PARTICIPANT INFORMATION AND CONSENT FORM

Melatonin, Nightshift Work and DNA Damage (MEND) Study

Short title: MEND

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Sponsor: BC Cancer Foundation and Canadian Cancer Society

Your participation is voluntary

You are being invited to take part in this clinical trial because you responded to a posting at Vancouver Coastal Health, or the study information sheet via e-mail from your union representatives. Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving. If you decide that you want to terminate your participation in this study, you should notify the study staff.

This consent form describes the procedures that are being carried out for research purposes. Please review the document carefully when deciding whether or not you wish to be part of the research study, and discuss it with others if you wish. Please ask the study staff to explain any information that you do not understand. If you wish to participate in this study, you will be asked to sign this form.

Who is conducting this study?

The principal investigator has received financial compensation from the BC Cancer Foundation and the Canadian Cancer Society for the work required in conducting this clinical trial.

Background

Nightshift work has been linked with increased risks of multiple cancers. Given how common nightshift work is in Canada (~1.8 million Canadians work between the hours of midnight and 5 am), its link with cancer represents an important public health concern that has not been addressed.

Free radicals are molecules in our body that cause damage to cells and lead to the development of cancer and other health conditions. Research has shown that lack of sleep and poor quality of sleep among nightshift workers, are associated with increased cell damage and reduced ability to repair DNA once it has occurred. This research aims to examine the effects of melatonin supplementation, which is a natural health product shown to improve sleep quality. Health Canada has approved the sale and use of melatonin to improve sleep quality in people suffering from sleep restrictions or altered sleep schedules such as nightshift workers.

What is the purpose of the study?

This is a Phase IV study. A Phase IV study is a study of an approved health product which is conducted to obtain additional information regarding the product's benefits and optimal use. The purpose of this phase IV trial is to determine whether:

- Melatonin supplements consumed by nightshift workers before going to sleep during the day will improve their sleep quality and, therefore, reduce the production of cellular damage; and
- Melatonin supplements consumed by nightshift workers before going to sleep during the day will improve their sleep quality and, therefore, improve the ability to repair cellular damage caused by free radicals.

Who can participate in this study?

You may be able to participate in this study if you*:*

- Are 18-50 years of age;
- Have Body Mass Index or BMI within the range of 18.5-30;
- Live and work in the Greater Vancouver region;

- Primarily work nightshifts of 7 or more hours in duration that end no earlier than 6 am at least 2-3 nights per week over the past 6 months or more;
- Sleep 5 - 6 hours each day after completing a nightshift;

Who should not participate in this study?

You will not be eligible to participate in this study if you:

- Are currently using any illicit drugs;
- Have a personal history of hormonal disorders, seizures disorders or chronic medical condition (e.g. cancer, diabetes, kidney disease, liver disease, asthma, cardiovascular disease, infectious disease etc.)
- Are currently pregnant;
- Are currently breast feeding;
- Have travelled across more than one time zone in the past 4 weeks or are planning to travel across more than one time zone during participation in the study;
- Have been diagnosed or are suspected to have circadian or sleep disorders (e.g. sleep apnea, narcolepsy);
- Are currently using melatonin supplements

These are the main reasons why you may not be able to participate. The study staff will discuss the eligibility criteria with you in more detail.

What are my responsibilities?

If you decide to participate in this study, you will be asked to read and sign this consent form. In total, your participation will take **two hours** during the one-month study period. The procedures you can expect at your appointments will include the following:

1. You will meet with a study staff member, at a location convenient to you, to review and sign the consent form (Table: first appointment, day 1). The interviewer will then measure your height and weight, and work with you to complete a general questionnaire which collects demographic, medical and work history data. Additionally, as you will be asked to provide urine samples during the study period, the interviewer will provide you with materials and instructions for urine sample collection. Finally, you will receive an actigraphy device and instructions for its use. This is a watch-like device that is worn on your non-dominant wrist that measures sleep quality during sleep periods and physical activity levels during wake periods.

