



# The Women's Health Initiative (WHI): Investigator Data

February 18, 2021

**Michael Pennell**  
College of Public Health



**THE OHIO STATE UNIVERSITY**  
CENTER FOR CLINICAL AND  
TRANSLATIONAL SCIENCE

# Today's Goals

1. Become more familiar with the **WHI investigator datasets** and how they can be used for your research.
2. Learn about the process for accessing the data and proposing manuscripts.

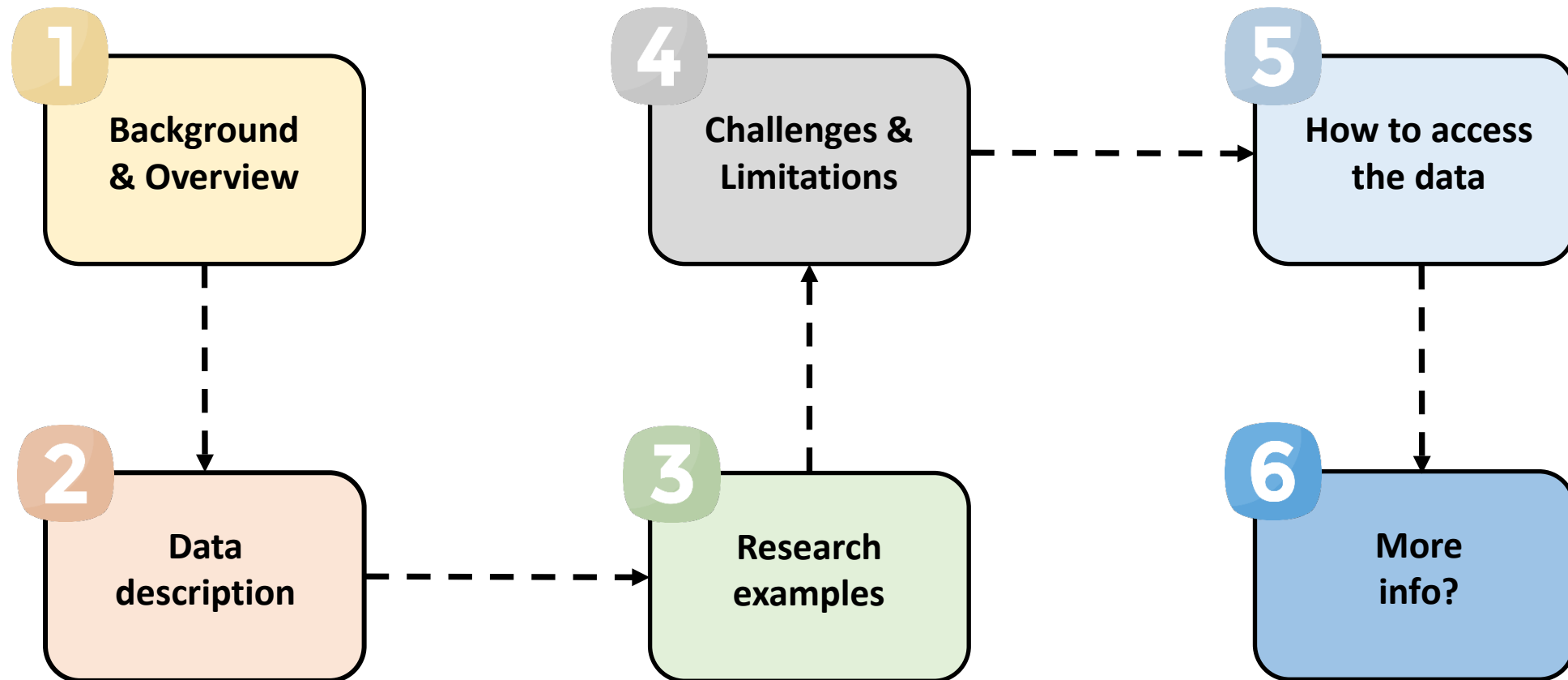


# Acknowledgement

- The majority of these slides were prepared by Amy Lehman, former member of WHI, Midwest Regional Center.
- All the bells and whistles are due to her efforts!



