Publications and Presentations Committee
Manuscript Review Process

• Submit manuscript proposals by the fifteenth of the month to Alyssa Smith at the WHI Clinical Coordinating Center. Electronic copies in Word are encouraged. Please email to: absmith@whi.org. If you do not have access to email, please mail a hard copy of your proposal plus a floppy copy to:

   Alyssa Smith, P&P Program Assistant
   WHI Clinical Coordinating Center
   Fred Hutchinson Cancer Research Center
   1100 Fairview Ave N MP-1002
   Seattle, WA  98109-1024

   • The manuscript proposal must be no more than six pages and conform to the manuscript template (see attached) or it will be returned for immediate revision.

• There can only be 3 co-authors, including the convener, listed on the proposal. All other authors are added during the writing group nomination process.

• The manuscript proposal is sent to two committee members who review the proposal and prepare a brief presentation for the next conference call (second and fourth Thursday of every month). Other committee members receive the proposals with the agenda and prepare discussion points for the conference call. Approval status is voted on at the meeting.

• Once approved, writing groups are formed. (The convener and proposed authors may or may not be a part of the writing committee depending on the number of papers already participating on). An email is sent to all investigators describing the paper and soliciting nominations. Nominations are open for two weeks. Investigators may nominate themselves or another investigator and/or WHI staff. Nominations of junior investigators are encouraged. Nominations are accepted by email absmith@whi.org or fax 206-667-4142.

• Once nominations are closed, Alyssa gathers the nominations and forwards the list to the chair of the P&P Committee. The chair forms the writing using the following criteria: 1) expertise; 2) participation in other writing groups.

• Writing group chairs and members are notified and mailed the Analysis Plan Guide to assist in developing a detailed analysis plan.

• A Clinical Coordinating Center statistician is assigned to the paper once an analysis plan is approved. Contact the Statistics Unit Manager at the CCC concerning any questions about analysis plans.

• Prior to submission to the journal, final manuscripts are reviewed by P&P and the NIH Project Office.
INTRODUCTION

Over the past decade, increasing interest has been focused on the role of antioxidant nutrients in disease prevention. The carotenoid pigments, which number over 500, are well known for their antioxidant properties. Only β-carotene has been studied extensively; the other major carotenoids found in the human body have garnered much less attention. Of this group, lycopene is particularly important because it comprises roughly half the total carotenoid concentration of human serum. Dietary lycopene is primarily derived from tomatoes and tomato products.

Early research found that intraperitoneally injected lycopene improved survival rates of irradiated mice (1). Interest in this nutrient was renewed following the 1989 publication by Di Mascio et al. which reported that lycopene has the greatest ability of all the common carotenoids to quench singlet oxygen, a mechanism by which protection from the damaging effects of reactive oxygen species is thought to occur (2). Recent biologic evidence suggests that lycopene is a more effective inhibitor of human endometrial, mammary, and lung cancer cell proliferation in cell culture than α- or β-carotene (3). Although there is conflicting evidence, in some observational epidemiologic studies this nutrient has been found to be associated with a decreased risk of prostate cancer (4, 5), cervical intraepithelial neoplasia (6), stomach cancer (7), pancreatic cancer (8), and myocardial infarction (9).

Although research conducted over the past 8 years suggests that lycopene may play an important role in disease prevention, there is little information about predictors of serum lycopene. It is the only major carotenoid found to decrease with age and does not appear to be higher in women than men, as are other carotenoids (10), thus, lycopene status may be particularly important in older women. There are conflicting results regarding the relationship of serum lycopene levels to both cigarette smoking (10-12) and alcohol consumption (10, 13). As lycopene intake among African-American male health professionals was found to be substantially less than among their Caucasian counterparts (4), ethnicity may be an important determinant of serum lycopene. By investigating the factors associated with serum lycopene in a subset of older women, a better understanding of the relationship between this potentially important nutrient and certain disease processes may be gained.

OBJECTIVES
1. To evaluate the relationship of serum lycopene with dietary lycopene intake, foods high in lycopene and other dietary factors as estimated by the baseline FFQ.

2. To assess the relationship of serum lycopene with lifestyle, demographic, and biochemical factors of WHI participants at baseline.

The ethnic diversity of the WHI also offers a unique opportunity to study the determinants of serum lycopene among the various ethnic groups.

**ANALYSIS PLAN**

**Statistical Analysis**

We propose to analyze baseline data from CT participants in the 6% serum subsample whose blood samples have been analyzed. Over 1500 such blood samples have been analyzed to date and include a large percentage of minority participants.

We will describe the intake and serum concentration of lycopene and the demographic characteristics of the study population (Table 1).

The relationship between serum lycopene and other factors will be assessed by Pearson correlation coefficients and multiple linear regression. Pearson correlation coefficients will be presented, adjusted for age and other covariates, if appropriate (Table 2). The results of multiple regression analysis of dietary, biochemical, demographic, and lifestyle factors on serum lycopene will be presented in Table 3. Log transformation of lycopene and other variables will be used if distributions are found to be skewed. For factors that are found to be associated with serum lycopene, e.g. lycopene intake, we will test for modification of the effect by age, ethnicity, and smoking status (current, former, or never). If any of the findings differ by these variables, the results will be stratified by these variables.

*Pertinent variables*

1. Serum lycopene
2. Lycopene intake
3. Total caloric intake
4. β-carotene intake
5. α-carotene intake
6. Total carotenoid intake
7. Fruit and vegetable intake
8. Fiber intake
9. Intake of specific foods high in lycopene
10. Vitamin supplement intake/use- multivitamins, vitamin C, vitamin E
11. Serum β-carotene
12. HDL
13. LDL
14. Triglycerides
15. HRT use
16. Age
17. Alcohol consumption
18. Cigarette smoking
19. BMI

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CONCLUSIONS

We expect that serum lycopene will be positively associated with dietary sources of lycopene and negatively associated with sources of oxidative stress, in particular cigarette smoking.

TABLES

Table 1. Demographic and physiologic characteristics

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<thead>
<tr>
<th>Variable</th>
<th>Mean or percentage</th>
<th>SD</th>
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<tbody>
<tr>
<td>Serum lycopene</td>
<td></td>
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<tr>
<td>Lycopene intake</td>
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<td>Total caloric intake</td>
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<td>Select demographic variables</td>
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Table 2. Pearson correlations (r) of serum lycopene with dietary estimates, blood measures, and personal characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum Lycopene</th>
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<tr>
<td></td>
<td>Crude</td>
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<td>Adjusted</td>
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Table 3. Multivariate regression analysis of serum lycopene on physiologic and personal characteristics

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<tr>
<th>Independent Variable ( Intercept)</th>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>Significance</th>
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\[ R^2 = \]
REFERENCES