2. On day 2, you will be asked to collect all urine produced during your day sleep, including the first void immediately after waking from sleep. Urine will be collected in a single opaque bottle which will be kept in a cooler that we provide. Prior to the start of the urine collection period, you will void your bladder and discard the urine. After waking from your day sleep, you will be asked to complete a urine sample collection form to note situations that may have compromised the sample (e.g. spillage) and a post-sleep questionnaire. A study staff member will meet with you at a location of your choosing to retrieve the urine sample and completed forms and to provide you with new urine collection materials (table: second appointment).

3. During your nightshift work starting on day 2, you will be asked to collect all urine produced, including the first void immediately after completing your nightshift. You will be asked to record the time of each urine void and note any situations that may have compromised the sample. You will be asked to fill out at a brief form to report feelings of sleepiness during the beginning, middle and end of your work period and a post-work questionnaire at the end of your work period. Finally, you will meet with a study staff member, at a location of your choosing, to return the actigraph device and to receive melatonin/placebo supplements and (table: third appointment).

4. You will be randomly assigned to consume either melatonin or placebo supplements for a 4-week period. The placebo supplements will looks identical to the melatonin supplements but will contain an inactive substance. To obtain valid results, it is important that neither you nor the interviewer know which supplement (melatonin or placebo) you are receiving. You will be asked to consume the supplements with a meal at least 1 hour before your intended day sleep bedtime and cannot drive or operate heavy machinery for at least five hours after consuming the supplement. Near the end of the 4-week period, you will be asked to repeat the Day 1, Day 2 and Day 3 procedures (table, appointments 4 to 6).

It is important to remember the following things during this study:

- Ask a study staff member if you have any questions or concerns;
- Tell a study staff member if anything about your health has changed.

Table. Time Commitment and procedures:

Timeline	Visits	Procedures	Total time of contribution
Before 4-week intervention commences	Day 1: First appointment	Obtain informed consent	60 min
		Measure height and weight and complete questionnaire	
		Receive actigraphy device and urine collection materials and review instructions	
	Day 2: Second appointment (after sleep period)	Collect urine and complete sample collection form and questionnaire	20 min
		Meet interviewer to receive new urine collection materials	
	Day 3: Third appointment (after work period)	Collect urine and complete sample collection form and questionnaire	30 min
		Report feelings of sleepiness at the beginning, middle and end of nightshift on provided form	
		Meet with interviewer to receive either melatonin or placebo supplements and instructions	
During final days of 4-week intervention period	Day 1: Fourth appointment	Receive actigraphy device and urine collection materials	10 min
	Day 2: Fifth appointment (after sleep period)	Collect urine and complete sample collection form and questionnaire	10 min
		Meet interviewer to receive new urine collection materials	
	Day 3: Sixth appointment (after work period)	Collect urine and complete sample collection form and questionnaire	20 min
		Report feelings of sleepiness at the beginning, middle and end of nightshift on provided form	
Total time			**150 min**

Will my research data be used in future research?

In addition to the current study, investigators at BC Cancer would benefit from being able to use the data and urine samples you provide for future cancer studies. All new use of your data and samples by the current study team or by other researchers must have the approval of a properly constituted Research

Ethics Board before that new research is conducted. The samples and data will be used for non profit research purposes only and will not be sold.

What are the possible harms and discomforts?

The protocol poses some risk, beyond ordinary daily activity as follows:

1. Collection of urine samples at the workplace may be embarrassing to some individuals
2. The intervention agent (melatonin) may cause sedative affects

What are the potential benefits of participating?

There will be no direct benefits of this research to you as a participant or any immediate benefits to others.

What if new information becomes available that may affect my decision to participate?

You will be advised of any new information that becomes available that may affect your willingness to remain in this study.

What happens if I decide to withdraw my consent to participate?

