Study Title:

Association between food/nutrient intake and sleep quality in middle aged and older population

Study ID: *NCT03554954*

Study Protocol

31 October 2019

STUDY PROTOCOL

1. Specific Aims:

The purpose of is research project is to assess the association between food/nutrient intake and pattern and sleep quality in middle-aged and older population.

Specific aim 1: Will assess the associations among dietary protein intake, blood amino acid concentrations, and sleep quality

Specific aim 2: Will assess the associations among fruit and vegetable intake, skin carotenoid status, and sleep quality

2. Introduction:

Sleep is essential to health and indexes of sleep including duration, quality, and patterning are related to the incidence of obesity, type 2 diabetes, cardiovascular disease, hypertension, and premature death. Changes in sleep patterns are a part of the aging process and as people age, they tend to have a harder time falling asleep and more trouble staying asleep than when they were younger. Certain cross-sectional studies have shown that food/nutrient intake may be associated with sleep duration, quality, and patterns. However, limited research examined the association between food/nutrient intake and indexes of sleep in middle-aged and older population.

3. Preliminary Studies:

Previously, Prof. Kim and colleagues found that the consumption of a greater proportion of energy from dietary protein while dieting may improve sleep quality in US overweight and obese adults. The results of the study suggest that the dietary protein intake may be associated with sleep quality in Singapore population.

Ref: Zhou J, **Kim JE**, Armstrong CLH, Chen N, Campbell WW. *Am J Clin Nutr*. 103(3):766-74.

4. Methodology:

This is a cross-sectional study and participants require a 1-day visit. Generally healthy middle-aged and older population will be recruited and after the phone screening, validated participants will complete the medical history questionnaire and bring on the day of visit. During the visit, participants will stay approximately 3-h to complete the testing. After complete the consent form, fasting-state blood collection and general health assessment will be conducted. Then participants will be asked to complete the questionnaires to assess sleep quality dietary intake.

On the testing day, participants will arrive at the NUHS Investigational Medicine Unit with 10-h overnight fast. After completing the consent form, fasting-state blood (20mL) will be collected by a certified phlebotomist and height, weight, waist circumference, blood pressure, and skin carotenoid status will be measured by trained research staffs. Once participants complete the health-related assessment, snack will be provided and trained research staffs will work with participants to complete

the questionnaires including Pittsburgh Sleep Quality Index, lifestyle questionnaire, 3-day food record, and food frequency questionnaire to assess sleep quality dietary intake. The collected blood samples will be stored in -80°C, until they are ready to be analyzed.

5. Subject Recruitment:

This study will recruit 130 subjects from NUS and around Singapore over a period of 1.5 year. About 103-130 subjects will be involved in this study. The following are the criteria of subjects that will be recruited for the study.

Inclusion criteria

1. Ability to give an informed consent
2. Age ≥ 50 years
3. Not taking dietary supplements which may impact the out of interests (i.e. dietary protein and vitamin supplements, and others)
4. Did not have significant dietary changes for the past 1 year (i.e. weight loss, vegetarian diet, and others)
5. Having sufficient venous access to allow the blood collection
6. Willing to follow the study procedures

Exclusion criteria

1. Unable to give an informed consent
2. Age < 50 years
3. Taking dietary supplements which may impact the out of interests (i.e. dietary protein and vitamin supplements)
4. Had significant dietary changes for the past 1 year
5. Not having sufficient venous access to allow the blood collection
6. Unwilling to follow the study procedures

INFORMED CONSENT FORM

1. Study Information

Protocol Title:

Association between food/nutrient intake and sleep quality in middle aged and older population

Principal Investigator & Contact Details:

Principal Investigator

Dr. Khoo Chin Meng
National University Hospital (S) Pte Ltd
Department of Endocrinology
5 Lower Kent Ridge Road
Singapore 119074

Email: mdckcm@nus.edu.sg

Site Investigator (NUS)

Dr. Gregory Chung Tsing Chan
University Health Centre
20 Lower Kent Ridge Rd.
National University of Singapore
Singapore 119080

Email: gregchan@nus.edu.sg

Co-Investigator (NUS)

