



Recruitment and Retention of Women's Health Research Participants: Lessons Learned From NIH Trials (And Errors)

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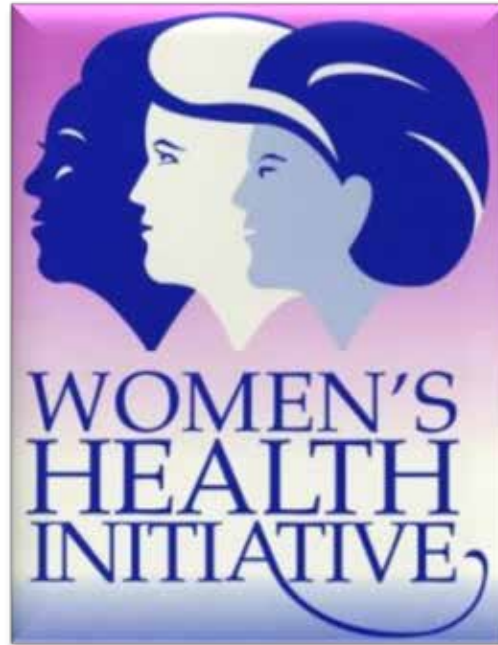
SoWH CyberSeminar, January 17, 2013

Poll Question #1

- What is your primary role in VA?
 - student, trainee, or fellow
 - clinician
 - researcher
 - manager or policy-maker
 - other

Poll Question #2

- Which best describes your research experience?
 - have not done research
 - have collaborated on research
 - have conducted research myself
 - have applied for research funding
 - have led a funded research grant



The WHI is funded by the
National Heart, Lung, and Blood Institute,
National Institutes of Health,
U.S. Department of Health & Human Services

(through contracts N01WH22110, 24152, 32100-2, 32105-6, 32108-9,
32111-13, 32115, 32118-32119, 32122, 42107-26, 42129-32, and 44221)

Why WHI?

- Address major causes of morbidity and mortality in postmenopausal women:
 - coronary heart disease
 - breast cancer
 - colorectal cancer
 - osteoporotic fractures
- Inadequate research on women's health
 - concerns about hormonal cycles and pregnancy
 - lack of women investigators
- Inadequate research in minority populations





Department of Health and Human Services

National Institutes of Health

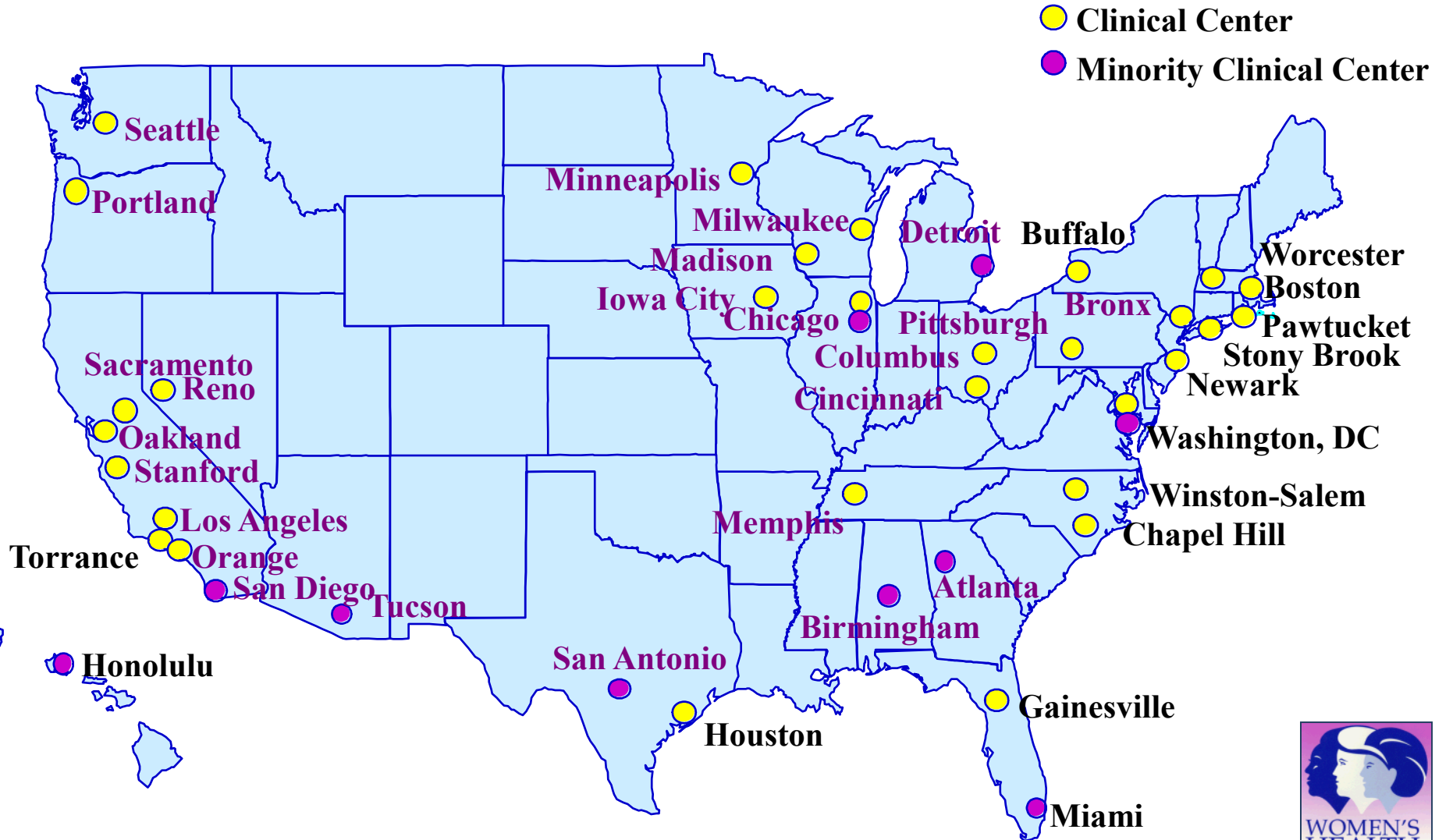
National Heart, Lung, and Blood Institute

WOMEN'S HEALTH INITIATIVE

A Vast Scientific Undertaking ...