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw later, you have the right to request the withdrawal of your information [and/or samples] collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data [and/or samples] will not be able to be withdrawn for example where the data [and/or sample] is no longer identifiable (meaning it cannot be linked in any way back to your identity) or where the data has been merged with other data. If you would like to request the withdrawal of your data [and/or samples], please let the study staff know.

Can I be asked to leave the study?

In case of any change in your health status or travel across more than one time zone during participation in the study (criteria listed in the section: Who should not participate in this study section?), the study staff may withdraw you from the study.

How will my taking part in this study be kept confidential?

Your confidentiality will be respected. All information is collected and used in strict accordance with the *Freedom of Information and Protection of Privacy Act* and other applicable legislation. Further details about these laws are available on request to the researchers conducting this study or the UBC /BCCA Research Ethics Board. You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name and date of birth to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

As a requirement of ongoing ethical and research oversight, however, research records, and health or other source records identifying you may be inspected, in the presence of the Investigator or his or her designate, by representatives of the UBC/ BCCA Research Ethics Board for the purpose of monitoring the research.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request.

Your actigraphy data will be downloaded, processed, stored and analyzed by study personnel at BC Cancer. Your urine samples will be delivered to BC Cancer for processing and storage. Urine samples, which will be labelled with only your unique study number, will be sent to a laboratory outside Canada for analysis. By signing this form, you are consenting to the transfer of your de-identified bio-specimen to researchers located outside of Canada. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law. Data and urine samples will be kept for at least 5 years after the study result is published.

Any study related data [and/or samples], sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada.

What happens if something goes wrong?

If you become ill or physically injured as a result of participation in this study, you will be referred for appropriate treatment. No funds have been sent aside to compensate you for incidents such as lost wages, disability, or discomfort in the event of injury or illness related to the study procedures. You do not waive any of your legal rights for compensation by signing this form.

What will the study cost me?

There will be no costs for participating, nor will you benefit from participating. Your participation may increase the knowledge of factors associated with reducing cancer risk among night workers.

Remuneration

You will receive $300 after completing the study to compensate you for your time and effort.

Who do I contact if I have questions about the study during my participation?

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can contact the study staff .

Who do I contact if I have any questions or concerns about my rights as a participant?

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

“Please reference the study number H19-00780 when contacting the Complaint Line so the staff can better assist you.

When and where can you learn about the study findings?

Results of this project will be published in scientific journals and presented at meetings; never disclosing individual results; and always acknowledging the generous contribution of study information by participants. We expect study results to be available starting in 2024.

Participant Consent

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.

- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.

I will receive a signed copy of this consent form for my own records.

It may be possible to use the information and sample that you provided for this study for other studies at the BC Cancer. Please check the desired boxes below:

❑ I allow my information and sample to be used for other cancer studies at the BC Cancer
❑ I am willing to be contacted for possible participation in other cancer studies at the BC Cancer

I consent to participate in this study

_____	_____	_____
Participant's Signature	Printed name	Date

_____	_____	_____
Signature of Person Obtaining Consent	Printed Name of Person Obtaining Consent	Date

Was the subject assisted during the consent process?

☐ Yes ☐ No

If yes, please ensure that the consent form was read, explained to the subject in his or her language, and apparently understood by the subject.

_____	_____	_____	_____
Signature of Person Assisting in the Consent Process	Printed Name	Relationship to Participant	Date

If this consent process has been done in a language other than that on this written form indicate:
Language:_____

Complete the following declaration only if the participant has limited proficiency in the language in which the consent form is written and interpretation was provided as follows:

- The informed consent discussion was interpreted by an interpreter, and,
- A sight translation of this document was provided by the interpreter as directed by the research staff conducting the consent.

Interpreter declaration and signature:
By signing the consent form I attest that I provided a faithful interpretation for the discussion that took place in my presence, and provided a sight translation of this document as directed by the research staff conducting the consent.

_____	_____	_____
Signature of Interpreter	Printed Name	Date