STUDY INFORMATION SHEET

A randomised, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of LactoSpore® (*Heyndrickxia coagulans* MTCC 5856) in peri-menopausal women.

Principal Investigator:	**Dr Adrian Lopresti**
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Background

There is preliminary research to suggest probiotics may help reduce menopausal symptoms. Therefore, the aim of this study is to investigate the effects of a probiotic called LactoSpore® on hot flushes, night sweats and other menopausal-related symptoms (e.g., changes in mood, sleep, energy, libido, cognition, weight, digestion, or joint pain) in perimenopausal women experiencing, on average, at least 3 hot flushes/ night sweats a day. Furthermore, to help understand how LactoSpore® works, changes in blood markers that may influence menopausal symptoms will be examined over time.

This study will be conducted by Dr Adrian Lopresti and Dr Stephen Smith (Clinical Research Australia).

Information about the funding source and declaration of interests

This study is funded by Sabinsa Corporation, the company that produces LactoSpore®. However, this study is being independently managed by Clinical Research Australia (CRA) without external influence from the study sponsor.

What does participation involve? **(see study flow chart on page 3)**

This study will comprise several steps as outlined below:

Step 1: Completion of initial online screening

This questionnaire takes approximately 10 minutes to complete. It provides us with information relating to the eligibility criteria. If, based on the screening questionnaire results, you are assessed as 'likely' eligible, you will be contacted for a phone interview. Ineligible volunteers will be informed by email that they do not fulfil the eligibility criteria.

Step 2: Phone Interview for an assessment of eligibility

If you are potentially eligible to participate in the study, you will be interviewed by a researcher. The interview will be conducted over the phone (approx. 20 minutes). The purpose of this interview is to obtain relevant background information (e.g., medication use, current treatments, menopausal symptoms, general health, etc.) and assess other relevant eligibility criteria. We will also provide you with further details about the study. If you meet our eligibility criteria and agree to participate in the study, you will proceed to the next step.

Step 3: VISIT 1 (Day -7): Face-to-face assessment (total time approx. 45 mins)

The face-to-face assessment will comprise the following:

a. Measurement of vital signs and anatomical measurements: A researcher will measure your sitting blood pressure, height, weight, and temperature.

b. Completion of self-report questionnaires: You will complete a series of questionnaires.

c. Provision of a 12-week supply of the study capsules: You will be given one bottle containing capsules with either LactoSpore® or a placebo.

d. Provision of Gift Voucher. You will be given a $30 gift voucher.

Step 4: DAY -7: Collect a blood sample

Immediately after your visit, a blood sample will need to be collected. This will be collected at a Western Diagnostics Pathology (WDP) clinic located near our office. This blood sample will be used to assess changes in your sex hormones, thyroid function, blood lipids, blood sugar balance, liver function, renal function and blood count.

Step 5: DAYS -6 to 0: 7-day baseline record of your hot flushes and night sweats

You will receive notifications on your phone for 7 days, where you will record your hot flashes (completed in the evening) and night sweats (completed in the morning upon waking).

Step 6: DAYS 1 TO 84: Start taking your capsules

In this study, we will be using a randomised, double-blind, placebo-controlled design. This means that half of the participants will be placed on placebo capsules and the other half on capsules containing LactoSpore®.

Neither you nor the investigator will know which group you have been placed in. This random allocation is important for us to assess the true effects of the probiotic supplement.

You will be required to take **ONE** capsule, approximately 30 minutes before breakfast. If you don't have breakfast, you can take it with your first meal of the day (e.g., lunch). It is extremely important that you take these capsules every day.

* Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain maltodextrin (a plant starch).

Step 7: DAYS 22 to 28: 7-day record of your hot flushes and night sweats

You will receive notifications on your phone for 7 days, where you will record your hot flashes (completed in the evening) and night sweats (completed in the morning upon waking).

Step 8: DAY 28: questionnaires (online)

You will complete questionnaires online, which will take approximately 10 to 15 minutes

Step 9: DAYS 50 to 56: 7-day record of your hot flushes and night sweats

You will receive notifications on your phone for 7 days, where you will record your hot flashes (completed in the evening) and night sweats (completed in the morning upon waking).