- 161,808 participants followed ≤ 12 years in main WHI (1993-2005)
- 115,403 enrolled in WHI Extension Study (2005-2010)
- Over 93,000 enrolled in Extension Study-2 (2010-2015)
- 40 Clinical Centers in urban, suburban and rural areas
 - 3 CCs designated bone density centers
 - 10 CCs with satellite sites
 - 10 minority centers w/access to American Indian, African American, Asian American/Pacific Islander, Hispanic populations

WHI Clinical Centers



WHI Components & Primary Outcomes

3 Controlled Trials

27,347

Hormone Therapy Trials:

Coronary Heart Disease & Fractures
Adverse effect for Breast Cancer?
(16,608 E+P; 10,739 E-Alone)

36,282

Calcium/Vitamin D Trial:

Fractures & Colorectal Cancer

48,835

Dietary Modification Trial:

Breast & Colorectal Cancers & Coronary
Heart Disease

1 Observational Study

93,676

Observational Study

161,808 women total

Enrollment Goals

- Study component (HT, DM, CaD, OS)
- Age group:
 - ⊕ 10% 50-54 years
 - ⊕ 20% 55-59 years
 - ⊕ 45% 60-69 years
 - ⊕ 25% 70-79 years
- Minority centers - 60% racial/ethnic minority participants to ensure proportions representative of general population



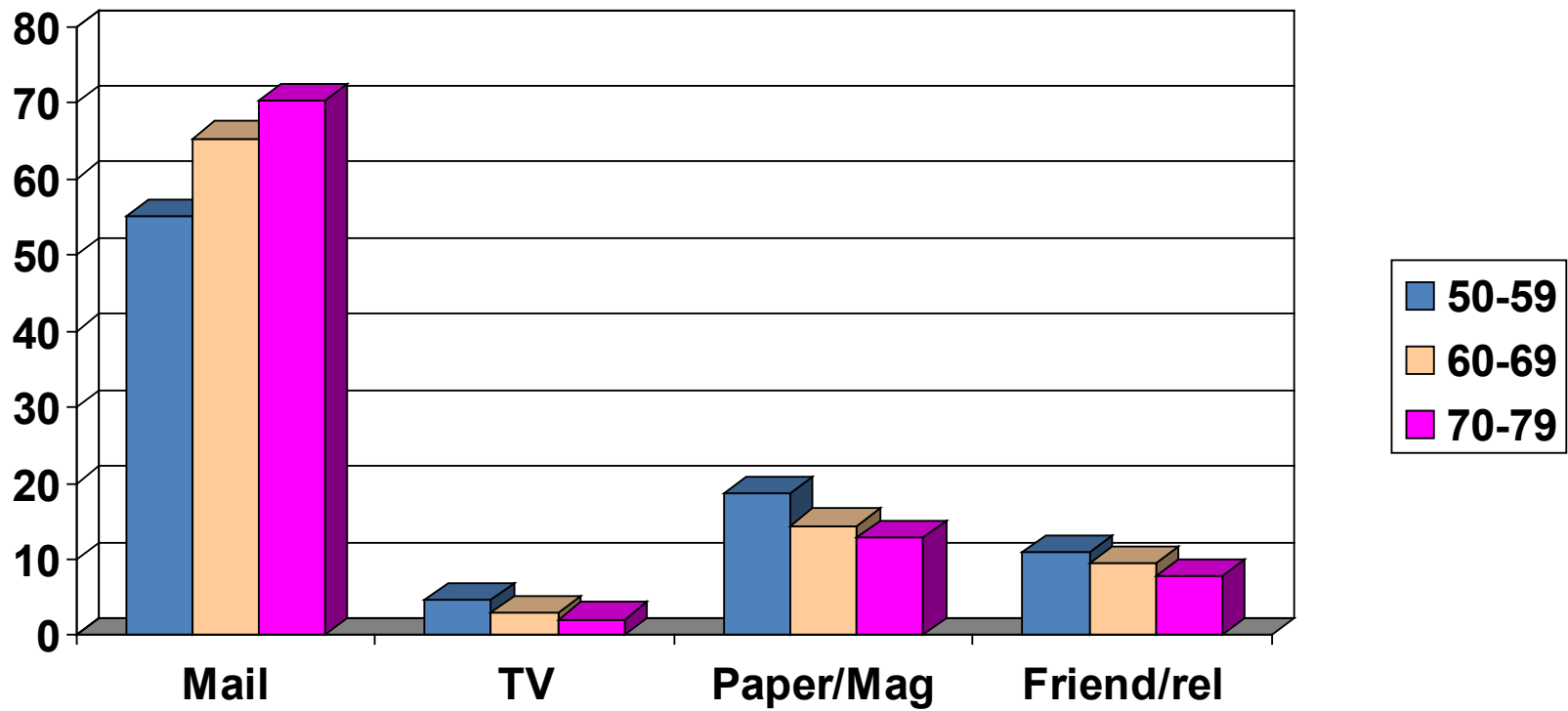
WHI Timeline

- Recruitment/screening: 1993 to 1998
 - Vanguard CCs started in September 1993
 - New CCs started in February 1995
- Follow-up for 7-12 years
 - CT: *contacts* every 6 months
 - OS: annual mailings; 3-year clinic visit
- Close-out: Oct. 2004 – Mar. 2005
- WHI Extension Study: 2005-2010
- WHI Extension Study-2: 2010-2015

