Official Title: Association between Melatonin Use and Improved Sleep Quality after Total Knee Arthroplasty

NCT Number: Not yet assigned

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INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Study Title:	Association between Melatonin Use and Improved Sleep Quality after Total Knee Arthroplasty		
Protocol No:	Version 1		
Principal Investigator:	Alejandro Gonzalez Della Valle, MD	**Phone Number:**	(212) 774-7124
Research Coordinator:	Christian Ong	**Coordinator Contact:**	ongc@hss.edu
Sponsor:	Hospital for Special Surgery		
IRB #	2021-0150		

Participating Site(s)	Location	Participating Investigator	Site Phone Number
HSS Main Campus	East Side, NY	Alejandro Gonzalez Della Valle, MD	(212) 774-7124

1. OVERVIEW OF KEY INFORMATION REGARDING THIS RESEARCH STUDY.

You are being asked to take part in a research study conducted by Hospital for Special Surgery (HSS). You are being asked to participate in this study because you are undergoing a total knee arthroplasty (TKA).

The information in this form is meant to help you decide whether or not to participate in this research study.

- Your **participation is voluntary.**
- You may decide not to participate in this research study.
- If you do participate, you may withdraw from the research study at any time.
- You do not have to participate in this study to receive treatment for your condition.

This document provides you with information about this study, including:

- Information about the procedures and the research, including risks and benefits, so you can make an informed decision about participating.
- Description of how your information will be used and shared.

Ask your study doctor or study staff to explain any words or information in this document that you do not understand. You may take home a copy of this document to consider or discuss with family and friends before making your decision. You will need to sign this document to participate in this research.

Funding for this study will be provided by departmental funds.

DOES THIS STUDY INVOLVE GENETIC TESTING OF YOUR BIOLOGICAL SAMPLES?

_x_ No, there is no genetic testing of your biological samples involved with this Study.
___ Yes, the Study involves genetic testing of your biological samples.

A. WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if melatonin is effective in improving sleep quality in patients after they undergo TKA. This study will compare the sleep quality of patients taking melatonin to patients taking a vitamin C placebo.

Melatonin and vitamin C have not been FDA approved as sleep medications. Both are currently used as over the counter dietary supplements. The goal of this study is to see if melatonin can aid in postoperative sleep in patients who undergo TKA.

A total of 130 subjects will participate in this study at HSS.

HSS may use the results of the study to gain scientific knowledge, as described in Section 1(E) of this document (BENEFITS OF PARTICIPATING IN THE RESEARCH STUDY).

B. YOUR INVOLVEMENT:

- Besides the usual pre-/post-operative visits, no additional in-person visits will be required.
- Upon hospital discharge, you will be provided with 42 pills of either melatonin or placebo
    - This will be randomized and double-blinded (neither you nor your surgeon will know which medication you receive) [See more on this in Section 2]
- You will be instructed to take 1 pill each night 30 minutes before bedtime for 6 weeks
- You will be asked to complete a weekly compliance survey for 6 weeks, and again at 90-days, and 1-year postoperatively.
- You will be asked to complete the Pittsburgh Sleep Quality Index survey (PSQI) preoperatively, and at 6-weeks, 90-days, and 1-year postoperatively.
- Compliance and PSQI surveys will be administered physically (written) during routine follow-up appointments, or if you cannot be reached during these times, they will be administered electronically through email via REDCap.
- Please see the chart listed in Section 2 below for additional information.

Your responsibilities as a participant in this study include:

- Signing this informed consent form;
- Following all study rules;
- Telling the study doctor truthfully about your complete medical history and other medications and supplements you are taking;
- Reporting any new problems, illnesses, or changes in medication during the study;
- Following the instructions of the study doctor and staff, including attending all your scheduled visits and taking the study drug only as directed;
- Telling other doctors, nurses, and health care providers who provide treatment to you about your participation in this study; and

- Refraining from participating in any other studies while you are participating in this study unless your first notify your study doctor and discuss with your study doctor any potential risks posed by participation in more than one study.

