Diverse Women in Clinical Trials

Marsha Henderson, MCRP
Assistant Commissioner for Women’s Health
U.S. Food and Drug Administration
October 16, 2016
Faculty Disclosure

In compliance with ACCME Guidelines, I hereby declare:

I do not have financial or other relationships with the manufacturer(s) of any commercial services(s) discussed in this educational activity.

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Assistant Commissioner for Women’s Health
U.S. Food and Drug Administration

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Advocate for the inclusion of women in clinical trials and analysis for sex/gender effects

- Policy
- Science
- Outreach
How FDA Addresses Sex Differences and Women in Clinical Trials

- Regulations and Guidance
- Regulatory Research
- Assessment of Product Applications
- Health Professionals Training
- Workshops and Outreach
- FDASIA 907 Action Plan
WHAT IS THE PURPOSE OF DRUG TRIALS SNAPSHOTS?

Drug Trials Snapshots provide consumers with information about who participated in clinical trials that supported the FDA approval of new drugs. The information provided in these Snapshots also highlights whether there were any differences in the benefits and side effects among sex, race and age groups. Drug Trials Snapshots is part of an overall FDA effort to make demographic data more available and transparent.

HOW TO USE SNAPSHOTS:

Each Snapshot contains information about the drug in a question and answer format. At the end of each section of the Snapshot, there is a shaded bar with the words “MORE INFO”. Click the “MORE INFO” bar for more technical and detailed content. At the bottom of each Snapshot, there is a link to the drug’s Package Insert as well as the medical review.

LIMITATIONS OF SNAPSHOTS:

The Snapshot is intended as one tool for consumers to use when discussing a drug’s risks and benefits with their physician. Do not rely on Snapshots alone to make decisions regarding medical care. Do not use Snapshots to substitute for advice from your health care professional. Conclusions regarding how effective and safe a drug is among different sex, race, and age groups cannot always be made, often because the numbers of patients in some groups are too limited to allow for meaningful comparisons to other groups and to the overall results.

GLOSSARY

CLINICAL TRIAL: Voluntary research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, other therapies, or new ways of using existing treatments.

COMPARATOR: A previously available treatment or placebo used in clinical trials that is compared to the actual drug being tested.

EFFICACY: How well the drug achieves the desired response when it is taken as described in a controlled clinical setting, such as during a clinical trial.

PLACEBO: An inactive substance or “sugar pill” that looks the same as, and is given the same way as, an active drug or treatment being tested. The effects of the active drug or treatment are compared to the effects of the placebo.

SUBGROUP: A subset of the population studied in a clinical trial. Demographic subsets include sex, race, and age among others.
<table>
<thead>
<tr>
<th></th>
<th>WOMEN</th>
<th>BLACK/AFRICAN AMERICAN</th>
<th>ASIAN</th>
<th>WHITE</th>
<th>AGE 65 AND OLDER</th>
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<td>7%</td>
<td>12%</td>
<td>75%</td>
<td>22%</td>
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Diverse Women in Clinical Trials Initiative
www.fda.gov/womeninclinicaltrials
Collective Approach

FDA

Industry

Community

Healthcare Professionals
Join Us

- Website: www.fda.gov/womens
- Twitter: @FDAWomen
- Pinterest: www.pinterest.com/usfda/womens-health/
Diversity in Clinical Research: The New Expectation and What It Means

Luther T. Clark, MD, FACC, FACP
Global Director
Scientific, Medical and Patient Perspective
Office of the Chief Medical Officer
Merck

October 16, 2016
Faculty Disclosure

In compliance with ACCME Guidelines, I hereby declare:

I am an Employee of Merck & Co

Luther T. Clark, MD, FACC, FACP
Global Director, Scientific, Medical and Patient Perspective
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The Compelling Data Reality (All Disease Areas)

Prevalence of disease is not reflected in US trial populations
• African-Americans constitute 12% of the U.S. population but only 5% of clinical trial participants.
• Hispanics make up 16% of the population but only 1% of clinical trial participants.
• Gender distribution in cardiovascular device trials is 67% male, 33% female

Trends (by 2050)
• Current racial and ethnic minorities will constitute >50% of the US population
• Hispanics will make up 29% of the U.S. Population

Minority Volunteer Disparities in Clinical Research

<table>
<thead>
<tr>
<th>Category</th>
<th>All Minorities</th>
<th>White</th>
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</thead>
<tbody>
<tr>
<td>Total US Population</td>
<td>33.1%</td>
<td>66.9%</td>
</tr>
<tr>
<td>Participants in NIH-Funded Clinical Research</td>
<td>36.1%</td>
<td>63.9%</td>
</tr>
<tr>
<td>Participants in Industry-Funded Clinical Trials</td>
<td>16.7%</td>
<td>83.3%</td>
</tr>
</tbody>
</table>

Sources: US Census Bureau; NIH; Tufts CSDD 2013
Disparities in Disease Prevalence and Risk

• The most important diseases that disproportionately affect ethnic minorities include:
  – type 2 diabetes
  – cardiovascular disease
  – stroke
  – infectious diseases (HIV/AIDS, HCV, STDs)
  – different types of cancer (colon, prostate, cervix, lung)

Reference: Successful Strategies for Engaging Women and Minorities in Clinical Trials; The Society for Women’s Health Research United States Food and Drug Administration Office of Women’s Health; September 22-23, 2011
Controlled clinical trials provide a critical base of evidence for evaluating whether a medical product is effective before the product is approved for marketing.

