PARTICIPANT INFORMED CONSENT FORM

Study Title: Dietary Supplements to Reduce Symptom Severity and Duration for People with SARS-CoV-2: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

OHSN REB: 20210072-01H
CCNM REB: CCNMREB036.Seely.Wilson

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Sponsor: Ottawa Hospital Research Institute

Funding Agency: Ottawa Integrative Cancer Centre Foundation and private support from Mavis and Martin Sacher

Emergency Contact Number: Please dial 911 or proceed to the nearest emergency department

Non-emergency contact numbers are noted at the end of this document under the section heading "contacts."

Introduction

You are being asked to participate in the above clinical trial (a type of study that involves research). You are invited to participate in the study because you have been diagnosed with SARS-CoV-2, also known as Coronavirus 2019 or COVID-19, in the Ottawa community. This consent form will help you make an informed choice about your participation. Please read this form carefully before you decide if you would like to participate. Ask the study doctor and study team as many questions as you like. We encourage you to discuss your options with family, friends or your healthcare team. The study staff will tell you about the study timelines for making your decision.

Participation in this study is completely voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you might receive outside the study.

Do the investigators have any conflicts of interest?

Dr. Dugald Seely, the Principal Investigator on this trial, is the Co-Founder & CEO of the Centre for Health Innovation (CHI), and the Executive Director of Research & Clinical Epidemiology for the Canadian College of Naturopathic Medicine (CCNM). Although CCNM will be paying the CHI and the Ottawa Hospital Research Institute (OHRI) to conduct the study, the Principal Investigators and these institutions do not otherwise benefit financially from the study. There are no other conflicts of interest to declare related to this study.

Vitazan Herbs and Supplements Inc. is the supplier of product for this study and will be providing it to the research staff free of charge. This study is also receiving funding from an outside source. The suppliers or funders did not have any role in the design of the study, nor will they play a role in the collection, analysis, or interpretation of the data, the writing of the final manuscript, or the decision to submit the manuscript for publication.

What is the background information for this study?

The purpose of this study is to determine the effects of specific dietary supplements for people who have SARS-CoV-2 (COVID-19) who are not in the hospital (staying at home during recovery). The dietary supplements being studied are vitamin D, vitamin C, vitamin K2 and zinc.

More specifically, this trial will study the effects of these supplements on your overall health, the seriousness of your COVID-19 symptoms, and length or your symptoms. We will also study to see if these supplements change the need for hospital admissions and medical care.

Currently, there are no approved treatments for COVID-19 in the community. Health Canada, the regulatory body that oversees the use of drugs and natural health products in Canada, has not approved the sale or use of vitamin D, vitamin K2, vitamin C, or zinc for the treatment of COVID-19; however, Health Canada has allowed all of these products to be used in this study.

Why is this study being done?

The purpose of this study is to determine whether or not taking these dietary supplements will improve the overall health and decrease symptom severity and duration of people diagnosed with COVID-19. To do this, half of the participants will receive these supplements and the other half will receive a placebo. A placebo is a harmless pill that looks and tastes like the supplements but does not contain any active ingredients (in this case vitamin C, vitamin D, vitamin K2 and zinc will be absent). The placebo is not intended to have any effect on your symptoms and is used to make the study more reliable.

What other choices are there?

You do not have to take part in this study. There may be other clinical trials for COVID-19 that you are eligible for. If you choose not to participate, you will not be denied any treatments that may be given to you

by your healthcare providers. We recommend you continue to follow the advice given to you by Ottawa Public Health and The Ottawa Hospital

How many people will take part in this study?

We hope to enroll 200 people from the Ottawa community in this study over the next 4 months. The trial should take 7 months to complete and the complete results should be known in 9-12 months.

What will happen during this study?

Assignment to a group

If you decide to participate in this study, you will be "randomized" to a group that receives either the dietary supplements or a placebo. Randomization means that you are put into a group by chance (like flipping a coin). You will have an equal (50%) chance of being placed in either group. Neither you, the study staff, nor the study doctors can choose which group you will be put in. This is a double-blind study, meaning you, the study staff, study doctors, and your usual healthcare providers will not know which group you are in. Your group assignment can be identified if medically necessary.

