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Title: Aerobic Exercise for Optimizing Cognitive and Brain Health in Remitted Late-Life Depression

Short Title: Fitness for Brain Optimization for Late-Life Depression (FIT BOLD)

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KEY INFORMATION SUMMARY: You are being asked to take part in a research study because you are an adult at least 60 years old with who has had depression in the past but now has few or no symptoms, called “remitted depression.” The main purpose of this research study is to evaluate the effects of exercise on memory and thinking in geriatric psychiatric populations. If you consent to participate, you will be asked to complete a handful of assessments including evaluations of fitness, cognition, brain health, blood sampling and depression. You will also be randomized to complete a 6-month aerobic exercise (AE) or social

engagement (SE) intervention. Randomized means assigned by chance, like a flip of a coin. All participants will be invited to complete an optional smartphone-based assessment of thinking and memory. Your participation in this study is completely voluntary. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.

Although staff have developed procedures to minimize risks associated with participation in this research study, potential risks include: The risk of a breach of confidentiality

- Injury or illness resulting from exercise
- Feelings of boredom, fatigue, or frustration in response to depression and cognitive assessments
- Health and safety risks associated with MRI scans
- Additional risks are associated with the optional use of personal smartphone devices

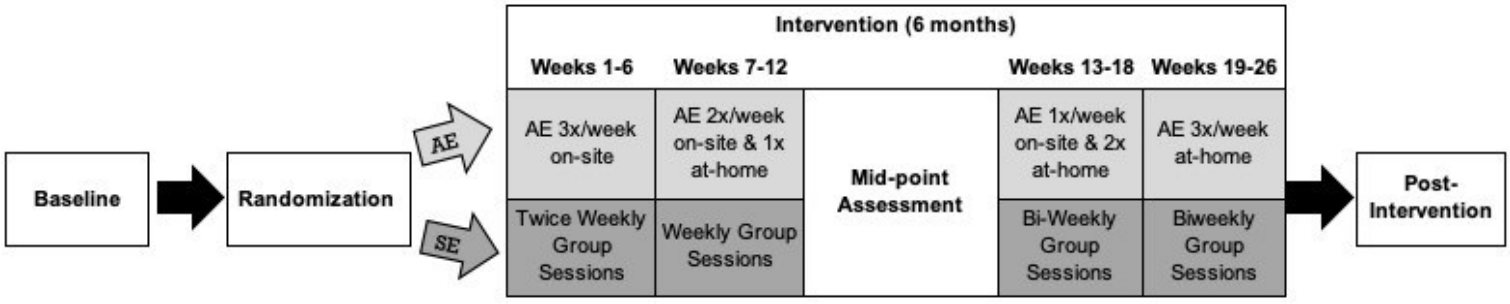
Potential benefits to participants:

- You may benefit both physiologically and psychologically from the increase in physical exercise.
- Your level of fitness and physical functioning will be enhanced, resulting in possibly less injury and illness
- You may experience possible improvements in independent and effective daily functioning, as well as in your thinking ability and mood.

DESCRIPTION: You are being asked to take part in a research study because you are an adult at least the age of 60 with “recently remitted” depression. The goal of this study is to better understand whether moderate-intensity aerobic exercise training, above and beyond the effects of increased social engagement, uniquely influence thinking, memory, and brain health in older adults with recently remitted depression.

Approximately 50 people, of both sexes and all races, will be asked to participate in this study. Participation in this entire study will last approximately 1 year. If you agree to participate, you will undergo the procedures listed below.

STUDY PROCEDURES:



Baseline Assessment: You will be asked to complete several assessments prior to starting the intervention portion of this research study. The baseline assessment includes magnetic resonance imaging (MRI), physical activity monitoring, a fitness test, an evaluation of depression, and cognitive testing. These assessments can be done on the same day or split into a few visits depending on your schedule and will occur at University of Pittsburgh facilities. Prior to the fitness test, your primary care provider must clear you to participate.

MRIs: You will be asked to undergo a brain scan known as a Magnetic Resonance Imaging (MRI) scan in a 7-tesla MRI scanner. The baseline MRI will take approximately 60 minutes to complete and will take place at the 7T MRI Center at the University of Pittsburgh within UPMC Presbyterian. Magnetic resonance imaging (MRI) is a technology that uses strong magnetic fields ("magnetic") and radio frequency fields ("resonance") to produce detailed pictures of soft tissues in the body, including the brain. For this study, we will be using MRI to take pictures of your brain's structure and your brain's function.

