

# Using WHI Outcomes Data

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# Focus on:

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- What has been collected in WHI
- Which outcomes are adjudicated
- Changes between WHI and the extension studies (WHIX1 and WHIX2)
- What data is available on the [WHI website](#)
  - Format
  - How to use

# Clinical Outcomes in the CT

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- Defined as: primary or secondary
- Each study component (HT, DM, CaD) has 1 or 2 primary, and multiple secondary

# Clinical Outcomes in the OS

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- Same process for outcomes collection as in the CT
- No primary/secondary designation
- Fewer outcomes are adjudicated

# Adjudication and Confirmation

- Most outcomes start as a self-report on Form 33
- → Form 33D used to collect more information
- → Defined set of medical records obtained for selected outcomes
- Adjudication process confirms or denies the self-report (two levels: local and central)

# Cardiovascular Outcomes, WHI

Outcome	HT	DM	CaD	OS	Form
Cardiovascular:					
Coronary heart disease	1 <sup>o</sup> - C	2 <sup>o</sup> - L	L	L	121
Stroke	2 <sup>o</sup> - C	2 <sup>o</sup> - L	L	C	121/132
Congestive heart failure	2 <sup>o</sup> - C	2 <sup>o</sup> - L	L	L	121
Angina	2 <sup>o</sup> - C	2 <sup>o</sup> - L	L	L	121
Peripheral vascular disease	2 <sup>o</sup> - C	2 <sup>o</sup> - L	L	L	121
Carotid artery disease	L	L	L	L	121
Coronary revascularization	2 <sup>o</sup> - C	2 <sup>o</sup> - L	L	L	121
Total cardiovascular	2 <sup>o</sup>	2 <sup>o</sup>			

# Cancer Outcomes, WHI

<b>Outcome</b>	<b>HT</b>	<b>DM</b>	<b>CaD</b>	<b>OS</b>	<b>Form</b>
Breast cancer	2 <sup>0</sup> - C	1 <sup>0</sup> - C	2 <sup>0</sup> - C	C	122/130
Endometrial cancer	2 <sup>0</sup> - C	2 <sup>0</sup> - C	C	C	122/130
Colorectal cancer	C	1 <sup>0</sup> - C	2 <sup>0</sup> - C	C	122/130
Ovarian cancer	2 <sup>0</sup> - C	2 <sup>0</sup> - C	C	C	122/130
Other cancer	L	L	L	L	122
Total cancer	2 <sup>0</sup>	2 <sup>0</sup>	2 <sup>0</sup>		

# Fracture Outcomes, WHI

<b>Outcome</b>	<b>HT</b>	<b>DM</b>	<b>CaD</b>	<b>OS</b>	<b>Form</b>
Hip fracture	2 <sup>o</sup> - C	C	1 <sup>o</sup> - C	C	123
Other fractures	2 <sup>o</sup> - L	L	2 <sup>o</sup> - L	L*	123
Total fractures	2 <sup>o</sup>		2 <sup>o</sup>		

\* Only for participants at the 3 BMD clinical centers



# Other Outcomes, WHI

Outcome	HT	DM	CaD	OS	Form
Pulmonary embolism	2 <sup>o</sup> - C				126
Deep vein thrombosis	2 <sup>o</sup> - C				126
Diabetes mellitus requiring therapy	S	2 <sup>o</sup> - S	S	S	33
Death from any cause	2 <sup>o</sup> - C	2 <sup>o</sup> - C	2 <sup>o</sup> -C	L	124

- 1<sup>o</sup> - Primary outcome
- 2<sup>o</sup> - Secondary outcome
- C – Centrally adjudicated
- L – Locally adjudicated
- S – Self-report

# Self-reported Outcomes

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- Source: Form 33 v. 5, question 8
- “Since the date given on the front of this form, has a doctor told you **for the first time** that you have any of the following specific conditions?”
  - Glaucoma, osteoporosis, osteoarthritis, rheumatoid arthritis, intestine or colon polyps or adenomas, gallbladder disease or gallstones, lupus, kidney or bladder stones, cataracts

