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Diversity in Research

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1

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2

Agenda

3

- Background
- What is Diversity and Inclusion in Research
- Importance of Diversity in Research
- Benefits of Diversity in Research
- Why Some Communities Have Not Been Part of Research
- NIH and Its Attempts to Close the Health Disparity and Address Diversity in Research

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3

Agenda

4

- Federal and State Law Protections of Vulnerable Populations
- FDA Guidance on Drug Apps
- More Recent Developments
  - MRCT Diversity Center
  - PhRMA
  - "Hybrid" Remote Trials
- Where to Improve Research in the Context of Diversity

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4

Background

5

- The COVID-19 pandemic has brought into focus issues of health inequality (or health disparity) and the disproportionate disease burden experienced by underrepresented groups, compared with the population as a whole.
- High-quality research is essential for an evidenced-based approach to effectively delivering health care to the population. But the quality of research may be compromised by misrepresentation of the population (often by underrepresentation of subgroups).
- By studying data from diverse groups of people, researchers can ensure that research is generalizable, benefits all of society (by improved treatment and disease prevention), and does not perpetuate existing inequalities.

Example of Alzheimer Research

6

- African-Americans are twice as likely than non-Hispanic whites to be diagnosed with Alzheimer's disease.
- Latinos are 1.5 times more likely than non-Hispanic whites to be diagnosed with Alzheimer's disease.
- But African-Americans and Hispanics make up 30% of the U.S. population and account for only 6% of all participants in federally funded clinical trials.

See Alzheimer's Impact Movement – Alzheimer's Association, *Race, Ethnicity, and Alzheimer's* (March 2020); National Institute of Health, *Studies Explore Alzheimer's Risk Factors, Biomarkers in Latinos* (December 12, 2018).

Diversity and Inclusion in Research

7

Diversity of participants

Participants are from different races, ethnicities, age groups, and regions of the country; they are also diverse in gender identity, sexual orientation, socioeconomic status, education, disability, and health status.

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7

Importance of Diversity in Research

8

- Research is typically performed using a small portion of the overall population with the goal of providing effective treatment for the entire population.
- Without diverse groups of participants, however, researchers will not know whether the results can be applied to all people equally.

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8

Importance of Diversity in Research

9

Some of the top reasons diversity is important:

1. Some groups of people suffer more from certain diseases than other groups.
2. The cause of a disease may not be the same for all groups of people.
3. Medical treatments may not be equally effective for all groups of people, and some groups of people may experience more side effects from medications than other groups.
4. Individuals within the same racial or ethnic group can respond differently to the same treatment.
5. Diversity in genetic samples and databases is needed to guide personalized medicine based on an individual's genetic makeup.

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9

Benefits of Diversity in Research

10

1. Better identify what makes people more likely to develop a disease.
2. Better understand and address "minority health."*
3. Find out how environment, lifestyle, and genes can impact health.
4. Build better tools for detecting a health condition and encouraging healthy habits.
5. Development better treatments effective for the entire U.S. population.

*__Minority health__ refers to the distinctive health characteristics and attributes of racial and/or ethnic minority groups that can be socially disadvantaged due in part to being subject to potential discriminatory acts.

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10

Why Some Communities Have Not Been Part of Research

11

Studies focusing on the lack of minority representation in research offered several possible reasons for the continued disparity gap:

1. Cultural differences;
2. Linguistic differences;
3. Financial constraints;
4. Time constraints;
5. Logistical challenges;
6. Lack of studies in minority communities;
7. Lack of incentive to recruit or retain;
8. Reluctance and distrust based on past unethical practices of lack of information/clear communication; fear of exploitation;
9. Higher presence of other health issues that exclude the minority populations.