Study Intervention

Group 1 (treatment group)

If you are randomized to the treatment group, the interventions will include three products: one bottle with capsules containing vitamin C and zinc, one bottle with one capsule containing an initial dose of vitamin D, and one bottle with liquid drops containing a mix of vitamin D and vitamin K2.

Group 2 (control group)

If you are randomized to the placebo group, you will receive similar-looking products to the treatment group, but the capsules and liquid drops will not contain the supplements.

The instructions for taking the study products are the same regardless of what group you are placed in and are described in the section "Treatments" below.

What are the study procedures?

Throughout the study, you will be asked to take the required pills and liquid drops, complete questionnaires, and be available for six phone or online check-ins. If you choose to participate, you will receive an information sheet with all the information below.

Treatments

Participation in this study will involve you taking dietary supplements or a placebo each day for 21 days at your own home. Instructions for when to take each supplement are as follows:

Vitamin D (or placebo): One capsule (50,000 units) once on day 1 (this is called a "loading dose," a larger dose that you take only once)

Vitamin D + Vitamin K (or placebo): 4 drops twice daily at breakfast and dinner for 21 days. Each day you will take 240 mcg vitamin K and 1000 units Vitamin D (or placebo).

Vitamin C + Zinc (or placebo): 3 capsules 3 times daily at breakfast, lunch, and dinner for 21 days. Each day you will take 6 g vitamin C and 75 mg zinc (or placebo).

The Vitamin D and Vitamin C + Zinc capsule placebos are made of a compound called "microcrystalline cellulose," and the Vitamin D + Vitamin K liquid placebo is made of "medium chain triglyceride (MCT) oil." Microcrystalline cellulose, or "cellulose," is a common non-medicinal ingredient added to most supplements and prescription drugs. MCT oil is the non-medicinal ingredient in the Vitamin D + Vitamin K treatment.

You will be asked to *not throw out any study product at the end of the 21-day period*. The product must be disposed of properly. You may do this by returning the study product to the CHI after the 21 day period or by taking them to your local pharmacy and asking the pharmacist to destroy them. More detailed instructions will be given to you by the research staff when it is time to dispose of the products.

Questionnaires

If you choose to participate in the study, you will be asked to fill in short questionnaires at different time points during the 12 weeks that you are enrolled in the study. Before starting the study products, you will fill in a demographics questionnaire that asks about your height, weight, age, sex, race, vaccination status, and health conditions. The next questionnaire set asks about the symptoms you are experiencing and your overall health. This will be filled out each day you are taking the study products (i.e., once daily for 21 days). The final questionnaire asks about five dimensions of your health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. This questionnaire will be filled in before you start any study products, as well as once during weeks 1, 2, 3, 4, 8, and 12 of the study. Each of these questionnaire sets should take no longer than five minutes to complete.

Questionnaires can be completed on paper or through the internet using software called Research Electronic Data Capture (REDCap). REDCap is the software we will be using to collect data for the study. If you choose to answer questionnaires through REDCap, you will receive an email with a link to each questionnaire. This process will be explained in detail by the research staff if you choose this option.

Phone Check Ins

As part of the study, a member of the research team will contact you once during weeks 1, 2, 3, 4, 8, and 12 to ask you about any side effects or concerns and ask you a few questions. Each check-in will take between 5-15 minutes. The check-ins will be done by phone. They will be scheduled ahead of time.

Taking Your Temperature

You will be asked to take and write down your oral temperature on the daily questionnaire each day for 21 days. You will be provided with an oral (by mouth) thermometer and detailed instructions on how to use it.

Following Public Health Procedures

Participation in this study does not change any public health directives and we ask that you follow all instructions given to you by Ottawa Public Health (or another public health agency) and The Ottawa Hospital. Any questions regarding public health measures should be directed to Ottawa Public Health or your primary healthcare provider.

Hospitalization

If you are hospitalized at any point during the study, you will stop all study activities. This means you will not take the study product, answer questionnaires, or participate in phone check-ins while you are in the hospital. Once you are back home, you may resume all study procedures.

What are the responsibilities as a study participant?

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

- Talk to the study staff if you have any questions or concerns.
- Tell the study staff if anything about your health has changed.
- Tell the study staff about all prescription and non-prescription medications, including natural health products, you are taking while taking part in the study
- Follow the product intervention instructions provided to you.
- Do your best to participate in all phone call check-ins from research staff.
- Complete all of the questionnaires to the best of your ability.
- Call the study doctor or one of the study staff if you experience any side effects, even if you are unsure whether they have anything to do with this study.