# Self-reported Outcomes (cont)

- Source: Form 33 v. 5, question 9
- “Since the date given on the front of this form, has a doctor prescribed **for the first time** any of the following pills or treatments?
  - Pills for diabetes, insulin shots for diabetes, pills for high blood pressure

# Other Sources of Outcomes Data

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- ECG results (CT only)
- BMD results from DEXA (subset of CT & OS at 3 clinical centers)
- Form 33, question 3 (falls), question 10 (exams, tests, and procedures)
- OS follow-up questionnaires (Form 48, Forms 143-148) – 19 conditions

# Some Changes in outcome data (WHI vs WHIX1 vs WHIX2)

- There are no local adjudications in WHIX1/WHIX2, all adjudications are done centrally
- Angina and CHF were locally adjudicated in WHI, they are only self-reported in WHIX1/WHIX2 (though we now have UNC HF adjudicated for the MRC Supercohort throughout WHI/WHIX1/WHIX2)
- Deaths – central (CT) and local (OS) adjudications during WHI; central only during WHIX1; central (MRC) and self-report (SRC) during WHIX2
  - National Death Index (NDI) deaths
- Fracture – only hip fracture is adjudicated in WHIX1/WHIX2, all other fractures are self-report (fracture was adjudicated in the CT & OS BMD clinics in WHI)
- Some endpoints were only collected in WHI (e.g., ECG data) and a few endpoints were added during WHIX2 (atrial fibrillation, heart valve disease, aortic aneurysm/dissection)

# Some Changes in outcome data (WHI vs WHIX1 vs WHIX2) (cont)

Table 1: WHI adjudicated outcomes by study period and WHI cohort

Outcome	WHI 1993-2005				Extension 1 2005-2010	Extension 2 2010-2015	Extension 2 2010-2015	Form
	HT	DM	CaD	OS	CT/OS	MRC	SRC	
<b>CARDIOVASCULAR:</b>								
MI	C	L	L	L	C	C	S	121
Stroke	C	L <sup>1</sup>	L <sup>1</sup>	C <sup>1</sup>	C	C	S	121/132
WHI congestive heart failure	C	L	L	L	S	S	S	121
UNC heart failure	C <sup>2</sup>	C <sup>2</sup>	C <sup>2</sup>	C <sup>2</sup>	C <sup>2</sup>	C <sup>2</sup>	S	135/136
Angina	C	L	L	L	S	S	S	121
Peripheral artery disease	L	L	L	L	C	C	S	121
Carotid artery disease	L	L	L	L	C	C	S	121/132
Coronary revascularization	L	L	L	L	C	C	S	121
TIA	C	L	L	L	S	S	S	121/132
Atrial fibrillation						C	S	121
Heart valve disease						C	S	121
Aortic aneurysm/dissection						C	S	121
<b>CANCER:</b>								
Breast cancer	C	C	C	C	C	C <sup>3</sup>	C <sup>3</sup>	122/130
Endometrial cancer	C	C	C	C	C	C <sup>3</sup>	C <sup>3</sup>	122/130
Colorectal cancer	C	C	C	C	C	C <sup>3</sup>	C <sup>3</sup>	122/130
Ovarian cancer	C	C	C	C	C	C <sup>3</sup>	C <sup>3</sup>	122/130
All other cancers	C	C	C	C	C	C <sup>3</sup>	C <sup>3</sup>	122/130
<b>FRACTURES:</b>								
Hip	C	C	C	C	C	C	S	123
Non-hip fractures	L	L	L	L <sup>4</sup>	S	S	S	123
<b>OTHER:</b>								
Pulmonary embolism	C	S	S	S	C (HT)	C	S	126
Deep vein thrombosis	C	S	S	S	C (HT)	C	S	126
Hysterectomy	C	S	S	S	C (HT)	S	S	131
Death from any cause	C	C	C	L	C	C	S	124

C - Centrally adjudicated

L - Locally adjudicated

S - Self-reported

<sup>1</sup> Used central adjudication data when available, and local adjudication data otherwise

<sup>2</sup> Adjudication by UNC is only done for the HT and Black/Hispanic participants. Data for events in Extension 2 is not yet available.

