

Selection of Cases and the Subcohort

Cases

1) An incident cancer case will be defined as a primary tumor of the colon, rectum, breast, or endometrium diagnosed for the first time, 24 months or more after the baseline study visit.

Notice the change to 24 months (from the 18 months originally proposed). This change is intended to make cases and controls more comparable, as selection based on 18 months of follow-up is not possible for controls, given annual follow-up.

This change will have to be revisited if the observed incidence of colorectal or endometrial tumors suggests that too few cases would be available as of June 2004. That is, we will want the last batch of specimens one year before the end of the study, to leave time for testing and analyzing data/writing papers. That means the last shipment of specimens would be at the end of 2004 (with the grant ending end of 2005), and the cases would have had to have been diagnosed approximately 6 months earlier or before to be in the central database. Thus, the question is will there be enough cases as of June, 2004?

Given that enrollment was conducted between 1993 and 1998, there will be roughly 8.5 years of follow-up on average by June 2004, or 6.5 years if we exclude the first 24 months.

Endometrial = $0.11\%/yr = 0.0011 \times 92,000 \text{ women} \times 6.5 \text{ years} \times 60\% \text{ with uterus} = 395 \text{ cases}$

Colorectal = $0.12\%/yr$ more than the 500 cases

2) Those with a primary tumor diagnosis prior to enrollment in WHI, or during the first 24 months of follow-up, will be excluded from participating as a case for that cancer, but only that cancer.

3) A second primary tumor diagnosed during observation that is unrelated to the first, involving a different site, will be treated as a new case. Thus, in theory, a person can contribute data as more than one case.

4) The schedule for selection of subjects is shown in the table. In the first year, we will randomly select 167 colorectal, 300 breast, and 100 endometrial cancer cases from all available cases, meeting the above criteria. In years #2 and #3, we will repeat this process exactly, except that subjects previously selected as a case for a particular cancer will be excluded from selection again as a case for that same cancer, but only that cancer. That is, a subject can be selected a second time as a case, for a second cancer, but their specimen only needs to be drawn once.

Year of testing	Number of Specimens to be Tested			
	Subcohort	Colorectal Ca.	Breast Ca.	Endometrial Ca.
Year 1 (3-15 mo)	500	167	300	100
Year 2 (16-26 mo)	200	167	300	100
Year 3 (27-36 mo)	200	167	300	100

Subcohort ("Controls")

1) The subcohort will be a stratified random sample of all subjects enrolled in WHI for at least 24 months. (Since data are only collected annually, it is not practical to consider using 18 months).

2) Women who develop cancer within 24 months of enrollment will be excluded from the subcohort, since including them in the comparison group but not in the case group could result in bias towards the null.

3) Colorectal, breast, and endometrial cancer incidence increases with age. Therefore, the cancer cases in this study are expected to be disproportionately older than the cohort as a whole. To make the subcohort more comparable to the cases in terms of age, we will use stratified random sampling to select comparison group subjects. Specifically, based on age strata at baseline:

Age at Baseline	Fraction of Subcohort
50-59	20%
60-69	40%
70-79	40%

A more exact approach to determining the appropriate distribution of comparison group subjects is not practical, since the age distributions of colorectal, breast, and endometrial cancer are not precisely the same.

4) The schedule for selection of the subcohort is shown in the table. In the first year, we will randomly select 500 subjects from all available individuals, meeting the above criteria. In years #2 and #3, we will repeat this process exactly, except that we will select just 200 subjects in each year, and that those previously selected for testing will be excluded from selection a second time.