WHI MANUSCRIPT PROPOSAL GUIDELINES

To be considered for Publications and Presentation (P&P) Committee calls, which usually occur on the second and fourth Thursday of each month, manuscript proposals must be submitted by the fourth or second Friday of the month to the P&P Program Coordinator at the WHI Clinical Coordinating Center. Please email proposals to the P&P Coordinator (p&p@whi.org).

- The manuscript proposal must be no more than six pages, not including references or tables, or it will be returned for immediate revision.
- It must conform to the manuscript template, or it will be returned for immediate revision.
- Non-WHI investigators must be sponsored by a WHI Principal Investigator (PI).
- The proposal cannot have more than five co-authors, including the convener and the sponsoring PI, or it will be returned for immediate revision. Exceptions to this rule are noted in the P&P Committee Policies. Other authors are added during the writing group nomination process.
- Authors are encouraged to include “Women’s Health Initiative” and the name of the ancillary study (if applicable) in the manuscript title.
- Authors are encouraged to check for existing literature in their area of interest. Failure to identify overlap could lead to cancellation of the paper, even if overlap is identified after proposal approval.
- Consortium papers—WHI requests that it be represented in proportion to the number of cases it contributes to the overall cohort.
- If the writing group will be performing their own analysis, they will be expected to download the necessary data from www.whi.org. Prior to this, a WHI Data Distribution Agreement must be signed.
- Prior to submission to the journal, all final manuscripts are reviewed by the P&P.

Please see Process Schematic for a more thorough explanation of the manuscript process.
Manuscript Proposal Template

Title:

Proposal authors (List names of up to 5, which includes the convener/lead author and Sponsoring PI – strongly recommend inclusion of junior and/or biostatistical investigators): (please include name, email, clinical center, address, fax, and phone of the lead author)

Is the lead author new to WHI? □ Yes □ No

Is the lead author currently leading a paper that falls outside of WHI P&P submission timeline requirements?*

• Authors have yet to submit a draft manuscript for Committee review and >3 years has passed since the original proposal was approved?
  □ Yes □ No

• Manuscript was approved by P&P Committee in the last year but the manuscript has yet to be submitted to a journal for publication?
  □ Yes □ No

*If “yes” is selected, please work with the P&P Coordinator (p&p@whi.org) and the Committee Chairs to resolve the outstanding issues. Please reference the P&P Committee Policy for further information.

**Required**

Name of Sponsoring PI/Senior Investigator*:

*(only WHI PIs are eligible to sponsor paper proposals. A list of PIs is available here: https://www.whi.org/researchers/SitePages/WHI%20Investigators.aspx). WHI co-investigators and Associate Members may submit their own proposals without a PI sponsor, but they are not eligible to sponsor papers for others.

We confirm sponsoring PI/senior investigator has reviewed/approved this proposal: □ Yes

What is your primary outcome?:

What data source are you using to identify this outcome (check all that apply):

□ Adjudicated outcomes
☐ Self-report  
☐ Medicare data  
☐ Other (please describe and justify this selection):

Is data from a WHI Ancillary Study (AS), Core Study, and/or BAA Study included in this proposal: ☐ Yes ☐ No

If yes, list the study number(s):

If yes, was the source of funding for this study a commercial entity? ☐ Yes ☐ No

If using AS data, has all AS lab data been submitted to CCC?:

Does this proposal utilize National Death Index data?:

Does this proposal utilize CMS data?:

Does this proposal utilize data from a supplemental questionnaire (Form 156, Form 157, Form 158)?:

Keywords (include at least 5):

Will this proposal use data from studies other than WHI? ☐ Yes ☐ No

If yes, is the data from publically-available datasets, or are you working with investigators from other studies? If the latter, please see information regarding consortium studies and fill out a consortium application.

Have you checked for overlap with published and in-process WHI manuscripts?  
Failure to identify overlap could lead to cancellation of the paper, even if overlap is identified after proposal approval.

☐ Yes ☐ No

Have you considered whether you have adequate sample size and/or power to conduct these analyses and each aim? ☐ Yes ☐ No – Please show power calculations in the proposal.

If this proposal stems from a discussion within a WHI Scientific Interest Group (SIG), please mark which SIG.  
Investigators are strongly encouraged to consult a SIG (if applicable) prior to submission to P&P. Proposals that benefit from SIG input tend to be stronger, which can result in a quicker approval from P&P. Visit the WHI website for a list of SIG Chairs and their contact information.

☐ Aging: Cognition & Functional Status  
☐ Bone/Fracture & Body Composition  
☐ Cancer
Correlates of serum lycopene in older women
(Example of a MS proposal with all the required elements)

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  
20. Physical activity  
21. Ethnicity  
22. Years of education  
23. Income  
24. Region of the US  
25. Month of blood draw

**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**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean or percentage</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum lycopene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lycopene intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total caloric intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Select demographic variables</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 Crude</th>
<th>Adjusted</th>
</tr>
</thead>
</table>
2         |                      |          |
Table 3. Multivariate regression analysis of serum lycopene on physiologic and personal characteristics

<table>
<thead>
<tr>
<th>Independent Variable (Intercept)</th>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>Significance</th>
</tr>
</thead>
</table>

\[ R^2 = \]
REFERENCES