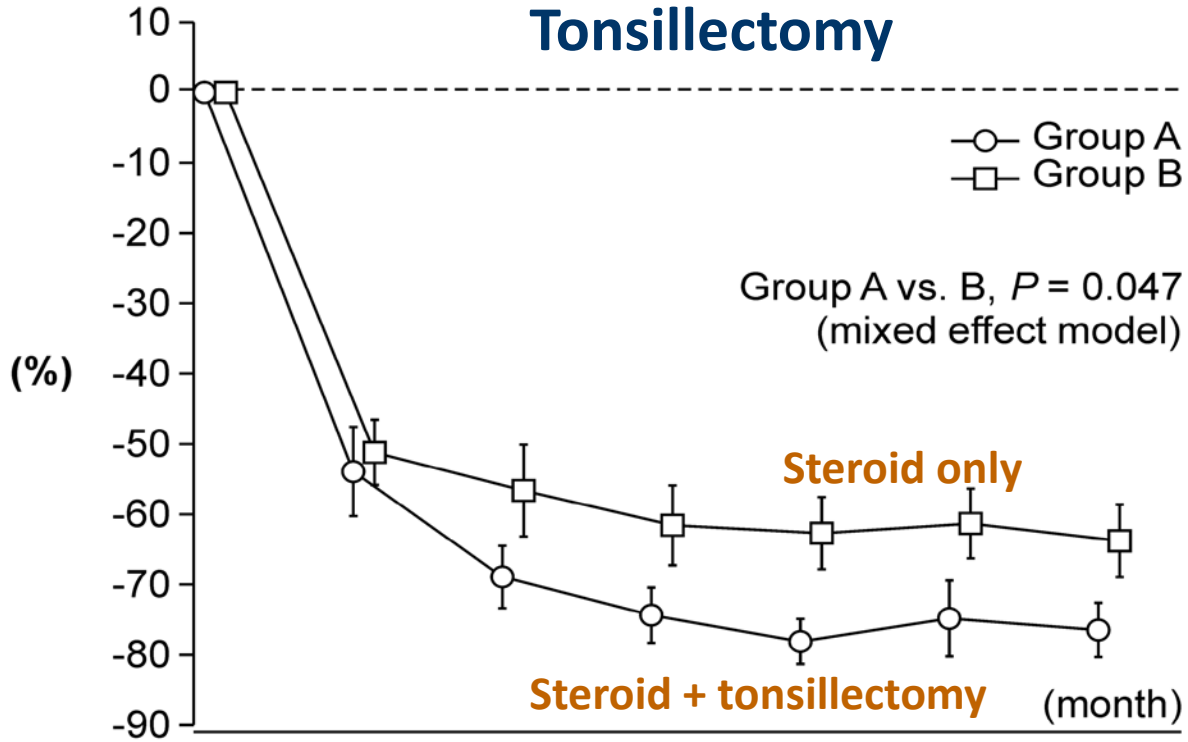
KHI KIDNEY HEALTH INITIATIVE

Low Minority Enrollment in Recent High Impact Nephrology Clinical Trials



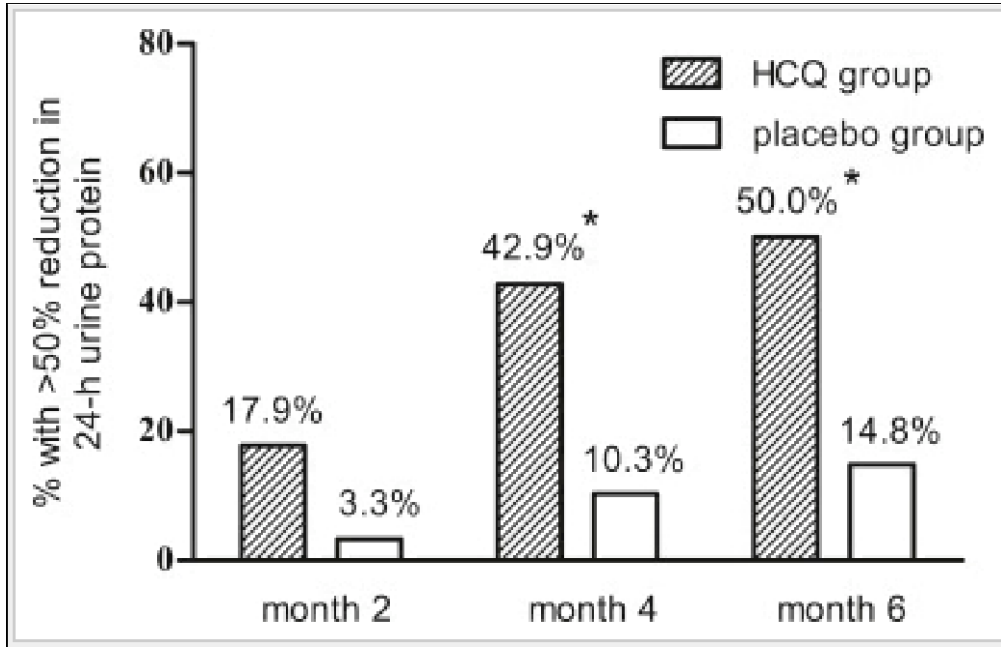
Positive Data Not Always Generalizable - IgAN