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11

Why Some Communities Have Not Been Part of Research

12

- **Distrust** – some racial and ethnic populations may not wish to participate in research due to unethical studies conducted in the past.
  - *Messaging about a clinical trial may include information on participants rights and protections (e.g., Declaration of Helsinki, The Belmont Report, and the Common Rule).*
- **Financial/Time Constraints** – People with lower incomes often cannot afford to take time off of work, commute long distances, or find child care. Households with an income of less than $50,000 per year were 27% less likely to participate in research.
  - *Prepare clear messaging about time requirements and other participant expectations, and identify opportunities for flexibility.*

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12

Why Some Communities Have Not Been Part of Research

13

- **Higher Presence of Other Health Issues** – Sometimes minorities are more likely to have other health issues such as high blood pressure and diabetes, compared to white Americans. For some studies, stringent trial criteria disallow participation of patients with multiple conditions regardless of race and ethnicity.
  - *Prepare messaging with the study rationale; use requirement as an opportunity for further discussion*

The National Institute of Health's Attempt to Close the Health Disparity

14

NIH has designated the following subgroups of the U.S. population as U.S. health disparity populations:*

- ❑ American Indians/Alaskan Natives;
- ❑ Asian Americans
- ❑ Blacks/African Americans
- ❑ Hispanics/Latinos
- ❑ Native Hawaiians and other Pacific Islanders
- ❑ Sexual and gender minorities
- ❑ Socioeconomically disadvantaged populations
- ❑ Underserved rural populations

See National Institute on Minority Health and Health Disparities, *Overview: Health Disparity Populations* (May 5, 2021).

The National Institute of Health's Attempt to Close the Health Disparity

15

NIH Revitalization Act of 1993
In an attempt to remove the healthcare disparity gap, the NIH mandated including women and racial and ethnic minorities in federally funded research pursuant to its authority under the NIH Revitalization Act of 1993.

21st Century Cures Act (enacted December 13, 2016)
Entities conducting applicable clinical trials must submit results of valid analyses by sex/gender, race, and ethnicity in Clinicaltrials.gov. The statute further requires that NIH consider, as appropriate, whether the entity has complied with this reporting requirement when awarding any future grant to that entity; and that NIH encourage the reporting of these results of valid analysis through any additional means determined appropriate.

Federal and State Law Protections of Vulnerable Populations

16

The Code of Federal Regulations

The CFR outlines specific requirements to enhance protection for 3 groups:

1. Pregnant women, human fetuses, and neonates (45 CFR 46, Subpart B)
2. Prisoners (45 CFR 46, Subpart C)
3. Children (45 CFR 46, Subpart D)

Federal and State Law Protections of Vulnerable Populations

17

- New York State Law on Human Subject Research applies to research not covered by federal law (e.g., the Common Rule)—research neither federally funded nor otherwise subject to federal oversight.*
- **NYS Public Health Law Section 24-1 – Protection of Human Subjects**
  - Explicitly identifies protection of participants in research as the primary goal of the law;
  - Addresses the necessity of voluntary informed consent;
  - Lays the mechanisms by which a Human Research Review Committee ("HRRC"; New York State's equivalent to an IRB) may review proposed research protocols.

*See New York State Public Health Law Sec. 2445 ("The provisions of this article shall not apply to the conduct of human research which is subject to, and which is in compliance with, policies and regulations promulgated by any agency of the federal government for the protection of human subjects.")

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17

Federal and State Law Protections of Vulnerable Populations

18

- **The New York State Task Force on Life and the Law Report & Recommendations for Research with Human Subjects Who Lack Consent Capacity**
  The Report and Recommendations represents the advisory opinion of the NYS Task Force on Life and the Law. The Report provides guidance and best practices that will assist research institutions, investigators, IRBs, and legally authorized representatives, and others in the ethical conduct and responsibility of research involving cognitively impaired adults.
- **Primary Focus on Informed Consent**
  For Minors, Incompetent Persons, Mentally Disabled Persons, and Prisoners.

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18

FDA Guidance on Improving Diversity in Clinical Trials for Medical Products

19

- FDA recognizes the importance of encouraging developers of any medical product (such as drugs and devices) to include diverse populations to understand their risks or benefits across *all* groups.
- It is important that people who are in clinical trials represent the population most likely to use the potential medical products.

