PRYSMS STUDY
Data and Safety Monitoring Plan

A. Confidentiality

1. Protection of Subject Privacy – During this study, a limited physical examination will be performed and questionnaires will be administered. Fasting blood tests, oral glucose tolerance test, salivary cortisol tests, and abdominal CT scans will be done periodically. Data will be kept in strict confidence. No information will be given to anyone without permission from the subject. This statement guarantees confidentiality. Confidentiality is assured by use of identification codes. All data, whether generated in the laboratory or at the bedside, will be identified with a randomly generated identification code unique to the subject. Health Information Portability and Accountability Act (HIPAA) guidelines of the two clinical sites will be followed. (See VI. Informed Consent and HIPAA)

2. Database Protection – The database is secured with password protection. The informatics manager receives only coded information, which is entered into the database under those identification codes. Electronic communication with outside collaborators involves only unidentifiable information.

3. Confidentiality during AE Reporting –AE reports and annual summaries will not include subject-identifiable material. Each will include the identification code only.

B. Adverse Event Information

1. Definition - An adverse event (AE) is any untoward medical occurrence in a subject temporally associated with participation in the clinical study. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.) or any combination of these.

2. Classification of AE Severity –AEs will be labeled according to severity which is based on their impact on the patient, per this Event Grading Scale:

Grade 1	**Mild**	Transient of mild discomfort; no limitation in activity; no medical intervention/therapy required.
Grade 2	**Moderate**	Mild to moderate limitation in activity – some assistance may be needed; no medical intervention/therapy required.
Grade 3	**Severe**	Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible.
Grade 4	**Life-Threatening**	Extreme limitation in activity, significant assistance required significant medical intervention/therapy required, hospitalization or hospice care probable.

3. AE Attribution Scale –AEs will be categorized according to the likelihood that they are related to the study intervention. Specifically, they will be labeled either definitely, probably, possibly or unrelated to the study intervention.

4. Expected Risks – Expected risks to the subject are mild injury due to Restorative yoga therapy or stretching therapy. These risks are considered to be minimal and are addressed in the protocol and consent form. Participants will have a contact number to report any potential adverse events that occur in between scheduled study visits. They will also have an opportunity to privately discuss any musculoskeletal or other physical complaints due to yoga or stretch therapy with the yoga/stretch instructor(s) on a weekly basis.

There is minimal risk associated with participating in the Restorative yoga intervention. Risks are rare but may include muscle soreness and muscle or ligament strain. The instructors providing instruction for these classes are certified yoga instructors with years of experience instructing people with chronic pain conditions. We will be using props such as blocks and straps to help participants perform the yoga postures to minimize muscle strain.

There is minimal risk associated with participation in the group stretching intervention. Rare risks include muscle soreness and muscle or ligament strain. The trained instructors will have physical therapy or training backgrounds and will provide instruction on gentle stretches that have been approved for use by our Physical Therapist consultant.

5. SAE Reporting - SAEs that are unanticipated, serious (grades 3 and 4), and/or possibly related to the study intervention will be reported to the Independent Monitor, IRB, CTSA at UCSF, and NIH in accordance with requirements. Anticipated SAEs or those unrelated to the study intervention will be reported to the same individuals/entities in accordance with requirements.

If abnormal lab values are discovered during the study, the PI will be notified and will address this issue as early as possible. Abnormal lab values will be reported as adverse events only when the site investigator deems them to be clinically significant. When an "alert" laboratory value occurs the UCSF Coordinating Center will contact the site study staff to request a brief report on how the abnormal value was managed. A table summarizing all 'alert' values will be reviewed by the Date Safety Monitor.

C. Data Quality and Safety Review Plan and Monitoring

1. Data Quality and Management
   a. Description of Plan for Data Quality and Management – The PI will review all data collection forms on an ongoing basis for data completeness and accuracy as well as protocol compliance. A statement reflecting the results of the review will be sent to the NIH in the annual report.

