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Title of Study: Predictors of Response to Insomnia Treatments for Gulf War Veterans	eProtocol #38548
Principal Investigator: **Jerome Yesavage, MD**	VAMC: VA Palo Alto HCS

Predictors of Response to Insomnia Treatments for Gulf War Veterans

Informed Consent

Your participation in this study will be completed:

_____ Via telehealth. All study sessions will be conducted via secure video conference call (via Zoom) on your computer or other digitial device.

_____ In person. All study sessions will be conducted in person at the Palo Alto Health Care System.

PURPOSE OF RESEARCH

You are invited to participate in a research study of non-drug treatments for insomnia in Gulf War Veterans. We hope to learn which of two treatments works best for adults with specific sleep problems. Specifically, we will compare and contrast sleep restriction therapy and cognitive therapy. You were selected as a possible participant in this study because you may have insomnia.

This project plans to enroll about 100 research study subjects with insomnia to participate in this study. The VA Palo Alto expects to enroll up to 35 participants. The study will be conducted at the three VA WRIISC centers, at VA Palo Alto Health Care System (VAPAHCS), VA New Jersey Health Care System, and Washington, DC VA Medical Center.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care you are entitled to. You have the right to refuse to answer particular questions.

DURATION OF STUDY INVOLVEMENT

If participating via telehealth, all sessions will be conducted via a secure video conference call on your computer or other device (via Zoom). If participating in person, all sessions will be conducted in person at the VAPAHCS. Across both methods of participation, a screening session (this may be split across two days), six treatment sessions- once per week for six consecutive weeks, one session at end of treatment and one visit approximately six months after completion of the treatment for follow-up, for a total of approximately six months.

PROCEDURES

If you decide to participate in the study, you will go through a series of screening steps to determine the nature of your sleep problem. The order of these steps may vary. If at any point during the

evaluation portion of this study, we determine that our treatments are not appropriate for your sleep problem, we will end your participation in this study and suggest possible referral resources.

Procedures: Screening Session (Applies to both telehealth and in person participation).

During the primary screening session, we will ask you to complete a number of psychological tests, standardized clinical interviews, and questionnaires about the nature of your sleep problem. You will also have a chance to bring up issues you believe are relevant to your sleep problem. At the first screening session, we will also do a brief physical examination and a standard evaluation of your sleep issues, to determine if your sleep problem has a physiological basis. If necessary, this session can be split into two visits. For telehealth (via Zoom), video must be on to complete study measures.

Medications. Participants may take medications, drugs, herbal remedies, or hormones specifically prescribed for treating sleep disturbances while participating in the study. Sleep medications are acceptable if stable (at least 4 weeks of same dose/timing/formulation) at the time of recruitment. The responses to questions concerning illegal drug use could be self-incriminating and harmful to you if they became known outside the study. As explained in the confidentiality statement of the consent, we do not intend to disclose this information.

Sleep Reports. During this screening session, we will show you how to complete daily sleep reports. A sleep report is designed to gather information about your daily sleep pattern. You will be asked to keep a daily sleep report a week following your screening session, a week prior to the start of treatment, the entire six-week treatment period and for one week at the end of treatment follow up and again at the six-month follow-up.

Procedures: Additional In Person Screening Session (Applies to in person participation only).

If you are participating in person, the screening session will be split across two in-office screening visits. In addition to the psychological tests and questionnaires. If our treatment appears appropriate for your sleep problem, you will complete a one-night ambulatory, overnight sleep recording that you will have set up in our lab and sleep with in your own home. You will return to the lab the next morning to have the equipment removed. At this time, we will also do a blood draw and urine screen.

Blood Draw. We will take a blood sample of approximately one teaspoon at the end of screening to look for inflammatory markers, and to analyze for DNA.

Urine screen. We will analyze a urine sample of approximately two tablespoons at the end of screening, end of treatment, and at the 6 month follow up to verify that you are not taking any drugs that are not allowed by this study. Analysis will be done immediately and the urine samples discarded. If the drug screen is positive for an illicit drug and is subpoenaed or somehow disclosed, an unlikely event, it could be incriminating. As explained in the confidentiality statement of the consent, we do not intend to disclose this information.