On the day of the scan, a trained staff member at the MR Center will review your safety screening and will assist you with preparation for the brain scan. You will be given hospital garments if your clothing contains metal pieces that cannot be removed, such as buttons and/or zippers. A locker will be provided to secure your belongings. A member of the research staff will join you at this visit.

The MRI involves lying on a table, which then moves into a hollow machine that contains a powerful magnet. While you are lying in the MRI scanner, you will hear a variety of loud knocking noises. You will always be able to talk with a study team member and MR technologist during the course of the scan. You will be given earplugs, which are required and will provide a barrier to the loud noise. Additionally, a pillow or cushion will be placed under your head and around your ears. These cushions serve two purposes: to stabilize your head to reduce movement and to serve as another barrier to the loud noise. While in the MRI scanner, you should try to remain as still as possible during the scans. Movements will not be dangerous to you in any way, but the movements will blur the picture of your brain.

It is important to note, you may be removed from the study if you are unable to complete this MRI scan. If you are unable to complete this scan for reasons out of your control, such as scanner issues, all attempts to reschedule the scan will be made. If you are unable to complete the scan for reasons such as claustrophobia, discomfort, or personal choice, you may be removed from the study.

Because this is a research MRI, not a clinical MRI, your scan will not be read by a radiologist. The MR technologists at the MR Center are trained to examine brain images as they are acquired, and if any abnormality is suspected, a radiologist will immediately review the images. If anything previously unknown is found on the MRI that is of clinical significance, the reviewing radiologist or another study physician will review the findings with you, and you will be given an appropriate referral.

Cognitive Performance Assessment: You will undergo some basic cognitive testing prior to the intervention period. These tests will assess verbal ability, your ability to identify visual and spatial relationships among objects, attention/processing speed, memory, and executive function, which are things like thinking on your feet and self-control. These tests have standard administration protocols and will be administered by a trained member of the team including a research specialist or project coordinator. These tests will take approximately 2 hours and 55 minutes. If the tests shows that there is a problem with thinking ability, it may mean you need to be removed from the study. These tests will take place at Bellefield Towers, the Oxford Building, or Western Psychiatric Hospital.

Physical Activity and Fitness Assessments: You will be asked to monitor your physical activity for one week at three timepoints in the study: at baseline, the mid-point assessment (3months), and the follow-up assessment (6-months). You will be equipped with an Actigraph, a physical activity-monitoring device worn on the wrist. The device does not contain any confidential or private information. You will be asked to wear the device 24-hours a day, except while showering or swimming, for a period of one week at each monitoring timepoint. Infrequently it may itch or you may get a mild skin irritation while wearing the device. You will be provided with a phone number to the lab if you experience any problems or have any questions with the use of the device.

You will also undergo a Cardiopulmonary Exercise Test (CPET) to assess cardiorespiratory fitness. Cardiorespiratory fitness will be measured via a maximal exercise test performed on a motorized treadmill. “Maximal” means the intensity will increase every two minutes by increasing the treadmill’s incline in stepwise amounts. This is done to get you to the point that you report you are walking as hard as you can (or maximal).

To start the test, you will work with the exercise test leader to set the walking speed that is comfortable for you. The speed will stay the same and only the incline will get higher. Once you reach a level of incline when you are breathing hard and working at what feels like you can’t work any harder, the test will conclude, with the study team taking the incline back to zero and you catching your breath and cooling down. The air that you breathe out will be collected and analyzed by a machine. You will wear a mask on your face to allow the air to be collected.

In addition, strength and flexibility will be assessed. The fitness assessment will take place at The Brain Aging & Cognitive Health Exercise Lab. You will be asked to wear loose comfortable clothing and walking shoes for the fitness test and all subsequent structured exercise visits. On the day of testing you will be asked to do the following:

- No heavy meal, caffeine, or smoking 3 hours prior to test time.
- No vigorous exercise 24 hours prior to test time.
- Be appropriately dressed for exercise (for females, please avoid wearing a bra with underwire, we recommend a sports bra).
- Please wear comfortable athletic/walking shoes.