C. MOST COMMON POSSIBLE RISKS AND DISCOMFORTS ASSOCIATED WITH YOUR PARTICIPATION IN THE RESEARCH STUDY:

All research has some risk, which may include some side effects that make you feel unwell or uncomfortable or that could harm you. Ask the study doctor or staff if you have any questions about the risks or discomforts that may occur during this study.

During the study, you may have risks, discomforts and side effects from the study procedures. Most of these are listed in this informed consent form. Risks, discomforts and side effects may vary from person to person. Everyone taking part in the study will be watched carefully; however, doctors do not know all the risks, discomforts and side effects that may happen. These may be mild or serious, and in some cases may be very serious, long-lasting, or may never go away. If we learn about new risks that may affect your willingness to continue your participation, we will make you aware of them and you will be asked to re-consent to continue your participate in the study.

Let your study doctor know immediately if you experience any side effects or other health issues. Ask your study doctor to explain any side effects that you do not understand. If your side effects are severe, your study doctor may advise you to withdraw from the study.

Possible risks, discomforts and side effects that you may experience after taking melatonin include:

- Headache
- Dizziness
- Nausea
- Drowsiness

Possible risks, discomforts and side effects that you may experience after taking vitamin C include:

- Nausea
- Heartburn
- Headache
- Skin flushing

Participation in this research involves the potential risk of a breach of confidentiality to your stored health information. HSS tries to minimize those risks by (i) removing some direct identifiers from stored information [(i.e., names, social security numbers, medical record numbers); (ii) securing, in a separate location, and limiting access to information that would identify you; and (iii) limiting access to information stored to HSS investigators.

D. BENEFITS OF PARTICIPATING IN THE RESEARCH STUDY:

This study includes experimental/investigational procedures. While it is possible that these procedures may improve your sleep quality after your surgery, their benefits are not yet fully known. So, it is possible that you will not benefit from the procedures.

The knowledge gained from this study may benefit others in the future. Specifically, this study may help scientists to advise patients on methods for improving sleep quality after TKA.

E. ALTERNATIVES TO BEING IN THE STUDY

You do not have to participate in this study to receive treatment for your condition. If you decide not to participate in this study, you may receive the standard treatment for your condition. There may be other studies available that you could participate in.

Melatonin is available as an over the counter dietary supplement. Melatonin has not been FDA approved as an over the counter sleep medication.

You should ask the study doctor about other alternative treatments that may be available for your condition.

F. WHAT HAPPENS IF YOU CHANGE YOUR MIND?

Your participation in this study is voluntary. You may decide not to participate at any time by informing your study doctor in writing that you no longer wish to participate in the study. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you decide to leave the study before the last study visit, it is important that you tell the study doctor so that the study doctor can evaluate risks to you and discuss any follow-up care that could be helpful to you. It is helpful if you could explain your reasons for leaving the study.

If you decide to leave the study, no new information or samples will be collected from you after you withdraw. Information collected about you before you withdraw may be used by HSS in connection with the study for certain reasons, such as to check the accuracy of the study, maintain the integrity of the study data, or account for you leaving the study.

2. WHAT WILL YOUR PARTICIPATION REQUIRE?

If you decide to be in this study, the following procedures will be performed:

Study Visit #	Surveys	Study Drug	Randomization	Surgery	Physical Exam
#1 (Pre-surgical screening)	RES				SOC
#2 (Surgery day)			RES	SOC	
#3 (Week 6)	RES	RES			SOC
#4 (Day 90)	RES				
#5 (Day 365)	RES				SOC

Study Visit Outline:

#1 – At your pre-surgical screening visit, you will sign this consent form. You will also be asked to complete the PSQI survey.

#2 – On your surgery day, you will be randomized into one of two groups: 1) melatonin or 2) placebo. Upon discharge from the hospital, you will be provided with enough pills to take 1 each evening for 6 weeks (42 days/42 pills). You should take the pill each night, 30 minutes before getting into bed.