Step 10: DAY 56: questionnaires (online)

You will complete questionnaires online, which will take approximately 10 to 15 minutes

Step 11: DAY 60 Onwards: Blood collection

After you have been taking your capsules for at least 60 days (we will notify you when this milestone is reached), you will need to have your second blood sample collected.

1. This blood collection should occur 1 to 7 days after you have experienced bleeding
2. If your bleeding is light or stops and starts frequently, then you will get your blood sample collected as soon as possible after spotting/ bleeding has occurred.
3. If you do not have a period before your second visit, then you will simply get your blood collected at visit 2.

You will complete questionnaires online, which will take approximately 10 to 15 minutes

Step 12: DAYS 78 to 84: 7-day record of your hot flushes and night sweats

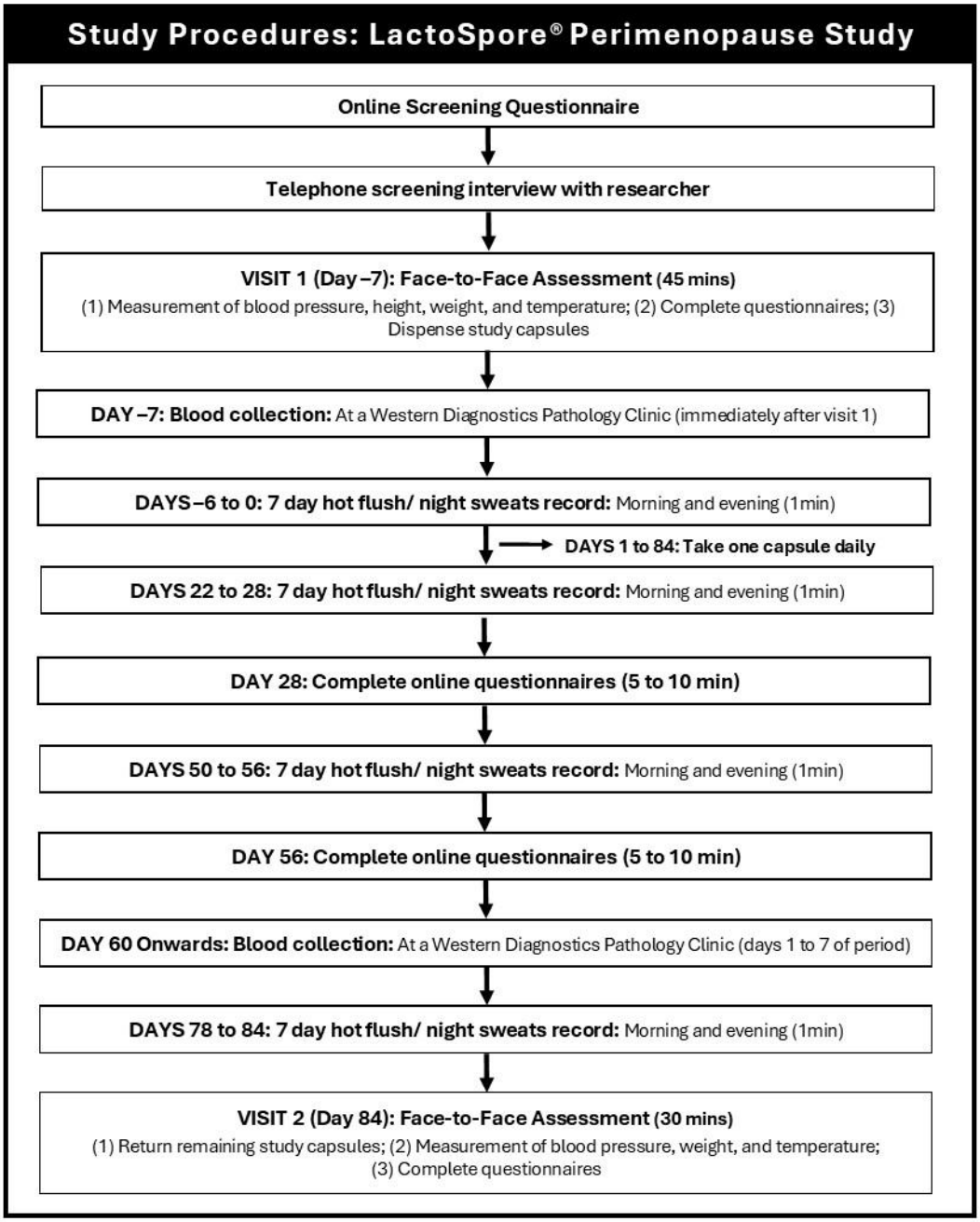
You will receive notifications on your phone for 7 days, where you will record your hot flashes (completed in the evening) and night sweats (completed in the morning upon waking).