- Please avoid bath oil, lotion or baby powder to the upper body/chest area.
- Drink plenty of fluids upon arriving for the test, water is available for you before and after the test

This fitness assessment will ensure your safety to participate in the exercise intervention group and allows for tailoring of the exercise regimen for participants assigned to this group. It is important to note that all participants must safely complete the fitness test to continue participation in the study. If the study team has concerns about your ability to safely exercise, you may be removed from this study.

Evaluation of Depressive Symptoms: Given that all participants will have a recent history of depression and may have lingering low level symptoms or may even relapse, depressive symptoms will be assessed at baseline and throughout your involvement in the study. Additionally, given the link between depression and anxiety rates, we will also assess symptoms of anxiety. A trained member of the research team (a Research Specialist or Project Coordinator) will administer these measures. If clinical or safety concerns related to depression or anxiety severity arise, we will inform your primary care or mental health provider.

Blood samples for research: We would like to collect about 4 teaspoons of blood. Some of the blood that we collect will be used as part of this current study. We would like to use additional blood samples from this study for other future research projects studying mental health. If you agree, this will mean that your sample will be used for studies going on right now as well as studies that are conducted in the future. The studies may include genetic analysis; although none is planned for this study the sample may undergo an analysis called “whole genome sequencing” (WGS). WGS is identifying your entire unique genetic information from your biological parents. Other genetic studies involve looking at single genes or parts of genes. The blood tests will be for research and not expected to have results that could affect your medical care.

We would like your permission to share your data and blood sample without identifiers with other researchers. These researchers may be at the University of Pittsburgh, or at other research institutions or at other research centers. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories, only qualified researchers, who have received prior approval from individuals who monitor the use of the data, will be able to look at your information. The only risk of future use of your data is a breach of confidentiality. This means that someone might be able to identify which of the data is yours. Because we use a code number when we are working with your data and when we share it, this risk is very low.

You won’t experience any medical or financial benefit from us using or sharing your sample. By agreeing to participate, you make a free and generous gift of your blood sample for research that might help others. This research might create new tests, treatments, or cures. If it does, you will not get any money or ownership rights to these products.

The risks associated with genetic studies include the potential for a breach of confidentiality which could affect future insurability, employability, or reproduction plans, or have a negative impact on family relationships and/or result in paternity suits or stigmatization.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies and group health plans to use genetic information in making decisions regarding your eligibility or premiums. GINA also makes it illegal for employers with 15 or more employees to use your genetic information when making decisions regarding hiring, promoting, firing, or setting the terms of employment. This new Federal law does not protect you against genetic discrimination by companies that sell life, disability, or long-term care insurance. GINA does not protect you for genetic diagnoses that have already been established.

Again, letting us use and share your sample is voluntary. If you refuse to provide a blood sample for genetic analysis and future research, you may still participate in the rest of the study.

Intervention Period: After approval from your primary care physician has been obtained and you have completed the baseline assessments, you will be randomized to either the aerobic exercise (AE) intervention group or social engagement (SE) group. Both intervention groups will last for 6-months. Because both interventions involve group-based activities, there may be a waiting period before you are able to begin the intervention to which you have been assigned.

Aerobic Exercise (AE) Intervention: Participants who are randomly assigned to participate in the 6-month exercise intervention will attend exercise sessions three times per week for the first six weeks then will complete a combination of on-site and home-based exercise sessions for the remainder of the intervention period with a graded decline in supervision. All on-site sessions will be conducted in Dr. Erickson's Exercise Lab on the campus of the University of Pittsburgh.

Supervised AE will occur in groups, though each participant’s AE prescription will be personalized based on baseline exercise capacity, as assessed by the fitness test. All supervised sessions will start and end with 5-minute warm-up and cooldown. During supervised and home-based AE sessions, participants will exercise so that their heart rate is approximately 65% of their peak heart rate and gradually increase the intensity of exercise so that their heart rate is between 70 and 85% of their peak heart rate. All participants will wear heart rate monitors (wrist worn Polar A370 device) during exercise and will be encouraged to exercise in their target heart rate zone. Participants will complete weekly home exercise logs including the mode, time, and intensity of exercise, which will regularly be shared with the exercise trainer via mail, e-mail, telephone, or videoconferencing. Intensity of exercise during each session will be assessed using the self-reported Borg rating of perceived exertion (RPE) scale, which you will be trained to use during initial in-person supervised exercise sessions.