Ambulatory Overnight Recording. The ambulatory recording is a method for screening participants for possible sleep apnea (a condition causing a person to stop breathing briefly during sleep), and periodic leg movement disorder (PLMD, periodic contractions of the limb, usually the lower leg, during sleep, followed by awakenings). Sleep apnea and periodic leg movement disorder are medical conditions not treated by our study. These recordings will be taken again at the end of the 6 week treatment and at the 6 month follow-up session. If your recordings shows evidence of any of these

or other medical conditions, we will inform you so that you may discuss appropriate medical treatment with your primary care physician.

Procedures: Treatment.

When you have completed all of the evaluation sessions described above, we will determine if our study is appropriate for you. If so, you will be randomly assigned to one of two treatments. You have an equal chance of being assigned to either of the two treatments: Sleep Restriction Therapy or Cognitive Therapy.

Sleep Restriction Therapy will regulate the time you spend in bed on the basis of information collected about your sleep from sleep diaries during the evaluation and during treatment. Sleep restriction therapy is designed to improve your sleep quality by matching the opportunity you give yourself for sleep to the amount of average sleep ability you exhibit on your sleep diaries. Once the quality of your sleep has improved then then sleep quantity is gradually increased by slowly increasing your sleep opportunity. Sleep restriction therapy will also attempt to strengthen your bed sleep connection by focusing on what activities you engage in when you are awake in the middle of the night.

Cognitive Therapy is designed to identify incorrect ideas about sleep, challenge their validity, and replace them with correct information. This therapy tries to reduce worry, anxiety, and fear that one won't sleep by providing accurate information about sleep.

The treatment part of the study lasts six weeks. During the treatment, you will meet with the therapist for a total of six sessions: once per week for six consecutive weeks. Each session lasts approximately 60 minutes. We will make an audio or video recording of each treatment session, which will be evaluated by a research psychologist for quality control. All audio or video recordings will be kept in a locked cabinet or on an encrypted VA server for the VA-required period of 6 years after study closure, then destroyed.

_____ Yes, I give permission for audio/video recordings to be made, as set forth above.

_____ No, I do not give permission for audio/video recordings to be made.

Procedures: End of Treatment Follow-up.

At the end of the 6-week treatment period, you will be asked to complete a 7-day sleep log, and then either return to the clinic or conduct a visit over telehealth to repeat some of the psychological tests and questionnaires that you completed at the beginning of the study. At this time, if you are participating in the in-person study, we also repeat the overnight sleep recording. As in the in-person screening session, we will set you up in the lab with sleep recording equipment (Polysomnography, PSG) that you will sleep with overnight in your own home. You will return to the lab the next morning to have the equipment removed. After the equipment is removed, we will repeat the urine screen.

Procedures: 6 month Follow-up.

We expect the benefits of your treatment to continue and improve with time, thus we encourage you to continue practicing the treatment instructions to maintain your progress. Six months after you have completed the treatment, we will ask you to complete a 7-day sleep diary and an updated medication list. We will ask you to return either to the Palo Alto VA or a teleconference room in order to complete the psychological tests and questionnaires for a third time. If you are completing the study in-person, we will also set you up in our laboratory with overnight sleep recording equipment that you will sleep with in your home for a third time. You will return to the lab the next morning to have the equipment removed. After the equipment is removed, we will repeat the urine screen and blood draw.

Telehealth Protocol:
If you participate in the telehealth protocol, you will complete all study sessions through Zoom and you will not need to come to any study visits in person. You also will not complete the study physical, blood draw, urine screen or overnight recording. You will be required to have your video on during all study visits.