How long will participants be in the study?

Your participation in the study will last 12 weeks in total. You will only take the study product for the first 21 days.

Can participants choose to leave the study?

You can choose to end your participation in this research (called withdrawal) at any time without providing a reason. This decision will not affect your future care at the hospital or the CHI. If you decide to withdraw from the study, please note the following:

- If you decide to stop your study intervention you should contact the study doctor or the study team first. They will discuss the related issues or possible safety concerns for you.
- If you choose not to participate, a final visit(s) may need to be completed to ensure your safety and well-being.
- If you withdraw your consent, the study team will no longer collect your personal health information for research purposes, unless it is needed for review of safety. Information that was recorded before you withdrew will be used for the purposes of the study, but no information will be collected or sent to the sponsors after you withdraw your permission.

If you wish to withdraw your consent, the research team will ask if it is OK to continue to collect information from your medical chart and to contact you for follow-up if necessary. You can choose to accept or decline both of these requests. If you accept, you will still be considered a study participant but will not have to fill in any more questionnaires or participate in any check-ins.

Can participation in this study end early?

The study doctor will stop your participation in this study early, without your consent, for reasons such as:

- The study doctor feels it is in your best interest
- The sponsor cancels the study
- Regulatory authorities (such as Health Canada) or research ethics boards withdraw permission for this study to continue
- You do not follow the study staff's instructions

What are the risks or harms of participating in this study?

If you are randomized to the dietary supplement group you will be required to take vitamin C, vitamin D, vitamin K2 and zinc each day. The risks we know about the short-term consumption of each supplement are listed below; however, there could be additional risks we do not know about when taking these study products. Please note that there are more risks associated with longer-term consumption of some of these products. If you wish to continue supplementation after the end of the study, please discuss this with your family doctor, naturopathic doctor, or pharmacist.

Vitamin D

- **Rare**: nausea, constipation, upset stomach, high blood calcium levels

Vitamin C

- **Rare**: stomach upset, nausea, headache, apparent decrease in blood uric acid levels
- **Common but not serious**: mild diarrhea

Vitamin K2

- **Rare:** stomach upset

Zinc

- **Rare:** low blood copper levels, vomiting
- **Common but not serious:** stomach upset, indigestion, nausea*

* *These side-effects become rare when zinc is taken with food*

Certain medications and conditions are contraindicated with the study products, meaning they cannot be taken at the same. Please inform the study team if there are any changes to the medications or natural health products you are taking. Please stop taking the study product and immediately inform the study staff if the following happens:

- You are placed on a vitamin K-antagonist anticoagulant (i.e., a blood thinner. E.g., Warfarin)
- You are placed on cephalexin or tetracycline antibiotics (e.g., tetracycline, doxycycline)
- You are diagnosed with kidney stones, hypercalcemia (high blood calcium), or hypervitaminosis D (high blood vitamin D)

What are the benefits of participating in this study?

If you agree to take part in this study, the study products may or may not be of direct benefit to you. Your participation may help the researchers to determine if there are beneficial effects of a combination dietary supplement involving these ingredients for people with COVID-19. This may benefit people who are diagnosed in the future.

How will participant information be kept confidential?

If you decide to participate in this study, the investigator(s) and study staff will look at your personal health information held at The Ottawa Hospital and collect only the information they need for this study.

"Personal health information" is health information about you that could identify you because it includes information such as your name, address, telephone number, date of birth, new and existing medical records, or the types, dates and results of various tests and procedures. Records identifying you will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical and study records at The Ottawa Hospital or the Centre for Health Innovation where these records are held to check that the information collected for the study is correct and follows proper laws and guidelines:

- The Ottawa Hospital Research Institute, the sponsor of the study
- Researchers at the CHI or TOH who are involved with the study,
- The Ottawa Health Science Network Research Ethics Board and Canadian College of Naturopathic Medicine Research Ethics Board, who oversee the ethical conduct of this study,

- Health Canada, as they oversee the use of therapeutic drugs and natural health products in Canada.