Exercise staff will work individually with each participant to maintain AE adherence during supervised and home-based portions of the intervention, along with monitoring intensity and safety. Supervised AE sessions will involve the treadmill, elliptical, and/or bike, and routines will be varied to promote adherence. Supervised AE sessions will gradually increase to 50 minutes per session; however, participants will be encouraged to engage in home-based AE sessions according to their own preference of length and frequency in order to achieve 150 minutes of AE per week. Exercise staff will work with participants to overcome barriers to AE adherence through encouragement in-person and over the phone. If persistent barriers to AE adherence arise, participants will be given the choice to return to on-site AE sessions.

Social Engagement (SE) Intervention: This group will be designed to control for the social component of the AE intervention. Participants assigned to this group will enjoy a variety of group-based activities centered around wellness will be scheduled throughout the 6-month intervention. This condition will involve one 1-hour-long meetings per week. To promote adherence, FITBOLD staff will track session attendance.

Mid-Intervention Assessment: 3 months into the intervention, regardless of group assignment, you will be asked to complete a mid-point assessment which includes an evaluation of depression and cognitive testing and wearing a physical activity monitoring device for one week (wrist Actigraphy).

Other during-intervention-period activities: In addition to baseline, mid-point, and postintervention, depression symptoms will be assessed monthly throughout the intervention period.

Follow-up/Post-intervention Assessment: You will be asked to complete a follow-up assessment, which will include MRI, blood draw, physical monitoring, a fitness test, an evaluation of depression, and cognitive testing. This will occur after the 6-month intervention regardless of group assignment. The testing will be identical to what was done at the baseline assessment. Similarly, remote activities may be offered.

All participants, regardless of timepoint or group assignment, may be offered virtual options where possible. Our team will be as flexible as possible. Please discuss any questions or hesitations with on-site or virtual sessions with a staff member.

OPTIONAL:

Smartphone-based sessions:
You will be invited to participate in 2 optional phone-based assessments of thinking and memory, each lasting approximately 10 days.

During each session, you will receive a text message from our provider NeuroUX to your smartphone device 4 times per day with a link to complete the study assessment. This link will be viable for about 90 minutes from the time it is received. Each assessment will:

- arrive approximately 3 hours apart

- take only about 3 minutes to complete
- be sent during times to avoid disrupting your sleep
- include a brief questionnaire asking about your current activities and two quick tasks (brain games) that assess cognition. For example, you may be asked to remember a list of words or match shapes into pairs.

What are the possible risks and discomforts of this research study?

Risks of the MRI: The risks involved with the scans are small and limited to the risks present during routine MRI examinations. There is no radiation exposure associated with MRI scans. There are no known dangers of exposure to the magnetic fields used for the brain imaging in this study. During an MRI scanning session, there is potential for the powerful magnetic field to attract metal objects towards the magnet. For this reason, you will be carefully screened for previous exposure to metal fragments or clips that may be inside your body. You will be asked to place all metal and magnetic objects in your possession (e.g., keys, bank cards) in a locker outside the magnetic room. Some people feel claustrophobic, meaning uncomfortable in confined areas, in the scanner, and if that is a problem for you, the MRI will be discontinued, and you may be removed from the study. Finally, the MRI machine is noisy, which has the potential to irritate your hearing. You will be given earplugs to minimize this risk.

Although the MRI is being done for research purposes, there is a possibility that the scan could show something that is unusual or different. In this case, the MR tech will refer the scan to a specialty physician to review. The physician will advise the study team and the study team will inform you if further medical follow up should be done. The physician will be available to discuss the result with your PCP. Your research scan will not be entered in your medical record.

Risks of breach of confidentiality of research data: There is a possibility that your private research data could be seen by someone not associated with the study team.

Risk of depression, anxiety, and cognitive assessments: There is a possibility that you may feel a sense of frustration, fatigue or other discomfort when performing the cognitive tests or completing assessments of depression and anxiety. To reduce discomfort, we allow participants to take frequent breaks between assessments.

