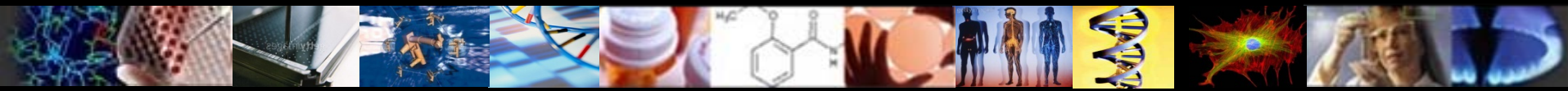


Women in Interventional Cardiology
October 16-17, 2009

Representation of Women in NHLBI-supported Studies



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U.S. Department of Health and Human Services
National Institutes of Health

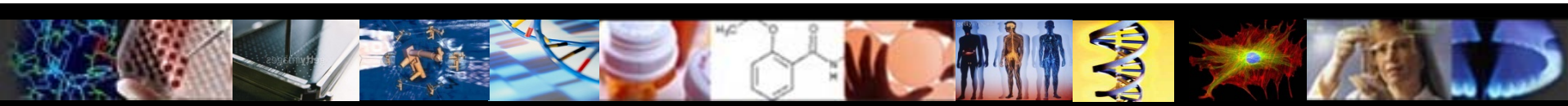


**National Heart
Lung and Blood Institute**
People Science Health

Women in Interventional Cardiology

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Women Enrollment in NHLBI-supported Studies



- **Historical perspective: NIH & NHLBI policies & experience**
 - WHI and other cohorts
 - Barriers for women
- **Strategies to include women**
- **Challenges for clinical trials**



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Background

- **Cardiovascular Disease is the primary cause of death for all populations.**
- **NHLBI is committed to improving the CV health of the nation.**
- **Sex differences in CVD often results in the need for sex-specific investigations/**analyses** with women as controls.**
- **Despite federal law, NIH and NHLBI policies and identified needs, enrollment of women, especially in clinical trials, is challenging.**

Background and environment

- **NHLBI-supported research enrolls more women than men in clinical studies, even when WHI is excluded.**
- **CVD disproportionately burdens women. Women receive less aggressive treatment and/or sub-standard care. Current overall CVD trials enroll 25 percent women.**
- **Treatment guidelines often lack evidence for sex-specific recommendations.**
- **Women are commonly underrepresented in phase III-IV treatment trials.**

Revitalization Act of 1993 (PL 103-43)

- **The law requires inclusion of women and minorities proportional to population and disease in federally-funded research.**
- **1994 Inclusion Policy: numbers of women and minorities in human subject research are tracked by NIH centrally.**
- **2000 update requires that NIH must:**
 - **ensure that women and minorities and their subpopulations are included.**

Revitalization Act of 1993 (PL 103-43) continued

2000 update requires that NIH must:

- **for Phase III trials, ensure valid analyses of subgroups**
- **cost is not acceptable reason for excluding groups or analyses**
- **initiate programs and support for outreach**

Women Enrollment

What is the report card?

- Numbers of women as study participants has increased.
- Attitudes about inclusion have changed – routine exclusion of pregnant women and elderly are nearly eliminated.
- Women receive fewer invasive (life-saving) procedures.
- Women remain under-represented in phase III & IV trials.
- Evidence for women in treatment guidelines is lacking relative to men.

Women Enrollment

Two models

- Single sex cohort
 - Sufficient numbers but data may not be generalizable impeding marketing, insurance coverage, and guidelines
- Both sexes (with over-sampling)
 - Generalizable, but
 - Sex comparison rather than women as controls

Women Enrollment

Challenge is Different:

- Observational Studies are usually successful (Framingham, WHI, WISE)

- Clinical Trials have marginal success.

ALLHAT, the largest trial of active treatment for blood pressure recruited 33% minorities. With over 42,000 study participants analyses for population subgroups is well powered. The minority target was target was 50%

Why do women participate in medical research?

- heightened sense of susceptibility to disease
- research question is viewed as important and ethical
- desire to contribute to medical progress now and for future generations
- understand and support need for medical research

Barriers for women

- financial constraints - single parent, widow, elderly- often under insured,
- logistical barriers - time needs, co-morbidities, transportation
- cultural barriers - care givers, myth and misinformation, mistrust
- environmental stressors - individual choice is heavily influenced by environment

Identified barriers are understood and are commonly effectively addressed.

Challenges in clinical trials

- Overall costs are increasing
 - Regulatory requirements
 - Human subject safety and confidentiality
 - Mortality versus surrogate endpoints
- Competition with men for enrollment
 - Women are more difficult to identify and more often not eligible
 - Physician and patient bias exists.
 - Age, size, symptoms, diagnostic tests may be sex-specific.
 - Invasive procedures are underutilized.
 - Cost and time for outreach may be excessive.

Strategies to increase women enrollment

- Target clinical centers to recruit target population
 - WHI solicitation was specific for minority vs. majority recruiting centers.
- Evaluate how eligibility criteria and enrollment process influence enrollment of women and be proactive to reduce obstacles.
- Pre-determine numbers of women needed and maintain open enrollment until all identified subgroups are completed.
 - Observational studies: Dynamic registry

Strategies to increase women enrollment

■ Community involvement

- Prepare your messaging and outreach through use of focus groups and partnering with community leaders and organizations such as beauty parlor or church. (WHI, Jackson Heart Study)

■ Physician/Investigator buy-in

- This is key for most CV conditions. In any trial the primary endpoint is jeopardized by lengthy and difficult enrollment. In this setting enrollment of women and other subgroups is a second priority. This must be challenged!

Women enrollment summary

- **Appropriate women enrollment in CV Trials is essential**
- **Federal law support inclusion**
- **Greatest barriers to enrollment of appropriate numbers of women include:**
 - **investigative priorities,**
 - **sex differences in disease, and**
 - **differential effect of eligibility criteria,**
 - **logistic and environmental burden to women.**

Women Enrollment Conclusions

- **Inclusion of women in CV trials is essential to improve outcomes.**
- **Law and policies support appropriate inclusion of women.**
- **Continued improvement in women enrollment requires buy-in by research community (i.e., sponsor and researcher).**