## eAppendix 1.

Model Participant Information Sheet and Consent Form (May Vary Slightly to Accommodate Local Requirements)[a]

**Title of Project:** Build Better Bones With Exercise (B3E)

**Primary Investigator:**

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**Students or Trainees**: Caitlin McArthur, Dr. Jenna Gibbs, Eric Bowman

**Sponsors:** Canadian Institutes of Health Research

### Introduction

You are being invited to participate in a research study. We have outlined the study here and will discuss it with you. Please read this information carefully. Ask questions about anything that you want to know more about.

### Why is this research being done?

Exercise is often recommended to those with osteoporosis. There are very few studies that examine how effective and safe it is for people with spine fractures to participate in exercise.

### What is the purpose of the study?

Our team wants to investigate whether exercise can improve health and prevent fractures in individuals who have had a spine fracture. We need to do a really large study to achieve this goal. The current study will recruit 160 women with spine fractures at 7 centers in Canada and Australia. It will be the first step in finding out if it is feasible to do a really large study. The current study will also help us understand whether exercise can improve function and quality of life for women with spine fractures.

### What will your responsibilities be if you decide to take part in the study?

You will be asked to participate in one visit to St. Mary's General Hospital at the beginning of the study and one study visit at the end of the study, or 12 months later. The study visit will take approximately 2 hours and will include the assessments listed below. If you cannot complete an assessment, or do not wish to, you can still remain in the study. The only assessments that are mandatory are the x-ray, memory tests, and medical history at the start to confirm that you are eligible to participate. We also may ask you to describe the study back to us in your own words so we can be sure you understand what we are asking you to do.

*Study assessments during study visits at the start and 12 months later:*

- X-rays of your spine to confirm the number and severity of fractures. If you have had spine x-rays in the last 3 months, we will examine those; otherwise, we will have a new x-ray taken.

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- A physical assessment that includes assessing your height, your balance, your posture, and your walking speed over 4 m and your back and arm endurance. Balance tests include a measure of how far forward you can reach with your arm, how many times you can step on a block with your foot in 15 seconds, your ability to stand with your eyes closed, and how well you can get out of a chair 5 times or get out of a chair and walk 3 ft and come back to the chair. The posture assessment requires you to stand against the wall and have your height and the distance between your head and the wall measured. The back and arm endurance test requires you to hold two 2-lb weights straight out in front of you for a maximum of 2 minutes.
- The team doctor at your site, their delegate, or the research assistant will review your medical record to obtain the date of your most recent spine fracture and for any measurements of vitamin D that were performed.
- You will be asked to wear an activity monitor for 7 days at the beginning and end of the study.

*Other assessments:*

- You will be provided with monthly calendars to keep track of your activity, whether you have had a fall, and whether you are taking your osteoporosis-related medication (if applicable) or used any health care services.
- You will be contacted halfway through the study to complete questionnaires over the telephone. The questionnaires will ask about your health, your physical activity level, the health services you use, your physical function, and perceived quality of life.
- You will be contacted monthly to see how you are doing and whether you have had any illnesses or injuries. If you have, you may be asked questions about the injury or illness and any health services you used. A telephone number will be provided so that you can report any falls, injuries, or health problems.
- If you experience a bone fracture at any point during the study, we will ask for access to your medical records to see the x-rays and details about the fracture.

Everyone in the study will be provided with a year's supply of vitamin D supplements (1,000 IU per day, in the form of Ddrops). All participants will be visited in home by the study physical therapist 6 times over the 12-month study period. Each home visit will be approximately 45–60 minutes. Once you complete the first study visit, you will be randomly assigned to 1 of 2 groups. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor your doctor can choose what group you will be in. Participants in group 1 will be given an exercise program during the home visits with the physical therapist as well as an exercise band and exercise materials. The exercise program will be tailored to individual ability and will include aerobic, strength, and balance training to be performed at least 3 times weekly. Participants in group 2 will receive educational materials and will discuss general health or other topics during the home visits. They will receive a tailored exercise program identical to that received by participants in group 1 and all of the exercise materials 12 months later. You will be asked not to disclose what group you are in to the research assistant performing assessments.

**What are the possible benefits of the study for me and/or society?**

We will provide you with the results of your assessments at the end of the study so that you can see how you did. You will be allowed to keep all of the exercise materials, and you will receive an exercise program from a physical therapist. We will host a social event and information session at the end of the study that you can attend if you wish. Our study will be a first step in providing more evidence about the safety and effectiveness of exercise in women with spine fractures. We also will look at factors, such as numbers of spine fractures or memory, that influence who sticks to an exercise program or completes the study.

