Engagement or Non-Engagement: That is the IRB Oversight Question

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Engaged in Research?

- Learning Objectives:
  - Learn about OHRP Guidance and HRPP Policies on engagement in human subjects research
  - Discuss the different types of reliance agreements put in place when the BMC/BU Medical Campus IRB is the IRB of record for external sites, organizations, and individual investigators
  - Differentiate between engagement and non-engagement through the evaluation of detailed case studies and examples

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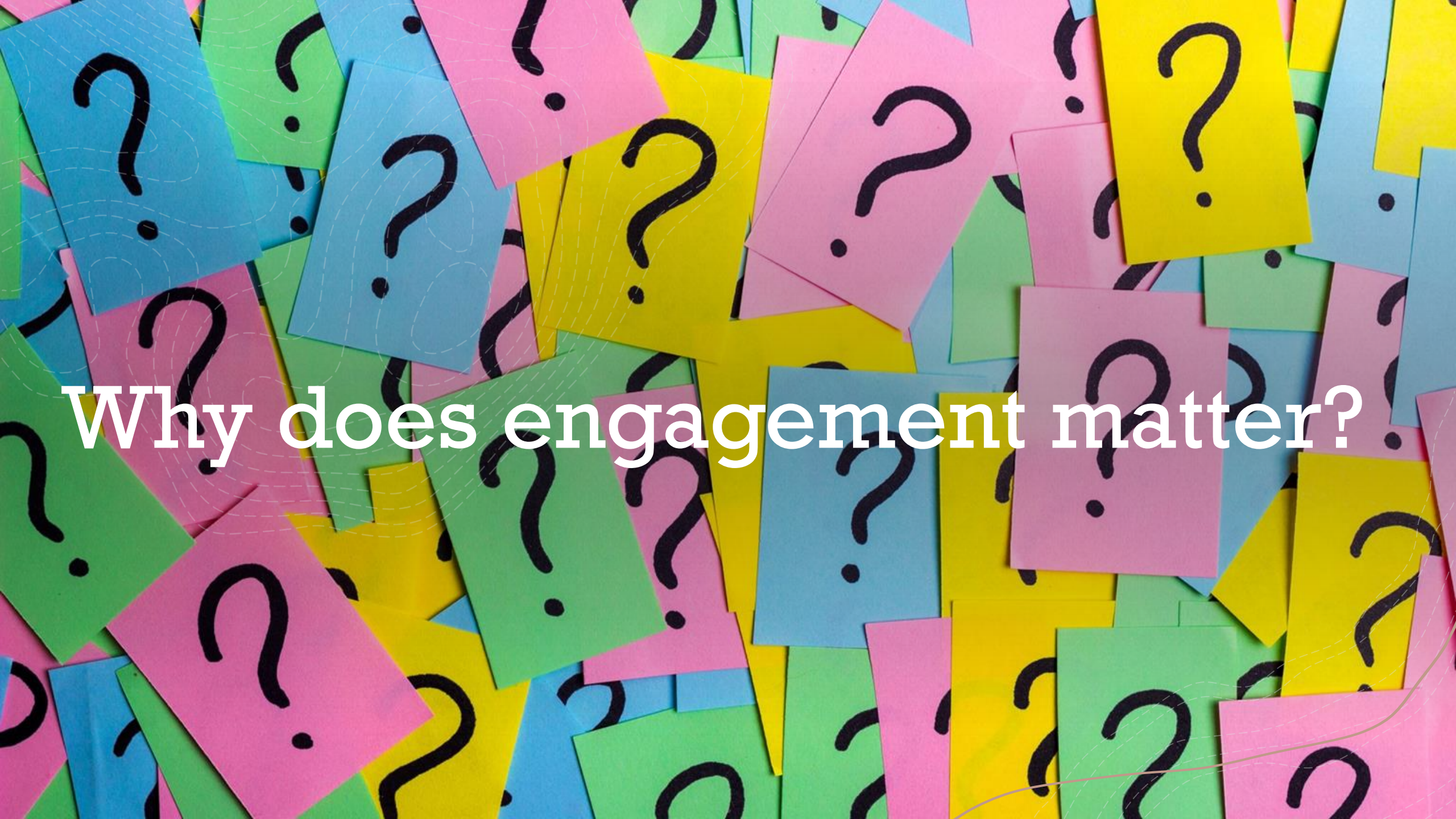

Why does engagement matter?