# The Women's Health Initiative (WHI)



# 1 Background and Overview

“The Women's Health Initiative (WHI) is a long-term national health study focused on strategies for preventing heart disease, breast and colorectal cancer, and osteoporotic fractures in postmenopausal women.”

- <http://www.whi.org>
- National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI)
- Launched in 1993:
  - Main study: 1993 – 2005
  - Extensions: 2005 – 2010, 2010 – 2020
  - Ancillary studies
- **Fred Hutchinson Cancer Research Center** in Seattle, WA

“Investigator Data”

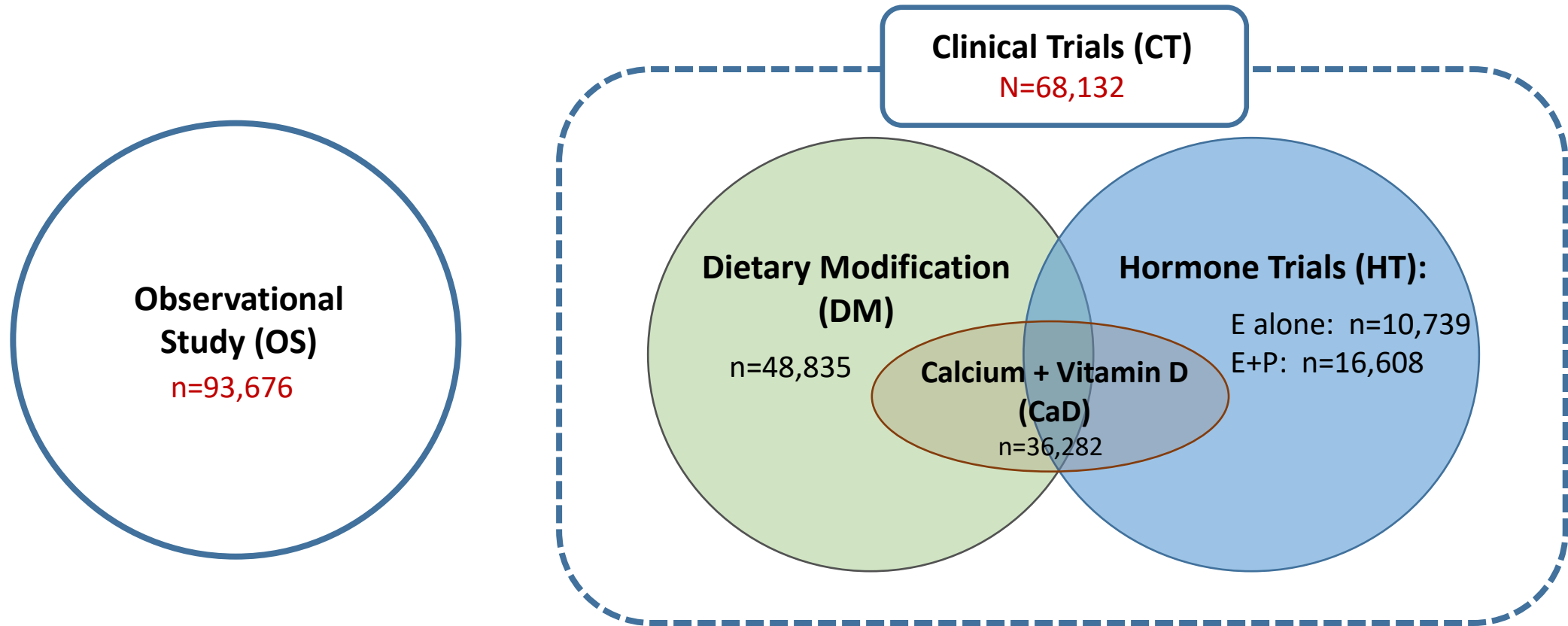


THE OHIO STATE UNIVERSITY  