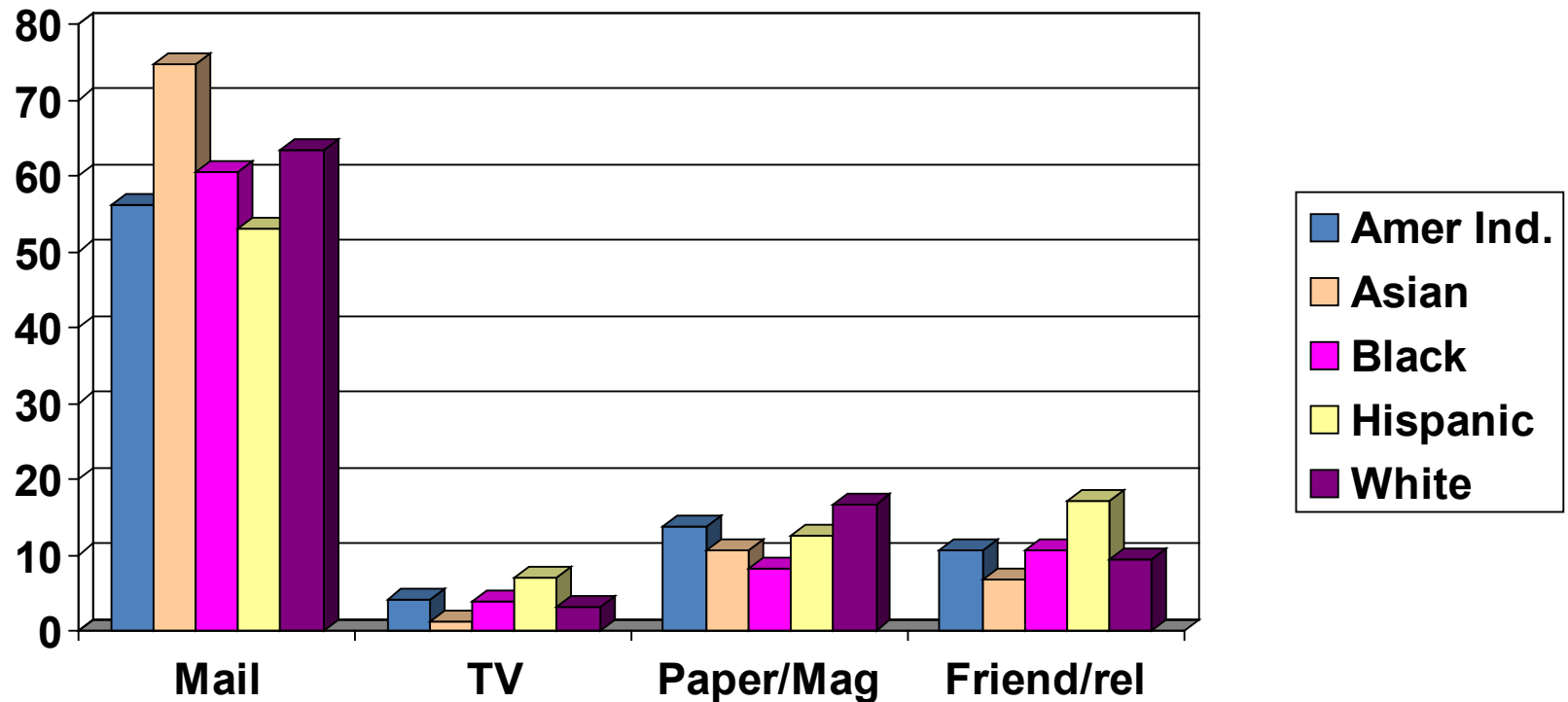
Eligibility Criteria

- General criteria for inclusion in CT and OS:
 - Ages 50 to 79 years
 - Postmenopausal
 - Planning to reside in the area for ≥ 3 years
 - Able/willing to provide written informed consent
- Additional eligibility criteria specific to each study component, related to:
 - Safety
 - Competing risk
 - Adherence/retention

Type of Initial Contact with WHI



Type of Initial Contact with WHI



WHI Initial Screening

- Mass mailing of recruitment brochure
 - provided basic information
 - postage-paid return postcard to indicate interest
- Telephone screening by trained interviewers
- Clinic visits
 - 3-5 for randomization in Clinical Trial (HT or DM)
 - 1 for enrollment in Observational Study





Retention and Adherence

Primary Prevention




During screening:

- Fully inform participants about study burden, do not minimize inconvenience and effort required
- Fully inform that benefits may not accrue to the participant in a research trial
- Fully inform about the meaning of randomization
- Inquire about their past intervention behavior
- Have a “trial run” (*HT run-in, 4-day food record, CaD taste test*)
- Attend to subtle and overt cues during screening visits (*rescheduling, lateness, difficulty contacting, hesitancy*)

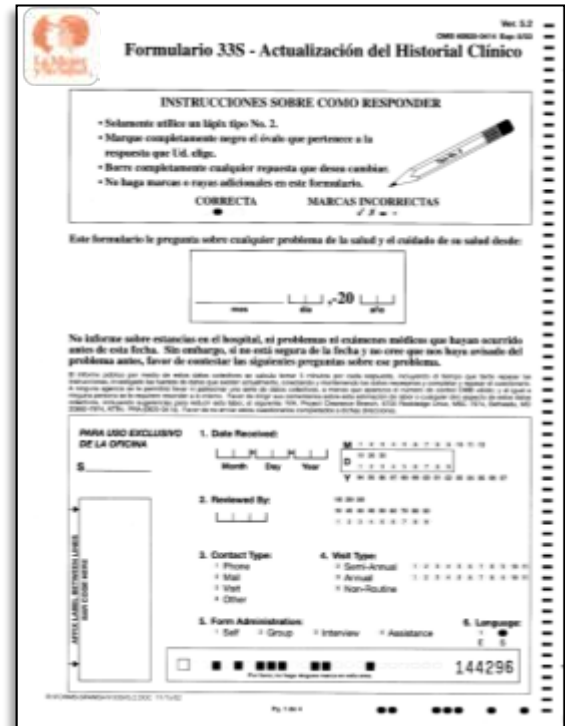


Baseline Characteristics of WHI Final Enrollment Participants

	HT		DM		CaD		OS	
	N=27,347		N=48,835		N=36,282		N=93,676	
	N	%	N	%	N	%	N	%
<i>Race/Ethnicity</i>								
American Indian	131	0.5	203	0.4	149	0.4	422	0.5
Asian/Pacific Island'r	527	1.9	1107	2.3	722	2.0	2671	2.9
Black	2741	10.0	5266	10.8	3317	9.1	7639	8.2
Hispanic	1543	5.6	1854	3.8	1507	4.2	3623	3.9
White	22027	80.5	39760	81.4	30153	83.1	78013	83.3

Notes about Data Collection

- Data collection protocols (forms & frequency) based on study component, study year, WHI priorities, and subsampling
- All participant materials, including self-report forms, available in Spanish
- Self-report forms:
 - Most were scannable
 - Most could be completed by interview or w/assistance
- Follow-up outcome reports obtained from participants, proxies (as needed & available), National Death Index (vital status)



Formulario 33S - Actualización del Historial Clínico

INSTRUCCIONES SOBRE COMO RESPONDER

- Soloamente utilizar un lápiz tipo No. 2.
- Marque completamente según el óvalo que pertenece a la respuesta que Ud. elige.
- Borrar completamente cualquier respuesta que desee cambiar.
- No haga marcas o rayas adicionales en este formulario.

CORRECTA MARCAS INCORRECTAS

Este formulario le pregunta sobre cualquier problema de la salud y el estado de su salud desde:

_____ años, _____ días, _____20_____ años

No informe sobre episodios en el hospital, ni problemas ni exámenes médicos que hayan ocurrido antes de esta fecha. Sin embargo, si no está segura de la fecha y no cree que sea muy distinto del problema antes, favor de contestar las siguientes preguntas sobre ese problema.

PARA USO EXCLUSIVO DE LA OFICINA

1. Date Revisado: _____

2. Revisado By: _____

3. Contact Type: _____

4. Visit Type: _____

5. Form Administration: _____

6. Language: _____

144296

Notes about Coordinating and Monitoring Recruitment Efforts

- Recruitment Coordinator (RC) at each site & CCC RC liaison
- Weekly national RC calls & email newsletter to share ideas
- Use of logo, study colors, & catch-phrase on all recruitment materials (*central review*)
- Performance Monitoring Committee focus on recruitment and assistance

HEALTH NEWS

Study of Women's Health Issues Focuses on Disease Prevention

(NIH) - Women 50 and over currently have an opportunity to participate in one of the largest studies on women's health ever conducted in the United States.

Called the Women's Health Initiative, the study is focusing on strategies to prevent heart disease, breast and colorectal cancer, and osteoporosis in women. Strategies being studied include hormone replacement therapy, low-fat dietary changes, and calcium and vitamin D supplementation.