#3 – This will be your final week of taking the study drug. After your final day (day 43 postoperatively), you will be asked to complete the PSQI and the compliance survey. Most surgeons will ask you to come in for a standard-of-care check-up at week-6 as well, during which you will complete the PSQI/compliance survey in a written format. If you cannot be reached during this time, these surveys will be administered electronically through email via REDCap. We will ask for you to bring your leftover pills to this office visit so that one of the study investigators can count the number of unused pills.

#4 – You will be asked to complete the PSQI and a study compliance survey at postoperative day-90.

#5 – You will be asked to complete the PSQI and a study compliance survey at postoperative day-365 (1 year). Some surgeons may ask you to come in for a standard-of-care check-up at 1 year as well.

All surveys will be administered physically (written) during routine follow-up appointments. If you cannot be reached during these times, surveys will be sent electronically through email using a secure research software called RedCap. Visits that require survey administration only do not require you to come back to the hospital. Surveys can be answered remotely.

The PSQI contains 10 multiple-choice/short answer questions concerning your sleeping patterns and overall mood, (i.e. how would you rate your overall sleep quality?) and should only take 5 minutes to complete.

This study will select your treatment by chance. You will be assigned at random to one of 2 study groups that will receive different treatments. The randomization process is comparable to (or similar to) the flip of a coin. It is not known if any treatment you receive will benefit you. It is hoped the knowledge gained will benefit others in the future.

During the study you will be "blinded" to whether you are receiving melatonin or placebo, which means you will not know if you are receiving the melatonin or placebo. In the event of an emergency, the "blind" can be broken. The research will be "double blind" which means that during the course of the study, neither you nor your surgeon will know if you are receiving the melatonin or placebo.

3. COST TO YOU

The items and services that you receive because you are participating in the study will be provided to you at no charge. These research procedures are marked as "RES" in Section 2 of this document.

You or your insurance company are financially responsible for the costs of routine medical care provided to you over the course of the study that you would have received as part of the treatment of your condition even if you were not participating in the study. These procedures are marked as "SOC" in Section 2 of this document. You will be responsible for any co-pays, deductibles, and co-insurance associated with your medical care, just as you would be for any costs billed to your health insurance outside of this study, and any costs for procedures marked "SOC" that are not covered by your health insurance. Financial assistance may be available in certain cases. To learn about whether financial assistance may be available in your case, please call (212) 606-1505 to speak with a Financial Assistance Counselor or you can visit the following site: https://www.hss.edu/financial-assistance.asp.

4. PREGNANCY

Due to the risks associated with total knee replacements, pregnant women may not receive the type of intervention needed to participate in this research. Therefore, women who are pregnant or nursing a child are not permitted to participate in this study. For the safety of

yourself and any unborn child, before participating in this study, women are required to confirm that, to the best of your knowledge, you are not now pregnant, and that you do not intend to become pregnant during the next 6 months. If you suspect that you have become pregnant during this study, you must notify the study doctor immediately. Additionally, if you are capable of getting pregnant and are sexually active with someone of the opposite gender, you must use a form of contraception that has been approved by your study doctor while participating in the study. In some cases, your study doctor may instruct you and/or your partner to use two forms of contraception, such as birth control (IUD, pill, etc.) and a condom.

5. PAYMENT FOR PARTICIPATION

You will not be paid for your participation in this study.

