

Ancillary Study #165: Subclinical Hypothyroidism and Risk of MI and Stroke

Summary of Cohort and MI Case Selection

March 20, 2013

This memo addresses details of the MI case and joint cohort selection. Stroke selection will occur following completion of central adjudication.

Study Population:

All WHI Observational Study participants were considered for the MI and stroke cohorts. Because the MI and stroke cohorts have slightly different exclusion criteria, a common cohort with the characteristics belonging to at least one cohort was selected here. All locally adjudicated cases of incident fatal and nonfatal clinical myocardial infarction reported as of December 15, 2004 within this population were selected as potential MI cases. A total of 1684 cases out of a cohort of 93,676 were initially eligible.

Potential cases and controls were excluded based on the following hierarchical criteria:

	<i>Eligible Cases</i>	<i>Eligible Cohort</i>
No exclusions	1684	93,676
1) Lack of available serum (0.6 mL)	1418	90,983
2) History of thyroid disease at baseline	1016	68,428
3) Use at baseline of medication that could influence TSH or T ₄ levels, including thyroid medication, amiodarone, daily oral corticosteroids, dopamine, lithium, immunomodulators and immunosuppressive agents (including interferons), hydantoins (including phenytoin), carbamazepine	960	66,354
4) History of MI (<i>MI cases</i>) or both MI and stroke (<i>cohort</i>) at baseline	841	66,235
5) History of CABG (<i>MI cases</i>) or both CABG and carotid endarterectomy (<i>cohort</i>) at baseline	808	66,209
6) <i>Cohort only</i> : History of both 1) MI and carotid endarterectomy or 2) stroke and CABG at baseline	NA	66,175
7) Unknown race/ethnicity on both Form 2 and Form 41 ¹	803	65,897
8) No outcomes forms after baseline	803	65,517

Out of the original 1684 cases and 93,676 participants, 803 cases and 65,517 participants met the eligibility criteria and were available for case or cohort selection.

MI Case and Cohort Selection:

A set of 800 out of the 803 eligible MI cases were chosen by simple random sampling. The 3200 members of the cohort were chosen by simple random sampling stratified on 10 year age category. The stratification frequencies were determined by weighting the 10-year age distributions of the 803 eligible MI cases and 402 eligible centrally confirmed ischemic stroke cases known as of December 15, 2004 by the percentage of MI and projected stroke cases in the final dataset. Specifically, in the women with

¹ Defined hierarchically as any 1) Hispanic, 2) African-American, 3) Native American, 4) Asian or Pacific Islander, or 5) white racial identification

qualifying MI's, 13.0%, 41.8%, and 45.2% were of ages 50-59, 60-69, and 70-79, respectively. In the women with qualifying stroke's, 10.4%, 44.0%, and 45.5% were of ages 50-59, 60-69, and 70-79, respectively. Since there will be 800 MI and up to 750 stroke cases for a total of up to 1550 cases in the final dataset, the percentage of 50-59 year old women in the cohort was calculated as a weighted sum of the possible MI distribution, $(800/1550)*13\%$, and the stroke distribution, $(750/1550)*10.4\%$, for an overall percentage of 11.7%. In the same way, the overall percentages of 60-69 year olds and 70-79 year olds in the final cohort were calculated to be 42.9% and 45.5%, respectively. Since there will be 3200 women chosen for the cohort, $11.7\%*3200$ or 376 women will be chosen from the 50-59 year age strata, $42.9\%*3200$ or 1373 women will be chosen from the 60-69 year age strata, and $45.5\%*3200$ or 145 women will be chosen from the 70-79 year age strata.

Matching summary:

A total of 800 MI cases and 3200 cohort members were chosen in this selection step for a total of 3936 unique participants. The MI case and cohort groups had similar distributions with respect to age category, summarized below. The average follow-up time among the MI cases and cohort from enrollment to the last follow-up date was 84.4 (SD = 20.4) and 86.0 (SD = 18.6) months, respectively.

<i>Variable</i>	<i>Level</i>	<i>MI Cases %</i>	<i>Cohort %</i>
Age category	50-54	4.25	5.03
	55-59	8.75	6.72
	60-64	18.00	20.94
	65-69	23.88	21.97
	70-74	27.63	31.63
	75-79	17.50	13.72