SOF Analysis Plan Submission Form

Date: 8/21/2012

Investigator’s Name: Daniel Evans

Clinical Center: San Francisco CC

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Other investigators who will be working on this analysis: Daniel Evans, Greg Tranah, Katie Stone, Steve Cummings, Susan Redline, and others who are interested.

Analysis Plan Title: Replication of findings from a genome-wide association study of sleep onset latency.

Data sets to be used: SOF genome-wide HapMap imputed SNP data, SOF Visit 8 data.

Primary variables to be used in the analysis: HapMap imputed GWAS data and self-reported sleep onset latency from the Pittsburgh Sleep Quality Index (PSQI) administered at SOF Visit 8 (variable name V8PSLPM).

Does this analysis plan involve a consortium or meta-analysis project? ☑ YES ☐ NO

If YES,
1. Does this plan propose to use GWAS data? ☑ YES ☐ NO
2. Who is the investigator leading the analysis? Najaf Amin
   a. If not a SOF investigator, please note the lead investigator’s affiliations. Erasmus MC
3. What other cohorts are involved in the consortium or meta-analysis? EGP, ERF, KORA, KORCULA, MICROS, NESDA, ORCADES, EGcut, Rotterdam study, FHS, CHS, and ARIC.
4. What are the definitions of the primary phenotypes of interest? Sleep latency in minutes based on self-report on the Pittsburgh Sleep Quality Index (PSQI).
5. Describe any authorship policies of the consortium. CHARGE authorship policy.

Do you plan to submit an abstract based on these results? ☐ YES ☑ NO
If YES, when is the abstract due?

Who will perform the analyses?
☑ Coordinating Center
☐ Other local analyst, please specify:

Is this the first analysis plan you are submitting to utilize SOF data? ☐ YES ☑ NO
If YES, please provide 2-3 sentences about your professional background and research interests.
Replication of findings from a genome-wide association study of sleep latency.

Investigators: Daniel Evans, Greg Tranah, Katie Stone, Steve Cummings, and others who are interested.

Background

The prevalence of insomnia increases with age (Ancoli-Israel 2009). Among over 9,000 participants aged 65 years and older in the National Institute on Aging’s multicentered study entitled “Established Populations for Epidemiologic Studies of the Elderly” (EPSES), 19.2% reported trouble falling asleep and 28.7% had symptoms of insomnia (Foley, Monjan et al. 1995). Insomnia is a risk factor for various aspects of poor mental health, such as depression and anxiety disorders (Taylor, Lichstein et al. 2003).

Sleep onset latency, i.e., minutes from “lights off” to sleep onset, is used as one of the criteria for insomnia (Lichstein, Durrence et al. 2003; Edinger, Bonnet et al. 2004; Lineberger, Carney et al. 2006). Sleep onset latency has been reported to be heritable (Tafti 2009). A large study of 1554 monozygotic and 2991 dizygotic twin pairs estimated the heritability of sleep onset latency to be 0.41 (95% confidence interval: 0.37 - 0.46) (Hublin, Partinen et al. 2011). An on-going meta-analysis of genome-wide association studies of sleep onset latency identified significant genetic associations, and we would like to contribute results from SOF in the replication phase.

Phenotypes

The primary phenotype will be self-reported sleep onset latency from the Pittsburgh Sleep Quality Index (PSQI) administered at SOF Visit 8 (variable name V8PSLPM). Self-reported sleep latency from the PSQI is being used rather than objective measures of sleep latency that are available in SOF in an effort to stay consistent with results reported from the other cohorts participating in the meta-analysis.

Statistical Analysis

Imputed single nucleotide polymorphism (SNP) allele dosage from the HapMap release 22 imputed dataset will be used. Prior to genotype imputation, poor quality genotyped SNPs were removed using standard QC filters, such as minor allele frequency (MAF) < 0.01, Hardy-Weinberg equilibrium test P-value < $10^{-4}$, SNP call rate ≤ 0.98, or > 1 discordant genotype call between duplicates. Imputed SNPs with MAF < 0.01 or imputation quality (measured by R2MACH) < 0.3 will be removed.

Participants of non-European ancestry will be excluded from analysis. Participants reporting taking sleeping pills will be excluded (variable name V8PSLMED). Linear regression models will be used. Sleep onset latency will be transformed by taking the natural log to create a normal distribution of the dependent variable. Covariates will be age, clinic site, and the first four PCs estimated in SOF participants of European ancestry.
The three SNPs to be replicated are: rs9900428, rs9907432, and rs7211029.

Mock Tables

Table 1. Meta-analysis SNP association with sleep duration.

<table>
<thead>
<tr>
<th>SNP</th>
<th>nearest gene</th>
<th>coded allele frequency</th>
<th>n</th>
<th>β</th>
<th>SE</th>
<th>P-value</th>
<th>Heterogeneity (I²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs123</td>
<td>YFG1</td>
<td>0.3</td>
<td>40,000</td>
<td>0.50</td>
<td>0.09</td>
<td>1.4x10⁻⁸</td>
<td>0.0</td>
</tr>
</tbody>
</table>

References