Assistant Professor Kim Jung Eun
Food Science & Technology Programme
c/o Department of Chemistry
Block S14 level 6, S14-06-01
3 Science Drive 3
Lower Kent Ridge Road
Singapore 117543

Email: chmkje@nus.edu.sg

Study Sponsor:

NUS

Sleep is essential to health. Quality of sleep, measure through indexes of sleep, is related to the incidence of obesity, type 2 diabetes, cardiovascular disease, hypertension, and premature death. Sleep pattern changes as people age. They tend to have a harder time falling asleep and more trouble staying asleep than when they were younger. Studies have shown that food/nutrient intake may be associated with sleep duration, quality, and patterns. Singapore's population is aging rapidly and improving their indexes of sleep may result in their health promotion.

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Nevertheless, before you take part in this research study, the study will be explained to you and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign this informed consent form. You will be given a copy of this consent form to take home with you.

You are invited because we want to study the effect of nutrition on sleep quality. This study is carried out to find out the association between the food and nutrient intake and sleep quality in middle-aged and older adults. This study will recruit *130* subjects from *NUS and around Singapore* over a period of *1.5 year.* About *103-130* subjects will be involved in this study.

3. What procedures will be followed in this study

If you take part in this study, you will be screened via phone according to the inclusion and exclusion criteria. Once your eligibility for the study is validated, you will send a medical history questionnaire by **mail** which will need to be completed and brought on the day of the visit. You will also be required to fast from 10pm the night before or from approximately 10-12hr prior to the study visit. During the visit the following procedures will be done:

1. Sign the study consent form
2. Fasting-state blood collection
3. Anthropometric measurements: height, weight, waist circumference
4. Blood pressure measurement
5. Body composition measurement by measuring body impedance/electrical resistance.
6. Skin scan *by using a visible light scan (Raman Spectroscopy)* to measure the level of carotenoid storage, indicator of fruits and vegetable intakes in the skin
7. Dietary assessment via 24-hr recall and food frequency questionnaires *(two additional 24-hr dietary recall will be required **after the study visit** and sent back to our study team by either email or mail. Each 24-hr recall will take approximately 10 minutes to complete)*

   Participants will be provided with a pre-paid envelope if they choose to send their two additional 24-hr dietary recall by mail.
8. Sleep quality assessment via Pittsburgh Sleep Quality Index questionnaire and sleep evaluation questionnaire
9. Perceived stress evaluation questionnaire

In total, *20mL (4 teaspoons)* of blood will be taken as part of this study.

These procedures will be performed at the following address:
Investigational Medical Unit (IMU)
MD6 (Centre for Translational Medicine), level 7
14 Medical Drive, Singapore 117599

NUS Occupational Health Clinic
20 Lower Kent Ridge Rd, Singapore 119080

NUS Department of Chemistry
6 Science Drive 2, Block 16, Singapore 117546

With your consent, your research data and blood samples obtained during the course of this study will be stored for a minimum of 10 years in freezers owned by the research group in NUS, for use in this research study and general nutritional research. When the 10-year period ends, your blood sample and research data will be destroyed

During the duration of the storage, your collected blood samples will **NOT**:

1. Be used for future human biomedical research involving human-animal combinations
2. Transferred outside of Singapore

To ensure your privacy and confidentiality, your collected blood samples and research data will be coded and no subject identifiers will be attached to them Only the PI, Co-PI and assigned research staff of this study will have access to these codes identifying these research materials. Research data and biological samples will be used only for the current or future research.

There will not be any incidental findings arising in this research. “Incidental findings” are findings that have potential health or reproductive importance to research participants like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study. These findings may affect your current or future life and/or health insurance coverage

However, there is a possibility that tests conducted in future research might unintentionally uncover new information about your health condition. These are considered as “incidental findings”. You will be asked to indicate whether you wish to be re-identified and notified in the case of a clinically significant incidental finding that is related to you.

If you agree to be re-identified and notified, you will be advised to consult with a healthcare professional regarding this incidental finding. For this purpose, please inform the Principal Investigator or any of the study contact persons listed in this document whenever there are changes in your contact details. You may wish to do more tests and seek advice to confirm this incidental finding.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by the study team. You should be prepared to visit the hospital *once* and undergo all the procedures that are outlined above.