WOMEN'S HEALTH INITIATIVE

Troubling Numbers

There are startling statistics about women and health:

- About 90 percent of all heart disease deaths among women occur after menopause.
- About 39 percent of women who have heart attacks die within one year, compared to 31 percent of men. This is because heart disease in women often goes undetected and untreated until it is severe.
- One in eight women can expect to develop breast cancer.
- In 1990, nearly 2 million women were unable to carry out major life activities or were limited in their ability to do so because of osteoporosis.

Searching for Answers

Traditionally, medical research has not focused on women's response to treatment or preventative approaches to chronic disease. We do know that women and men respond differently to certain treatments, including some used for heart disease, the No. 1 killer of women in the United States.

Researchers hope to enroll 164,500 women in the study sponsored by the National Institutes of Health. About 100,000 of these women will participate in an observational study that looks at the relationship between lifestyle, health, risk factors and disease.

The study will also help to clear up conflicting results of previous preventative studies about nutrition and hormone therapy. WHI will provide, for example, definitive answers about the use of hormones in preventing heart disease.

To help get these answers, large numbers of women are being asked to join the study for eight years or more.

WHI is open to all women over 50, especially women in their 60s and 70s, and African American, Hispanic, Native American and Asian American women.

To learn more about the Women's Health Initiative, call (800) 54-WOMEN.

WHI Websites

- WHI Study - www.whi.org
 - Scientific resources - assist scientists with proposing papers or ancillary studies using WHI data or biospecimens
 - Participant information - for lay public
- NHLBI - www.nhlbi.nih.gov/whi

Thanks to the WHI participants!



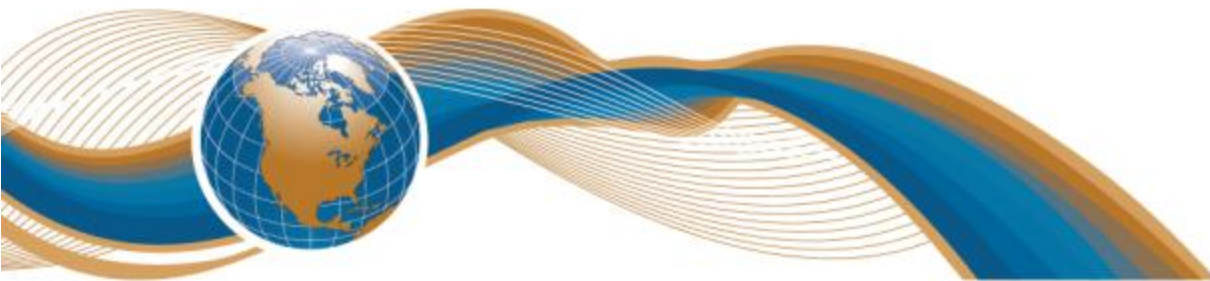
WHI Investigators *(A Short List)*



Program Office: (NHLBI, Bethesda, Maryland) Barbara Alving, Jacques Rossouw, Shari Ludlam, Linda Pottern, Joan McGowan, Leslie Ford, and Nancy Geller.

Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Ross Prentice, Garnet Anderson, Andrea LaCroix, Charles L. Kooperberg, Ruth E. Patterson, Anne McTiernan; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker; (Medical Research Labs, Highland Heights, KY) Evan Stein; (University of California at San Francisco, San Francisco, CA) Steven Cummings.

Clinical Centers: (Albert Einstein College of Medicine, Bronx, NY) Sylvia Wassertheil-Smoller; (Baylor College of Medicine, Houston, TX) Jennifer Hays; (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn Manson; (Brown University, Providence, RI) Annlouise R. Assaf; (Emory University, Atlanta, GA) Lawrence Phillips; (Fred Hutchinson Cancer Research Center, Seattle, WA) Shirley Beresford; (George Washington University Medical Center, Washington, DC) Judith Hsia; (Harbor-UCLA Research and Education Institute, Torrance, CA) Rowan Chlebowski; (Kaiser Permanente Center for Health Research, Portland, OR) Evelyn Whitlock; (Kaiser Permanente Division of Research, Oakland, CA) Bette Caan; (Medical College of Wisconsin, Milwaukee, WI) Jane Morley Kotchen; (MedStar Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Northwestern University, Chicago/Evanston, IL) Linda Van Horn; (Rush Medical Center, Chicago, IL) Henry Black; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (State University of New York at Stony Brook, Stony Brook, NY) Dorothy Lane; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Alabama at Birmingham, Birmingham, AL) Cora E. Lewis; (University of Arizona, Tucson/Phoenix, AZ) Tamsen Bassford; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of California at Davis, Sacramento, CA) John Robbins; (University of California at Irvine, CA) F. Allan Hubbell; (University of California at Los Angeles, Los Angeles, CA) Howard Judd; (University of California at San Diego, LaJolla/Chula Vista, CA) Robert D. Langer; (University of Cincinnati, Cincinnati, OH) Margery Gass; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Hawaii, Honolulu, HI) David Curb; (University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Massachusetts/Fallon Clinic, Worcester, MA) Judith Ockene; (University of Medicine and Dentistry of New Jersey, Newark, NJ) Norman Lasser; (University of Miami, Miami, FL) Mary Jo O'Sullivan; (University of Minnesota, Minneapolis, MN) Karen Margolis; (University of Nevada, Reno, NV) Robert Brunner; (University of North Carolina, Chapel Hill, NC) Gerardo Heiss; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (University of Tennessee, Memphis, TN) Karen C. Johnson; (University of Texas Health Science Center, San Antonio, TX) *Robert Brzyski*; (University of Wisconsin, Madison, WI) *Gloria E. Sarto*; (Wake Forest University School of Medicine, Winston-Salem, NC) Denise Bonds; (Wayne State University School of Medicine/Hutzel Hospital, Detroit, MI) Susan Hendrix.