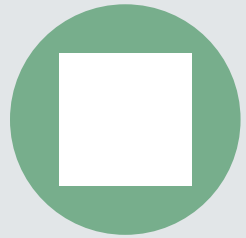
Big Commitments:

DOES THE BIOSTATISTICIAN WE HIRED NEED TRAINING?

A COLLEAGUE IS PASSING OUT FLYER, ARE THEY AN INVESTIGATOR?

PARTNERING WITH A LOCAL NON-PROFIT THAT DOESN'T DO RESEARCH, DO THEY NEED TO GET AN IRB?

DOES EVERYONE LISTED IN THE GRANT NEED TO BE IN INSPIR?



CAN I BE AN AUTHOR ON THE PAPER?

Engagement in Human Subjects Research = IRB Oversight and subject to all applicable regulations, laws, policies, and requirements

When to think about engagement?

+ Once we've concluded that any activity in your project constitutes human subjects research, we need to determine who (individuals and/or institutions) is *engaged* in research since not every person nor every institution involved in a human subjects research project requires IRB oversight.

Human Subjects Research

Human subject: a living individual about whom an investigator conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private* information.(**Private**: situations where you expect what you say, do, or write to not be made public. **Identifiable**: the identity is readily ascertainable to the investigator.)

Research: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Engaged?

OHRP: Engagement of Institutions in Human Subjects Research (2008)

- When an institution is *engaged* in non-exempt human subjects research that is conducted or supported by HHS, it must satisfy HHS regulatory requirements related to holding an assurance of compliance and certifying institutional review board (IRB) review and approval.
- ...this guidance should be used to determine whether an *institution* involved in some aspect of the research is *engaged* in that human subjects research, because if it is, certain regulatory requirements apply.
- OHRP recognizes that many institutions and individuals (e.g., the principal investigator, statistical centers, community physicians, educators, data repositories) may work together on various aspects of a human subjects research project. However, not all participating institutions and individuals need to be covered by an FWA or certify IRB review and approval of the research to the HHS agency conducting or supporting the research. This guidance aims to assist institutions in determining whether they must meet those requirements, that is, whether they are *engaged* in activities covered by the regulations.

OHRP Engagement Guidance:

- **III. Interpretation of Engagement of Institutions in Human Subjects Research**
  - In general, an institution is considered *engaged* in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.
- Section A. Institutions Engaged In Human Subjects Research
  - Lists 6 scenarios where institutions would be engaged.

BMC/BUMC HRPP Policies:

- 2.4 Engagement in Research
  - Submission to the IRB is required for all research in which a Boston Medical Center or Boston University Medical Campus constituent or entity relying on the IRB is engaged in human subjects research. **Boston Medical Center or Boston University Medical Campus IS engaged in human subjects research if:**

Note: while the next few slides refer to activities done by BMC/BUMC employees/agents, since our policies model OHRP guidance, it's very likely that other institutions would be engaged if doing the same study procedures.

BMC/BUMC is engaged if:

- Boston Medical Center or Boston University Medical Campus **receives a direct Federal award** through a grant, contract, or cooperative agreement for human subjects research, even where all activities involving human subjects are carried out by employees or agents of another institution; or
- Boston Medical Center or Boston University Medical Campus employees or agents:
  - **intervene** for research purposes with any human subjects of the research by performing invasive or noninvasive procedures or by manipulating the environment; or
  - **interact** for research purposes with any human subject of the research; or
  - **obtain the informed consent** of human subjects for the research; or
  - **obtain** for research purposes **identifiable private information or identifiable biological specimens** from any source for the research. Obtaining identifiable private information or identifiable specimens includes, but is not limited to:
    - observing or recording private behavior; or
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; or
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of either institution or the investigators.

OHRP Engagement Guidance:

- **B. Institutions Not Engaged in Human Subjects Research**
  - Institutions would be considered **not** engaged in an HHS-conducted or -supported non-exempt human subjects research project (and, therefore, would not need to hold an OHRP-approved FWA or certify IRB review and approval to HHS) if the involvement of their employees or agents in that project is **limited to one or more** of the following. The following are scenarios describing the types of institutional involvement that would make an institution **not** engaged in human subjects research; there may be additional such scenarios:
  - Lists 11 scenarios where institutions would NOT be engaged

BMC/BUMC is NOT engaged if:

- Assisting with the recruitment of subjects by:
  - informing prospective subjects about the availability of the research; or
  - providing prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators; or
  - providing prospective subjects with information about contacting investigators for information or enrollment; or
  - seeking or obtaining the prospective subjects' permission for investigators to contact them.*
    - *Submission to the IRB may be required depending on population and use/release of PHI – contact us
- Example: A BMC clinician who provides patients with literature about a research study occurring at another institution, including a copy of the informed consent document, and gives the patient contact information for the investigators.

