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**The TEMPO Diet Trial: Type of Energy Manipulation for Promoting optimum  
metabolic health and body composition in Obesity**

**INFORMATION FOR PARTICIPANTS**

**What is the study about?**

You are invited to participate in the TEMPO Diet Trial. This research study compares the long-term effects of fast versus slow weight loss on body fat content and distribution, muscle mass and strength, and bone density in postmenopausal women.

For many years health professionals have recommended 'slow and steady' weight loss. In recent years however, an increasing number of health professionals have begun prescribing very low energy diets (VLEDs). VLEDs can induce fast weight losses of approximately 0.5 to 2 kilos per week, which some people find motivating. Moreover, some people report not feeling hungry while on a VLED.

While VLEDs are known to be safe and effective in the short-term, the long-term consequences are unknown. There is some concern that compared to slower weight loss, VLEDs may increase the likelihood of weight regain, particularly in the abdominal region, and this could increase the risk of cardiovascular disease. Additionally, VLEDs may cause greater losses of muscle, muscle strength and bone compared to slower 'conventional diets', but this has never been tested. This

study will demonstrate whether or not there is any difference between the effects of weight loss via VLED or conventional diet on fat, muscle and bone for 3 years after commencement of the diet.

### **Who is carrying out the study?**

The study is being conducted by the above named investigators through the Boden Institute of Obesity, Nutrition, Exercise & Eating Disorders at the University of Sydney. The study is being funded by a competitive research grant from the National Health & Medical Research Council of Australia.

### **What does the study involve?**

If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

You will then be requested to undertake activities that fall into one of the following three categories:

- **Preparation** for weight loss and clinical testing.
- **Clinical support** to help you lose excess weight and learn how to keep it off.
- **Clinical testing** as outlined below.

The timetable for these activities will be outlined on Page 7.

### **Preparation for weight loss and clinical testing**

You will need to complete the following activities prior to starting the weight loss program. You will also need to complete some of these preparatory activities at various times during the 3-year trial, as outlined in the timetable on Page 7.

- **Blood tests and bone scan.** You will be asked to show us the results from any blood tests or bone scans that you have had in the past 6 or 24 months, respectively. Depending on what tests you have had done, we may request that you go for additional blood tests at a specified external pathology service, or a bone scan in our facility on a later date. These blood tests and bone scan enable us to determine whether or not the dietary regimes to be used in the TEMPO Diet Trial are medically suitable for you, and whether or not you are eligible for the trial.
- **'Homework tasks'**. Some preparation involves activities that you will be required to complete after your visit to us, and bring with you at your next visit.
  - **Home weighing.** After your first visit and before starting the weight loss diet assigned to you, you will be asked to weigh yourself and record your weight every day at home for at least 2 weeks and to follow our instructions for maintaining your weight during this time.

- **Home water sample.** We will give you a small empty container and ask you to bring a sample of drinking water from a tap in your home.
- **Athletic bra.** You will need to purchase a firmly fitted athletic bra, free of metal (e.g. from fasteners or underwire), to wear during determination of body composition during clinical testing.
- **Food, activity and sleep diary.** We will give you a pocket-sized paper diary and ask you to keep a written record of what, when and how much you eat, as well as your physical activity patterns, for 7 days.
- **Accelerometry and temperature tracking.** We will ask you to wear an accelerometer (a pedometer-like device), which includes a temperature tracker, plus a pedometer for 7 days. The accelerometer must be worn on your upper arm and should only be removed for bathing. The pedometer must be worn in your pocket or bra. This test measures your total level of physical activity as well as daily variations in body temperature. It will be performed in the same week as your food, activity and sleep diary.
- **SMS, e-mail or telephone reminders.** We will need to contact you prior to clinical support or clinical testing appointments in order to confirm appointments and remind you of things you need to do before or bring to your next appointment. We may also need to contact you to help you with the weight loss or weight maintenance diet. This contact will be via SMS, e-mail or telephone.