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Recruitment and Retention of Women's Health Research Participants: Lessons Learned from NIH trials (and errors)

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School of Nursing & Irving Institute for Clinical & Translational Research

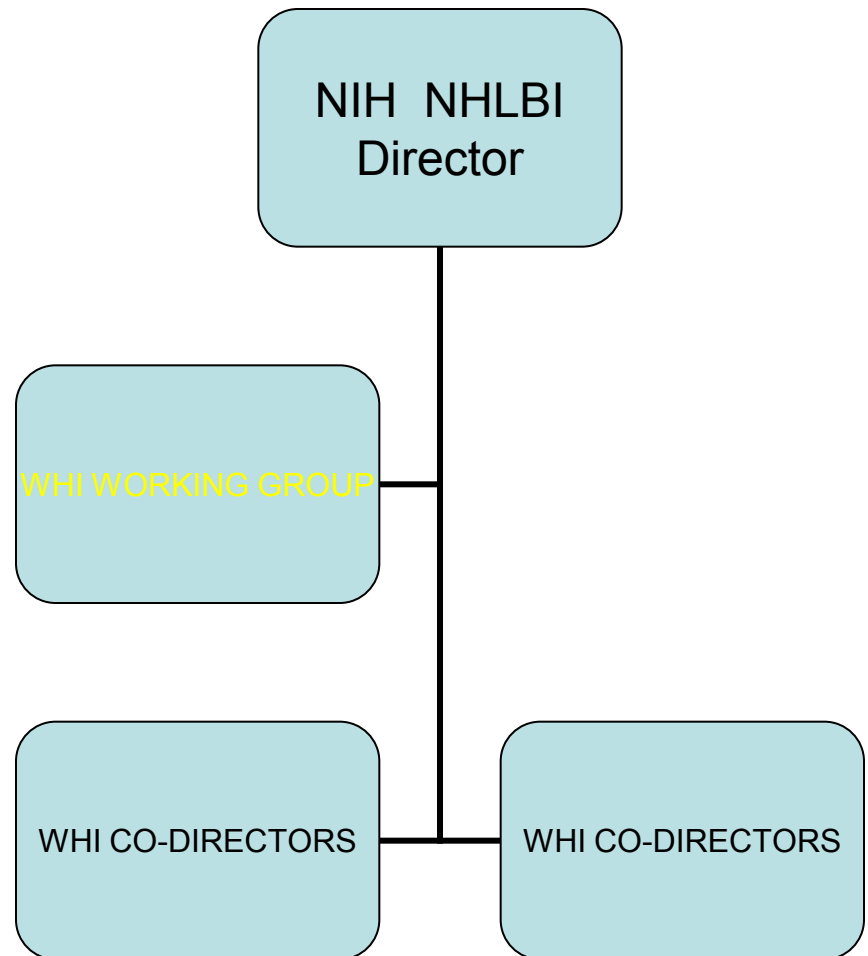
Columbia University, New York, NY

With contributions by **Barbara Cochrane, PhD, RN**

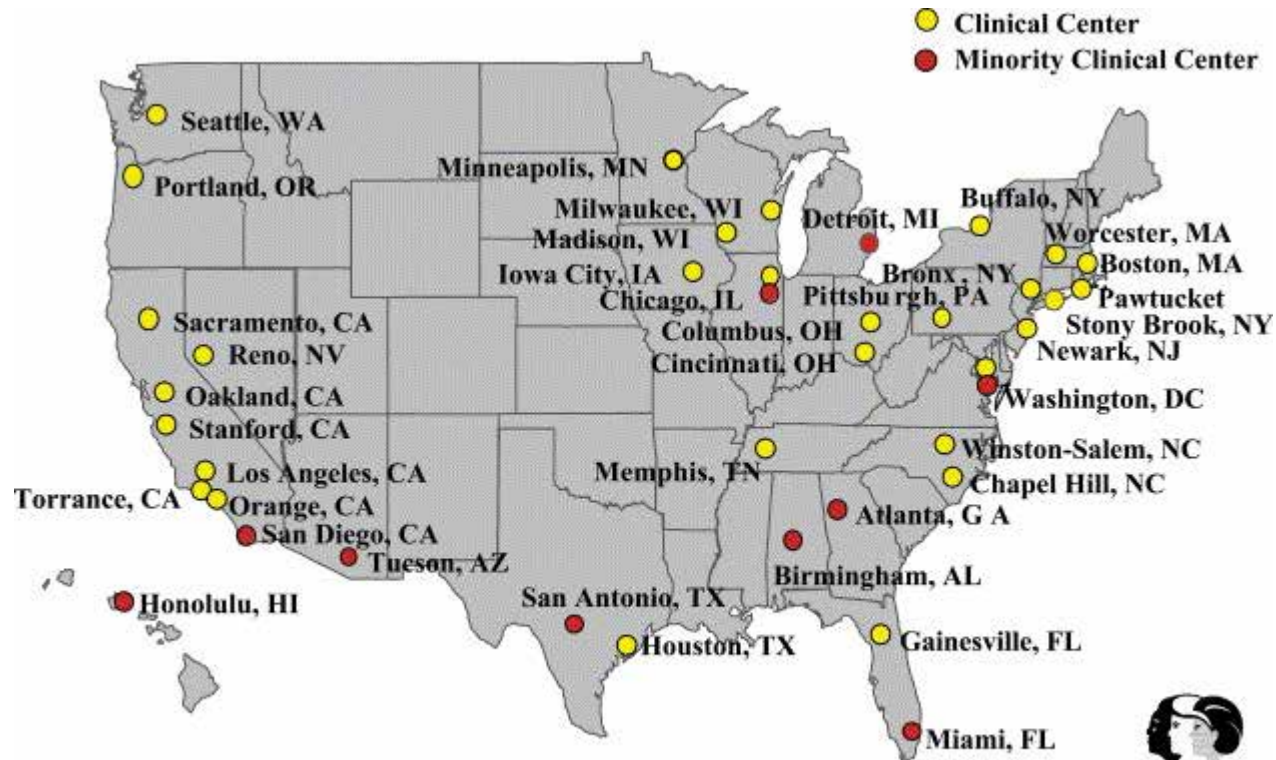
School of Nursing, University of Washington

WHI Working Group: advisory role to the NHLBI Director

- Judith Hochman, MD
- Linda Burhansstipanov, DrPH
- Deborah Dingell
- Stephen Fortmann, MD
- Lou Glasse, MSW
- Elmer Huerta, MD, MPH
- M. Margaret Kemeny, MD
- Gennell Knatterud, PhD
- Shiriki Kumanika, PhD
- Eugene Passamani, MD
- Alfred Poindexter, MD
- Nancy Reame, PhD, RN



WHI recruitment sites



Minority = 60% women of color;
Other sites = proportional to their
general population; GOAL: 20%
minorities enrolled