Tonsillectomy



	baseline	2	4	6	8	10	12
Group A	33	31	33	32	29	28	32
Group B	39	38	36	37	34	36	36

Hydroxychloroquine

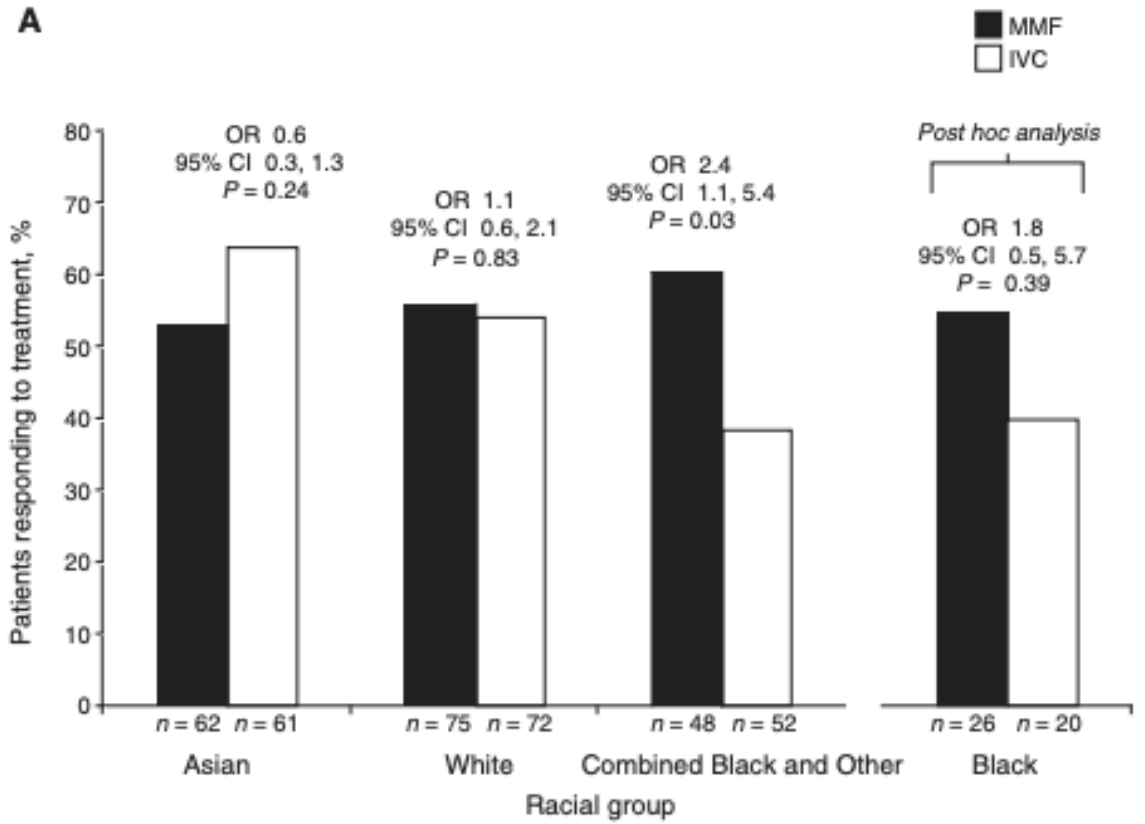


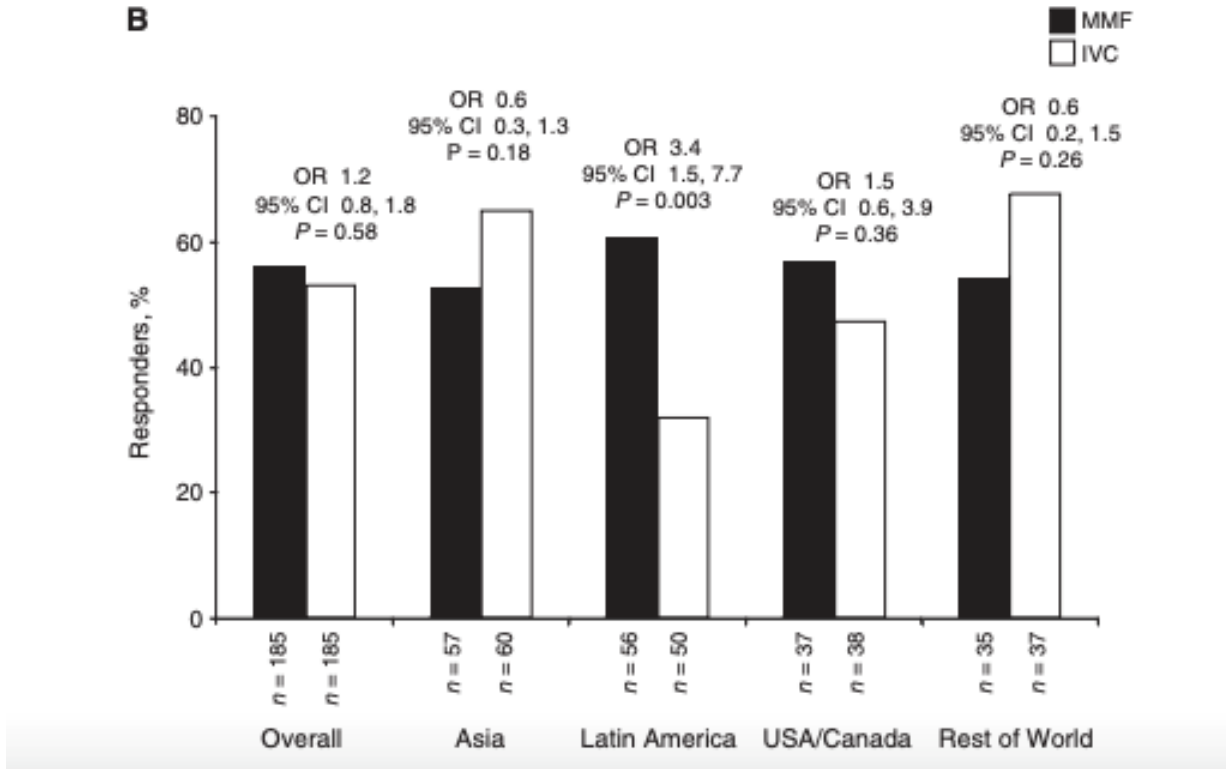
Liu et al., AJKD 74: 15-22, 2019

Kawamura et al., NDT 29:1546-53. 2014

KHI KIDNEY HEALTH INITIATIVE

Lessons from the ALMS Lupus Nephritis Study





