

Considering Inclusion in Research:
Scientific and Policy Perspectives

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Outline and Learning Objectives

The importance of diversity in clinical studies

Considering inclusion as essential to good science

NIH Revitalization Act: 1993

Intersection of good science and policy compliance

Know the requirements for addressing inclusion of women, minorities, and children in NIH grant applications

What's on the radar?

Conclusion

Obstacles in Translating Discovery to Health

Benefits from Inclusion

Advances in knowledge from research

Incorporating knowledge into education, training

Implementing new concepts into practice

Changing standards of practice, public health

Providing access to sex/gender and ethnic/racial/culturally sensitive and appropriate healthcare

Need diversified workforce to design studies, recruit participants, implement findings

Diabetes Prevention Program (DPP) – Lessons Learned:

- (1) a method for ongoing assessment and revision of recruitment strategies is valuable;
- (2) a range of recruitment strategies may be useful;
- (3) the most effective methods for recruiting potential subjects may vary according to the gender, age, and race/ethnicity of those individuals;
- (4) recruitment strategies vary in the amount of staff time required to randomize a participant;
- (5) a stepped screening may make it easier to identify and recruit volunteers who understand the requirements of the study.

Biased Enrollment Criteria – Selecting out women

The NIH Outreach Toolkit is intended to help principal investigators and their research teams fulfill their responsibilities to include women in clinical research.

The toolkit includes:

A review of research on recruitment and outreach best practices

Information on Federal laws, regulations, and NIH policies on the inclusion of women in clinical research

Case studies featuring researchers' experience with including women in their studies

Barriers to Recruitment and Retention of Women and Minorities in Clinical Trials

Fear and distrust of research enterprise

Lack of knowledge

Lack of transportation

Interference with work and/or family responsibilities

Burden as a result of participation

Financial costs

Facilitators to Recruitment and Retention of Women and Minorities in Clinical Trials

Cultural and linguistic adaptation of recruitment strategies

Translation of materials into appropriate languages

Enlisting culturally and linguistically competent research staff

Including families and communities in a dialogue

Partnering with community organizations

Including investigators and staff from the same targeted communities as participants and retaining the same staff and interviewers over time to ensure continuity.+

An NIH Outreach Toolkit: How to Engage, Recruit, and Retain Women in Clinical Research

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NIH Inclusion Policies

Inclusion of Women and Minorities

Must be included in NIH-defined clinical research unless exclusion is justified for scientific reasons

Justify the proposed sample in the context of who is at risk for the disease/condition and the scientific goals of the specific study

Plans for outreach and recruitment

Provide Inclusion Enrollment Report form(s) with proposed sex/gender, race, and ethnicity of the sample

For Phase III clinical trials, address considerations of trial design and analysis

Inclusion of Children

Children must be included in clinical research unless there are scientific or ethical reasons not to do so

“Children” are defined by the NIH as individuals <18 years

Applicants should justify the proposed age range of the participants, with specific attention to justifying the inclusion/exclusion of individuals under 18

Defining the Universe

What is subject to the statute/policies?

All studies (intramural, extramural, contracts) that meet the NIH definition of clinical research

NIH definition of clinical research: (1) Patient-Oriented Research: Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual (e.g., IRB Exemption 4). Patient-oriented research includes (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical studies, or (d) development of new technologies; (2) Epidemiologic and Behavioral Studies; and (3) Outcomes Research and Health Services Research

Additional requirements for NIH-defined Phase III clinical trials related to unbiased design and assessment of potential differences

Bottom line:

If you answer yes to human subjects and not E4, you should address inclusion.

But what does it mean to include?

Purpose Statement: NIH supported clinical research should address/include the population(s) at risk for the disease or condition under study. The purpose of NIH Inclusion Policies is to ensure that the distribution of study participants by sex/gender, race, ethnicity, and age reflects the population needed to accomplish the scientific goals of the study, rather than enumeration of research participants. All NIH-funded studies that meet the NIH definition for clinical research are subject to NIH Inclusion Policies, regardless of funding mechanism*. (*Funding mechanism includes any activity code associated with extramural grants, R&D contracts, and cooperative agreements as well as intramural projects and R&D contracts)

Bottom line: Thinking more broadly about inclusion→

Does the study have the right people for the science?

NIH Inclusion Re-Engineering Project

NIH Inclusion Task Force (2010)

Reorganized governance structure (2011)

Business Process Modeling and data system redesign (2011-2014)

Identification of pain points in management of inclusion policies

Release of new Inclusion Management System (IMS) (2014)

Data system used to collect and report sex/gender, race, and ethnicity

New functionality continues to be added (2015-present)

Updates to procedures for monitoring inclusion (2013-present)

Revise forms for data collection

Updated reviewer guidelines and review templates

Eliminate exception codes

Standardize reporting process

Inclusion Policy Governance Structure

E-SIG Co-Chairs:

Janine Clayton, Director, NIH Office of Research on Women's Health

Marie Bernard, Deputy Director, National Institute on Aging

Staffed by NIH Inclusion Policy Officer

Membership includes:

NIH Institutes/Centers with small, medium, or large clinical research/clinical trial portfolios

Representation from different business areas: extramural, intramural, contracts, review, legal, technical/system

Function:

To provide guidance and oversight regarding inclusion policies and procedures

What's required for inclusion in a competing NIH application?