Step 12: VISIT 2 (Day 84): Face-to-face assessment (total time approx. 30 mins)

The face-to-face assessment is similar to visit 1 and will comprise the following:

a. You will need to return your study bottles/ capsules
b. Measurement of vital signs and anatomical measurements: A researcher will measure your sitting blood pressure, weight, and temperature.
c. Completion of self-report questionnaires: You will complete several questionnaires.

d. Provision of Gift Voucher. You will be given a $140 gift voucher



Compensation for participating in this study

To compensate participants for travel costs and time associated with participating in this study, you will receive a $30 gift voucher at visit 1 and a $140 gift voucher at visit 2.

At the end of the study, volunteers in the placebo group will also be offered a complimentary 12-week supply of LactoSpore® to try.

Criteria for inclusion/ exclusion in this study

To be included in the study, the following inclusion criteria must be met:

1. You are a female aged 40 to 55 years
2. For at least 3 months, you have experienced changes in your menstrual cycle (e.g., changes in bleeding days, heaviness of bleeding, or days between menses)
3. You are experiencing, on average, at least 3 hot flushes and/or night sweats a day
4. You have been a non-smoker for at least 12 months

5. You have a body mass index between 18 and 35 kg/m^2
6. You have no plan to commence new treatments over the study period.
7. You understand, are willing and able to comply with all study procedures.
8. You are willing to provide a personally signed and dated informed consent form detailing all pertinent aspects of the trial.

If any of the exclusion criteria below are met, you will not be suitable for participation in this study:

1. Your menopause has been induced through surgery such as bilateral oophorectomy or salpingo-oophorectomy, chemotherapy, radiation, or drugs.
2. You have had a partial or total hysterectomy
3. You are currently receiving any treatment for your menopausal symptoms
4. You are suffering from a recently diagnosed or unmanaged medical condition, including but not limited to diabetes, hypertension, cardiovascular disease, gastrointestinal disease, biliary disease, autoimmune disease, endocrine disease, or chronic/acute pain condition.
5. You have a history of cancer (any type)
6. You have a history or presence of gastrointestinal, hepatic or renal disease, or any other condition known to interfere with the absorption, distribution, metabolism, or excretion of drugs (i.e., Crohn's disease, short bowel, acute or chronic pancreatitis or pancreatic insufficiency).
7. You have a neurological disease (e.g., Parkinson's disease, Alzheimer's disease), have experienced a significant neurological injury (e.g., intracranial haemorrhage, or head injury), or currently have a major psychiatric condition that significantly affects daily function.
8. You have experienced an acute infection in the month before study commencement
9. You regularly take probiotic-containing supplements, or in the last 3 months, have taken probiotics
10. In the last 3 months, you have commenced or changed pharmaceutical medications (including antibiotics), which are likely to affect treatment outcomes, or you expect to change medications during the study duration
11. In the last 3 months, you have commenced or changed nutritional or herbal supplements, which are likely to affect treatment outcomes, or you expect to change them during the study duration
12. You have a sensitivity, intolerance, or allergy to probiotics or other excipients in the capsules
13. You plan on making major lifestyle or dietary change during the study period.
14. Your alcohol intake is greater than 14 standard drinks per week
15. You have a current or 12-month history of regular illicit drug use
16. You are pregnant, breastfeeding, or intend to become pregnant during the study period.
17. In the last year, you have had a significant surgery that affects your general health or daily function, or you have a planned surgery during the study period.
18. You have participated in any other clinical trial in the last month

Voluntary participation and withdrawal from the study

It is essential that you understand your involvement in this study is entirely voluntary. While we appreciate your participation, we respect your right to decline. There will be no consequences to you if you decide not to participate, and this will not affect any future treatment/service. If you decide to discontinue participation at any time, you may do so without providing an explanation. If you withdraw, any assessments already conducted may continue to be used for analysis.