CENTER FOR CLINICAL AND  
TRANSLATIONAL SCIENCE



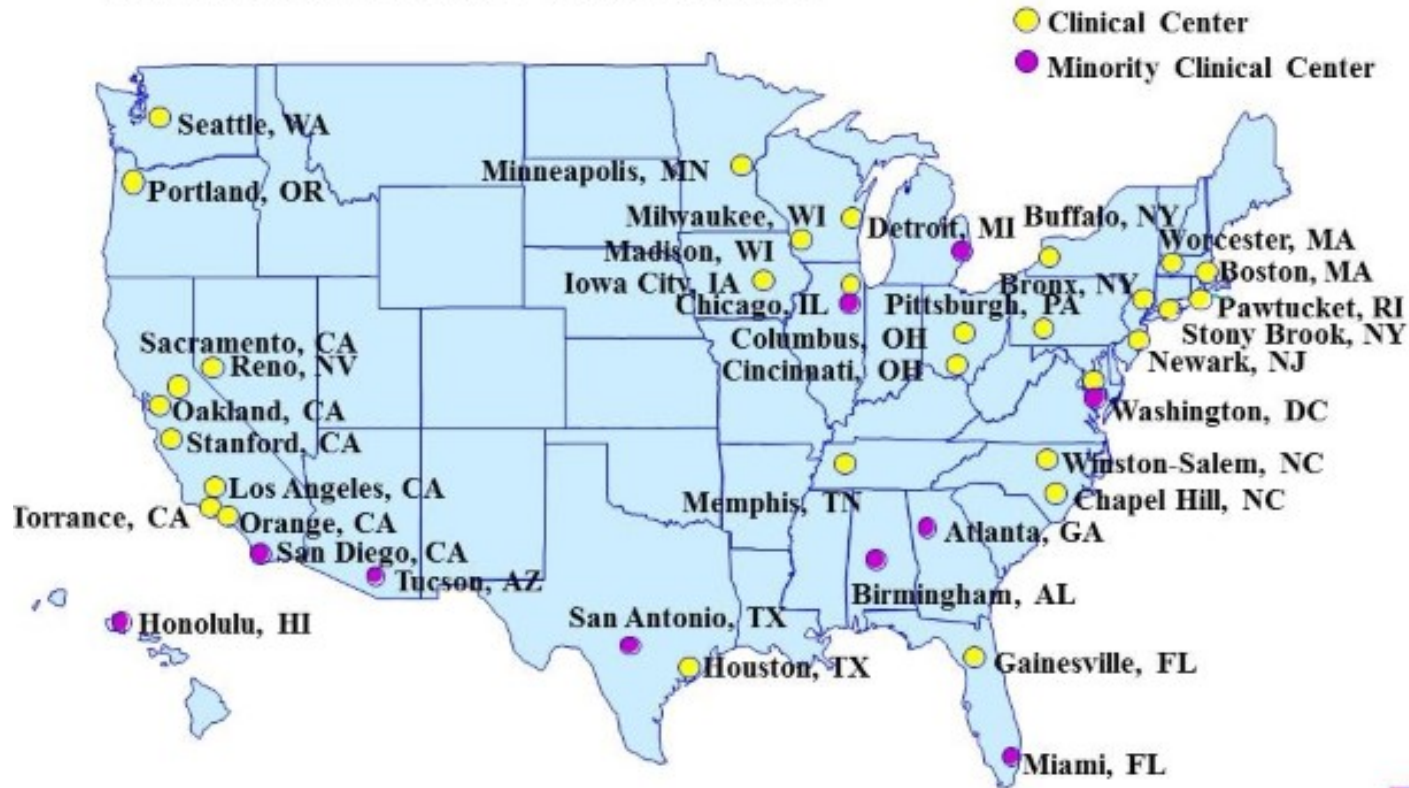
# Who is in WHI?

- 161,808 post-menopausal women
- Mean age at enrollment = 63.6 years (Range: 49 – 83 years)



# WHI Clinical Centers

## WHI Clinical Centers



- CT + OS conducted at **40** major clinical centers across the United States

Race/Ethnicity	N (%)
American Indian or Alaskan Native	713 (0.4%)
Asian or Pacific Islander	4,190 (2.6%)
Black (not of Hispanic origin)	14,618 (9%)
Hispanic/Latino	6,484 (4%)
White (not of Hispanic origin)	133,541 (82.5%)
Other	1,849 (1.1%)
Missing	413 (0.3%)
<b>Total</b>	<b>161,808</b>