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19

FDA Guidance on Improving Diversity in Clinical Trials for Medical Products

20

Enhancing the Diversity of Clinical Trial Populations-Eligibility Criteria, Enrollment Practices, and Trial Designs (2020)

- This FDA guidance aims to provide recommendations for how sponsors can increase enrollment of underrepresented populations in their clinical trial.
- It offers recommendations on how product sponsors can improve clinical trial diversity by accounting for logistical and other participant-related factors that could limit participation.
- Provides recommendations on broadening clinical trial eligibility criteria for clinical trials of investigational drugs intended to treat rare diseases and recommendations on improving enrollment and retention of participants with rare diseases.
- Includes other high-level considerations about inclusion of other important groups, including but not limited to: women, including pregnant women, racial and ethnic minorities, children, and older adults, and provides references to more specific guidance.

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20

FDA Guidance on Improving Diversity in Clinical Trials for Medical Products

Sec. 907 of the Food and Drug Administration Safety and Innovation Act ("FDASIA")

Directed FDA to investigate how well demographic subgroups (sex, age, race, and ethnicity) in applications for medical drugs – drugs, biologics and devices, submitted to the agency for marketing approval:

1. Are included in clinical trials generally; and
2. Are represented in subgroup-specific safety and effectiveness data

More Recent Developments

Multi-Regional Clinical Trials ("MRCT") – Center of Brigham and Women's Hospital and Harvard

- Version 1.0 of "*Achieving Diversity, Inclusion, and Equity in Clinical Research*" Guidance (Aug. 2020)
  - Aims to clarify the importance of, advance the goals of, and provide practical and actionable ways to improve diverse representation of participants in clinical research.
  - Current Version 1.2 – contains minor editorial updates, and was released in Jan. 2021.
- Associated Toolkit was released in 2021 – for practical resources to improve diverse representation of participants in clinical research.

More Recent Developments

Pharmaceutical Research and Manufacturers of America ("PhRMA") *Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results* (2020)

- Enhancing education about the role of clinical trials through the medical community and enhancing diversity among clinical investigators;
- Increasing clinical trial awareness and participant diversity by improving individual health literacy and community outreach;
- Enhancing diversity in clinical trials depends on identifying and reducing barriers to clinical trial access and participations;
- Using real-world data to enhance information on diverse populations beyond product approval; and
- Enhancing information about diversity and inclusion in clinical trial participation.

More Recent Developments

"Hybrid" Remote Trials

- FDA Guidance – *Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency* (Mar. 2020; updated Aug. 2021)

  FDA issued guidance to provide a policy to help expand the availability and capability of non-invasive remote monitoring devices to facilitate patient monitoring while reducing patient and healthcare provider contact and exposure to COVID-19 for duration of the COVID-19 PHE.

More Recent Developments

25

"Hybrid" Remote Trials

- FDA recommends the use of central and remote monitoring programs to maintain oversight of clinical sites if planned on-site monitoring visits are no longer possible.
- Other nonbinding recommendations include:
  - Conducting remote (virtual) clinic visits;
  - Remote clinical outcome assessments;
  - Remote site monitoring visits

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25

Where to Improve Research in the Context of Diversity

26

Considering target population and ethnicity information at trial design/conceptualization phase.

- ❑ Prepare a more accurate and detailed data on English proficiency in diverse populations to better assess the need to provide language translations as part of the clinical trials/research.
- ❑ Prepare and implement robust translation methods to be employed during the research/trial.

<u>Example solutions to improve translation</u>:

1. Employ forward and backward translation methods with inputs from multiple translations *and* clinical reviewers.
2. Emphasize achieving conceptual equivalence and appropriate readability in document translations.

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26

Where to Improve Research in the Context of Diversity

27

Improving language accommodations – under-served ethnic minorities may have low English literacy, health literacy, or English language proficiency.

- Training translators – despite accurate translations, use of the same word or the direct-translated equivalent word might convey different concepts to the non-English speaking participant.
- Document translation – ensure that the document translation convey essential information as clearly as possible.

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27

Where to Improve Research in the Context of Diversity

28

Consider other possible solutions, such as:

- Locating study sites in areas with diverse residents.
- Providing travel support.
- Create culturally sensitive informational materials that detail how data will be collected and used (to assuage participants' distrust).

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28

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29

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30