Risks associated with exercise testing and exercise intervention: There is a possibility that during or after participation in aerobic exercise, you may incur an injury to a joint or muscle, or experience muscle soreness of fatigue. Other infrequent risks include dehydration and heat exhaustion. Falling is another infrequent risk involved in exercise participation, although this risk will be minimized by the close monitoring of on-site exercise sessions and frequent followup during home-based exercise by an experienced exercise physiologist.

Very rare risks associated with exercise tests are the possibility of having a heart attack or serious change in your heart rhythm, which may require hospitalization. The FIT BOLD staff

recognizes the risk involved in maximal exercise tests (1 myocardial infarction or death per 2500 tests). In accordance with American College of Sports Medicine (ACSM) and American Heart Association (AHA) guidelines, the FIT BOLD trial will perform tests under the following conditions:

- Careful considerations for when exercise testing should not be done
- Under direction of a trained exercise physiologist with a qualified physician available by phone for emergencies
- Appropriate safety measures in place

Risk of using internet communication to collect, transmit, and/or store research data (this includes videoconferencing for virtual sessions): There is always a risk that messages or communications transmitted through the internet could be intercepted or sent to the wrong address. Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed. It is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study. Virtual sessions will not be recorded nor stored.

Risks associated with blood draws: Removal of blood by a needle and syringe poses a small risk (10-25 out of 100 people) of pain, soreness, or bruising at the site of the needle stick, but this is temporary. Some people may experience fainting or dizziness, lightheadedness, or blood clotting (1-10 out of 100 people) and there is also a slight risk (less than 1 out of 100 people) of bleeding or infection at the site of the needle stick. To minimize these risks, experienced medical personnel will handle all the blood drawing procedures and sterile conditions will be maintained.

Suicide is a possible risk of depression. Worsening depression may be associated with an increase in suicidal thinking and suicidal behavior. Tell a member of the research study immediately if you are having any thoughts or feelings about hurting yourself. You will be assessed regularly for the occurrence of depressive, anxiety, and suicidal symptoms during your participation in the study. If you become suicidal or if you experience psychosis (such as hearing voices that others do not hear, beliefs that others do not share), the research team may take steps to protect your life. These steps may involve removing you from the study, informing your family members, providing resources or referrals for care, or taking steps to hospitalize you.

Smartphone-based assessments:

- You may find these assessments boring or frustrating
- The assessments are sent via text message, so message and data rates may apply.
- Completing the assessments will use some of the smartphone battery.
- Your phone information will be temporarily used by NeuroUX in order to complete the smartphone-based assessments. NeuroUX is HIPAA compliant and has security measures in place to protect any personal information.

In addition, to ensure your safe participation in this study, you are being asked to designate someone to be an emergency contact. This should be someone whom the research team can contact if they have questions about/are concerned about your well-being and/or are unable to reach you. This should be someone who has frequent contact with you and who can contact the study staff in case of emergencies. You may not participate in the study if you do not provide a name of someone whom the research team can contact.

What are the potential benefits from taking part in this research study?

There is no guarantee that you will receive any benefit from participating in this research study. However, the program will provide regular, structured, and prescribed exercise for relatively inactive older adults who might benefit both physiologically and psychologically from it. You may benefit from becoming aware of your physical activity and fitness levels. You may additionally benefit from participating in regular aerobic exercise for 6-months. Aerobic exercise can and has shown to improve both physical and brain health. Enhancing your level of fitness and physical functioning could result in less injury and illness, an increase in independence and effective daily functioning, and improvements to your cognitive functioning and mood. You may also benefit from an increase in social interaction and engagement in enjoyable group-based activities. Social engagement in older adulthood improves mood and lowers the risk of decline in your thinking ability.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

You will be promptly notified if any new information, either good or bad, about this study develops, which may cause you to change your mind about continuing to participate.

Will you save my research data to use in future research studies?

As part of this study, we are obtaining data from you. We would like to use this data and your blood samples for studies that may be conducted in the future. These studies may provide additional information that will be helpful in better understanding depression. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. You will not share in any money that the investigators, the University of Pittsburgh, or their agents may receive.

If you change your mind and do not want us to store and use your data and samples for future research, you should contact the research team member(s) identified at the top of this document. The data and samples will no longer be used for research purposes. However, if some research with your data and samples has already been completed, the information from that research may still be used. Also, if the data or samples have already been shared with other researchers it might not be possible to withdraw it to the extent it has been shared.

