

Clinical Research at Harvard: Representative Scenarios

All of these examples illustrate research carried out at Harvard that can be supported by grants submitted through Harvard, with Harvard as the prime awardee. The examples are intended to illustrate the meaning of *clinical research* and *clinical research with a clinical care component*, and the additional review *clinical research with a clinical care component* may receive, either at the proposal stage or in parallel with IRB evaluation.

Psychology:

- A study of the effects of exercise on mental states: intervention is a regime of regular exercise (brisk walking) to be monitored by FitBit, and measures will include standard psychological assessment instruments.
 - Studies such as this meet the definition of *clinical research* but they would not be considered to have a *clinical care component* so they would not require any review under the guidance except normal IRB review
- An App to reduce NSSI (nonsuicidal self injury) behavior: Building on previous studies showing the benefit of creating a personal “library” of particular types of positive memories to access when the urge to self harm appears, participants who have engaged in self harm will customize an App on their smart phone with their own library of images and text. In one arm of the study participants will be instructed to access the App routinely and be reminded to do so by text messages. In another arm, participants will access the App “as needed.”
 - This study would meet the definition of *clinical research* and it would be considered to have a *clinical care component* since it is studying a means to treat a condition. As such, it would be forwarded for Provost’s Review. Assuming the intervention would be deemed minimal risk by the IRB, the Provost’s Review would be completed either before, or in parallel with IRB review, by considering the relevance of the following for the researcher or research team members: professional training; malpractice insurance; specialized facilities or resources; licensure or credentials.
- New approaches to cognitive behavioral therapy: a group of clinicians at outpatient psychiatric clinics will be trained in a new method of monitoring patient progress and tailoring treatment based on a structured review of recordings of previous sessions. The methodology has been developed by the Researcher, who will oversee the training of clinicians, and who will recruit comparable clinics using Standard of Care methods as controls.
 - This is *clinical research with a clinical care component*, presumably to be deemed minimal risk by the IRB. Provost’s Review would be carried out either before, or at the same time as IRB review. Upon

confirming that the care takes place in established treatment sites, and the intervention treatment is rendered by licensed, insured clinicians, and that the Researcher is appropriately licensed and insured, approval would be expected to follow in the same time frame as IRB review and approval.

- A clinical psychologist is PI in a project studying the effectiveness of computerized training programs to improve neurocognitive skills in patients with schizophrenia and in individuals identified as having 'clinical high risk' for developing psychosis. These studies involve pre- and post-fMRI scans with training sessions occurring off site. Patients for these studies are recruited from area hospitals and clinics and from the community. These studies are done in collaboration with investigators at affiliate hospitals who provide clinical consultation and care as needed for the study subjects.
 - This is *clinical research* with a *clinical care component*; the intervention is minimal risk, and Provost's Review would focus on the allocation of roles and responsibilities between the PI, who possesses the requisite training and experience for the project, and the collaborators at affiliate hospitals, who are well situated to provide care to subjects as appropriate. Adequacy of facilities is a consideration when clinical care is involved, and including the hospitals is an assurance in this case.

Economics:

- Farmers from across a district in India are recruited to a study designed to test the effects of several different incentives, or "nudges," on their participation in a program providing fertilizer, improved seed strains, and instruction to optimize yields. Seven hundred villages are involved, three hundred each randomized to one of two treatments, and another hundred serving as a control, receiving instruction but not fertilizer or new seed strains.
 - While the term "*clinical trial*" is often used interchangeably with "*randomized trial*," this case is an example of a randomized trial that has nothing to do with clinical research or clinical care. This guidance is concerned with clinical research with a clinical care component, not to all classes of research that involve a randomized trial methodology.
- Health insurance payment records and patient medical records are analyzed in health care outcomes research.
 - While such studies fall under the definition of *clinical research* and they are about *clinical care*, they do not have a *clinical care component*, when they have no element of prospective intervention, and are based on existing data that was not generated as part of the study design.

