Responses to Comments for Kashyap LOI

Comment: Is it ethical not to change depression medication following randomization

Response: I agree that this would not be ethical. I've changed the outcome measure analysis of depression to include use of anti-depressant medication and dosing. It will be interesting to observe the impact of Vitamin D supplementation on use of medication for treatment of depression.

Comment: The committee has raised concerns about the use of any inventor that will detect suicidal thoughts/ideation and the responsibility of the investigative site.

Response: We agree that this is a sensitive and medical-legal issue for investigative sights. The Beck Depression Inventory does not monitor suicidal ideation but rather asks about symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. A copy of the results of the questionnaire could be shared with the primary provider for the subject to initiate care.

Comment:How many participating sites will be required?

Response: We anticipate 6-8 sites may be required to enroll the 400 individuals.

Comment: Please address parts 2 and 3 for methods.

Response: The vascular function study takes about 60 minutes and the questionnaire takes 10-15 minutes on average. These studies could be done on a subsequent day following the closest visit to 12 and 24 months. Since the brachial artery reactivity will be related to markers of inflammation collected from blood obtained at 12 and 24 months, the tests should be done at the annual visit.

Funding- We will target a R01 submission for 2/5/2015

Sample volume: We will need 50 uL per subject at each visit (baseline, 12 and 24 months) for the three markers (CRP, fibrinogen, adiponectin). Approximately 200ml total volume will be needed from 400 subjects at baseline, 200ml at 12 and 200ml at 24 months.