<sup>3</sup> All cancers centrally adjudicated on all Extension Study 2 participants

<sup>4</sup> Done only at the BMD centers

# Some Changes in outcome data (WHI vs WHIX1 vs WHIX2) (cont)

Table 2: WHI self-reported outcomes for CT/OS participants by study period

Outcome	WHI 1993-2005	Extension 1 2005-2010	Extension 2 2010-2015
<b>Condition</b>			
Cataracts*	X	-	-
Colorectal polyps/adenomas	X	X	X
COPD	-	-	X
Dementia, Alzheimer's	-	X	X
Diabetes diagnosis, ever	-	X	-
Fainted/blacked out	X	-	-
Falls	X	-	X
Fractures (non-hip)	X	X	X
Gallbladder disease/stones	X	-	-
Glaucoma	X	-	-
Kidney/bladder stones*	X	-	-
Macular degeneration	-	X	X
Osteoarthritis*	X	X	X
Osteoporosis	X	-	-
Parkinson's disease	-	X	X
Rheumatoid arthritis	X	-	-
SLE	X	X	X
<b>Exams/Procedures</b>			
Barium enema X-ray*	X	X	-
Blood in stool	X	X	X
Blood pressure*	X	-	-
Bone density scan	-	X	X
Breast biopsy/aspiration	X	X	X
Breast exam	X	X	X
Breast exam, other (MRI/ultrasound)	-	X	X
Cholesterol	X	-	-
D&C	X	X	-
ECG	X	-	-
Endometrial biopsy	X	X	X
Eye exam*	X	-	-
Flex sig/colonoscopy	X	X	X
Hysterectomy	X (non HT)	X (non HT)	X
Mammogram	X	X	X
PAP smear	X	-	-
Physical exam*	X	-	-
Rectal exam	X	X	-
<b>Medication/treatments</b>			
Anxiety pills	-	X	-
Depression pills/therapy	-	X	-
Diabetes, diet/exercise	-	X	X
Diabetes, insulin	X	X	X
Diabetes, pills*	X	X	X
Estrogen pills	-	X	-
High blood pressure pills*	X	X	X
High cholesterol pills	-	X	-
Shots for DVT*	X	-	-
Osteoporosis calcium pills	-	X	-
Osteoporosis non-calcium pills	-	X	-

\*Not on all versions of Form 33

# Data on the WHI website

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- Visit forms, clinical measures, and other study data (baseline and follow-up visits)
- Clinical outcomes and detail data files (Currently through Sep 2015—includes extension study data)



# September 2015 Outcomes Data on the [WHI website](#)

- Clinical outcomes and detail data files:
  - Adjudicated outcomes (CT+OS, CaD)
  - Self-reported outcomes (CT+OS, CaD, MRC, SRC)
  - F121 cardiovascular detail (CT+OS, CaD)
  - F121/132 stroke/CAD detail (CT+OS, CaD)
  - F122/130 cancer detail (CT+OS, CaD)
  - F122/130 breast cancer detail (CT+OS, CaD)
  - F123 fracture detail (CT+OS, CaD)
  - F124 death & all discovered death detail (CT+OS)
  - F126 DVT/PE detail (HT)
  - F131 Hysterectomy (HT)
  - UNC heart failure detail (MRC Supercohort)
  - Aging (Survival) (CT+OS)
  - (Corresponding ``.dat'`, ``.sas'`, and ``.pdf'` files)

# CaD Trial Outcomes

- 91% of CaD participants were randomized at year 1 of the CT
  - 8% at year 2 of the CT
  - 1 % at other visits
- ➔ Timing of events in CaD participants uses CaD randomization date as the starting point

# Format of data for each outcome

(adjudicated outcomes file, outc\_ct\_os\_inv.dat)

- Three variables:
  - Indicator that outcome occurred (yes/no)
  - Days from randomization/enrollment to date of outcome
  - Source of adjudication (local, central, cause of death, ECG)

IMPORTANT:

Outcomes are first occurrence only

Outcome from 'best' adjudication only

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**STROKE****Stroke****Col#59**

<b>Value</b>	<b>Description</b>	<b>N</b>	<b>%</b>
0	No	155,247	95.9
1	Yes	6,561	4.1

**Usage Notes:**

Defined as the first occurrence of Stroke or a Death due to Cerebrovascular. Stroke was adjudicated for CT and OS participants through Ext1. In Ext2 it is only adjudicated for the Medical Record Cohort. In order to be able to classify strokes, WHI uses central adjudications if possible, even though Strokes were only fully centrally adjudicated in HT participants. See the DEATH and DEATHSRC variables for details about the death adjudication process. Includes inpatient strokes for the core WHI study and inpatient and outpatient strokes after the core study closeout.