Similar response to MMF versus Cyclophosphamide overall, but Black and Latino patients had a superior response to MMF

Isenberg et al., Rheum, 2010

KHI KIDNEY HEALTH INITIATIVE

PATIENT ADVOCACY GROUP PERSPECTIVE

Lauren Lee

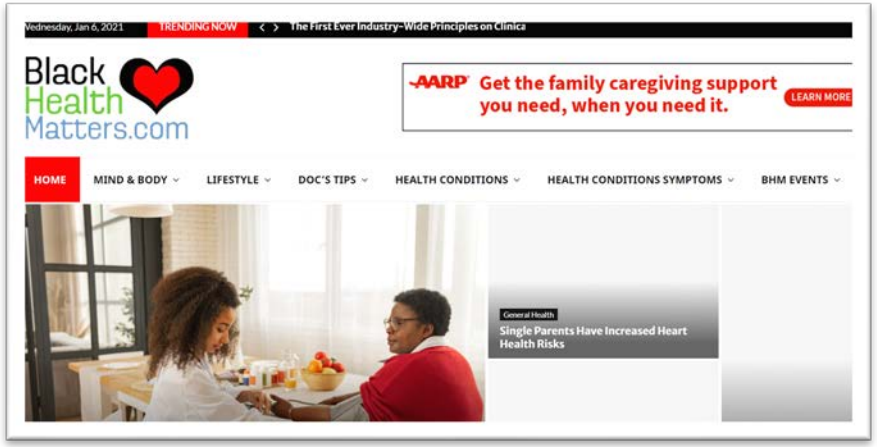
Start as you mean to go on: Practical Considerations