Who will pay if I am injured as a result of taking part in this study?

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not, however, waive any legal rights by signing this form

Are there any costs to my insurance carrier or me if I participate in this study?

There will be no costs to you for participating in this study, nor will your insurance provider be billed for study activities including the MRI visits, blood draws, research assessments, fitness test, or equipment used in this study. If you require medical care outside of the study, you will be billed in the standard manner for any procedures performed for your routine medical care, including any applicable co-pays, coinsurances, and deductibles. If you need to be hospitalized due to a worsening of your depressive symptoms, you or your insurance provider will be billed for the costs associated with this hospital stay. If you are referred for treatment outside of the study, and you decide to pursue this treatment (such as to a private practitioner or to your PCP), you will be responsible for the costs of such treatment including any applicable co-pays, coinsurances, and deductibles.

Will I be paid if I take part in this research study?

You will be compensated up to $130 for baseline assessments, up to $30 for mid-point assessments, and up to $130 for follow-up assessments (Grand Total = $290). In addition, you will be reimbursed $5 for travel costs for each on-site intervention session attended. For AE group participants, travel reimbursement can total $180 and for SE group participants travel reimbursement can total $125.

Compensation ($290):
Baseline ($130): MRI ($50) + fitness testing and activity monitoring ($40) + clinical and cognitive evaluation ($40)
Mid-point ($30): clinical/cognitive assessment/activity monitoring ($30)
Follow-up ($130): MRI ($50) + fitness testing and activity monitoring ($40) + clinical and cognitive evaluation ($40)

You may earn up to an additional $80 for completing the optional smartphone-based assessments ($40 per session). Grand total that can be earned in this study is $370.

No additional compensation will be provided for the blood draws.

Reimbursement ($5 per session attended):
AE group (up to $180) *$5 x 36 sessions*

SE group (up to $120) *$5 x 24 sessions*

AE group participants who maintain an average exercise volume of at least 80% of prescribed weekly exercise (120 out of 150 minutes) throughout the intervention and SE group participants who attend at least 20 out of the 24 SE sessions will receive a bonus payment of up to $50.

Participants in the AE group can receive total compensation up to $520 and those in the SE group can receive total compensation up to $460 over the duration of the study.

You will be paid on a reloadable debit card. Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 76% of the expected payment.

Who will know about my participation in this research study?

Any information about you obtained from or for this research study will be kept as confidential (private) as possible. As a participant, you will be assigned an identification number. This number, instead of your name, will be used in all data analysis and records. The database for which your identifiable information is located will be password protected and will have limited accessibility. Information not recorded electronically will be stored on file in a secured storage cabinet within a locked office also with limited accessibility. You will not be identified by name in any publication of the research results unless you sign a separate form giving your permission (release).

Will this research study involve the use or disclosure of my identifiable medical information?

Your medical records, including both inpatient and outpatient records, will be reviewed 1.) in order to complete screen for metal or other MRI contraindications and 2.) to review for pertinent eligibility criteria or other contraindications that would make an exercise intervention unsafe. This will help FIT BOLD staff ensure your safety and integrity of the research. Pertinent records include, but are not limited to, history and physicals, surgical history, operative reports, laboratory reports, physician orders, progress notes, radiology reports, EKG reports, emergency department reports, consults, and discharge summaries. If necessary, we will also record information about your mental health that we are unable to obtain during your interviews, such as the symptoms and history of your depression.

Who will have access to identifiable information related to my participation in this research study?

In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information related to your participation in this research study:

- Authorized representatives of the University of Pittsburgh's Office of Research Protections may review your identifiable research information for the purpose of monitoring the appropriate conduct of this research study.
- NIMH, the funding entity for this research study, reserves the right to inspect and/or monitor the study data.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., MRI) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e., quality assurance).

To protect your confidentiality, all personal identifiers (such as your name, social security number, birth date) will be removed (de-identified) and replaced with a specific code number. The information linking this code number to your identity will be kept in a separate, secure location. The investigators on this study will keep the data indefinitely.

We will take the following steps to ensure confidentiality. A research number will be assigned to you and your name will not be used. The only people who will have access to your individual identity are (investigators and staff).