      Data quality will be assessed using measures such as time from study visit to data entry, time to resolution of data queries, number of missing forms, and proportion of all study variables queried. Guidelines for concern regarding these measures are outlined below:

Measure	Goal Value	Acceptable Value
time from visit to data entry	< 1 week	< 2 weeks
time to resolution of queries	<2 week	< 2 weeks
number of missing forms	0	< 5%
proportion of variables queried	5%	<10%

b. Frequency of Review –The frequency of data review depends according to the type of data and is summarized in the following table.

Data type	Frequency of review	Reviewer
Subject accrual (adherence to eligibility criteria, stratified randomization)	Annually (beginning of each wave)	Principal Investigator and Independent Monitor
Adverse event rates (injuries)	Quarterly	Principal Investigator and Independent Monitor
Compliance to treatment	Quarterly	Principal Investigator and Independent Monitor
Out of range laboratory data	Monthly (PI) Annually (Monitor)	Principal Investigator Independent Monitor
Stopping rules report regarding statistical power implications of drop outs and missing data	Annually	Principal Investigator, Independent Monitor

2. Subject Accrual and Compliance

a. Measurement and reporting of subject accrual, adherence to inclusion/exclusion criteria –Review of the rate of subject accrual, adherence to inclusion/exclusion criteria will occur monthly during the 4 month recruitment phase. Review will occur at the end of each recruitment wave of 40 participants per clinical site (25% of subject enrollment) to assure that participants meet eligibility criteria and ethnic diversity goals outlined in the grant proposal.

b. Measurement and reporting of participant compliance to treatment protocol – Data on compliance to the treatment protocol will be collected monthly by research staff and reviewed quarterly by the Steering Committee and the Data Safety monitor. Compliance on the part of participants will be evaluated for the 1) group class attendance and the 2) individual home practice logs. Compliance will be reviewed quarterly and if the safety officer or Steering Committee has concerns about whether compliance has reached a level that might inhibit the ability of the study to test its primary hypotheses, he/she will suggest a conference call for study investigators to discuss methods for improving compliance. There is no available data on expected compliance to the proposed yoga/stretch protocol that can be used to determine a 'trigger point' for this action.

3. Stopping Rules – This study will be stopped prior to its completion if: (1) study recruitment or retention is too low for the study to provide meaningful results; (2) any new information becomes available during the trial that necessitates stopping the trial; and (3) other situations occur that might warrant stopping the trial. Given that the trial intervention is relatively safe, we will not monitor efficacy and will not stop the trial prior to planned completion for unexpected *efficacy*. If the intervention is efficacious at 6 months, it will still be important to determine the extent to which its benefits are maintained at 1 year. Conversely, if there is no apparent efficacy after the second wave completes the 6 month visit, longer term patterns might still be of interest, and little would be gained by stopping the study early at that late point. The trial will be stopped early if the data and safety monitor finds that the *harm* to study participants outweighs the benefit of the scientific evidence to be accrued by continuing the trial. Finally, the trial will be stopped early if the data and safety monitor finds that new information from sources outside the trial provides definitive information that the intervention is effective or harmful. The PI will include an assessment of futility in the annual progress report to

NIH and will consult with a biostatistician if necessary to assess the impact of significant data loss due to problems in recruitment, retention or data collection. The detailed Data and Safety Monitoring Plan will include parameters for stopping the study early for the reasons listed above.

4. Designation of an Independent Monitor – Dr. Andrew Avins (Senior Investigator Kaiser Division of Research and Adjunct Professor of Medicine at UCSF) will be the Independent Monitor who will perform an independent review of ongoing safety.

D. Safety Review Plan

Study progress and safety will be reviewed monthly by the PI. Progress reports, including patient recruitment, retention/attrition, and adverse events will be provided to the Independent Monitor annually for independent review. An annual report will be compiled and will include a list and summarization of adverse events. In addition, the annual report will address (1) whether adverse event rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study; and (5) conditions whereby the study might be terminated prematurely. The annual report will be signed by the Independent Monitor and will be forwarded to the appropriate IRB and NIH, the UCSF CTSA on an annual basis.