Study staff from the Centre for Health Innovation (CHI) will receive and retain your name, telephone number, and email address in order to conduct the phone check-ins and communicate with you at other time points if necessary. A Master List provides the link between your identifying information and the study number. This list will only be available to Dr. Dugald Seely and his staff at the CHI and will not leave these sites. The Master List and coded study records will be password protected and stored on a secure server with limited access. All information collected during your participation in this study will be identified with a unique study number (for example participant # 001) and will not contain information that identifies you. Documents leaving the CHI will only contain the coded study number.

Your contact information, including name and address, will also be sent to Vitazan Professional in order to facilitate the shipment of study product and study materials.

Communication via e-mail is not absolutely secure. We do not recommend that you communicate sensitive personal information via e-mail.

You will not be identified in any publications or presentations resulting from this study. Research records will be kept for 25 years, as required by Health Canada. At the end of the storage time, all paper records will be shredded, and all electronic records will be securely deleted. Your de-identified data from this study may be used for other research purposes. If your study data is shared with other researchers, information that links your study data directly to you will not be shared.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

Will family doctors or healthcare providers know who is participating in this study?

The study staff will not inform your family doctor or other healthcare providers about your participation in the study nor the interventions you are receiving unless you specifically request that they do so. You are free to inform your family doctor or other healthcare providers yourself with regards to your progression through the study.

Will information about this study be available online?

A description of this clinical trial will be available on http://clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. This research study can be found on the above listed website by using the clinical trial registration number NCT04780061.

What is the cost to participants?

There is no cost to participating. All study materials and interventions will be provided to you free of charge.

Are study participants paid to be in this study?

You will not be paid for participation in this study. The products listed in the study protocol will be provided to you free of charge if you are participating in the study. Any shipping or postage costs you might incur will be reimbursed to you by the study team.

In the event of a study-related injury or illness, you will be provided with appropriate medical treatment and care. Financial compensation for lost wages, disability or discomfort due to an injury or illness is not available through this research.

What are the rights of participants in a research study?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. You have a right to be informed of the results of this study once the entire study is complete. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor, sponsor, or involved institutions for compensation, nor does this form relieve the study doctor, sponsor, or their agents of their legal and professional responsibilities. You will be given a copy of this informed consent form prior to participating in this study.

Whom do participants contact for questions?

If you have any questions about this study, or if you feel that you have experienced a study-related injury or illness, you can talk to one of the study doctors. Those people are:

Centre for Health Innovation
Dugald Seely, ND, MSc
429 MacLaren Street, Ottawa ON K2P 0M7
613-792-1222 ext. 2
dseely@thechi.ca

Ottawa Hospital Research Institute
Kumanan Wilson, MD, MSc, FRCPC
1053 Carling Avenue, Ottawa, ON K1Y 4E9
613-737-8899 ext. 17921
kwilson@toh.ca

You may also contact the study staff at 613-792-1222 ext. 1.

If you have any questions about your rights as a study participant or about ethical issues related to this study, you may contact the Ottawa Health Sciences Network Research Ethics Board Chairperson at 613-798-5555, extension 16719 or the Canadian College of Naturopathic Medicine Research Ethics Board Chairperson at REBChair@ccnm.edu.

Study Title: Dietary Supplements to Reduce Symptom Severity and Duration for people diagnosed with SARS-CoV-2: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

Signatures

- I understand I am being asked to participate in a research study about the effects of dietary supplements on people diagnosed with COVID-19.
- I have read, or someone has read to me, all pages of this consent form and all my questions were answered to my satisfaction.
- I understand that I can withdraw my consent from this study at any time for any reason.
- I voluntarily agree to participate in this study.
- I will be given a copy of this consent form for my records.

_____	_____	_____
Participant Signature	Printed Name	Date

Investigator or Delegate Statement

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

_____	_____	_____
Signature of Person conducting consent and Role	Printed Name	Date

Study Title: Dietary Supplements to Reduce Symptom Severity and Duration for people diagnosed with SARS-CoV-2: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

Participant Assistance

Complete the following declaration only if the participant is unable to read:

☐ The consent form was read to the participant and the person signing below attests that the study was accurately explained to, and apparently understood by, and consent was freely given by the participant.

Signature of Impartial Witness	Printed Name	Date

Relationship to Participant

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:

☐ The person signing below acted as an interpreter, and attests that this study as set out in the consent form is accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and in additional discussion arising from this process.

Signature of Interpreter	Printed Name	Date