Please note that if you choose to commence treatment to reduce your stress levels, improve your mental health, or require medical treatment for any other condition during the study, this may result in your withdrawal from the study. Your health is the utmost priority, and your choice/need to commence new treatment before completing this study is respected and supported.

Your privacy

Your privacy is of the utmost importance to us. Your participation in this study and any information provided will be treated in a confidential manner. Your name and identifying details will not be used in any publication arising out of the research. Following the study, the data will be stored in a de-identified format in a locked cabinet in the Investigator's office and will be retained for statistical analysis and potential future publication. Re-identified codes will be retained for 6 months in case they are needed and will then be destroyed.

Possible benefits

Distressing menopausal symptoms, including hot flushes and night sweats, are experienced by up to 80% of women. Therefore, identifying safe and effective methods to alleviate menopausal symptoms is crucial. If LactoSpore® supplementation is effective, it will provide us with a natural option to help reduce menopausal symptoms in women experiencing perimenopause.

Possible risks

Participation in this study carries minimal risk, and numerous measures will be in place to minimise the likelihood of potential risks. LactoSpore® is an over-the-counter supplement available in several countries and is well-tolerated with no reports of serious adverse reactions. Several studies conducted on LactoSpore® have shown that it is well-tolerated with limited adverse effects. However, mild adverse and typically transient gastrointestinal reactions are possible with probiotics, including gas, bloating, and diarrhoea.

In this study, we will collect a blood sample from your vein (venepuncture). Although venepunctures are very safe, there is a possibility of bruising at the site of the needle puncture. This usually appears within 24 hours and may range in size from a small spot to a large purple bruise. While bruising can be unsightly, it is not dangerous and typically disappears over a few days. Very rarely, a small artery that contains blood at a much higher pressure than in veins will lie unusually close to, or underneath, a vein. In this situation, the artery may be accidentally punctured during venepuncture. Bruising on the lower arm may develop over the next 2 to 3 days. Again, this is not dangerous and will gradually disappear over a couple of weeks. Although extremely rare, some people may have a small branch of one of the sensory nerves in the arm running over the surface of a vein. Rarely, the needle will hit this tiny nerve on the way into the vein. This may cause a sharp, electric-shock-type pain. This may be all that occurs, but in some cases, a tingling type of pain may persist for 1 to 4 weeks as the nerve heals. This is inconvenient and may be unpleasant, but it eventually subsides. Another rare complication is the formation of a small clot (or thrombus) in the vein at the site of the venepuncture. This is noticed as a small firm lump just under the skin at the venepuncture site. The lump may be tender, and it will typically subside over a couple of weeks. Finally, although extremely rare, an infection can occur at the site of puncture. Please notify us immediately if this occurs. To minimise all these risks, blood collections will be collected by a qualified and experienced phlebotomist using current best practices.

What to do if you experience significant side effects

If you experience any significant illness, injury, or side effect that has commenced since starting your capsules, please contact Dr Adrian Lopresti or Dr Stephen Smith immediately (contact details are below). You may be asked to stop participating in the study and to seek medical advice.

Dr Stephen Smith: Ph: 9448 7376 | Mob: 0412 813 518 | Email: steve@clinicalresearch.com.au

Dr Adrian Lopresti: Ph: 9448 7376 | Mob: 0411 969 797 | Email: adrian@clinicalresearch.com.au

Feedback on study results

It is estimated that the results of this study will be finalised in late 2026. A summary of the results obtained from all participants in this study will be emailed to you when they have been published in a peer-reviewed journal (usually 6 to 12 months after the completion of the study).

Questions

If you would like to discuss any aspect of this study, please contact the principal investigator, Dr Adrian Lopresti, on 08 9448 7376 or email adrian@clinicalresearch.com.au

This study has been approved by the National Institute of Integrative Medicine (NIIM) Human Research Ethics Committee (HREC) (Trial Reference Number: 0164E_2026). If you have any reservations or complaints about the ethical conduct of this research and wish to talk with an independent person, you may contact the NIIM Research Ethics Office (Tel. 03 9804 0646) or email hrec@niim.com.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.