### **Clinical support**

We will provide 12 months of clinical support to help you lose excess weight and learn essential skills for weight maintenance. Clinical support will be provided via 16 individual clinical consultations. All clinical support is overseen by clinicians from the Metabolism & Obesity Services at Royal Prince Alfred Hospital (RPAH).

During the TEMPO Diet Trial you will be requested to follow either a VLED or a conventional diet. As a participant in this randomized controlled trial, you will not be able to choose which weight loss diet you will follow. The VLED is Prima Health Solutions KicStart™, an approximately 3,360 kilojoule (800 calorie) per day diet consisting of meal replacement shakes. No other foods will be consumed during the VLED except for low calorie jelly, strained broth and certain vegetables. The VLED is used for a minimum of 4 months and a maximum of 5 months, after which time participants will switch to the conventional diet. The conventional diet involves making healthier food and beverage choices.

### **Clinical testing**

In addition to attending preparatory and clinical support appointments, as a participant in this study, you will be requested to undergo a combination of clinical tests at our institute. In most cases you will be asked not to eat or drink anything except water from 10 pm on the night before each visit.



- **Questionnaires.** We will ask you questions about your physical and mental health, weight history, any medications you may be taking, as well as about your food intake, moods, sleep and physical activity.
- **Anthropometry.** We will measure your height, weight, waist and hip circumference while you are wearing leggings and an athletic bra.
- **Calorimetry.** This test determines how many calories you burn while lying down resting. A ventilated plastic hood will be placed over your head and shoulders, and samples of inspired and expired air will be collected for 40 minutes.
- **Blood pressure measurement** will be made using standard techniques.
- **Doppler fluxometry.** Using a device placed on your finger while you are sitting down, this test measures blood flow under your skin and how it changes in response to deep inhalation. It is an indication of the activity of your sympathetic nervous system, which controls 'fight or flight' responses. During this test you will be requested to take 6 deep breaths at 1-minute intervals.
- **Blood, urine and saliva collection.** A trained investigator will collect 60-100 mL of blood from a cannula in a vein in your arm. You should not donate whole blood in the 3 months before, or for up to 15 months after, the start of the weight loss diet. Besides blood sampling, you will also be asked to provide a small urine sample using the toilets provided. Saliva collection involves spitting into a plastic vessel. These samples will be analysed as described under the heading '**What will happen to the samples collected from me?**'
- **Visual analogue scales.** You will be invited to rate how you feel before and immediately after consuming a standard breakfast (toast, margarine, eggs and orange juice) and then again 0.25, 0.5, 1, 2 and 3 hours later. This waiting time will be used for other tests from this list, following which you can read or watch TV if desired. A small amount of blood will be collected from a cannula in a vein in your arm at each of these 7 time points. The total volume of blood to be collected is outlined above.
- **Body composition assessment (fat distribution, muscle mass and strength, bone)**
  - **BodPod®.** This test determines your body density (kg/L). You will be required to wear leggings, an athletic bra and a swim cap and to sit without moving for a few minutes in a bubble-like capsule with a large transparent window.
  - **Deuterium dilution.** This test determines the total water content of your body. It entails drinking a dose of 'heavy water', also known as deuterium oxide ( $^2\text{H}_2\text{O}$ ). Heavy water weighs more than normal water because it contains deuterium ( $^2\text{H}$ ), the stable, naturally occurring and non-radioactive isotope of hydrogen (H). You will be requested to provide a single urine sample before and 6 to 6.5 hours after drinking the dose (0.05 g/kg body weight of deuterium). This test has been used for over 20 years and there are no known risks.