BMC/BUMC is NOT engaged if:

- Obtaining coded private information or biological specimens from another institution, provided that the recipient investigators will be unable to readily ascertain the identities of the subjects to which the coded information or specimens pertain (for example, by having a written agreement prohibiting the release of the key to the code);
  - Example: BU SPH Biostatistician performing analysis on a dataset without any direct identifiers and there is an agreement in place
- Authoring a paper, journal article, or presentation describing a human subjects research study without obtaining access to identifiable private information; or

BMC/BUMC is NOT engaged if:

- Performing commercial or other services for investigators provided that all of the following conditions also are met:
  - the services performed do not merit professional recognition or publication privileges; and
  - the services performed are typically performed by those institutions for non-research purposes; and
  - the institution's employees or agents do not administer any study intervention being tested or evaluated in the study;
- Examples: BMC employees obtain blood through a blood draw or collect urine and provide such specimens to investigators as a service.

BMC/BUMC is NOT engaged if:

- There are a few more listed in the policies and in OHRP guidance, including:
  - Accessing or using identifiable private information when visiting an institution that is engaged in the research, provided that their research activities as visitors are overseen by the IRB of the institution that is engaged in the research
  - Providing clinical trial-related medical services that are dictated by the study and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators, provided certain conditions are met
  - Administering the interventions being tested or evaluated in the study limited to a one-time or short-term basis, provided certain conditions are met

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What is “cede review”?

- Ceding, or “relying” is when an institution permits an IRB outside their institution to oversee the IRB review process on their behalf
  - “Relying” Institution cedes to the “Reviewing” Institution
  - In order to define the responsibilities of site, the “Reviewing” Institution enters into a reliance agreement with the “Relying” Institution
  - Ceding is only needed when both institutions are engaged in research

What is a “reliance agreement”?

- A formal, written document that provides a mechanism for an institution (or organization, or individual) engaged in research to delegate institutional review board (IRB) review to an external institution.
- Institutions that are engaged in human subjects research, where one institution will rely on the other institution’s IRB, must agree to the terms of the Reliance Agreement before research can begin.

What are the "terms" of a reliance agreement?

Sample Division of Responsibilities:

- Reviewing Institution:
  - Provide initial and continuing reviews of submitted research, reviews of amendments; reviews of unanticipated problems that may involve risks to subjects or others; reviews of noncompliance that may represent serious or continuing noncompliance
  - Provide Relying Institution with consent template to customize in limited sections
  - When appropriate, conduct on-site or remote post-approval monitoring or for-cause audits.
  - Review any research study personnel COI or financial conflict of interest ("FCOI") management plans specific to the Study submitted by the Relying Institution
  - Make available IRB meeting minutes and other relevant documentation (approval letters, consent forms) to Relying Institution

What are the terms of a "reliance agreement"?

Sample Division of Responsibilities:

- Relying Institution:
  - Provide the Reviewing Institution with any local context information applicable to the research, including local requirements pertaining to vulnerable subjects and recruitment.
  - Cooperate with and provide reasonable assistance to the Reviewing Institution in conducting for-cause audits, as applicable.
  - Obtain disclosures of, and review and manage, FCOI's
  - Provide Reviewing Institution with determinations from all required internal reviews (e.g., Institutional Biosafety, Radiation Safety).

What is a “reliance agreement”?

- So, are reliance agreements “one size fits all”? NO!

- At BMC/BUMC, we use 3 types of reliance agreements:
  - IRB Authorization Agreement (IAA)
  - Collaborating Institutional Investigator Agreement (CIIA)
  - Individual Investigator Agreement (IIA)

IRB Authorization Agreement (IAA)

- IAA's are used to document reliance between two engaged institutions with active Federalwide Assurances (FWAs)
  - A Federal Wide Assurance (FWA) is the documentation of an institution's commitment to comply with Federal regulations and maintain policies and procedures for the protection of human participants.
  - An institution must have an FWA in order to receive HHS support for research involving human subjects.
  - Under IAAs, the relying institution is responsible for assuring training and qualifications of their investigators

The most common IAA used now is done through SMART IRB.

What is a "SMART IRB"?