6. COMMERCIAL ISSUES: YOUR RIGHTS IN THE RESULTS OF THE STUDY

Use of the findings of this study, information derived from you participation in the study and/or samples you have donated which are used in research may result in new products, tests, or discoveries, including establishing a cell line that could be patented and licensed. In some instances, these may have potential commercial value and may be developed and owned by the investigators, by Hospital for Special Surgery and/or by others. There are no plans to provide financial compensation to you should this occur. Therefore, you would not share in any financial benefits from these products, tests, or discoveries or cell lines

7. AUTHORIZATION FOR USE AND DISCLOSURE OF PRIVATE HEALTH INFORMATION FOR THE STUDY.

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to see your information and why they will be able to see it. The study doctor must obtain your authorization (permission) to use or give out your private health information for purposes of this study. *Private health information* means the health information in your medical or other healthcare records that can identify you

Your Private Health Information Will Be Used and Disclosed to Accomplish the Study: We are asking you to authorize the use and disclosure (release of your private health information for this research study. The private health information that will be used and/or disclosed to accomplish the study include:

- Information in your medical and research records. For example, your diagnosis, past medical history, diagnostic procedures, and results of any tissue biopsies or blood tests, including results of genetic tests that were already done as part of your standard treatment.
- Records about phone calls related to the study
- Records about your study visits
- Records of physical exams
- Laboratory, x-ray, and other test results
- Questionnaires
- Records about any study device you received
- If you choose to participate in the optional research repository discussed below, information collected for the repository and the results of tests performed on your samples that are stored in the repository

HSS and the HSS Study Team Can Use and Disclose Your Private Health Information to accomplish the Study: By signing this consent, you permit the study doctor and the study doctor's research team at HSS to use your private health information for the study. You also permit HSS to release your private health information to the people and organizations listed below to accomplish this study.

With Whom HSS May Share Your Private Health Information to accomplish the purposes of the Research Study:

- The Principal Investigator and other Investigators for this study, including your study doctor.
- The research coordinator, research nurses, and other members of the HSS research team working on this study.

- The Patient Advocate or Research Ombudsman at these institutions.
- Staff members of HSS main campus or HSS satellite site(s) responsible for administering clinical trials and other research activities, as well as other administrative or management activities of HSS.
- Any laboratories and other individuals and organizations that analyze your health information for this study.
- Any health care provider that you have used in the past or may use up to the time this study ends.
- The sponsor of this study. "Sponsor" includes any persons or companies that are working for or with the sponsor, are owned by the sponsor, or acquire rights to the product under study from the sponsor.
- Any Contract Research Organization (CRO) the sponsor may use. (A CRO is an independent entity with which a research sponsor contracts to oversee and facilitate various aspects of the clinical research process on the research sponsor's behalf.)
- The United States Food and Drug Administration (FDA), the federal Office for Human Research Protections (OHRP), any federal agency that provides support for this study, and any federal, state, or local agency responsible for overseeing HSS, the study doctor, or any other member of the HSS research team involved in this study.
- The members and staff of the affiliated Institutional Review Boards (IRBs) at HSS, New York-Presbyterian Hospital, Weill Cornell Medical Center and Memorial Sloan-Kettering Cancer Center. An IRB is a committee of health care providers, community representatives, and others that initially approves and periodically reviews biomedical and behavioral research that involves human subjects in order to protect the rights, safety and welfare of study participants.
- HSS contractors to assist in achieving the purposes of the study but only where such contractors agree to keep your information confidential.
- Data Safety Monitoring Boards and others authorized to monitor the conduct of this study for safety or quality assurance, for example a Clinical Events Committee.

<u>The Purpose for Which Your Private Health Information Will Be Used or Disclosed:</u>

Your private health information will be released to the people and organizations listed above to carry out this study. Specifically, this information will be used to determine whether you meet the conditions for participation in this study; to compare your earlier test results to the findings from this study; to use your previous laboratory results in place of, or in addition to, some of the lab results needed for this study.

The sponsor of the study will use your private health information as part of its analysis and evaluation of the results of this study. People working for the sponsor also visit HSS and view your private health information to make sure this study is being done correctly.

Your private health information may be disclosed to the FDA and to governmental agencies in other countries so the sponsor can get approval to market new products or to continue marketing existing products. Your private health information may also be used to meet the reporting requirements of governmental agencies.

While the results of this study may be published in scientific journals or presented at medical meetings, your private health information will not be disclosed in any publications without your consent.