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**STROKEDY****Days enrollment to Stroke****Col#60**

Days enrollment to Stroke

<b>N</b>	<b>Missing</b>	<b>Min</b>	<b>Max</b>	<b>Mean</b>	<b>Std Dev</b>
6,561	155,247	0	7439	2,925.842	1,639.303

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**STROKESRC****Stroke ascertainment source****Col#61**

<b>Value</b>	<b>Description</b>	<b>N</b>	<b>%</b>
0	Local adjudication - form 121	331	0.2
1	Central adjudication - form 121	82	0.1
2	Central adjudication - form 132	5,535	3.4
9	Cause of death - form 124	613	0.4
	Missing	155,247	95.9

**Usage Notes:**

In order to be able to classify strokes, WHI uses central adjudications if possible, even though during the core WHI study Strokes were only fully centrally adjudicated in HT participants. See the DEATH and DEATHSRC variables for details about the death adjudication process.

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# Format of detail data files

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- One row per participant, per outcome (participants may have multiple rows)
- Variable indicating ascertainment source (central or local)
- Flags for each outcome included in the file (yes/no)
- Form level detail items



# Uses of Outcome Variables

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- Get counts of outcomes (event flags include COD only events)
- Compare timing of events using 'days' variables
- In 'time-to-event' analyses (survival)

# Example 1: select form 121 detail info for all clinical MI events and create time-to-event variable

- Read in pertinent datasets
  - Form 121 data (outc\_cardio\_inv.dat) – select rows where MI = 1. Variables to keep: ID, MI, MIDX, MIPROCTYP, etc.
  - Adjudicated outcomes file (outc\_ct\_os\_inv.dat). Variables to keep: ID, MI, MIDY, MISRC and ENDWHIDY, ENDEXT1DY or ENDFOLLOWDY.
- Merge the subsetted Form 121 file with the subsetted adjudicated outcomes file by participant id.
- Create time-to-event variable:
  - => had event (MI = 1):  $\underline{misurvtm} = MIDY$
  - => no event (MI = 0), censored (follow-up ends because of death or last contact):  
 $\underline{misurvtm} = ENDFOLLOWDY$



# Example 2: using the breast cancer dataset



## CT+OS Adjudicated Outcomes

**File Name**  
outc\_ct\_os\_inv.dat

**Data as of** Sep 30, 2015    **Population** CT+OS    **Data Collected** Main, Ext1, Ext2    **1 row per** Participant    **Rows** 161,808    **File Created** Dec 1, 2015

**BREASTINV**    Breast Cancer Invasive    **Col#104**

Value	Description	N	%
0	No	151,754	93.8
1	Yes	10,054	6.2

**Usage Notes:**

Defined as a breast cancer from a Death or the first adjudication where the form 122 or 130 details indicate an invasive cancer. Breast Cancer Invasive is adjudicated for CT and OS participants. See the DEATH and DEATHSRC variables for details about the death adjudication process. WHI adjudicated all reports of breast cancer for a ppt until the first invasive Breast Cancer. i.e. The first Invasive Breast Cancer may not be the first Breast Cancer.

**BREASTINVDY**    Days enrollment to Breast Cancer Invasive    **Col#105**

Days enrollment to Breast Cancer Invasive

N	Missing	Min	Max	Mean	Std Dev
10,054	151,754	1	7526	2,889.976	1,852.498

**BREASTINVSRC**    Breast Cancer Invasive ascertainment source    **Col#106**

Value	Description	N	%
1	Central adjudication - form 130	9,651	6.0
9	Cause of death - form 124	400	0.2
10	Initial report of death - form 120	3	0.0
	Missing	151,754	93.8

**Usage Notes:**

Central adjudications were done for Breast Cancer Invasive. If the central adjudication is not complete, local adjudication data is used. See the DEATH and DEATHSRC variables for details about the death adjudication process.

