MrOS Sleep Study
Medical Alerts and Participant Feedback

1. Medical Alerts and Adverse Events

1.1 Background and Rationale

Certain findings made at the time of the clinic visit or in-home PSG visit may require medical intervention. Although the PSG, ECG, blood pressure measures, and bone density tests performed as part of the MrOS Sleep Study are not considered diagnostic studies, the MrOS investigators have an obligation to intervene when medically necessary. The system that has been established is based on the urgency of the finding – either IMMEDIATE (requiring action prior to the technician leaving the participant's home, or prior to participant leaving clinic), or URGENT (requiring review by study physician by the next business day, with follow-up taken no more than 10 days after observation, or sooner if deemed medically necessary).

1.2 Documentation of alerts and adverse events

During the clinic visit, the examiner will indicate on the blood pressure and ECG forms whether any alert conditions were observed. In the event of any alert condition, an "Alerts and Adverse Events Action" form is completed, in order to document what, if any, action was taken. An ECG worksheet will be completed in the clinic before the ECG is done. The worksheet will include information about participants history of a-fib/flutter and current treatment of such conditions. This information will be relayed to the Reading Center.

Similarly, during the in-home PSG visit, the technician will indicate on the "Signal Verification" form whether any alert levels were observed upon hook-up. In case any adverse events are observed during the signal verification process, an "Alerts and Adverse Events" form (AE) will be completed.

Alerts identified by the central PSG Reading Center will be documented on the Sleep Study Status (SS) form, and actions taken at the Field Site upon receipt of the PSG Reading Center report.

Participants will also be screened for excessive bone loss based on comparison of their bone density values at the MrOS Sleep Study with values obtained during the MrOS baseline visit. An EBL form (Excessive Bone Loss) will be completed for participants meeting minimum rate of bone loss criteria for excessive bone loss, and action will be taken by the Field Site. These procedures and alert criteria are described in more complete detail in the DXA Quality Assurance Manual.

1.3 PSG determined values

The MrOS Sleep Study approach minimizes the use of specific threshold levels of apneic activity (e.g., RDI>15%) to judge "severity" or to trigger a recommendation for physician follow-up. Emphasize that, other than at the high extreme, a given RDI should not be used to grade abnormality. Rather, participants should be told that, if symptomatic, they should consider further medical evaluation (regardless of level of apnea).

There are levels of apneic activity/hypoxemia so high that the likelihood of health risks/functional impairment may be substantial. MrOS elected an RDI level of >= 50 and level of hypoxemic stress, defined as the time in desaturation (<75% sat.) for > 10% sleep time, as levels that merited investigator review (within 10 days of the sleep study), with tailoring of specific feedback to participants and (if requested by participant) to physicians caring for these participants.

1.4 Immediate Referrals

Immediate referrals are potential emergencies which may require immediate notification of the participant and (if so requested by the participant) his primary physican or other available health care provider. These are findings made at the time of the clinic visit, or during PSG setup in the participant's home. Because the technicians performing the physical measurements and PSG setup are neither trained nor licensed to perform clinical diagnostic assessments, all findings requiring immediate referral will be referred by the technician to a physician-investigator of the MrOS Sleep Study. The physician, based on information obtained from the technician and/or the participant, will determine whether immediate referral is indicated. Participants receiving immediate referrals are those who would be advised to go directly from home to their physician or to a hospital. With participant's consent (obtained verbally at the time of the alert), study physician would contact the participant's referring physician directly.

Notification of the participant should be performed by the MrOS Sleep Study physician-investigator and should occur prior to the participant leaving the clinic, or prior to the technician's departure from the home, depending on where the finding is observed.

<u>Findings requiring immediate referral at the time of the clinic visit are as follows:</u>

- Blood pressure (awake, seated) (on EITHER the second or third reading):

  Systolic blood pressure ≥ 210 mm Hg
  OR
  Diastolic blood pressure ≥ 120 mm Hg

- Indication of any of the following conditions on automated ECG interpretation:

  QRS > 120 ms AND heart rate > 120 (with symptoms*)
  OR
  ST segment elevation > 1 mm (acute infarction pattern) OR ST-T wave abnormalities consistent with ischemia, (with symptoms*)

  Heart rate > 140 or < 40 beats/min

  3rd degree or complete AV block

  *Symptoms include chest pain, shortness of breath, dizziness or fainting spells.

During the PSG hook-up, the following conditions will require immediate referral:

- Oximetry (awake):

  Oxygen saturation < 85% while at rest

- Heart rate (awake):

  >140 beats/min at rest
  <40 beats/min at rest

1.5 Urgent referrals

Urgent referrals are related to abnormalities detected at the time of the clinic visit or PSG hook-up, or upon subsequent review of the PSG study at the Reading Center, which require medical attention but generally not on an emergency basis. In most cases, notification of the participant should be sent by mail within 10 days. However, certain urgent referrals may require more immediate attention at the discretion (and responsibility) of the study physician. Therefore, all urgent referrals should be reviewed by the study physician no later than the next business day following the observation of the alert condition. If the study physician judges the condition to require more immediate attention, the study physician has the responsibility of contacting the participant directly by phone to seek consent to notify the participant's referring physician about the condition. If the participant refuses, then the study physician should minimally refer the participant to the ER and / or provide a listing of specialists (e.g. cardiologists or sleep specialists) the participant could contact for immediate medical care.

Clinic visit findings requiring urgent referral are as follows:

- Blood pressure (awake, seated) (on EITHER the second or third reading):

  Systolic blood pressure ≥ 180
  OR
  Diastolic blood pressure ≥ 110

- Indication of any of the following conditions on automated ECG interpretation

  Heart rate ≥ 120 (tachycardia)
  Wolff-Parkinson-White (WPW) ECG pattern or ventricular pre-excitation
  Mobitz type II AV block

Findings during in-home PSG hook-up and/or subsequent review of PSG studies requiring urgent referral:

- Any a-fib/flutter not previously diagnosed (upon review of study)
- A-fib/flutter that was previously diagnosed but HR>120 or <50 for 2 minutes duration (upon review of study)
- Heart rate >=150 or <=30 (no a-fib/flutter) (upon review of study)
- Non-sustained v-tach (3 beats duration at rate>120) (upon review of study)
- Oximetry (awake, during time of hook-up):

  Baseline awake O2 saturation <88% (but > 85%)

- Oximetry (asleep, found upon review of PSG):

  O2 saturation < 75% for > 10% of total sleep time

- Respiratory disturbance index (during sleep, found upon review of PSG):

  RDI ≥ 50 events/hour