THE OHIO STATE UNIVERSITY  
CENTER FOR CLINICAL AND  
TRANSLATIONAL SCIENCE



# WHI Regional Centers

Region	Regional Center Site	Institution	Principal Investigator
CCC	Seattle, WA	Fred Hutchinson Cancer Research Center	Garnet Anderson, PhD
Northeast	Buffalo, NY	University at Buffalo	Jean Wactawski-Wende, PhD
	Boston, MA	Brigham and Women's Hospital	JoAnn Manson, MD, DrPH
Southeast	Winston-Salem, NC	Wake Forest University	Mara Vitolins, DrPH
West	Palo Alto, CA	Stanford University	Marcia Stefanick, PhD
	Tuscon, AZ	University of Arizona	Cyndi Thomson, PhD, RD
Midwest	Columbus, OH	The Ohio State University	Rebecca Jackson, MD
	Iowa City, IA	University of Iowa	Jennifer Robinson, MD, MPH





# Primary Goals of WHI

## **Hormone Trials (HT)**

Combined hormones or estrogen alone →  
heart disease, osteoporotic fractures,  
breast cancer

## **Dietary Modification Trial (DM)**

Low-fat & high fruit, vegetable, grain diet →  
breast and colorectal cancers, heart disease

## **Calcium + Vitamin D Trial (CaD)**

Calcium and vitamin D supplementation →  
osteoporotic fractures, colorectal cancer

## **Observational Study (OS)**

Lifestyle, health and risk factors →  
disease outcomes



# Main Trial Findings of WHI

## Hormone Trials (HT)

Combined hormones or estrogen alone →  
heart disease, osteoporotic fractures,  
breast cancer

### Estrogen alone:

↑ risk of stroke, blood clots in the legs

↓ risk of hip fractures

No significant increase in heart disease  
and colorectal cancer risk, possible  
decrease in breast cancer risk

### E + P trial:

↑ risk of breast cancer, heart attack,  
stroke, blood clots

↓ risk for hip and other fractures and  
colorectal cancer

## Dietary Modification Trial (DM)

Low-fat & high fruit, vegetable, grain diet →  
breast and colorectal cancers, heart disease

No significant reduction in the risk of  
CHD, stroke, or CVD

Nonsignificant ↓ in breast cancer risk

## Calcium + Vitamin D Trial (CaD)

Calcium and vitamin D supplementation →  
osteoporotic fractures, colorectal cancer

Small but significant ↑ in hip bone  
density

No significant ↓ in hip fracture

↑ risk of kidney stones

# Impact of WHI Trials

ORIGINAL RESEARCH

Annals of Internal Medicine

“The Women’s Health Initiative E+P trial changed understanding of cHT risk–benefit balance and was a major driver of the precipitous and sustained decline in hormone therapy use in the United States between 2003 and 2012...Our findings suggest that these investments have yielded a return of approximately \$37 billion in net economic return in the past decade.”

**Target Population:** Postmenopausal women in the United States, aged 50 to 79 years, who did not have a hysterectomy.

**Time Horizon:** 2003 to 2012.

**Perspective:** Payer.

**Intervention:** Combined hormone therapy.

**Outcome Measures:** Disease incidence, expenditure, quality-adjusted life-years, and net economic return.

...tends with a substantial return on investment. These results can contribute to discussions about the role of public funding for large, prospective trials with high potential for public health effects.

**Primary Funding Source:** National Heart, Lung, and Blood Institute.

*Ann Intern Med.* 2014;160:594-602.

For author affiliations, see end of text.

[www.annals.org](http://www.annals.org)

Roth JA et al. *Ann Intern Med.* 2014 May 6;160(9):594-602. PMID: 24798522

One of the major debates in public funding of research is its overall return to society. In this context, studies that link National Institutes of Health (NIH)–sponsored research to changes in clinical practice patterns, patient outcomes, and costs are uncommon, although such information could inform debate about the role of publicly

2002, approximately 5.5 million U.S. women used cHT, largely based on clinical trial evidence of vasomotor symptom and osteoporosis benefit and observational evidence that suggested reduced cardiovascular disease risk (3–6). In July 2002, publication of the E+P trial results provided randomized, controlled trial evidence of increased cardiovascular disease among thromboembolism and breast cancer