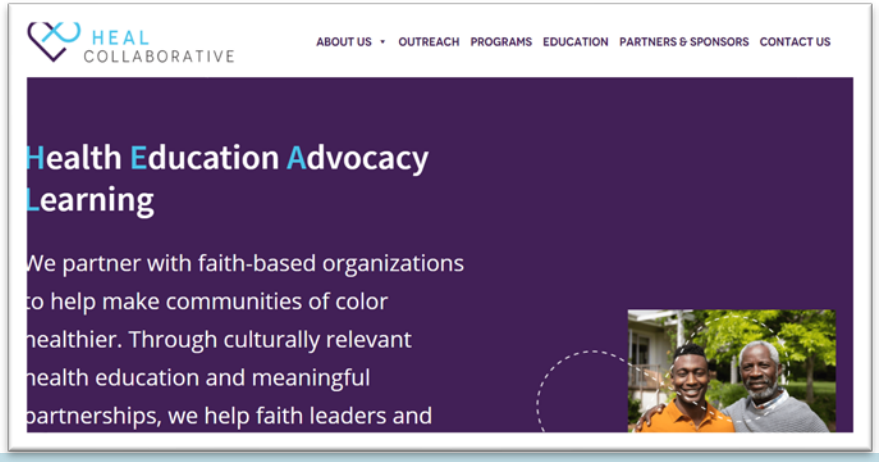
- *If you don't talk to your ~~customers,~~ patients how will you know how to talk to your ~~customers~~ patients?*
    - Study design and patient burden insights
    - Fears, beliefs, perceptions around clinical trials
    - Build bridges to support groups and advocacy organizations

- Study Team Alignment
    - Champion 'Trials are for everyone'
    - Trust, respect and transparency
    - Overcommunicate (PI to patient, PI to sponsor)

A Grassroots approach to equity and inclusiveness

- Community extends far beyond the trial site
  - Physician to physician
  - Faith based groups
  - Social Media outlets
  - Community Centers
  - Smart partnerships with like-minded organizations





CRO PERSPECTIVE

Owen Garrick, MD, MBA

New Aspects of the Guidance

Make Trial Participation Less Burdensome for Participants

Adopt Enrollment and Retention Practices That Enhance Inclusiveness by:

- “Consideration may be given to paying participants in exchange for their participation in research”
- “Remain engaged with communities after the conclusion of the clinical research and share trial updates”
- “Consider . . . community-based participatory research . . . which promotes the design of clinical research with the assistance of community members and leaders to more effectively meet the needs of potential participants.”
- “Consider holding [recruitment] events in non-clinical but trusted locations (such as places of worship or community centers), social commercial venues (such as barbershops and beauty salons) . . . as a means of connecting with diverse populations.”

OTHER STUDY DESIGN AND CONDUCT CONSIDERATIONS FOR IMPROVING ENROLLMENT

KHI KIDNEY HEALTH INITIATIVE

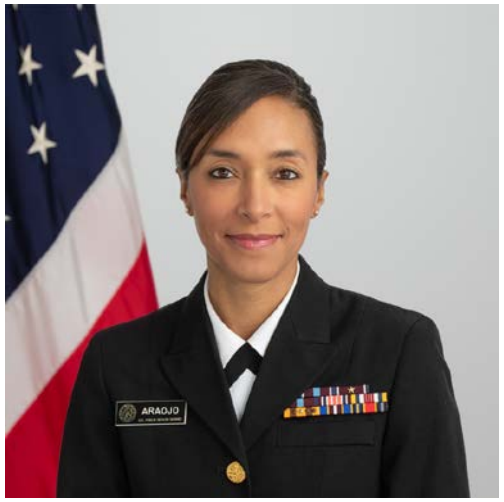
What Does it All Mean

As part of the overall study design, sponsors can improve the diversity of enrolled participants by accounting for logistical and other participant-related factors that could limit participation in clinical trials.

- Onus is on us as a research enterprise
- Need to consider cost versus efficiency interplay
  - Additional services are upfront and costs are pretty clear
  - Efficiency gains are on the back end and financial impact may need to be imputed
- These are nonbinding recommendations

FDA Encourages More Participation, Diversity in Clinical Trials

Panel Discussion



RADM Richardae Araojo, PharmD
FDA Office of Minority Health and Health Equity

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Icahn School of Medicine at Mount Sinai

Owen Garrick, MD, MBA
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David M. White
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Thank you to our speakers

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To access the recordings from previous KHI Member Townhalls, please visit the KHI website at https://khi.asn-online.org/pages/events.aspx