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information or documents protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

There may be future analyses of the research data conducted by the study investigators, as yet unplanned, dealing with other aspects of late-life mental health illnesses and/or exercise. In addition, your de-identified research data may be provided to secondary investigators for the purpose of conducting additional analyses (e.g. late-life mental health illnesses or physical exercise).

Additionally, you may be contacted after concluding your participation in this study by FIT BOLD staff and asked to complete additional questionnaires, measures, or activities related to this research. Furthermore, staff may contact you to invite you to participate in future research studies. Your involvement in these activities is voluntary and you may refuse to partake in any of these potential offerings.

If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include identifiable medical information) related to your participation in this research for at least seven years. The University of Pittsburgh policy for the retention of research records and/or data is seven years after the final reporting or publication of the study.

Is my participation in this research study voluntary?

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC Health System hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

May I withdraw, at a future date, my consent for participation in this research study?

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.). Any identifiable research information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC Health System hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If I agree to take part in this research study, can I be removed from the study without my consent?

You may be removed from the research study at any time by the investigators if:

- your healthcare provider does not provide approval for you to participate.
- you are determined by the research team as unable to follow the study requirements
- you present with any exclusionary criteria (e.g. current depressive episode, major health concern, severe cognitive impairment) throughout the course if the study.
- it is determined that engaging in exercise would exacerbate any health condition or diagnosis.
- you are identified as being acutely suicidal
- any severe neurological abnormality is found to present.

If study staff are concerned about a decline in your thinking ability over the course of the intervention (e.g., you appear repeatedly confused during interactions or are unable to understand task instructions), an investigator will meet with you, discuss pertinent cognitive concerns, complete a cognitive screening measure, and refer to the Alzheimer's Disease Research Center as appropriate.

If clinical or safety concerns related to depression severity arise, your mental health provider will be informed. If the study personnel identify that you have become acutely suicidal, you will be referred to a mental health professional for further evaluation and treatment. This may lead to a clinical intervention that is lifesaving and may not have occurred had you not been participating in the study.

There is the possibility that we may detect something unusual, a tumor, or something different on your MRI scans. The MRI scans in this study are done to answer research questions and not the type which reveal medical conditions. In the event that we detect such abnormalities in the scan, the MR technologist will refer the scans to a qualified specialist (neurologist or neuroradiologist) at the Magnetic Resonance Research Center (MRRC) for expertise in these situations, for further examination and professional opinion as soon as possible after the scan. We will contact you as soon as possible to have you meet with consulting specialist recommend further examination, in which case, you will work with our healthcare provider to decide if further examination or treatment is needed.

Any identifiable research information recorded for, or resulting from, your participation in this research study prior to the date you were withdrawn from participation may continue to be used and disclosed by the investigators.

Can we contact you by email and/or text messaging?

We would like to contact you by email or text for the purposes listed below. We may use email or text to verify appointment scheduling, confirm or clarify information, or communicate educational or follow-up materials (e.g. discuss exercise regimen or invitation of future research opportunities). Only the research team will have access to your email/text communications. If you have any questions or need to contact us for an urgent or emergent situation, please contact a coordinator identified at the top of this document. You should be aware that there are risks associated with sending information via email or text.

- There is always a risk that the message could be intercepted or sent to the wrong address.
- When using any computer, you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server. It is your choice whether you would like to communicate by email or not. Providing your email address to us will indicate that you agree to allow us to send your health information by email.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. 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

VOLUNTARY CONSENT

☐ By initialing this box, I agree to be contacted by text messaging and/or email

Please initial below that you either agree or refuse to allow your blood sample to be used for genetic analyses.

☐ By initialing this box, I agree to have my data and blood sample used to for future research, as described above.

Emergency Contact Information:

_____ _____

Name of contact person Relationship

_____ _____

Address Telephone number

_____

Alternate telephone number

The above information has been explained to me and all my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during this study, and that such future questions will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.
I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations if the research team is unavailable. By signing this form, I consent to participate and authorize the use and sharing of my medical record information in this research study. A copy of this consent form will be given to me.

_____ _____
Participant's Signature Date

_____
Printed Name of Participant

CERTIFICATION OF INFORMED CONSENT
I certify that I have explained the nature and purpose of this research study to the abovenamed individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____ Printed
Name of Person Obtaining Consent Role in Research Study

_____ _____
Signature of Person Obtaining Consent Date