<u>You Can Refuse to Authorize the Use and Disclosure of Your Private Health Information for the Research Study:</u> You do not have to give HSS permission to use or disclose your private health information. Such permission is voluntary. However, if you do not give HSS this permission, you will not be able to join the research study. Your decision to not sign this permission will not affect your current and/or future treatment, health care services, or eligibility for benefits you receive from HSS or your HSS health care providers.

<u>Expiration Date of This Authorization to Use and Disclose Your Private Health Information</u>: This permission to use and disclose your private health information will never expire unless you revoke it.

<u>Can You See the Private Health Information Collected as Part of the Study?</u> You have the right, in accordance with Hospital policy and applicable law, to review and copy your health information that is created or obtained in the course of this study. However, if you decide to

be in this study and sign this informed consent form, you will not be able to look at or copy your information until after the study is completed if doing so would impact the validity of the study (for example, if the study is "blinded" so that during the study you will not know what treatment or other intervention you are receiving).

You May Revoke This Authorization: You may change your mind and take back this Authorization at any time. If you take it back and no new health information that might identify you will be gathered. However, the researchers may still use the private health information they have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization. To take back the Authorization, you must write to the Principal Investigator at Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021.

Once Disclosed Your Private Health Information May No Longer Be Protected by the Privacy Laws: Some persons or organizations who receive your private health information may not be required by law to protect it in the same way as HSS, and they may share your information with others without your permission, if permitted to do so by laws governing them. Therefore, your private health information may be released to others without your permission.

8. CONFIDENTIALITY and PRIVACY.

Any and all private health information about you obtained through this study, including any results of genetic testing, is private and confidential, and will not be disclosed, unless permitted or required by law or by this consent form. If a disclosure of information is not authorized by law or by this consent form that disclosure will not be made without your further written informed consent.

Identifiers might be removed from your private health information or your identifiable samples and, after such removal, the information or biosamples could be used for future research studies by HSS or distributed to another investigator, institution or company for future research studies without HSS getting additional consent from you.

Subject privacy and confidentiality will be maintained through the storage of study data in a password-protected computer database maintained by the PI and accessible only to the principal investigator, in addition to other IRB approved study personnel. Each subject will be assigned a unique study number for identification in the study database. This unique study number will not be derived from or related to information about the individual. The key linking this unique study number to patient identifiers (i.e. name, medical record number, date of birth, registry number, etc…) will be maintained in a different password protected database.

9. CONTACTING YOU AFTER THE CONCLUSION OF THE STUDY:

Do you give the HSS researchers permission to contact you in the future? Such contact could be, for example, to get more information from you that may be needed for this research, to explain the results of this study, or to notify you of medical information that could help you or your family member, discuss how your samples might be used, or to discuss possible participation in another research project?

Yes ☐ No ☐

Please note that, except for the above with your permission, in no event will we contact your family members for clinical, research or other purposes without your consent with respect to the specific family members who will be contacted and the specific purpose of the contact.

Risks and Benefits of Allowing Future Contact: The risks of allowing us to contact you are that we may have information that cause some emotional distress, but the benefits are that we may have information that could help you in your medical planning and decision-making.

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. In order to comply with journal submission requirements, the Web site may also include a plan describing

how your de-identified data may be shared with other investigators. You understand that we may share your de-identified data with other researchers due to these requirements.

10.CONFLICT OF INTEREST NOTIFICATION

HSS is concerned about possible conflicts of interest in research, and has policies that require all investigators and senior research staff to report to HSS significant financial interests (such as stock ownership, royalty payments, and consulting agreements) and relationships (such as membership on a scientific advisory board) that are related to their research studies. When an investigator reports a significant financial interest or relationship that relates to one of his/her studies, HSS's Conflict of Interest Committee for Research reviews the information to evaluate the risk that the interest or relationship might influence how the investigator conducts the study or interprets the results of the study. HSS may also take steps to minimize that risk.

☒ The Conflict of Interest Committee for Research has determined that there are no conflicts of interest associated with this study.