UNIVERSITY



## 2 WHI Data

- Investigator data = **107** separate forms



Demographics, study  
status, eligibility &  
adherence



Diet



Medical history



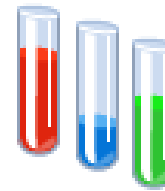
Medical & physical  
measurements



Medications



Psychosocial &  
personal habits



Specimen results



Outcomes, adjudicated  
& self-reported



# WHI Data

- Data collected at baseline and at selected time points over the study (longitudinal), depending on the form and study membership
  - Example - current medication use:
    - **Clinical trials (CT) participant:** baseline, years 1, 3, 6, 9
    - **Observational study (OS) participant:** baseline, year 3
- Adjudicated outcomes (and days from randomization/enrollment to first event) include:
  - Cardiovascular (eg. CHD, MI, stroke)
  - Cancer
  - Fracture
  - Death



### 3 Examples of Research with WHI (MW/OSU)

CARDIOVASCULAR DISEASE	
TOPIC	PMID
Stress, resilience, and cardiovascular disease risk among black women	30909729
Risk of cardiovascular disease among women with endometrial cancer compared to cancer-free women	29049937
Cardiovascular health and incident cardiovascular disease and cancer	26456876
STROKE	
Breastfeeding history and risk of stroke among parous postmenopausal women	30371157
Prestroke factors associated with poststroke mortality and recovery in older women	23869842
FRACTURE	
Age of menopause and fracture risk in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination	27801706
Dietary inflammatory index, bone mineral density, and risk of fracture in postmenopausal women	28019686
Postmenopausal weight change and incidence of fracture	25627698

CANCER	
TOPIC	PMID
COPD and lung cancer incidence	31958598
Rural-urban residence and stage at breast cancer diagnosis among postmenopausal women	30230942
Tubal ligation and risk of endometrial cancer	26825831
Statins and breast cancer stage and mortality	25736184
Bone health and survival in women with multiple myeloma	30049515
Change in longitudinal trends in sleep quality and duration following breast cancer diagnosis	29978034

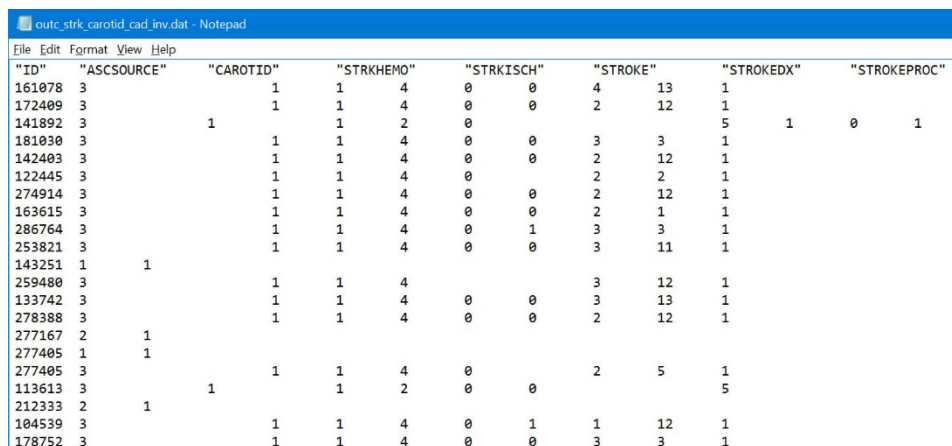


## 4 Challenges / Limitations of WHI Data

1. Data are observational – require consideration of confounders

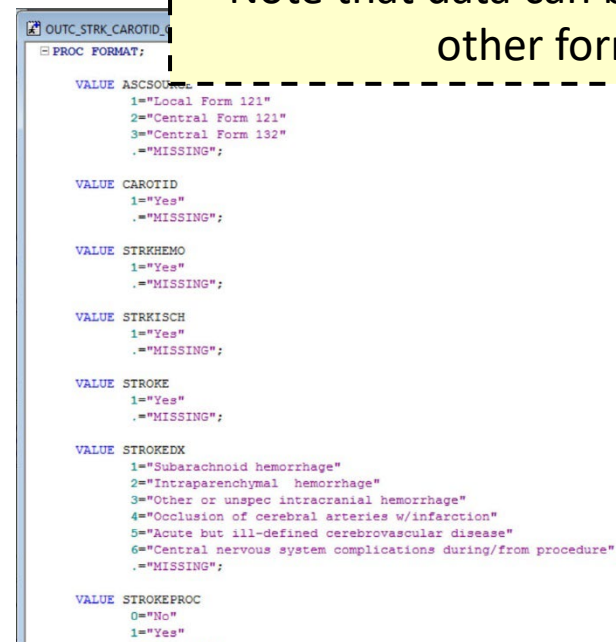
2. Data management:

- *Tab-delimited ASCII file with a header row containing the variable names and code to create SAS datasets*



"ID"	"ASCSOURCE"	"CAROTID"	"STRKHMO"	"STRKISCH"	"STROKE"	"STROKEDX"	"STROKEPROC"
161078	3	1	1	4	0	0	4
172409	3	1	1	4	0	0	2
141892	3	1	1	2	0	0	5
181030	3	1	1	4	0	0	3
142403	3	1	1	4	0	0	2
122445	3	1	1	4	0	0	2
274914	3	1	1	4	0	0	2
163615	3	1	1	4	0	0	2
286764	3	1	1	4	0	1	3
253821	3	1	1	4	0	0	3
143251	1	1	1	4	0	0	3
259480	3	1	1	4	0	0	3
133742	3	1	1	4	0	0	3
278388	3	1	1	4	0	0	2
277167	2	1	1	4	0	0	2
277405	1	1	1	4	0	0	2
113613	3	1	1	2	0	0	5
212333	2	1	1	4	0	0	3
104539	3	1	1	4	0	1	1
178752	3	1	1	4	0	0	3

+



```
PROC FORMAT;
VALUE ASCSOURCE
1="Local Form 121"
2="Central Form 121"
3="Central Form 132"
.= "MISSING";

VALUE CAROTID
1="Yes"
.= "MISSING";

VALUE STRKHMO
1="Yes"
.= "MISSING";

VALUE STRKISCH
1="Yes"
.= "MISSING";

VALUE STROKE
1="Yes"
.= "MISSING";

VALUE STROKEDX
1="Subarachnoid hemorrhage"
2="Intraparenchymal hemorrhage"
3="Other or unspec intracranial hemorrhage"
4="Occlusion of cerebral arteries w/infarction"
5="Acute but ill-defined cerebrovascular disease"
6="Central nervous system complications during/from procedure"
.= "MISSING";

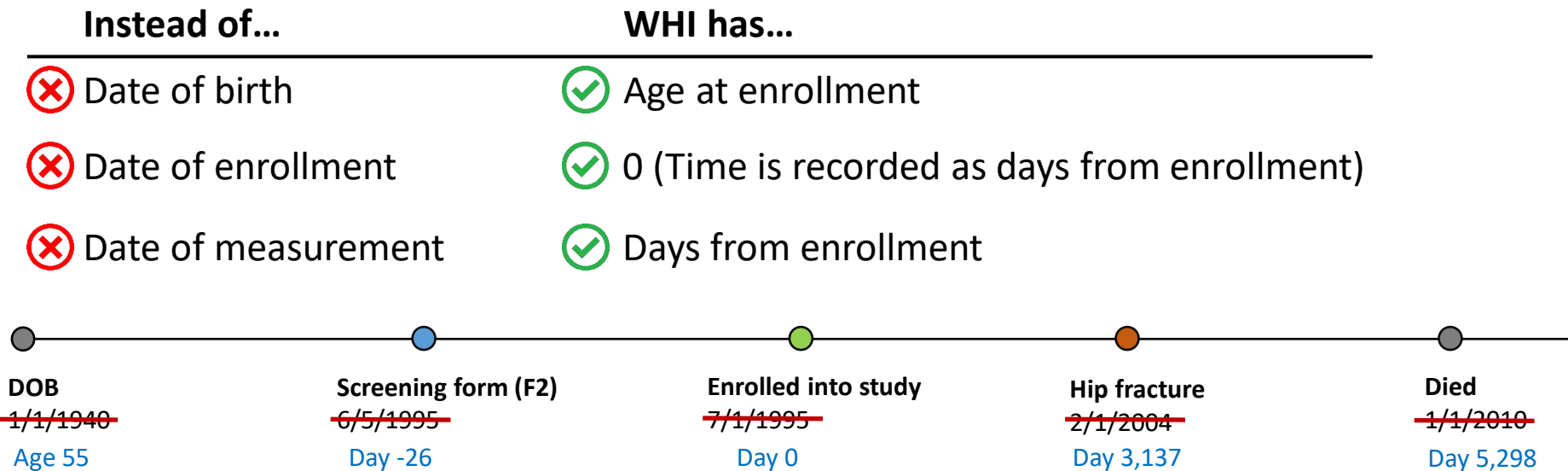
VALUE STROKEPROC
0="No"
1="Yes"
.= "MISSING";
```

Note that data can be converted into other formats...