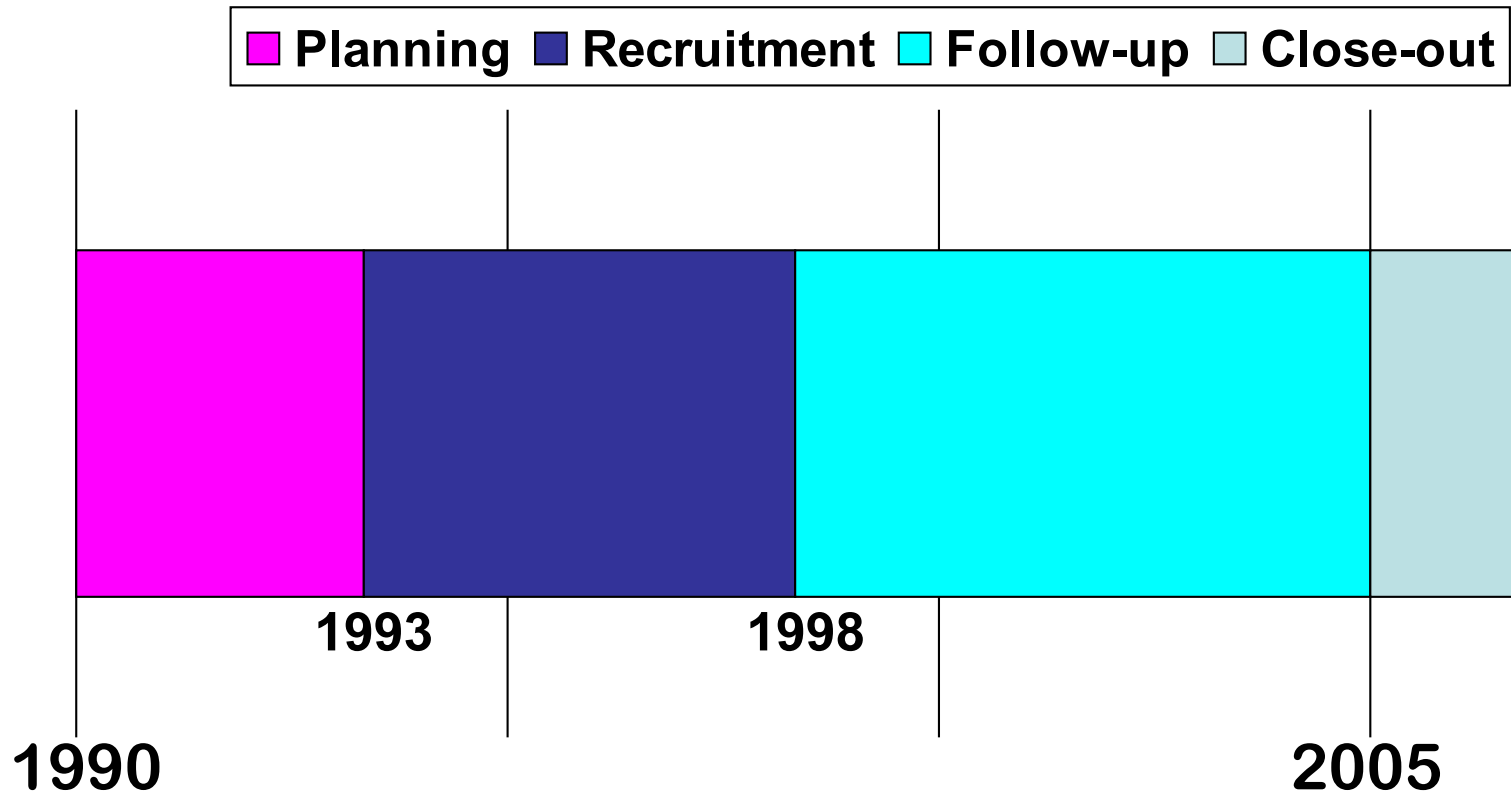
WHI Recruitment required wise planning!

Recruitment is a process, not a single step (Walson, 1999)

- Identifying & attracting the eligible patient populations
- Adequately explaining the study
- Recruiting an adequate, representative sample
- Obtaining true informed consent (in many cultures, this may hinge on family/spouse's views)
- Retaining participants until study completion
- Minimizing cost-benefit ratio



Women's Health Initiative Timeline



National Recruitment Activities



- Central development of materials (brochures, videos)
- Toll free national recruitment telephone line (1-800-54-WOMEN)
- National public awareness campaign to develop materials and aid with national media placement
- Central training and support of staff
- Study-wide advisory groups


WHI Special Strategies to Encourage a Diverse Population of Elderly Women



- Allowing extra time at screening visits for older women
- Providing extra assistance for women with physical limitations
- Using large size print, good color contrasts
- 6th grade reading level
- Spanish translation
- All materials printed with WHI logo/colors
- Consistent use of visual images (three heads logo)
- And verbal messages: “Be part of the answer,” passing on a legacy of good health

WHI “Branding”

- All materials printed with WHI logo/colors
- Consistent use of visual images (three heads logo)
- And verbal messages: “Be part of the answer,” passing on a legacy of good health



**WOMEN'S
HEALTH
INITIATIVE**

Be part of the answer!

The Women's Health Initiative is a major national research study of women and their health. It will help to decide how diet, hormone therapy, and calcium and vitamin D might prevent heart disease, cancer, and bone fractures.

You may be able to join if you are:

- a woman 50-79 years old
- past menopause or the “change of life”
- planning to live in the same area for at least 3 years

By joining this important study, you may help to improve your future health and the health of generations to come!

For more information, please call:
Berman Center for Clinical Research, 336-5743



¿Qué herencia
dejará Ud.
a sus hijas
y a futuras
generaciones?

Sea Parte de la Solución

La Mujer y Su Salud

Taking Calcium and Vitamin D Supplements

May reduce your risk for
bone fractures and *Might* reduce
your risk for colon, rectal and
perhaps even breast cancer.



What Legacy
Will You Leave
Your Daughters
& Future
Generations?

Be Part of the Answer

The Women's Health Initiative

Clinical Center Recruitment Strategies



Mass mailing was primary method for initial contact
Each CC mailed an average of 1000-5000 brochures per
month for 3-5 years!

Supplemental Strategies:

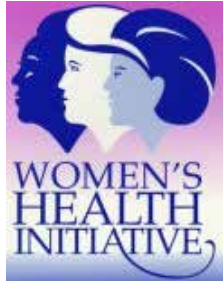
- Community presentations
- Local newsletter articles and ads
- Public service announcements (TV and radio)
- Name-a-friend programs
- Health fairs
- National and local press releases
- Health care provider referrals