Engineering:

- Wearable “smart” prosthetics may improve mobility for patients who are recovering from a stroke or who have other conditions that impair their walking ability. It is anticipated that improving mobility will lead to a range of health benefits. For this early stage research, healthy volunteers will be recruited initially, followed by rehabilitation patients, according to a carefully drawn set of inclusion and exclusion criteria. The plan is to run subjects at a lab on campus, and then to have rehabilitation patients participate at Spaulding Rehab and similar rehab center sites. In addition to the SEAS faculty PI, a Biological Anthropology faculty member from FAS will be a co-pi, and there will be investigators who are M.D.s at rehab center sites.
 - This project is *clinical research with a clinical care component*, that can be supported by sponsored research funding through Harvard, with subawards to affiliate and other rehab institutions as appropriate. Depending on the risks identified by the researcher and by the IRB in its review, the level of scrutiny by way of Provost’s Review will vary.

School of Dental Medicine:

- A randomized clinical study to compare the clinical outcomes of titanium-zirconium and titanium dental implants (both FDA approved products). The study will enroll patients that are receiving dental implants as part of their regular dental care at HSDM and will be evaluated for 3 years. One study-implant per patient will be placed and restored with a single crown. Outcome parameters will include procedure comparisons, healing, quantitative and qualitative measurements of the peri-implant soft tissue, implant and superstructure survival, and rate of complications. This study includes X-rays and dental molds and pictures of the site as a part of the data collection.
 - This clinical trial takes place in the setting of regular care of patients at the HSDM clinic. Issues that might be considered on Provost’s Review are satisfied: licensure of researchers, adequacy of facilities, liability insurance, familiarity with administration of clinical trials in a patient care setting. Since the trial involves the comparison of two products approved by the FDA for the study population, risk is no greater than minimal.

Public Health:

- In an East African country, a major concern is motivating HIV patients to comply with their medication regimen. Researchers will compare the effectiveness of a new program that involves having HIV patients meet with community health workers in their own neighborhoods, to the standard practice of having the patients travel substantial distances to special HIV clinical centers. The researchers will monitor the two approaches, review

- patient charts, and interview a sample of patients to gather qualitative insights about the barriers to consistent maintenance.
- Although the researchers will not be treating patients, assessing the two delivery models is *clinical research* that is closely related to *clinical care*. The international setting, as well as the vulnerable study population, will receive attention during review, though the nature of the study is entirely appropriate for Public Health.
- A randomized controlled trial is planned, to evaluate the effectiveness of using text messages to improve the knowledge, communication, and attitudes about reproductive health among adolescents in senior high schools in the capital city of a West African nation. There are significant gaps in knowledge about reproductive health on the topics of sex, pregnancy, sexually transmitted diseases, and contraception among these secondary school students. These gaps contribute to unwanted pregnancy and spread of sexually transmitted diseases. At the same time, phone ownership and use among young people has spread rapidly, especially in urban areas. The project will seek to use mobile phone messages to increase awareness of these reproductive health issues. By conducting a randomized controlled trial, it will be possible to statistically evaluate if the messages have had any effect on improving outcomes for adolescents in the areas of knowledge, communication, and attitudes. This work can help guide future programs that can scale up this intervention and ultimately improve the health and wellbeing of adolescents across the country.
 - Although this is a randomized trial whose ultimate goal is to reduce the incidence of disease and unwanted pregnancy, it does not have a *clinical care component*: the outcomes to be measured concern “knowledge, communication and attitudes.” On the other hand, the study meets another criterion for Provost’s Review, since it is international human subjects research.

Medical School:

- Faculty involved in patient centered outcomes research and Bioinformatics researchers at the Medical School propose to establish a Clinical Data Research Network in collaboration with clinicians at selected hospitals, both Affiliates and teaching hospitals in other states. In addition to patient clinical records, data to be collected, stored and analyzed at HMS would include online surveys of hospital patients, both during the course of treatment and post treatment. Data and analyses will be sent to the clinicians providing care to the patients.
 - This is research with a *clinical care component*, so it would require Provost’s Review. The allocation of roles and responsibilities is such that the proposal would not require a high level of scrutiny: the HMS investigators are not involved in direct delivery of care, and any

information provided to clinical collaborators at hospitals would supplement, not replace, information they might use in the course of providing care to patients.