- **Dual energy X-ray absorptiometry (DXA) scanning.** This test measures bone density. You will be requested to lie without moving on a bed for a few minutes while an X-ray emitting arm sweeps over your whole body and then over your lumbar spine and hip region. The dose of radiation used is very low (please see Risks). There will be 9 DXA scans in this study: One before commencement of the diet in preparation for the trial, one on the day the diet commences, and then again 1, 4, 4.25, 6, 12, 24 and 36 months later.
- **Magnetic resonance imaging (MRI) and spectroscopy (MRS).** This test is used to determine the amount and location of fat in your abdomen, as well as the amount of fat and muscle in your thigh. It consists of lying on a table, which then moves you feet or head first into a cylindrical magnet. You will be requested to stay very still for up to 30 minutes in the machine while readings are made. Some people feel claustrophobic while inside the cylindrical magnet, but at all times you will be able to talk to and hear the operator (a trained staff member from a commercial Nuclear Medicine provider in Camperdown), and you can stop the test at any time. MRI and MRS have been used in medical diagnosis for over 30 years and there are no known side effects. However, if you have loose metal in your body (e.g. a pacemaker, bullet or metal shavings), it is unsafe to undergo MRI or MRS testing. You will be required to walk from our institute to the Nuclear Medicine provider and back (8-12 minutes' walk each way).
- **Muscle strength** is assessed by dynamometry and 1 Repetition Maximum (1RM) testing. Dynamometry consists of repeatedly and intermittently pulling or squeezing a hand-held sprung device as hard as you can over several minutes. 1RM testing aims to determine the heaviest weight that you can push with both legs or lift with both arms, using strength training gym equipment (leg press and chest press, respectively).
- **Vascular health** tests will be performed immediately after you begin on the diet and again 3, 6, 24 and 36 months later.
  - **Flow-mediated dilatation (FMD).** We will use ultrasound to visualize blood vessels in your arm, before and after inflation of a blood pressure cuff to 240 mmHg (quite tight) for 5 minutes. This may cause some discomfort, but the test has no known side effects.
  - **Carotid intima-media thickness (cIMT).** We will use ultrasound to image the main blood vessels in your neck (the carotid arteries and jugular veins).

### **What are the known risks of participating in this study?**

All medical procedures involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study. The known risks of this study are:



**Blood sampling:** This involves some discomfort at the site at which the cannula is inserted and from which blood is taken, and there is a risk of some minor bruising at the site, which may last one to two days. Fainting and local infection can also occur when blood is taken, although these are rare.

**Exposure to radiation:** This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. The dose from routine diagnostic X-ray and nuclear medicine procedures is 2 mSv to 20 mSv. The effective radiation dose from this study is about 1.62 mSv (about 1.26 mSv in the first year and 0.18 mSv in each of years 2 and 3). At this dose level, no harmful effects of radiation have been demonstrated and the risk is very low.

Please inform us if you have participated in any other research studies using radiation in the last five years. Please keep this information in a safe place for the next five years in case you volunteer for any more studies using radiation, when you should show it to the Investigator.

**Muscle strength testing.** You may feel some soreness in your legs and upper arms for 2 to 3 days following 1 Repetition Maximum (1RM) testing. As with all activities involving gym equipment, there is a risk of injury if correct techniques (including breathing technique) are not followed. The procedure used for this test is overseen by an exercise physiologist.

## How much time will the study take?

Participating in the TEMPO Diet Trial will require you to visit or talk over the telephone with us at the University of Sydney in Camperdown 29 times over 3 years, for a total of 113 hours (excluding transport time). This is equivalent to 15 x 7.6-hour working days (or 3 x 38-hour working weeks) of your time over 3 years. All visits will be on weekdays between the hours of 8:00 am and 6:00 pm. In addition to visiting or talking on the telephone with our team in Camperdown, participating in the TEMPO Diet Trial will require you to complete some preparatory 'homework tasks' as described on pages 2-3 for a total of approximately 12 hours over 3 years. The visiting schedule will be as follows:

Time (relative to start of the weight loss diet)	Purpose	Duration
First visit	Meet, sign consent, preparation for diet and clinical testing, measure weight and height	1 hour
-2 weeks	Preparation for diet and clinical testing	4 hours
-1 weeks	Clinical support (individual), preparation, clinical testing	3 hours
0 weeks (start diet)	Clinical testing	9 hours
1 week	Clinical testing	8 hours
2 weeks	Clinical support (individual), preparation	½ hour
4 weeks	Clinical testing	8 hours
6 weeks	Clinical support (individual)	½ hour
8 weeks	Clinical support (individual), clinical testing	1 hour
10 weeks	Clinical support (individual)	½ hour
12 weeks	Clinical support (individual), clinical testing	1 hour
15 weeks	Clinical support (individual), preparation, clinical testing	3 hours
16 weeks	Clinical testing	9 hours
17 weeks	Clinical testing	8 hours
18 weeks	Clinical support (individual)	½ hour
21 weeks	Clinical support (individual), clinical testing	1 hour
25 weeks	Clinical support (individual), preparation, clinical testing	4 hours
26 weeks	Clinical testing	9 hours
26 to 51 weeks	Clinical support via ½ hour individual sessions	3 hours
29 weeks	Clinical testing	2 hours
51 weeks	Clinical support (individual), preparation, clinical testing	4 hours
52 weeks (1 year)	Clinical testing	9 hours
103 weeks	Preparation, clinical testing	4 hours
104 weeks (2 years)	Clinical testing	8 hours
155 weeks	Preparation, clinical testing	4 hours
156 weeks (3 years)	Clinical testing	8 hours

Your appointment schedule for the 3-year trial will be arranged just before you start the weight loss diet, taking into account your other engagements. You will thus know your appointment dates and times in advance. Please note that **once your appointments are booked there is limited scope for flexibility in appointment dates and times**. This is because your appointments with us involve several different health care and research professionals, and several different clinical services.

## **Costs**

To participate in this trial you will need to pay for blood tests that will cost you up to A\$110. Since these blood tests are for a clinical trial, the cost cannot be claimed through Medicare.

We will reimburse you for the cost of these blood tests at the end of the trial, provided that you give us the original results and receipts, complete the necessary forms for funds transfer, and attend all of the clinical testing days listed in the table above (i.e. at -1, 0, 1, 4, 15, 16, 17, 25, 26, 29, 51, 52, 103, 104, 155 and 156 weeks). If the blood test results reveal that the weight loss diets to be used in this trial are not medically suitable for you, or that you are not eligible for the trial, we will reimburse you the cost of the blood tests within 8 weeks of your providing the original receipts and completing the necessary forms for funds transfer.

You will be required to purchase a metal-free athletic bra to wear during long clinical testing days. This is necessary for the anthropometry and body composition assessments described on pages 4-5. Such bras can be purchased from department stores for approximately \$20 - \$30. As the bra must be firm fitting to ensure accurate and precise measurements, you may need to purchase a new bra after some time on the weight loss diet.

You will not be paid for participation in this clinical trial.

## **Can I withdraw from the study?**

Participation in this study is completely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you. However, please note that information or samples collected from a participant prior to withdrawal from the study cannot be withdrawn.

## **What will happen to the samples collected from me?**

### *Blood*

Your blood will be used to measure fasting concentrations of serum glucose, insulin, triglycerides, cholesterol, glycosylated haemoglobin and C-reactive protein. Together with waist circumference and blood pressure measurements, these analyses will be used to assess your metabolic health. Your blood will also be used to measure the concentration of hormones and factors that regulate appetite, body weight and body composition, including but not limited to free triiodothyronine (T3), free thyroxine (T4), reverse T3, thyroid stimulating hormone (TSH), adrenocorticotrophic hormone (ACTH), cortisol, luteinizing hormone, follicle stimulating hormone, progesterone, oestradiol, insulin-like growth factor 1 (IGF-1), peptide YY (PYY), ghrelin, macrophage inhibitory cytokine 1 (MIC-1) and leptin. Blood and serum ketone concentrations will also be investigated, as these are produced in higher levels during VLED and are thought to suppress appetite.