WHI Creative Local Strategies

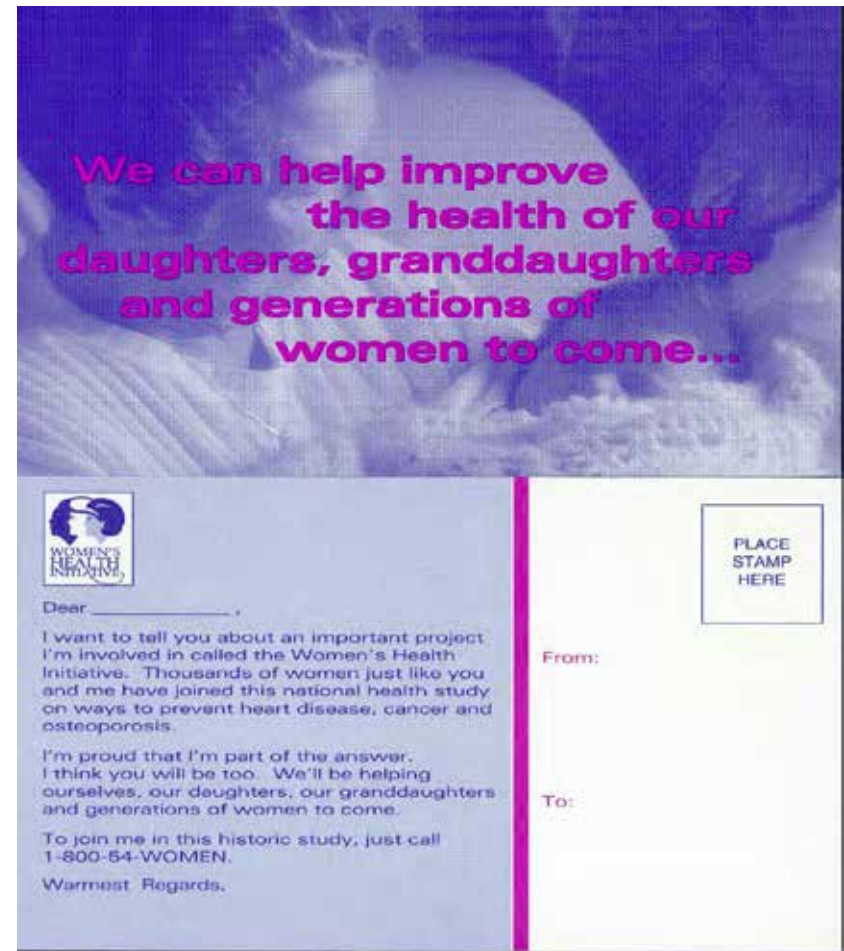


- Airplane message flying over OSU football game
- Local and national celebrities including Ms. Senior America, Olympia Dukakis
- Collaboration with local businesses to fund incentive items, newsletters, and transportation
- Planned events such as fashion shows
- Paid advertisements on buses, billboards, coupon packs, employee payroll stuffers

Engaging Volunteers in Recruitment: examples

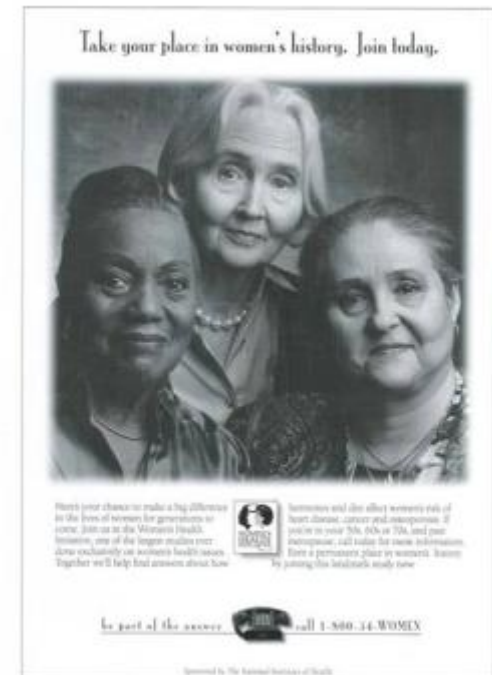


Postcards were developed for recruited women to mail to their friends and family



Focus Group Feedback is Key!

- Branding messages
- Celebrity testimonials
- Incentives
- Videos
- Posters and flyers
- Public Service Announcements for radio, TV, and print media
- WHI Logo magnets, buttons, stickers



Recruitment Issues: Making Trials “User-Friendly”

- *Engaging community gate-keepers/stakeholders in the research agenda*
Detroit Church pastors, Hispanic women city representatives in Miami
- *Tailoring Site-Specific recruitment strategies in response to focus groups*
- motivational messages “Be part of the Answer” ; “for the next generation”
- *Developing TRUST of the scientific/medical communities- listening to the participants about travel costs, clinic hours, communication methods*
- hiring participants to work as recruiters, educators, team members
- *Clinic site personnel and researchers should “look like me”*
- women of color represented in mass media alerts, recruitment flyers, websites
- at study onset, very few PIs were women!...





Adapting Study Questionnaires/Tools for WHI Populations: Physical Activity

- *Tracked self-reported “moderate” intensity physical activities that included child care, housework, occupation, and not just leisure-time conditioning and sports activities*
- *monthly 4-day sets of 24hr PA diaries x 6 mos, kept by AA women in Birmingham, Alabama and 107 NA residents of Pueblo or Navajo reservations in New Mexico*
- *top 5 PA: occupation, walking for exercise, house cleaning, child care, lawn & garden; few reported sports/conditioning*
- *ethnic differences in patterns and categories of exercise*

(Ainsworth et al, J Women's Health Gender-based Med, 1999)

Retention Issues: Making Trials “User-Friendly”



The Women's Health Initiative **PARTICIPANT WEBSITE**



- *Modifying interventions in line with lifestyle needs*
 - *Site-specific cooking classes, dietary modifications to reduce fat intake*
- *Active monitoring of recruitment goals successes & failures for timely recalibrations*



Improving Adherence in the CaD: A Case Example*



- Early CaD Adherence was low (~60% had >80% adherence).
- CCC performed survival analyses with time to first non-adherent visit as the outcome. Factors predicting poor adherence were:
 - younger age
 - minority ethnicity
 - unmarried status
 - not having a 4-week adherence phone contact
 - moderate to severe symptoms of gas or constipation
 - Women who stopped CaD reported problems taking the pills.

* (LaCroix, 2005)

Table 5.8
Reasons for Stopping CaD

Data as of: January 31, 1999

Reasons¹	(N=4008)	
Personal	227	6%
Travel	68	2%
Study Procedures	51	1%
Health	916	23%
Experiencing health problems or symptoms not due to intervention	512	13%
Worried about health effects of medical tests	21	1%
Worried about costs if adverse effects occur	11	(<1%)
Advised not to participate by health care provider	297	7%
Study conflicts with health care needs	212	5%
Expected more care	9	(<1%)
Intervention	1694	42%
Reports health problems or symptoms from WHI Intervention	1137	28%
Problem with Clinic Practitioner or other CC staff	3	(<1%)
Doesn't like taking pills	477	12%
Doesn't like DM requirements	9	(<1%)
Problems with DM group nutritionist or group members	3	(<1%)
Doesn't like DM eating patterns	4	(<1%)
Doesn't like randomized nature of intervention	161	4%
Expected some benefit from intervention	29	1%
Won't participate in safety procedures	17	(<1%)
Other	1284	32%
Not Given	517	13%

Improving Adherence in the CaD: A Case Example*

Increased awareness of problems with chewable formulation:

- taste
- consistency
- size
- Hardness



Taste test (7/96)

Participant material revisions (9/96)

4-week call (10/96)

CaD survey of 100 participants (late 1996)

New swallowable formulation (10/97)

Swallowable re-formulation (early 1998)

