NCT03850743

Biomarker Signatures of the Sleep-pain Enigma

July 12, 2019

WALTER REED NATIONAL MILITARY MEDICAL CENTER (WRNMMC)
BETHESDA, MARYLAND

This consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Research Study Entitled:

Biomarker Signatures of the Sleep-Pain Enigma; a CHIRP funded project

Principal Investigator:

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Attending Anesthesiologist, WRNMMC
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301-816-4710
Current Duty Station: USUHS/WRNMMC

Study site: _X_WRNMMC, __ FBCH, _X_USUHS, ___WRAIR, ___NMRC, ___JPC, ___OTHER

1. INTRODUCTION OF THE STUDY

You are being asked to be a part of this research study because you will be having an orthopedic surgery and may have problems with pain or sleep after your surgery.

Taking part in this study is voluntary. You may choose to be in or not be in the study. If you decide to be in this study, you may leave the study at any time. No matter what you decide, there will be no penalty to you and you will not lose any of the benefits you already have. Leaving the study will not affect your medical care. Please read the information below, and ask any questions you have, before you decide whether or not you want to be in the study. While you are in the study, the study team will let you know about any new information that may affect your decision to be in the study.

If you choose to participate in this study, you will be asked to do these three things:

- Fill out surveys that ask questions about your pain, sleep, and other things related to your health and well-being. Survey links will be emailed to you at six different time points over the course of 6-months and you can complete them online or at a clinical visit.
- Have your blood drawn at three time points over your first 6-8 weeks of being in the study. These blood draws will occur at your regularly scheduled clinical visits before and after surgery. We will draw about 2 tablespoons of blood at each of these time points.
- Wear an actigraph for a week before your surgery and a week after your surgery. An actigraph is a sleep and activity tracker about the size of a watch. This is optional.

The study is being done at Walter Reed National Military Medical Center (WRNMMC) and is funded by the Collaborative Health Initiative Research Program (CHIRP): Uniformed Services University and National Heart Lung and Blood Institute Collaborative Health and Readiness Research Program.

2. PURPOSE OF THE STUDY:

The purpose of this study is to learn about how sleep problems and pain are related before surgery and in the months following surgery. For this study, we are looking at small protein biomarkers and hormones that are in your blood. These proteins are like traffic lights and tell the body when to make more or less of something to help you heal or adapt to something new. What we learn in this study may help us find out why some people have long-term problems with pain and sleep after surgery.

3. PROCEDURES TO BE FOLLOWED:

If you agree to be in this study, you will complete the following tasks. The tasks will be in addition to your routine standard of care (information your doctor is collecting as part of your treatment). All survey data will be collected online in a database called the *Wounded, Ill and Injured Registry (WIIR)*. In addition, some information (mentioned below) will be collected from your electronic medical record.

On the **first day** of the study, before your surgery, you will be asked to**:**

- **Provide Information.** First you will be asked to provide background information like age, race, and date of surgery. This takes about 5 minutes. Then you will be asked to complete the standard of care (SOC) surveys that you would normally complete even if you were not in the study, and two extra surveys (about social activities and sleep) and a pain scale. You will do the surveys on a computer tablet at a clinical visit, at home using a computer by following a link that is emailed to you, or over the phone with a study team member. If you already did your SOC survey before surgery, we will ask you to do a couple of surveys that were not in your SOC surveys.

- **Give a blood sample (about 2 tablespoon or 20 mL)**. This takes about 5 minutes. A study nurse, or other person trained in drawing blood, will draw the blood in a private space.

- **Wear an actigraph for 3-7 days**: You will be given an actigraph to wear on your wrist, like a watch. It measures how much you move during the day and at night while you sleep. You will wear it in the days before your surgery and bring it with you to your surgery. Wearing the actigraph is optional.

One week after your surgery:

- You will be emailed a link to your "Week 1" surveys. These surveys are almost the same as the standard of care surveys you will do before surgery, plus two extra surveys and a pain scale. All of these surveys will be done for the study, and are not done as your standard of care. A study team member may call or text message you to remind you to do the surveys. Depending on your mobile device provider, data and messaging rates may apply. The surveys take about 10-15 minutes.

Two weeks after your surgery:

- You will be emailed a link to your "Week 2" surveys. Since you will most likely be returning to WRNMMC for a follow up clinical appointment, if you have not yet completed your survey by this 2 week appointment, a study team member will contact you with a reminder. We will meet you before or after your follow-up appointment to get another 20 mL blood sample.

10 days before your 6-week follow up:

- You will be mailed an actigraph, and asked to wear it for 3-7 days in a row. We will ask that you bring the actigraph to your 6-week follow-up appointment.