# Challenges / Limitations of WHI Data

1. Data are observational - can WHI answer your question?
2. Data management
3. No actual dates!



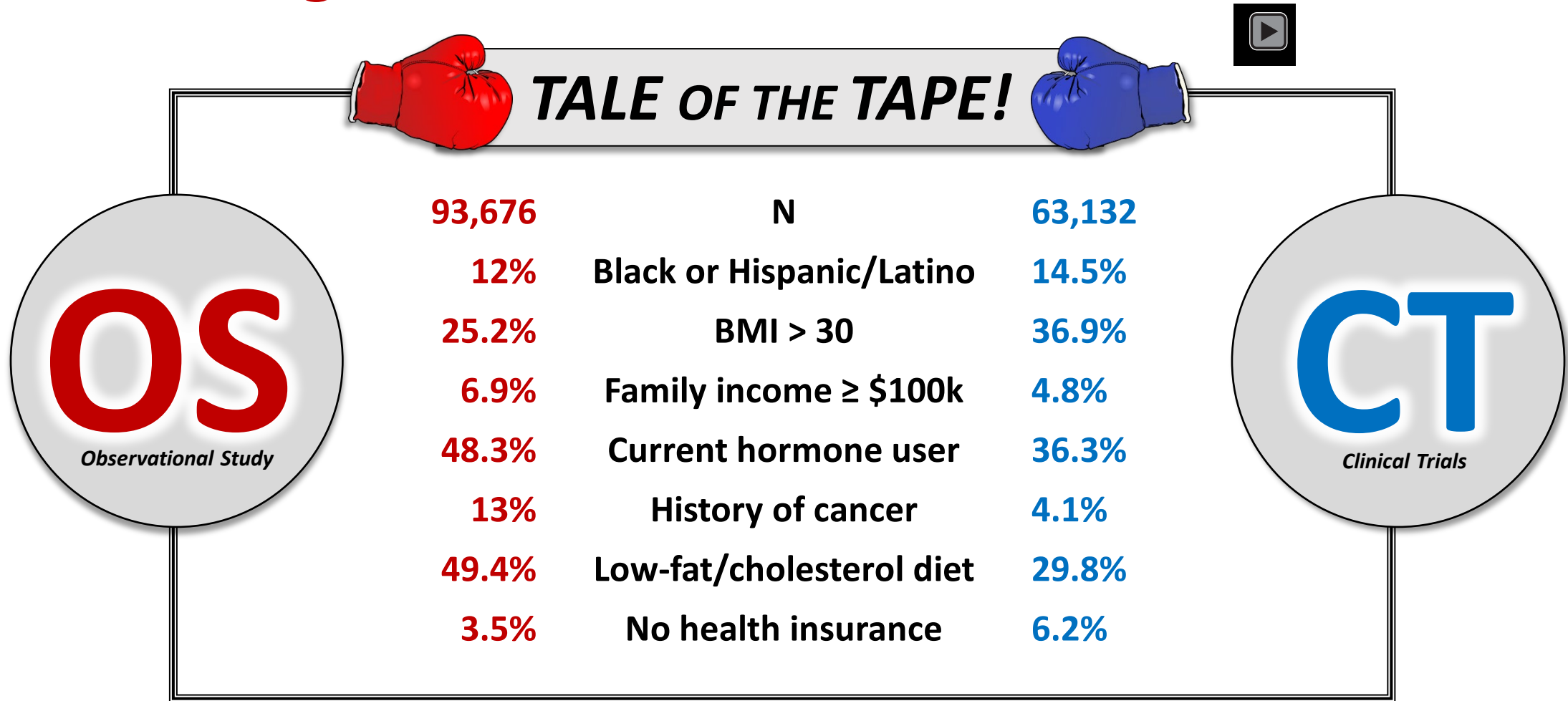


# Challenges / Limitations of WHI Data

1. Data are observational - can WHI answer your question?
2. Data management
3. No actual dates!
4. For adjudicated outcomes, only have first recorded event (no recurrence)
5. **Study population:**
  - Women close to an academic medical center (educated, more affluent  
→ not representative of all women)
  - CT vs. OS women – very different



# Challenges / Limitations of WHI Data



# Challenges / Limitations of WHI Data

## TUBTIED - Ever had tubes tied

Did you ever have an operation to have your tubes tied to prevent pregnancy?