Tissue Banking for Future Research (Applies to in person participation only)

As part of this research we would like to save any leftover blood samples for future research. Your blood samples will be stored at the Palo Alto VA and will be used for future research on problems concerning sleep. Your samples will continue to be stored and used for research until the sample is all used up. Your sample and information about you will be labeled with a code that does not contain your name, initials, SSN, date of birth, or other ways that identify who you are. The research we conduct with your blood is being done for research purposes only and we will not tell you or your doctor about the results of the research.

You may withdraw your permission for us to use your blood for future research at any time. Contact Dr. Goldstein-Piekarski at 650-493-5000 extension 65436 to withdraw your permission. If you take back your permission, the research team can continue to use information about you collected before you decided to take back your permission, but they will not collect any information about you going forward and any remaining samples will be destroyed.

The research we conduct using your blood may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. These inventions and discoveries may become financially valuable. You will not receive any money or other benefits from any commercial or other products that are made using your specimens.

If you are participating in the telehealth protocol, we will not collect any samples.

_____ Yes, I give permission for my samples to be saved for future research, as set forth above.

_____ No, I do not give permission for my samples to be saved for future research.

Tissue Sampling for Genetic Testing (Applies to in person participation only)

Genetic tests will be conducted on your samples. The tests we plan to do will allow us to study the impact of different genes on sleep disruption, its treatment, and its relationship to aging, and other problems or diseases related to aging. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications, and responses to treatment. Your sample and information about you will be labeled with a code that does not contain your name, initials, SSN, date of birth, or other ways that identify who you are. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. The research we conduct with your blood is being done for research purposes only and we will not tell you or your doctor about the results of the research.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

We will protect the confidentiality of your samples and information about you. Your samples will be stored in a locked area and all information about you will be stored in a locked file cabinet or on a password protected secure computer.

PARTICIPANT RESPONSIBILITIES

As a study participant, your responsibilities include:

- Follow the instructions of the investigators and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the investigators or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigators or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Keep your sleep diaries as instructed.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- Tell the investigators or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are **free to withdraw** your consent and stop your participation at any time. If you decide to withdraw from the study, you will not

lose any benefits to which you would otherwise be entitled and your decision will not affect your ability to receive medical care for any condition.

If you want to stop being in the study you should tell the investigators or study staff. You can do this by phone by calling Dr. Andrea Goldstein-Piekarski at 650-493-5000 extension 65436.

If you withdraw from the study for any reason, you must return any study-related equipment still in your possession.

The investigators may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the investigators and/or study staff.
- The investigators decide that continuing your participation could be harmful to you.
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions. This study involves the following risks, discomforts, and possible inconveniences:

Evaluation and testing. There are virtually no risks involved in the cognitive testing and psychological measurements other than the anxiety that can be associated with any test. It is possible that you might become tired or frustrated by some of our testing. You may find answering the questionnaires annoying, boring, or repetitive. If this happens, please tell us and we will take a break or skip a particularly difficult test. Evaluations of mood and mental status may be slightly frustrating or produce fatigue and boredom. If the research staff has reason to believe you may be having suicidal thoughts, you will be asked to speak to a clinician trained in suicidality risk assessment.

Sleep Log and Questionnaires. There are no harmful effects to filling out the sleep log and questionnaires, but you may find answering the questionnaires annoying or boring.

Sleep recording (Applies to in person participation only). The ambulatory overnight recording offers no risk other than a certain discomfort due to the attached sensors which may slightly affect your sleep quality during that night. The tape or glue used to attach the sensors to your skin might cause a minor skin irritation (rash). If this were to occur, we recommend putting lotion on the irritation. If you are completing the study over telehealth, there will be no sleep recordings.

There is always the possibility that your sleep might get worse during treatment. In general most patients benefit from the proposed treatments, but it is always possible that an individual can experience unwanted changes in their sleep pattern.

Sleep Restriction Therapy may cause you to feel overly sleepy, cranky, or disoriented during the first few days of treatment. It is recommended that you avoid driving, operating machinery, or doing activities that require close attention for the first few days of therapy. Sleep Restriction Therapy has

been known to trigger seizures in people with seizure disorders and to have possible negative effects on mood in people with bipolar disorder. For this reason, people with these disorders are not eligible for this study.