6 weeks after your surgery:

- You will be emailed a link to your "Week 6" surveys. You will most likely be returning to WRNMMC for a follow up clinical appointment and a study team member will contact you to remind you to do surveys if you did not do them. We will meet you before or after your follow-up appointment to get another 20 mL blood sample and the actigraph.

3 months after your surgery:

- You will be emailed a link to your "3 Month" surveys. You will most likely be returning to WRNMMC for a follow up clinical appointment and a study team member will contact you to remind you to do the surveys if you did not do them.

6 months after your surgery:

- You will receive an email with a link to your "6 month" questionnaires. You will most likely be returning to WRNMMC for a follow up clinical appointment and a study team member will contact you to remind you to do the surveys if you did not do them.

4. IDENTIFICATION OF YOUR BLOOD SAMPLES, HOW AND WHERE THEY WILL BE KEPT, AND WHO WILL HAVE ACCESS TO YOUR SAMPLES

a. Instead of using your name or social security number, you will be given a code number, called a study identification number "study ID." Your study ID number will be used to label your survey answers and any clinical information that is collected from your health record in this study. The only link between your study ID number and your name or medical record number, called the "Master list," will be kept in double-locked secure files and in a password-protected secure database.
b. The blood samples will be kept in a locked lab at the WRNMMC Department of Research and analyzed at the Uniformed Services University. The samples will be labeled with a unique barcode at WRNMMC and linked with your Study ID number on a SEPARATE spreadsheet at WRNMMC. Blood samples will be

tracked and kept in an existing Laboratory Inventory Management System (LIMS), which is made to track the exact location of your blood sample, where the sample came from, how much blood is in the sample, and where your blood sample has been.

c. Your blood sample will be stored until all analysis has been complete. You may be asked if you wish to participate in a "sister" biobank research study. If you are interested, the PI will review the consent form with you and answer any questions you may have. If you decide to participate, any amount of blood samples that are remaining after this study is complete, as well as study data, will be transferred to this biobank research study. If you choose not to participate, any remaining blood samples, after all analysis is complete, will be destroyed. If you do not want to be included in future research, then you should not agree to be approached for consent to the Biobank research study.

Please initial the sentences that reflect your choices.
_____ **I authorize** research staff to contact me for participation in the sister Pain Registry Biobank Study.
_____ **I do not authorize** research staff to contact me about in the Pain Registry Biobank Study.

5. ALTERNATIVE TO PARTICIPATION

Choosing to not take part in this study is your alternative to being in the study. No matter what you decide, you will get the same medical treatment.

6. AMOUNT OF TIME FOR YOU TO COMPLETE THE STUDY

You will be in this study for up to 6 months after surgery. The Week 1, Week 2, and 3 Month surveys will take about 10-15 minutes each. As part of your regular medical care, your provider will ask you to fill out the Day 1 (before surgery), Week 6, and 6 Month surveys. For this study, a couple of extra surveys will be added to those surveys that will take about 5 minutes longer than they normally would take. The times we ask that you give blood at your clinical visits will take about 5 minutes each. The total amount of time that you are asked to give to surveys and blood draws in this study is less than 2 hours over a six month period. If you choose to wear an actigraph for 3-7 days before surgery and 3-7 days before your 6-week follow up appointment, it may take a few seconds to put on the actigraph and take it off when you shower.

7. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

We expect to enroll 240 people in this study from WRNMMC.

8. POSSIBLE RISKS AND DISCOMFORTS FROM BEING IN THIS STUDY

We do not think you will have any health risks by being in this study. However, you may experience some discomforts or risks that we list below.

There may be some discomfort from having your blood drawn, and you may feel some pain, swelling, and bruising at the place of the needle stick. Some people feel dizzy or light-headed for a few minutes during or after their blood is drawn.

There is a possible risk that your personal information could be exposed. To reduce this risk, records are coded using Study ID numbers and stored on a secure and password-protected computer database and in locked file cabinets in a locked file room. Access to this data will be limited to trained and approved study team members.

As part of the analysis on your samples, the investigators will do genetic testing. 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, and reactions to medication and responses to treatment. Results from research using your data or specimens will not be provided to you or placed in your health record. In addition, the Genetic Information Nondiscrimination Act (GINA) of 2008 provides some protections as described below.

GINA is a new Federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this study.
- Health insurance companies and group health plans may not use your genetic information when making decisions about your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.
- All health insurance companies and group health plans and all employers with 15 or more employees must follow this law, dated 21 May 2010.

GINA's health insurance protections do not apply to members of the military who receive their healthcare through TRICARE and for veterans who receive their healthcare through the Veterans' Administration. While GINA's employment protections do not apply to military members and Federal employees, presently an Executive Order protects federal employees from genetic discrimination in employment, and the military has its own policies in place that may protect against genetic discrimination. GINA's protections should apply to a military member once he or she leaves the service.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance or higher rates for these kinds of insurance.