One challenge that remains for FDA is ensuring that research participants are representative of the patients who will use the medical product.

A wide range of people should have the opportunity to participate in trials, both for access to new therapies and to have the chance to contribute to better treatment of everyone, an important altruistic goal for many Americans.
## FDA Report Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products August 2013

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<th>Asian</th>
<th>Other</th>
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<tr>
<td>ALL</td>
<td>78%</td>
<td>10%</td>
<td>2%</td>
<td>10%</td>
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<td>5%</td>
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<td>1%</td>
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<td>8%</td>
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<td>1%</td>
<td>0%</td>
<td>0%</td>
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<tr>
<td>Melanoma (2)</td>
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<td>0%</td>
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<tr>
<td>Myelofibrosis</td>
<td>88%</td>
<td>2%</td>
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<td>8%</td>
</tr>
<tr>
<td>NSCLC</td>
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<td>30%</td>
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<td>Prostate CA</td>
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<td>4%</td>
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<tr>
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<tr>
<td>C.Diff</td>
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<td>9%</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Head Lice</td>
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<td>6%</td>
</tr>
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<td>HepC (1)</td>
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<td>HepC (2)</td>
<td>87%</td>
<td>9%</td>
<td>2%</td>
<td>3%</td>
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<tr>
<td>HIV</td>
<td>61%</td>
<td>23%</td>
<td>13%</td>
<td>3%</td>
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</table>

Merck, in collaboration with the Association of Black Cardiologists, academia, and Maslansky & Partners completed a uniquely intensive research plan with patients, investigators, referring physicians and study coordinators to investigate the barriers to minority participation in U.S. clinical trials, and to identify potential solutions with respect to implementation, recruitment and communication.

Data presented November 7, 2015 at the “Dr. Walter M. Booker, Symposium”; Annual Scientific Sessions of the American Heart Association, Orlando, FL.
Participant Criteria

Patients
• Cardiometabolic condition, and one of following
  o Have participated in a clinical trial
  o Asked to participate and declined
  o Have never been asked

Coordinators
• All with cardiometabolic clinical trials recruiting experience

Referring (Treating) Physicians
• All have referred patients to participate clinical trials conducted by others

Investigators
• All minority serving investigators who have led cardiometabolic clinical trials
Study Participants (Testing Phase)

**Pilot Testing**
- 6 Patients (2 participated, 2 declined, 2 never been asked)
  - 2 African-American, 3 Hispanic, 1 Asian
- 2 Referring doctors
- 2 Investigators
- 2 Coordinators

**Field Testing**
- 30 Patients (11 participated, 7 declined, 12 never been asked)
  - 14 African-American, 11 Hispanic, 5 Asian; 3 age 73+
- 5 Referring doctors
- 5 Investigators
- 5 Coordinators

**In Person Focus Group**
- 9 patients, all who have never been asked to participate in a clinical trial
Critical Barriers Identified and tested across the sample

Identified From Literature
1. Mistrust of process
2. Understanding the value
3. Fear
4. Stigma of participating
5. Family members’ opinions
6. Financial Burden
7. Time commitment
8. Transportation

Identified From Expert Interviews
1. Communication style from investigator/staff
2. Information
3. Compensation and Logistics

Grouped During The Barriers & Solutions Brainstorming and Randomized When Tested

1. MISTRUST
   • Understanding the value
   • Fear
   • Stigma of participating
   • Communication style from investigator/staff

2. LACK OF COMFORT WITH THE PROCESS
   • Mistrust of process
   • Fear
   • Family members’ opinions
   • Information

3. LACK OF INFORMATION
   • Fear
   • Stigma of participating

4. TIME AND RESOURCE CONSTRAINTS
   • Financial Burden
   • Time commitment
   • Transportation
   • Compensation & Logistics

5. AWARENESS
   • Understanding the value
   • Information
Commonalities among participant groups that stood out

**Patients’ own health comes first:**
- Patients are *concerned first and foremost about their own health* and the potential benefits of better outcomes and more comprehensive care.
- Potential benefit to the *community is a secondary* benefit, while a few stated that the community benefit and personal benefit were equal in importance.