Cognitive Therapy may lead you to challenge some of your thoughts and concerns about the way you sleep. The treatment may lead you to adopt a more flexible cognitive stance regarding your sleep. Some people may find this uncomfortable.

POTENTIAL BENEFITS

There may be no direct benefits to you for participation in this study. Your sleep may improve. Your participation may help us to learn more about the causes of insomnia.

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY DIRECT BENEFITS FROM THIS STUDY.

ALTERNATIVES

You do not have to participate in this research study in order to receive treatment for any medical condition. There are other behavioral treatments for sleep problems, as well as various drug treatments for sleep problems, that are not included in this study. Your study doctor can discuss any alternatives with you before you agree to participate in this study.

PARTICIPANT'S RIGHTS

Your participation is voluntary. You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY

We will keep your name and all the information you tell us in this study as confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

If you decide to participate in other studies at the VA or Stanford Sleep Center, data about you from this study may be combined with data about you collected for other studies.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that

may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

Exceptions: A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about you, without your consent. For example, we will voluntarily disclose information about incidents such as child abuse, and intent to hurt yourself or others. In addition, a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. Finally, the Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

FINANCIAL CONSIDERATIONS

Payments. This payment is to help cover any expenses you may incur in the course of your participation, such as costs of transportation and telephone calls to our offices. You will need to provide your Social Security Number to receive payment.

Telehealth Participation: If you are participating in the study through telehealth, you will receive $50 for the screening procedures. If you are determined to be eligible for the study, you will receive stipends of $25 for all 6 treatment visits thereafter and $25 for the follow up visit (7 x $25 = $175). If you complete all treatment visits and the follow up visit will receive a $50 completion bonus. Thus, if you complete all study visits, you will receive a total of $275.

In Person Participation: If you are participating in the study in person, you will receive $150 for completing both screening visits. If you are determined to be eligible for the full study, you will receive $25 for each of the 6 treatment visits thereafter and $25 for the end of treatment follow up visit (7 x $25 = $175). Participants who complete all treatment visits and return for the 6-month follow up visit will receive a $150 completion bonus. Thus, if you complete all the study visits, you will receive a total of $475.

Costs. You will not have to pay anything to be in this study.

Participation in this study is not a substitute for health insurance. You and/or your health insurance must pay for those services, supplies, procedures, and care that you may require for medical care that is not part of this research study. **You will be responsible for any co-payments and/or deductibles as required by your insurance.**

Sponsor. The Department of Veterans Affairs is providing financial support for this study.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on a number of factors. In most circumstances, the treatment must be provided in a VA medical facility. No other form of compensation for injuries is available. However, by signing this form you have not released the VA from liability for

negligence. For further information, you may call the Human Protections Administrator at (650) 493-5000, ext. 67593 or the V.A. Regional Counsel at (415) 750-2288.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the principal investigator, Dr. Jerome Yesavage, at 650-493-5000 ext. 64330. You should also contact the principal investigator or any member of the research staff at any time if you feel you have been hurt by being a part of this study.

Appointment Contact: If you need to change your appointment, please contact the research assistants at 650-849-0584.

If in the event of a medical emergency that may or may not be related to participation in the study please call 911 and notify your primary care physician.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Are you participating in any other research studies? _____ yes _____no

May we contact you (by phone or letter) about related studies that may be of interest to you?

_____ Yes. I would like to be contacted for future research opportunities.

_____ No. Do not contact me about future research opportunities.

Signing your name means you agree to be in this study and that you were given a copy of this consent form.

Signature of Participant Date

Print Name of Participant Date

Person Obtaining Consent:

Signature of Person Obtaining Consent Date

Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

Signature of Person Obtaining HIPAA Authorization confirmation Date

☐ Confirm the participant signed the VA HIPAA Authorization (VA 10-0493)

Add VA HIPAA form here