You should talk with the study investigator if you have any questions.

9. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You will not benefit from taking part in this study, but the information we learn may help us understand who is at risk for long term pain and sleep problems after surgery. In the future, this information could be used to create cutting-edge treatments.

10. CONFIDENTIALITY/PRIVACY OF YOUR IDENTITY AND YOUR RESEARCH RECORDS

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at:
http://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf..

The Principal Investigator will keep your study data in a locked file drawer in a locked file room with limited access, located in the secure DVCIPM research office. Staff from the WRNMMC Department of Research Programs, the Institutional Review Board, the DoD Higher Level Review, and other government agencies, such as Uniformed Services University, may look at your study data as part of their duties.

These duties include making sure the study participants are protected. Confidentiality of your information will be protected to the extent possible under current regulations and laws but cannot be guaranteed. Complete confidentiality cannot be promised, including for military personnel, because important information about your health may need to be reported to appropriate medical or command authorities (DoD 6025.18-R). Your study records may be disclosed outside of WRNMMC, but in this case, only a unique code number will identify you. Information about the code will be kept in a secure location and access limited to approved study team members. See section 17(9) of this form.

By signing this consent document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational reasons, and used generally to advance medical science. You will not be personally identified; all information will be presented as anonymous data. Also, you give your permission for your de-identified study data to be compared to data obtained in other future studies. Your name will not appear in any published paper or presentation related to this study.

Electronic research data that is stored outside the .mil network will be stored in the Research Electronic Data Capture (REDCap) system. All data stored for this protocol in REDCap will be coded (i.e. names and identifying numbers such as birthdays are removed and are replaced by a study ID number). No protected health information (PHI) nor personally identifiable information (PII) will be stored in REDCap for this protocol. Access to REDCap is restricted to authorized users only, who have completed annual trainings in HIPAA standards for research staff as well as training for this specific study. Each user of REDCap has a unique username and password; passwords must be changed every 3 months. Furthermore, activities are monitored on REDCap,

and any modifications to data or downloads of data are linked to the user who performed such action and logged.

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 results. You can search this web site at any time.

This research study meets the confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA).

11. CONDITIONS UNDER WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

Your taking part in this study may be stopped without your consent if being in the study might be dangerous or harmful to you. Your taking part in this study may also be stopped without your consent if the military mission requires it, or if you lose your right to receive medical care at a military hospital.

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

- The study is cancelled
- Other administrative reasons
- Unanticipated circumstances

12. ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

You are eligible to be in this study if you are:

- Active duty military or DEERS eligible individuals
- Between the ages of 18 and 60 years old
- Able to understand written and spoken English
- Eligible for healthcare within Military Health Systems
- Having an orthopedic procedure at WRNMMC

You will not receive any payment for being in this study.

13. COMPENSATION IF INJURED AND LIMITS TO MEDICAL CARE

You will not receive any compensation (payment) if you are injured as a direct result of being in this study. This is not a waiver or release of your legal rights. You should discuss this issue with the study investigator before you enroll in this study.

If you are injured as a result of your participation in this study, you will be given medical care for that injury at no cost to you.

Medical care is limited to the care normally allowed for Department of Defense health care beneficiaries (patients eligible for care at military hospitals and clinics). Necessary medical care does not include in home care or nursing home care. If you need to be hospitalized, you may have to pay the normal fees for subsistence (hospital meals), as per standard regulations.

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the Human Protection Administrator at the Department of Research Programs at: Phone: (301) 295-8239
Mailing Address: 8901 Wisconsin Ave, Building 17B, Floor: 3, Suite: 3C, Bethesda, MD 20889.

14. COSTS THAT MAY RESULT FROM TAKING PART IN THIS STUDY

Depending on your mobile device provider, data and messaging rates may apply if you choose to have a reminder text (with the survey link) sent to you.

15. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND THE INSTRUCTIONS FOR STOPPING EARLY

You have the right to leave the study at any time. There are two ways you can do this:

1. You can decide that you no longer want researchers to contact you to collect future surveys, blood samples, and actigraph data, AND
    - They can keep looking at your standard of care survey answers and personal medical information until the end of the study period,
      OR
    - You can decide that you do not want any contact with this study including allowing access to future standard of care survey answers and personal medical information.

When leaving the study, please note:

1. You cannot withdraw your samples or any information that has already been collected by the study team, AND
2. The Principal Investigator will include information and samples collected from you, before your withdrawal date, in the data analyses for this study.

If you want to leave the study, please send that request in writing to the address below.
By leaving the study at any time, you in no way risk losing your right to medical care.