☐ The Conflict of Interest Committee for Research has determined that there is a potential conflict of interest associated with this study. Please read the information below carefully.

11.COMPENSATION FOR INJURY

If you are injured as a result of participating in this study, the study doctor, other members of the research team, or other HSS professional medical staff will provide you with emergency medical treatment (or arrange to have such treatment provided to you), and will assist you in obtaining appropriate follow-up medical treatment. However, there is no plan to provide you compensation or reimbursement for medical care or other costs.

Your health insurance may or may not pay for treatment of injuries as a result of your participation in this study.

12. QUESTIONS

If you have any additional questions later on, or if you wish to report a medical problem that may be related to this study, Dr. Della Valle can be reached at (212) 774-7124 during office hours.

If you have any questions about your rights as a participant in this study or any questions about your participation that you would like to ask an institutional representative who is not part of this study, you can call the HSS Institutional Review Board at (212) 774-7123.

If you would like to have more information about the Hospital's financial disclosure review process in general, or in regard to this study, you may contact the Hospital's Office of Legal Affairs at (212) 606-1592. You may also ask the Hospital's patient advocate at (212) 774-2403, to arrange for you to have this information.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Agreement to Participate: Witnessing and Signature

To be in this study, you or your legal representative must sign the next page of this informed consent form. By signing the next page, you are voluntarily agreeing to be in this study at HSS.

Before signing, you should be sure of the following:

- You have read all of the information in this "Informed Consent to Participate in Research" form (or had it read to you).
- You have discussed the implications of your being in this study with your doctor, your study doctor and/or the study coordinator.
- You have had the chance to ask questions about this study.
- You received answers to your questions.
- If you did not understand any of the answers, you asked the study doctor or the study coordinator to explain them to you.
- The information given to you is based on what is now known about the study drug(s), device(s), or procedure(s). There may be other risks or complications that are not known at this time.
- You have had time to think about the information and decide whether or not to be in the study.

Please check one of the following:

☐ I AM NOT in another research study at this time.

☐ I AM in another research study at this time.

If you decide to be in this study:

- You are expected to follow the study procedures.
- You are expected to provide the information needed by the study doctor, the study coordinator, nurses, or other staff members for the study.
- You will be told in a timely manner of any significant new information that may affect your willingness to stay in the study.
- You may freely choose to stop being in the study at any time.

By signing below, you are voluntarily agreeing to be in this study.

You must be given a signed copy of this informed consent form to keep for yourself.

_____

Print Name of Participant Signature of Participant Date

_____

Print Name of Parent/Legal Guardian (if applicable)[1] Signature of Parent/Legal Guardian Date

_____

Print Name of Person Obtaining Consent Signature of Person Obtaining Consent Date

As an HSS representative, and the person obtaining consent, please sign here to indicate that you have given a signed copy of this informed consent form to the participant

_____

[1] The parent or legal guardian of a child participant should sign this form on behalf of the child. The signature of one parent is sufficient when the research is of minimal risk to the child, or when the research presents the prospect of direct benefit to the child. The signature of both parents is required when the research involves greater than minimal risk with no prospect of direct benefit to the child. The requirements for signature of both parents may be waived if one parent is deceased, unknown, incompetent, or not reasonably available, or when one parent has sole legal responsibility for the care and custody of the child. If the participant is a child who is capable of giving assent, the child should also sign the attached Assent Form.

IRB Administrative Use Only

Hospital for Special Surgery Institutional Review Board Approval
12/10/2021 Thru 7/26/2022

NOTE TO INVESTIGATORS:

- **THE ORIGINAL OF THIS INFORMED CONSENT FORM MUST BE PLACED IN THE PARTICIPANT'S STUDY FILE.**
- **A SIGNED COPY OF THIS INFORMED CONSENT FORM MUST BE GIVEN TO THE PARTICIPANT.**
- **A COPY OF THE INFORMED CONSENT FORM MUST BE PLACED IN THE PARTICIPANT'S ELECTRONIC MEDICAL RECORD**.