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**What are the possible risks and discomforts?**

There is a potential for exercise-related changes, such as muscle soreness and changes in blood pressure and heart rate, to occur during the assessments or exercise. Any physical exercise or performance-based test is associated with a risk of falls or cardiovascular complications. We aim to minimize the risks by having the exercise prescription done by a physical therapist and by having training for our staff. The x-rays involve exposure to radiation. The total dose at each of the 2 visits is approximately 3.2 mSv. For perspective, we are exposed to ~3mSv of natural background radiation each year. Radiation exposure can have a cumulative impact, so if you are concerned, you can discuss the risks with your physician.

We are asking you to be on 1,000 IU of vitamin D for the duration of the study (or remain on the vitamin D regimen recommended by your doctor if the dose is higher). Although significant side effects have not been reported when vitamin D is taken as directed, you should notify your doctor and the study staff immediately if you have any of the following: bone pain, muscle pain, nausea or vomiting, constipation, diarrhea, loss of appetite, metallic taste, dryness of mouth, weight loss, increased thirst, increase in amount and frequency of urination (especially at night), cloudiness or protein in the urine, irregular heartbeat, headache (continuing), drowsiness, unusual tiredness or weakness, calcium deposits (hard lumps) in tissues outside of the bone, itching of skin, loss of sex drive, mood or mental change, increased sensitivity of eyes to light or irritation of eyes, redness or discharge of the eye, eyelid, or lining of the eyelid, and runny nose.

**What information will be kept private and confidential?**

Your data will not be shared with anyone except with your consent or as required by law. All personal information will be removed from the data and will be replaced with an ID code. Your information will be stored at the study site as well as on a virtual (online) system that is managed by EmPOWER Health Research in London, Ontario. The system is highly secure, and it encrypts the data and protects it with a password that is known only by the research team. Paper and electronic records will be retained for 7 years after the study is complete, and study data will be retained for 25 years. All anonymized forms and study data will be stored in a locked office or on a password-protected online database. Only the research team will have access to the data. Some of the data may be examined by students doing thesis projects or research internships, but your name or other identifying information will not appear with the data. Data will be secured in accordance with University of Waterloo policies available at http://ist.uwaterloo.ca/security/policy/.

Information about you will be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form, you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorized representatives of the University of Waterloo or as required by law. By signing the Consent Form, you authorize release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published or presented in a variety of forums. The results will be presented in such a way that you cannot be identified, except with your permission. You may be asked if you would like to have your photo taken during study activities for use in oral presentations, training information, or publications. This is voluntary and not a requirement of the study. If you are to be photographed, you will be asked to sign a separate consent form.

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Information about your participation in this research project may be recorded in your health records.

**Can I end my participation early?**

Participation in this research is voluntary. If you do not wish to take part, you do not have to. You will receive the best possible care regardless of whether or not you take part. If you volunteer to be in this study, you may withdraw at any time. If you withdraw, you will be asked if there are some parts of the study you are still willing to complete (eg, telephone assessments only). You can opt out of only some parts of the study, or withdraw altogether. We will not withdraw previously collected data unless you request that we do. If you decide to withdraw from the project, please notify a member of the research team.

**Will I be paid to participate in the study?**

You will not be paid to participate in the study. We will reimburse parking or bus transportation costs for travel to study visits. If you lose your receipt, you will be reimbursed for parking or bus based on the time you spent at the clinic visit. If you do not have access to transportation, we will pay for a taxi within a reasonable distance from our center.

**What happens if I have a research-related injury?**

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing this form, you do not give up any of your legal rights against the investigators, sponsor, or involved institutions for compensation, nor does this form relieve the investigators, sponsor, or involved institutions of their legal and professional responsibilities.

If you have any urgent medical problem, injury, or illness that is related to your participation in this study or have any questions or concerns or would like to speak to the study team for any reason, please call: Day Emergency Number: Jenna Gibbs at (519) 888-4567, ext. 38779.

This project has been reviewed by, and received ethics clearance through, the Office of Research Ethics at the University of Waterloo. If you have any comments or concerns resulting from your participation in this study, contact Dr. Maureen Nummelin, Director, Office of Research Ethics, at (519) 888-4567, ext. 36005, or by e-mail at maureen.nummelin@uwaterloo.ca.

This project also has been reviewed by, and received ethics clearance through, the Tri-Hospital Research Ethics Board. If you have any comments or concerns resulting from your participation in this study, you can contact them by telephone at (519) 749-4300, ext. 5367, or by fax at (519) 749-4274.