Chester C. Buckenmaier III, MD
Attending Anesthesiologist, WRNMMC
Program Director, Defense and Veterans Center for Integrative Pain Management (DVCIPM)
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Associate Professor, Anesthesiology, USUHS
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301-816-4710
11300 Rockville Pike, Suite 709 Rockville, MD 20852

16. AUTHORIZATION FOR RESEARCH USE OF PROTECTED HEALTH INFORMATION

The Federal Health Insurance Portability and Accountability Act (HIPAA) includes a Privacy Rule that gives special safeguards to Protected Health Information (PHI) that is identifiable, in other words, can be directly linked to you (for example, by your name, Social Security Number, birth date, etc.). We must tell you how your PHI will be used. This authorization is effective until the end of the study.

(1) What information will be collected?

For this research study, we will be getting information about your medical history, inpatient and outpatient clinical notes, diagnostic radiology reports, labs, pain scores, medications, procedures, diagnosis codes and any other patient/provider contacts, along with:

- Name
- Age
- Dates directly related to an individual, including birth date, date of surgery, admission date, discharge date, follow-up appointment dates, and date of death
- Telephone number
- Email address
- EMR (electronic medical records)

(2) Who may use your PHI within the Military Healthcare System?

Study team members will have access to your PHI in order to email and call you for survey reminders, meet you at your clinical visits for blood draws and actigraph returns, monitor your progress, and analyze study data. Also, your PHI may be made available to groups such as the WRNMMC Department of Research programs and the WRNMMC Institutional Review Board.

(3) What persons outside of the Military Healthcare System who are under the HIPAA requirements will receive your PHI?

PHI that directly identifies you will not be given to persons outside of the Military Health Care System.

(4) What is the purpose for using or disclosing your PHI?

Study team members need to use your PHI in order to track your study activities and medical care.

(5) How long will the researchers keep your PHI?

All PHI will be coded and kept in a secure file cabinet in a locked file room, located at the DVCIPM office, 11300 Rockville Pike, Suite 709, Rockville, MD 20852 in the office of the

Principal Investigator and on a secure computer server for a period of six years following the end of the study. The master list will be destroyed as soon as data analysis is complete.

This consent form and HIPAA authorization will be kept for a period of six years after the study is finished.

(6) Can you review your own research information?

You will not be able to look at your research information.

(7) Can you cancel this Authorization?

Yes. If you cancel this authorization, you will no longer be in the study. The study team may use the study information collected before this cancellation. No more data will be collected after you cancel.

If you want to cancel your Authorization, please contact the Principal Investigator, in writing:
Chester C. Buckenmaier III, MD
11300 Rockville Pike, Suite 709
Rockville, MD 20852
301-816-4710

(8) What will happen if you decide not to grant this Authorization?

If you decide not to give this Authorization, you will not be able to be in this study. If you refuse to sign this Authorization, you will not have any loss of medical benefits to which you would normally receive.

(9) Can your PHI be disclosed to parties not included in this Authorization who are not under the HIPAA requirements?

There is a potential that your research information will be shared with another party not listed in this Authorization in order to meet legal or regulatory requirements. Examples of persons who may access your PHI include representatives of the DoD Higher Level Review, the Food and Drug Administration, the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP), and the DHHS Office for Civil Rights. This risk is unlikely to occur, but in that case, the HIPAA Privacy Rule would no longer protect your health information.

(10) Who should you contact if you have any complaints?

If you believe your privacy rights have been violated, you may file a written complaint with the WRNMMC Privacy Officer, located at 8901 Wisconsin Ave, Bethesda, MD 20889, Telephone: 301-319-4775.

Your signature at the end of this document acknowledges that you authorize WRNMMC personnel to use and disclose your Protected Health Information (PHI) collected about you for research purposes as described above.

17. CONTACTS FOR QUESTIONS ABOUT THE STUDY

If you have questions about the study, or if you think you have a study-related injury, you should contact the Principal Investigator, Chester Buckenmaier, at 301-816-4710. If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the Human Protection Administrator at the Department of Research Programs at:
Phone: 301-295-8239
Mailing Address: 8901 Wisconsin Ave, Building 17B, Floor: 3, Suite: 3C, Bethesda, MD 20889.

A signed copy of this consent form will be given to you.

SIGNATURE OF SUBJECT

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

_____
Printed Name of Subject

_____ _____ _____
Signature of Subject Date Time

SIGNATURE OF RESEARCH TEAM MEMBER OBTAINING CONSENT

My signature is intended to attest that the information in the consent document and any other information was explained to and apparently understood by the subject, that questions and concerns were addressed, and that informed consent was freely given.

_____
Printed Name of Person Obtaining Consent

_____ _____ _____
Signature of Person Obtaining Consent Date Time
(must be same as subject)