Value	Description	N	%	
0	No	132,711	83%	<div></div>
1	Yes	28,055	17%	<div></div>

## TUBTIEDA - Age when tubes tied

How old were you when you had your tubes tied?

**Usage Notes:** Sub-question of F31 V2 Q11 "Ever had tubes tied".

Value	Description	N	%	
1	Less than 30	4,250	15%	<div></div>
2	30-34	7,869	28%	<div></div>
3	35-39	9,510	34%	<div></div>
4	40-44	5,138	18%	<div></div>
5	45 or older	1,176	4%	<div></div>

- Recall only – no verification
- Self-report age range
- 112 missing age



# Challenges / Limitations of WHI Data

## Timing Example: BMI

- Collected on Form 80

Cohort	Baseline	1	2	3	4	5	6	7	8	9	Ext 1	Ext 2
CT	X	X	X	X	X	X	X	X	X	X		
OS	X			X								

2005 - 2010

2010 - 2020

MAIN STUDY: 1993 - 2005



# Challenges / Limitations of WHI Data

Cohort	Baseline	1	2	3	4	5	6	7	8	9	Ext 1	Ext 2
CT	X	X	X	X	X	X	X	X	X	X		
OS	X			X								

Timeline diagram showing the duration of the study:

MAIN STUDY: 1993 - 2005

2005 - 2010      2010 - 2020

- Differential follow-up
- Annual self-reported weight for OS vs. clinic visit for CT
- Adjudicated outcomes up to 3/1/2019 – time gap

## 5 How to Access WHI Data

- <http://www.whi.org>
  - **Paper:** Using existing data
  - **Ancillary Study:** New data
- 1. Submit a proposal to the **Publications & Presentations (P&P) Committee**
  - Need to collaborate with **WHI Sponsoring Principal Investigator:**  
<https://www.whi.org/sponsors>
- 2. Access to download data or work with WHI statistician



Note that all manuscripts need to be approved by P&P before submission!



THE OHIO STATE UNIVERSITY  
CENTER FOR CLINICAL AND  
TRANSLATIONAL SCIENCE



# WHI Query Builder

- Planning / feasibility
- Get numbers of participants by:
  - Study participation and time period (main, extension)
  - Race/ethnicity and age at screening
  - Outcomes
  - Specimen availability and test results



# WHI Query Builder (example)

**Q6102 returns 2,236 participants**

Participant was in the OS

AND has an outcome of Hip Fracture

Go to <https://www.whi.org/>  
and select 'Query Builder'  
under the Resources tab...

Ethnicity	Total	% of ppts	Ct	Ht	Dm	Cad	Os	Ext1	Ext2	Mrc	Src
Any Ethnicity	2236	100	0	0	0	0	2236	1701	1067	57	1010
White	2086	93.3	0	0	0	0	2086	1594	992	0	992
Black or African-American	71	3.2	0	0	0	0	71	55	38	38	0
Hispanic	32	1.4	0	0	0	0	32	23	19	19	0
Asian or Pacific Islander	21	0.9	0	0	0	0	21	14	8	0	8
Other	21	0.9	0	0	0	0	21	12	7	0	7
American Indian or Alaskan Native	5	0.2	0	0	0	0	5	3	3	0	3



**THE OHIO STATE UNIVERSITY**  
CENTER FOR CLINICAL AND  
TRANSLATIONAL SCIENCE





## 6 For More Information and BERD support:

- **WHI website:** <http://www.whi.org>
- **To request BERD support on a WHI paper:** <https://myccts.osu.edu/>
  - Alternatively, you could submit a ticket to the Center for Biostatistics:  
<https://medicine.osu.edu/departments/biostatistics/service-request-form>





Thank you!