5. What Is Not Standard Care or is Experimental in This Study

The study is being conducted because *the association of nutrition and sleep quality is* not yet fully understood We hope that your participation will help us to assess the how nutrition may have the potential to improve a person's sleep quality

These procedure(s) are only being performed for the purposes of the research, and are not part of your routine care.

6. Possible Risks and Side Effects

As this is a cross-sectional study, no actual experimental procedure will be performed other than non-invasive measurements, filling out of questionnaires and blood collection. Although there may be potential human risks, they are minimal and the research group members will consistently pay attention to assure your safety. The risks of drawing blood include slight pain and bruising. Some people may also experience dizziness when drawing blood which will usually go away when the person lies down. In the unlikely event that you are injured, first aid and proper health treatment will be administered. In addition, the Raman Spectroscopy procedure used to scan the skin carotenoid status pose minimal risk as the scan is non-invasive and done using visible light radiation for a short period of time (~30sec). Impedance measurements used for body composition measurement involves the application of alternating currents on the human body. As this is a commonly used method in health clinics and gyms to measure body composition and is non-invasive, it poses minimal risk.

7. Possible Benefits from Participating in the Study

There is no known benefit from participation in this study. However, your participation in this study may be used to design future research work targeted at improving the sleep quality for people aged 50 years and older

8.. Costs & Payments if Participating in the Study

You will be reimbursed $50 for your time, inconvenience and transportation costs by participating in this study. The participants will also be provided with a pre-paid envelope if they choose to send their two additional 24-hr dietary recall by mail. Research procedure will be performed at no cost to you as a participant.

9. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to discontinue your participation in this study, you can notify us by calling **(65) 6772 6174 and email mdckcm@nus.edu.sg**, and we will, according to your request, terminate your further participation and/or destroy any data that has not been analyzed. However, you retain your right to ask the Principal Investigator to discard or destroy any remaining samples if the biological sample(s) is individually-identifiable and has not been used for the research/future research or it has been used for research but it is practicable to discontinue further use of the biological sample(s) for the research/future research. Withdrawal of participation in the study will prevent your collected information from contributing to further research and analysis, but it will not be possible to remove your data from analyses that has already been done. Your blood samples for this study will be considered to be gifted to NUS and will not be returned to you, however you may request us to destroy any unused samples that could identify you. You will

also not have any right or claim to any share in the commercial gain derived from the research (if any).

Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you *(or your legally acceptable representative, if relevant*) will be informed in a timely manner by the Principal Investigator or his/her representative.

10. Compensation for Injury

In the unlikely event that you are physically injured during the process of this study, despite following the procedure carefully designed for this research, National University of Singapore (NUS) will pay the medical expenses for the treatment of the injury. By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence

11. Confidentiality of Study and Medical Records

The records of this study will be kept strictly confidential. Only the PI and authorized personnel will have immediate access to your identifiable information (e.g. names, contact, information, IC). Identifiable information will never be used in publication or presentation and all your identifiable health information and research data will be coded (i.e. only identified with a code number).

All collected data will be kept in accordance to the University's Research Data Management Policy. Research data used in the publication will be kept for a minimum of 10 years before being discarded.

However, NUH, NUS and NHG Domain-Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public.

Any biological samples and/or information containing your "Personal Data" that is collected for the purposes described in this Informed Consent Form will not be transferred out of Singapore.

"Personal Data" means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organization has or likely to have access. This includes medical conditions, medications, investigations and treatment history.

Research arising in the future, based on this Personal Data, will be subject to review by the relevant institutional review board.

Data collected and entered into the Case Report Forms are the property of NUS. In the event of any publication regarding this study, your identity will remain confidential.

12. Who to Contact if You Have Questions

If you have questions about this research study and/or in the case of any injuries during the course of this study, you may contact the following Principal Investigators:

Principal Investigator

Dr. Khoo Chin Meng
National University Hospital (S) Pte Ltd
Department of Endocrinology
5 Lower Kent Ridge Road
Singapore 119074

Email: chin_meng_khoo@nuhs.edu.sg/ mdckcm@nus.edu.sg

Site Investigator (NUS)

Dr. Gregory Chung Tsing Chan
University Health Centre
20 Lower Kent Ridge Rd.
National University of Singapore
Singapore 119080

Email: gregchan@nus.edu.sg

Co- Investigator (NUS)

Assistant Professor Kim Jung Eun
Food Science & Technology Programme
c/o Department of Chemistry
Block S14 level 6, S14-06-01
3 Science Drive 3
Lower Kent Ridge Road
Singapore 117543

Email: chmkje@nus.edu.sg

The study has been reviewed by the NHG Domain Specific Review Board (the central ethics committee) for ethics approval.