**Clear, guiding communication is key:**
- Introducing clinical trials in a manner that *eases fears* increases patient comfort and leads to greater participation.
- Offering *consistent reassurance* throughout all clinical trial stages is important for both patients and referring MDs.

**Directly address and contextualize any concerns:**
- Patients and referring docs want to know the potential AEs of study medications.
- Importance of *fully explaining* the known adverse events as well as *directly and openly* responding to patient concerns.
Partnerships

- Academic Research Centers
- Community Based Organizations
- Networks with Access to Diverse Populations

Investigator Sites
Many Key Stakeholders
Conclusions

- Increasing clinical trial diversity is a challenge for the pharmaceutical industry and the research community generally.

- Barriers and limited awareness of clinical trials among patients and referring physicians contribute importantly.

- Key barriers include mistrust and lack of comfort with the clinical trials process. Overcoming these must include clear communication that emphasizes the paramount importance of the patients’ health and safety, addresses all of their concerns, and provides reassurance of close monitoring.

- Working with organizations like the SCRS and the ABC provides an opportunity to help create sustainable solutions that will make diversity a standard part of the research model.
THANK YOU!
Discussion Questions

1. What is the one most important thing/solution (actionable) that you believe would accelerate representation of underrepresented minorities in U.S. clinical trials?

2. What is the one most important activity your organization is currently involved in that you believe will impact significantly (accelerate) clinical trial diversity in the U.S.?
Strategies for Increasing Minority Participation and Retention in Clinical Trials

Ola Akinboboye, MD, MPH MBA FACC FACP FAHA
Associate Professor of Clinical Medicine, Weill Medical College of Cornell
Medical Director, Queens Heart Institute, Rosedale.
What We Have Learned

• 70% of African Americans reside in 2,500 out of 38,000 zip codes
• 50% of Hispanics reside in 1,500 out of 38,000 zip codes
• These “minority” populations are served by approximately 500 hospitals and 40,000 primary care physicians
Participation and Retention in Clinical Trials is Particularly Challenging among “Minorities”

- African Americans represent 12% of the U.S. population but only 5% of clinical trial participants
- Hispanics make up 16% of the population but only 1% of clinical trial participants
- By 2020, “minorities” are projected to account for over 40% of the nation’s population
- By 2050, Hispanics will make up to 29% of the U.S. population (emerging “majority”)
The Current Picture: Industry Reality

• Average is < 5% in pivotal trials supporting drug safety and efficacy
• “No data available” is frequently cited
• “We can’t find ‘em”
• The race debate in medicine, “aren’t we all the same?”
The Current Picture: Minority Perspective

- “I don’t want to be a guinea pig”
- Lack of education about the process and value-added benefits of participation in clinical trials
- Lack of critical mass of minority physicians (particularly those doing research)
- Negative experiences with health care system
- Distrust due to tarnished industry image in the media
Why We Should All Be Concerned

Lack of minority physician and consumer participation affects:

- Product development, product approvals and standard of care.
- Targeted therapies based on genetics.
Barriers to Recruitment

• Patient
• Research Center
• Referring physician
Critical Patient Barriers

- MISTRUST
- Fear, communication style
- LACK OF COMFORT WITH THE PROCESS
- Information, Family members’ opinions
- Stigma of participating
- TIME AND RESOURCE CONSTRAINTS
- Financial Burden, time commitment, transportation, compensation & Logistics
Mistrust and Fear

• Mistrust of scientific investigators: Discussion about the past (Tuskegee), Safeguards that guarantee patient safety.
• Concern about impact on personal health: patient safety comes first, average number of patient exposure to study drug, and outcomes of other studies with study drug.
• Messenger is very important
Comfort With the Research Process

The Message:
• Concise and culturally sensitive education about the research process with emphasis on patient safety.

The Messenger:
• Care-giver - physician
• Opinion leaders in the community
• Racially diverse research team

Message Delivery:
• Open and respectful approach, eye-contact,
• No pressure, offer to participate in the discussion if patient wants to seek family member opinion.
Minimize financial impact on patient:

• Provide transportation when necessary
• Flexible schedules and extended hours including evenings and weekends
• Compensation for time
• Treatment of adverse effects
Research Center

- Protocol issues:
  - Adequate Funding (Personnel, advertisements etc.)
- Site Selection:
  - Match between site location and zip codes where black patients reside
- Development of a referral network
Referring Physicians

• Fear of losing a patient: Ensure patients returns for regular visits with referral source
• Loss of autonomy: Do not take over the management of the patient, provide regular updates
• Time constraints: offer assistance with in-office screening
• Lack of interest in clinical research
Conclusions

• Lack of awareness, mistrust of researchers and lack of understanding of the benefits of participation are probably the biggest obstacles
• Community involvement is imperative for enrollment to grow