Remember the "universe" to determine whether inclusion applies to your application

NOTE: Follow the scenarios described in Human Subjects' protection section to further understand what's expected for different scenarios

Plans for inclusion of women and minorities

Includes addressing plans for valid analysis if conducting an NIH-defined Phase III clinical trial

Plans for the inclusion of children

Inclusion enrollment report

Planned or Cumulative (actual) information depending on the study design

Missing plans may be subject to application return

Peer Review of Inclusion

Each reviewer will assess the inclusion plans

Plans for inclusion

Justification in the context of the science

http://grants.nih.gov/grants/peer/guidelines_general/Review_Human_Subjects_Inclusion.pdf

Peer review group will determine overall rating of “acceptable” or “unacceptable”

Summary Statement:

INCLUSION OF WOMEN, MINORITIES, AND/OR CHILDREN: UNACCEPTABLE (U CODE)

Unacceptable (U) code is a bar to award

Common Inclusion Concerns Identified in Peer Review

Inadequate information describing the sex/gender, race, ethnicity, and/or age(s) of the sample

Inadequate justification for proposed sample

Sex/gender, race, ethnicity, and/or age(s) breakdown not appropriate for the scientific goals of the study or not adequately justified

Unrealistic sampling

Appropriate from scientific perspective but not realistic

Collaborations and outreach plans may help

“Just-in-Time” Requirements

After peer review, for grants likely to be funded:

Work with Institute/Center staff to resolve unacceptable inclusion concerns, usually involves a written response to IC

Provide inclusion enrollment report(s) if missing or need update as a result of peer review and/or programmatic adjustments

After the Award...

Now What?

Funded investigators provide cumulative inclusion enrollment (e.g., actual enrollment) information at least annually or as frequently as specified by the funding Institute/Center

For NIH-defined Phase III Clinical Trial– report any analysis or findings related to outcomes by sex/gender, race, and ethnicity if available

Note progress (or challenges) in recruitment as needed in the progress report

Other Important Inclusion Information

Defining sex/gender, race, and ethnicity

Sex at birth vs. gender identity: What's important for your scientific question?

Race/Ethnicity

Required to use the OMB standards (Directive 15, revised in 1997)

Ethnic Categories

Hispanic or Latino

Not Hispanic or Latino

Racial Categories (select all that apply)

American Indian or Alaska Native

Asian

Black or African American

Native Hawaiian or Other Pacific Islander

White

More than one race (use this when more than one selected)

Inclusion Resources for Applicants and Investigators

Program staff at the Institute/Center you are applying to

Training and Guidance

FAQs

How To Videos and User Guides for working in the Inclusion Management System

Podcasts

Narrated slide decks

Guide notices and other policy related documents

Public websites

http://grants.nih.gov/grants/funding/women_min/women_min.htm

<http://grants.nih.gov/grants/funding/children/children.htm>

What happens to inclusion information?

High Level Inclusion Workflow

Trend of Enrollment by Sex/Gender
in NIH Clinical Research

Trend of Enrollment by Sex/Gender in
NIH-Defined Phase III Clinical Trials

Trend of Minority Enrollment in NIH Clinical Research
(US Populations Only)

Enrollment in NIH Clinical Research:
Racial Categories (US Populations Only)

Enrollment in NIH Clinical Research:
Ethnic Categories (US Populations Only)

Trend of Minority Enrollment in
NIH-Defined Phase III Clinical Trials
(US Populations Only)

Enrollment in NIH-Defined Phase III Clinical Trials:
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Enrollment in NIH-Defined Phase III Clinical Trials:
Ethnic Categories (US Populations Only)

What's on the radar?

Broader Context:

Congressional Interest in Inclusion

Minority enrollment in clinical trials

Recent articles highlight inclusion policy and peer review concerns

Inclusion of different age groups

Language in 21st Century Cures bill (House)

Development of trans-NIH workshop

Inclusion of women

Longstanding concern

FDA/Ambien

GAO study on the inclusion of women in clinical trials

GAO Study on Women in Clinical Trials Recommendations

Recommendation 1:

Make IC-level enrollment data readily available through public means, such as its regular biennial report to Congress on the inclusion of women in research, or through its website

Recommendation 2:

Examine approaches for aggregating more detailed enrollment data at the disease and condition level, and report on the status of this examination to key stakeholders and through its regular biennial report to Congress on the inclusion of women in research

Recommendation 3:

Ensure that program officers have a means of recording their monitoring of awardees plans for and progress in conducting analysis of potential sex differences;

Recommendation 4:

On a regular basis, systematically collect and analyze summary data regarding awardees' plans for analysis of potential sex differences, such as the proportion of trials being conducted that intend to analyze differences in outcomes for men and women

Recommendation 5:

Report on this summary data and analysis in its regular biennial report to Congress on the inclusion of women in research

Summary/Conclusions

NIH has made progress on addressing inclusion in clinical research

More to be done

Analysis and results reporting

Further understanding of inclusion in our research portfolio

Primary aim of policy is to collect scientific information leading to changes in standard of care

We have gained knowledge broadly applicable to health care

Questions?