**Consent of Participant**

I have read the information presented in the information letter about a study, Build Better Bones With Exercise, being conducted by Dr. Giangregorio and colleagues, or I have had it read to me in a language that I understand. I have had the opportunity to ask any questions related to this study and to receive satisfactory answers to my questions and any additional details I requested. I understand the purposes, procedures, and risks of the research described in the project.

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I am aware that I may withdraw from the study without penalty at any time by advising the researchers of this decision. With full knowledge of all foregoing, I agree, of my own free will, to participate in this study. I have been advised that I will receive a signed copy of this form.

**Consent Statement**

Name of Participant_____ Signature of Participant_____

Date_____

Person obtaining consent:

I have discussed this study in detail with the participant. I believe the participant understands what is involved in this study.

Name, Role in Study_____ Signature_____

Date_____

[a] The Model Participant Information Sheet and Consent Form may not be used or reproduced without written permission from the authors.

## eAppendix 2.

SPIRIT 2013 Checklist: Recommended Items to Address in a Clinical Trial Protocol and Related Documents[a]

| Section/Item | Item No. | Description | Page Found On |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | 2, 6 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | Not applicable |
| Protocol version | 3 | Date and version identifier | 2, 10 |
| Funding | 4 | Sources and types of financial, material, and other support | 1, 18 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | 1, 18 |
| | 5b | Name and contact information for the trial sponsor | 2, 18 |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 18 |
| | 5d | Composition, roles, and responsibilities of the coordinating center, Steering Committee, Endpoint Adjudication Committee, Data Management Team, and other individuals or groups overseeing the trial, if applicable (see item 21a for Data Monitoring Committee [DMC]) | 15, 18 |
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 3–4 |
| | 6b | Explanation for choice of comparators | 4, 9 |
| Objectives | 7 | Specific objectives or hypotheses | 4–5 |
| Trial design | 8 | Description of trial design, including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | 4, 6 |
| **Methods: participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected; reference to where list of study sites can be obtained | 6 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants; if applicable, eligibility criteria for study centers and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 6–8 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 7–9, Tables 1,2 |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | 9 |
| | 11c | Strategies to improve adherence to intervention protocols and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | 7–8, 11 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 7–8 |

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| Section/Item | Item No. | Description | Page Found On |
|---|---|---|---|
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended. | 10–14, Table 4 |
| Participant time line | 13 | Time schedule of enrollment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure). | 9, Table 3 |
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 4, 14 |
| Recruitment | 15 | Strategies for achieving adequate participant enrollment to reach target sample size | 13 |
| **Methods: assignment of interventions (for controlled trials)** | | | |
| Allocation | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers) and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enroll participants or assign interventions. | 6 |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 6 |
| Implementation | 16c | Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions | 6 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts) and how | 6, 10–11, 16 |
| | 17b | If blinded, circumstances under which unblinding is permissible and procedure for revealing a participant's allocated intervention during the trial | 10 |
| **Methods: data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known; reference to where data collection forms can be found, if not in the protocol | 10–13 |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 10, 14 |
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry, range checks for data values); reference to where details of data management procedures can be found, if not in the protocol | 10–11, 16 |
| Statistical methods | 20a | Statistical methods for analyzing primary and secondary outcomes; reference to where other details of the statistical analysis plan can be found, if not in the protocol | 14–15 |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 15 |

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| Section/Item | Item No. | Description | Page Found On |
|---|---|---|---|
| Statistical methods (continued) | 20c | Definition of analysis population relating to protocol nonadherence (eg, as randomized analysis) and any statistical methods to handle missing data (eg, multiple imputation) | 15 |
| **Methods: monitoring** | | | |
| Data monitoring | 21a | Composition of DMC, summary of its role and reporting structure, statement of whether it is independent from the sponsor and competing interests, and reference to where further details about its charter can be found, if not in the protocol; alternatively, an explanation of why a DMC is not needed | 16 |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 15 |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 12–13 |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 10–16 |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | 15–16 |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | 16 |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorized surrogates and how (see item 32) | 10 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | Not applicable |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 16 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 16 |
| Access to data | 29 | Statement of who will have access to the final trial dataset and disclosure of contractual agreements that limit such access for investigators | 16 |
| Ancillary and posttrial care | 30 | Provisions, if any, for ancillary and posttrial care and for compensation to those who are harmed from trial participation | |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, health care professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 16–17 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | 16 |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | 16–17 |
| **Appendixes** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorized surrogates | 27–32 |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | Not applicable |

[a] It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.