Additionally, the following parameters will be assessed in serum in order to determine possible reasons for any changes in bone mass: P1NP (procollagen type-I N-propeptide), CTX (C-telopeptide of type-I collagen), 25-OH vitamin D, 1-84 parathyroid hormone, calcium, phosphate, albumin and creatine.

DNA will be extracted from your blood and will likely be used to investigate the sequence of some of your genes or the DNA surrounding them. The genes likely to be investigated are those that have been implicated in the regulation of body weight. We envisage that these analyses will one day lead to genetic tests enabling people to be quickly matched to the most effective weight management strategy for their genetic makeup. As we will not be comparing your DNA with DNA from anyone else in your family (e.g. parents, spouse, siblings, children), these DNA analyses will not provide information about anyone other than yourself.

Your blood, urine and saliva will be used for metabolomics and proteomics analyses, which can detect thousands of metabolite and protein species and patterns. We expect that these patterns could lead to the development of diagnostic tools such as salivary or urinary test sticks that will make it easier for people to lose excess weight by identifying optimal times in which to restrict energy intake.

#### *Urine and saliva*

Urine will be used to determine the concentration of NTX (N-terminal telopeptide), which is used in the interpretation of your bone density data. Urine will additionally be used to measure the concentration of deuterium oxide ( $^2\text{H}_2\text{O}$ ) as described on page 4, for accurate determination of your body composition. Urine and saliva will be used for metabolomics and proteomics analyses as described above for blood.

#### *Long-term storage*

Some of your blood, DNA, urine or saliva samples may be stored for 15 years or longer, for as long as they are viable for biological analyses. The reason for this is that in the future, new hormones, genes or other factors are likely to be discovered that could provide useful biomedical insights if investigated in the samples collected in this study.

#### **Will anyone else know the results?**

In the event that your results suggest a medical condition that may require treatment, your results may be reported to your general practitioner. Otherwise, all the information collected from you for the study will be treated confidentially, and only the investigators named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

### **Can I tell other people about the study?**

We are recruiting 100 postmenopausal women for this study so please notify others if you think they may be suitable and interested.

### **Will the study benefit me?**

It is expected that participation in this study will benefit you directly. During the first 12 months of the study you will receive free clinical care in the form of individual clinical consultations, overseen by clinicians from the Metabolism & Obesity Services at Royal Prince Alfred Hospital. This treatment program is designed to help you to lose excess weight and learn skills that can help you to keep it off. By adhering to the prescribed diet, you may lose weight and improve your health (e.g. by lowering blood cholesterol levels and blood pressure). If you are assigned to the very low energy diet (VLED), meal replacement formulas (Prima Health Solutions KicStart™) will be provided free of charge for 4-5 months. If you are assigned to the conventional diet, you will be provided with a flexible and balanced menu planner that is tailored to your individual circumstances and preferences. All participants will be given educational materials outlining the principles of eating for health and weight maintenance, as well as a pedometer that can be worn in a pocket or in your bra. Throughout the study you will complete a number of test procedures to assess your health, at no cost. These procedures are expensive and unavailable to the general public. At the end of the study you will be provided with a detailed report of your health profile changes over the course of the study. In addition to these direct benefits, we expect that your participation in this project will help other people who are attempting to lose weight, by furthering knowledge of effective weight management.

### **What if I require further information about the study or my involvement in it?**

When you have read this information, Ms Michelle Hsu, Dr Radhika Seimon, Ms Alice Gibson or Associate Professor Amanda Salis will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact one of the above-named investigators on [tempo.diet@sydney.edu.au](mailto:tempo.diet@sydney.edu.au).

### **What if I have a complaint or any concerns?**

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 9515 6766 and quote protocol number X12-0081.

*This information sheet is for you to keep*