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain Specific Review Board Secretariat at 6471-3266. You can also find more information about the NHG Domain Specific Review Board at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

13. Consent to be contacted for future research (Optional)

You are being asked for permission to be contacted in the future for participation in research studies that you may be suitable for. If you agree to be contacted, your information and contact details will be entered and stored in a secured database in NUS. Your information and contact details will not be released to any parties outside NUS without your permission. When investigators from NUS identify you to be suitable for a particular research study, the investigators or authorised personnel from NUS will contact you to inform you about the research study. Your decision to be contacted for future research studies is completely voluntary and separate from your decision to participate in this study. Your decision will not affect your medical care or any benefits to which you are entitled. You may change your mind at any time by contacting ***Dr. Khoo Chin Meng at*** **(65) 6772 6174 and email mdckcm@nus.edu.sg**

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Principal Investigator & Contact Details:

Principal Investigator
Dr. Khoo Chin Meng
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Department of Endocrinology
5 Lower Kent Ridge Road
Singapore 119074

Email: chin_meng_khoo@nuhs.edu.sg/ mdckcm@nus.edu.sg

Site Investigator (NUS)
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University Health Centre
20 Lower Kent Ridge Rd.
National University of Singapore
Singapore 119080

Email: gregchan@nus.edu.sg

Co-Investigator
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Food Science & Technology Programme
c/o Department of Chemistry
Block S14 level 6, S14-06-01
3 Science Drive 3
Lower Kent Ridge Road
Singapore 117543

Phone: (65) 6516 1136
Email: chmkje@nus.edu.sg

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction.

By participating in this research study, I confirm that I have read, understood and consent to the NUS Data Protection Policy.

I hereby acknowledge that:

1. My signature is acknowledgement that I have agreed to take part in the above research
2. I have received a study information sheet that explains the use of my blood and data in this research. I understand its contents and agreed to donate my blood and data for the purpose of this research.
3. I can withdraw from the study at any point of time by informing the Principal Investigator and all my blood/tissue/data will be discarded if they have not been anonymized
4. I will not have any financial benefits from participating in this study
5. For the biological samples collected, please select any application options:

☐ I **agree** to donate my coded biological samples collected for this research to be used in future research OR

☐ I **agree** to donate my biological samples collected for this research to be used in future research. However, I would like all identifying information removed from my biological samples so that no one can link the sample to me OR

☐ I **agree** to donate my biological samples collected for this research to be used in future research which may include testing and development by commercial firms. However, I would like all identifying information removed from my biological samples so that no one can link the sample to me OR

☐ I **do not agree** consent to donate my biological samples collected for this research to be used in future research and would like to have my left-over biological samples destroyed after the completion of this research

☐ I consent to have the coded data made available for future research

6. Consent to be re-identified and notified in the case of an incidental finding.

☐ I **agree** to be re-identified and notified in the case of an incidental finding from future research. In the event that I cannot be reached, please contact my next of kin.

Name of next-of-kin: _____

Contact: _____

☐ I **do not agree** to be re-identified and notified in the case of an incidental finding from future research

7. Consent to be contacted for future research

☐ I **agree** to be contacted for future research that I may be eligible for

Phone: _____

Mail: _____

Email: _____

Others: _____

☐ I **do not agree** to be contacted for future research

_____	_____	_____
Name of Participant	Signature	Date

Witness Statement

I, the undersigned, certify that:

- I am 21 years of age or older
- To the best of my knowledge, the participant/ the participant's legally acceptable representative signing this informed consent form has the study fully explained in a language understood by him/ her and clearly understands the nature, risks and benefits of his/ her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant/ the participant's legally acceptable representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

_____	_____	_____
Name of Impartial Witness	Signature	Date

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

_____	_____	_____
Name of Investigator / Person administering consent	Signature	Date