# Example 2: using the breast cancer dataset



## Breast Cancer Outcome Detail (Form 122/130)

**File Name**  
outc\_bc\_inv.dat

**Data as of** Sep 30, 2015    **Population** CT+OS    **Data Collected** Main, Ext1, Ext2    **1 row per** Outcome Form    **Rows** 11,892    **File Created** Dec 1, 2015

This file has one row for every form 122 or 130 recording in situ or invasive breast cancer outcome(s). A participant may have more than one of these forms. Only the first occurrence of each outcome is counted, e.g. Limiting the file to rows where BREASTINV=1 will find a single row for each participant with a invasive breast cancer outcome. Breast Cancers derived solely from a cause of death do not have an associated form 122 or 130 so are not included.

**ID** WHI Participant Common ID **Col#1**

**ASCSOURCE** Ascertainment Source **Col#2**

Value	Description	N	%
1	Local Form 122	1	0.0
2	Central Form 130	11,891	100.0

**BREASTINV** Breast Cancer Invasive **Col#3**

Value	Description	N	%
1	Yes	9,651	81.2
	Missing	2,241	18.8

**Usage Notes:**  
Defined as a breast cancer from a Death or the first adjudication where the form 122 or 130 details indicate an invasive cancer. Breast Cancer Invasive is adjudicated for CT and OS participants. WHI adjudicated all reports of breast cancer for a ppt until the first invasive Breast Cancer, i.e. The first Invasive Breast Cancer may not be the first Breast Cancer. This file does not include cancers determined solely by the cause of death.

**BREASTINSITU** Breast Cancer In Situ **Col#4**

Value	Description	N	%
1	Yes	2,241	18.8
	Missing	9,651	81.2

**Usage Notes:**  
Defined as the first breast cancer where the form 122 or 130 details indicate an in situ cancer. Breast Cancer In Situ is adjudicated for CT and OS participants. Breast Cancer In Situ occurring on or after a Breast Cancer Invasive is not counted.

**ICDCODE** ICD-O-2 site code **Col#5**

N	Missing
11,891	1

**Usage Notes:**  
All centrally adjudicated cancers (F130) have an ICD-O-2 code. The only locally adjudicated cancers with a code are those marked as "other" on F122. F122 codes do not include a decimal. See the SEER coding section of the data prep/use document for details. A description of the ICD site codes can be found in the reference file seer\_icd\_site\_codes.dat by merging on the ICDCODE variable.

**BEHAVIOR** Tumor Behavior **Col#6**

Value	Description	N	%
1	Invasive	9,651	81.2
2	In Situ	2,241	18.8
3	Borderline	0	0.0
9	Unknown	0	0.0

**Usage Notes:**  
For cancers that have been SEER coded, tumor behavior comes from the 5th digit of the morphology (see MRPHHISTB). For cancers that have not been SEER coded, F130/Question 3 or

## Example 2: using the breast cancer dataset

- The 'N's for invasive breast cancer in the adjudicated outcomes file and the breast cancer detail file do not match. The detail file only contains events that were adjudicated, it does not contain events only found through cause of death.
- Set up an analysis file for invasive breast cancer just as described for MI in Example 1.
- Descriptions for the ICD-O-2 codes and histology codes are contained in separate files and will also need to be merged with your dataset (merging on ICD-O-2 code and histology code, respectively).

# Final thoughts

- Each time we release an updated set of outcome files, we remove the prior set from the website, so **download all files at one time, including the corresponding data prep document**
- Documentation is on the [WHI website](#) for outcome definitions and entire adjudication process
- Always study the forms associated with the data you are using to be sure you are “grabbing” the correct variables
- Other useful sources of information: [Data Preparation and Use document](#), Outcomes chapter in the baseline monograph, several links on the Dataset Documentation web page