* *LaCroix, 2005*

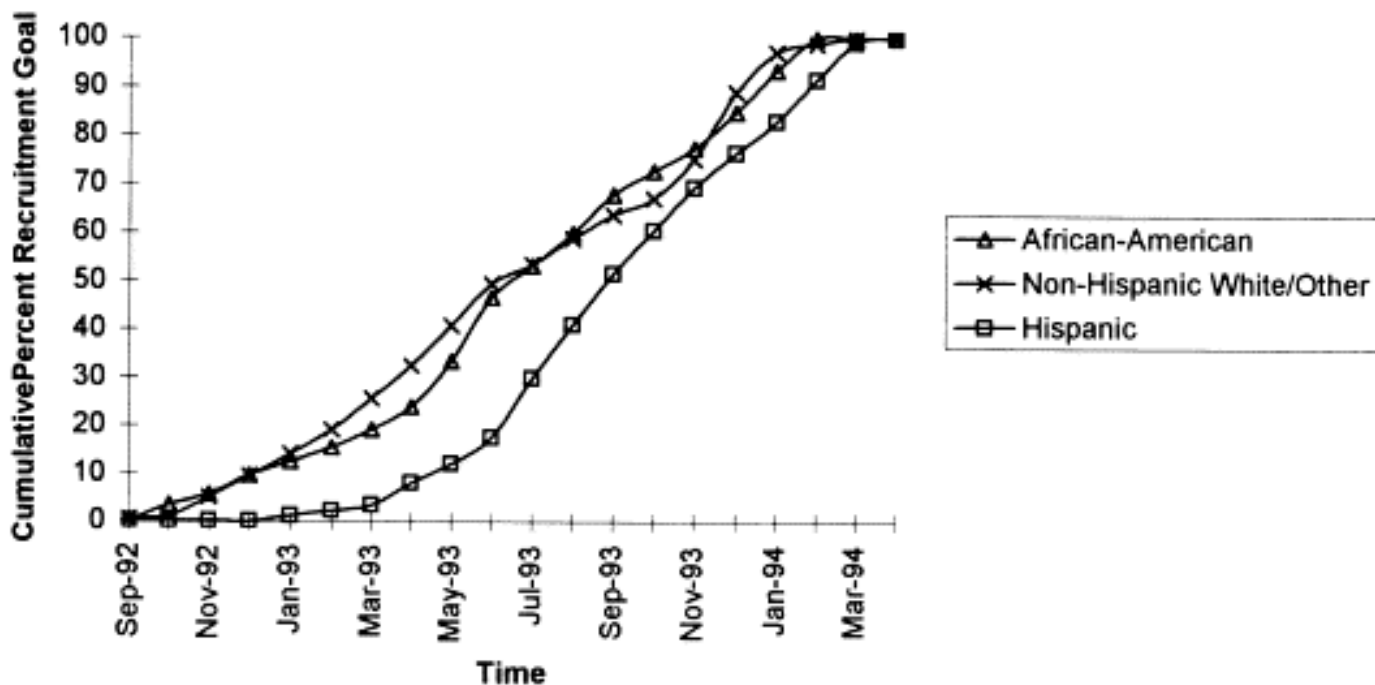
Hot Tips: Adherence*



- Screen for good adherers during recruitment
- Conduct the 4-week call to assess possible problems using consistent staff
- Develop a structure to support adherence:
 - designate a key retention staff person
 - have monthly retention committee meetings
 - identify candidates for and implement interventions
- Offer “step-down” and “step-up” options or pill “holidays”

*Lacroix, 2005

Feasibility of Recruiting Postmenopausal Women from Diverse Racial & Social Backgrounds into a Primary Prevention Trial Requiring Marked Reductions in Dietary Fat. (Lewis et al, 1998, fig 2)



Cumulative percent recruitment goal by ethnicity:
AA = 605, NHW- 1253, Hispanic = 350



Conclusions: WHI Recruitment*

1. Retention begins at recruitment, *really*.
2. WHI was privileged to have a national recruitment infrastructure and \$1 million to spend on national recruitment efforts.
3. Mass mailing was the backbone of our recruitment success.
4. Minority recruitment was a challenge, but tenacious effort paid off.
5. The greatest success comes from systematized pro-active efforts and individualized reactive efforts by staff.
6. Adherence monitoring and special studies can help to inform innovations that improve adherence.
7. Encouraging clinic staff (e.g. nurses) to become more data savvy is an important future direction.

*Trial Implementation II: Recruitment, Retention and Adherence, A. LaCroix, 2005

VULNERABLE OLDER WOMEN SYMPOSIA

From Gerontological Society of America
64th Annual Scientific Meeting
November 18 – 22, 2011:

*What Have We Learned from the WHI about
Racial/Ethnic Minority Women's Health?
Cochrane, Benavente, Coker*



Conclusions/Insights

Even with WHI's large numbers, our understanding of older racial/ethnic minority women's health continues to be challenged by:

- Comparisons of “white” with “non-white”
- Comparisons across groups
- Lack of subgroup differential analyses by racial/ethnic group:
 - Hispanic/Latinas
 - Asian/Pacific Islanders



Conclusions/Insights

- Future studies should include analyses by racial/ethnic group:
 - To gain new insights about potential mechanisms for study findings
 - To guide methods for future studies that incorporate alternative approaches to typical linear models used in epidemiology
 - Structural equation modeling
 - Interpretive/inductive methods
 - To generate hypotheses for future research



Effective Recruitment & Retention of Minority Research Participants



AK Yancey, AN Ortega, SK Kumanyika, *Ann Rev Pub Health*, 2006

- *Systematic review of 95 studies 1999-2005 of methods to increase minority participation*
- *“federally-defined” under-represented minority ethnic groups*
- *10 factors emerged re recruitment success:*
 - *6 related to features of the participants (religiosity, attitudes about disease, psychosocial health, trust of medical/scientific community; cultural adaptations)*
 - *4 related to the study design, sampling, incentives, community involvement*

Women's Health Research: Progress, Pitfalls & Promises: Recommendations (IOM, 2010)

1. Mainstream women's health: routinely assess sex differences in all health studies;
2. Govt agencies should develop targeted initiatives to enhance research on groups at highest risks/burdens
3. Outcomes research should include quality of life
4. Social determinants of health behaviors/disease risk
5. Sex-stratified analysis required for publication; add to journal guideline
6. Research on *how* to translate findings in clinical guidelines
7. HSS task force to develop evidence-based health messaging strategies to the public





Women's Health Research, 1990: "*We need a moon walk for women*" B. Healy, NIH Director.

- Until the 1990's, female subjects (humans and rats!) were underrepresented in biomedical research
- Women scientists <15% NIH grant awardees
- IN RESPONSE,
- * Offices of Women's Hlth/Minority Hlth
 - * The Women's Health Initiative (WHI)
 - * The National Centers for Infertility Research (U54)
- Legislation mandated that women be included in RCTs



Questions??