- SMART IRB is a *platform* (**not an IRB**) that enables IRB reliance among institutions who agree to collaborate under a pre-signed master SMART IRB global reliance agreement.
  - Online system
  - Paper forms
  - Resources for researchers and IRBs/HRPPs

- The SMART IRB agreement is a national **master agreement** that allows institutions to avoid having to negotiate individual agreements per study or group of studies.
  - The agreement lays out the responsibilities of the Relying and Reviewing Institutions

Collaborating Institutional Investigator Agreement (CIIA)

- CIIAs are used to document reliance between two engaged institutions when the relying institution does NOT have an active FWA
  - Ex. Dr. Smith is conducting a clinical trial randomizing children to an exercise intervention or usual activity. Staff from the Boys and Girls Club will recruit subjects and deliver the exercise intervention.

- Each separate engaged investigator at the non-FWA institution must sign their own CIIA.
  - Organizational Official (for example, Executive Director) also signs
  - Under CIIA, Reviewing Institution is responsible for certification of training/qualifications of external investigators

Individual Investigator Agreement (IIA)

- IIAs are used to document reliance between an engaged institution and an engaged individual investigator who is not affiliated with an institution.
  - Dr. Jones is evaluating whether trained peer counselors can deliver an intervention to increase self-esteem. The trained peer counselors do not normally work in research and are not affiliated with an institution.
  - Sometimes also used with international investigators or students from external sites who are not receiving academic credit
  - Terms and conditions are confirmations that the investigator understands and commits to compliance with rules and regulations
  - Under CIIA, Reviewing Institution is responsible for certification of training/qualifications of external investigators

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Time to get Engaged!

Scenario 1:

- An investigator at University of Maine is studying dental fillings. As part of an IRB-approved study, subjects need to complete a survey, provide a saliva sample, and have a dental x-ray. An x-ray technician at BUGSDM performs a dental x-ray and send the results to the investigator as a service. BUGSDM is not otherwise involved in the study.
- 1- BUGSDM is engaged in human subjects research
- 2- BUGSDM is not-engaged in human subjects research

Scenario 2:

- A BUMC researcher partners with a non-profit that helps veterans with PTSD. During a group session, the BUMC researcher obtains informed consent from the veterans and a buccal swab. However, since the study looks at changes over time, the busy BUMC researcher asks the non-profit employees to collect a buccal swab each week for a year and consent any new participants that join the group. Is the non-profit engaged in research?
- 1- Non-profit is engaged in human subjects research
- 2- Non-profit is not-engaged in human subjects research

Scenario 3:

- A collaborator at Tufts asks a BMC pathologist to review slides of tissue to assess the level of inflammation taken before and after exposure to a novel anti-inflammatory drug being tested in a federally-funded, IRB-approved research study. The slides are only labeled with a code and they've executed the appropriate agreements.
- 1- BMC is engaged in human subjects research
- 2- BMC is not-engaged in human subjects research

Scenario 4:

- A BMC PI is collaborating with MGB on a clinical trial. The BMC MD co-investigators will identify eligible patients from their clinical practice and introduce the study to them. If the patient is interested, the BMC co-Is will ask them to sign a HIPAA authorization to permit disclosure of their contact information to MGB. MGB will then reach out directly to the patients to discuss the study, and for those interested, MGB investigators will conduct the consent process.
- 1- BMC is engaged in human subjects research
- 2- BMC is not-engaged in human subjects research

Scenario 5:

- BU SPH has a subcontract with Tufts for a clinical trial. The Scope of Work describes BU SPH's activities as: Designing the protocol; providing expertise on interpretation of aggregate results; contributing to writing and publishing the manuscript as study authors.
- 1- BU SPH is engaged in human subjects research
- 2- BU SPH is not-engaged in human subjects research

Scenario 6:

- A BUSM PI is collaborating with Northeastern on a new text messaging study with medical students. The BUSM PI will identify eligible student participants and introduce the study to them. If they are interested, the BUSM PI will conduct the consent process and help them load the text messaging app onto their phone. They will then provide the list of consented subjects to Northeastern, who will conduct regular surveys and interviews with students about the app. The BUSM PI will receive de-identified data for analysis.
- 1- BUSM is engaged in human subjects research
- 2- BUSM is not-engaged in human subjects research

Scenario 7:

- BEDAC is acting as a data coordinating center for a small multi-site survey study under a subcontract. They will manage the secure storage of the study data, which consists of longitudinal questionnaires labeled with a code. The questionnaires are linked by the use of this anonymous code chosen by the study subjects. BEDAC will also contribute to the analysis of the data.
- 1- BEDAC is engaged in human subjects research
- 2- BEDAC is not-engaged in human subjects research

Scenario 8:

- A BMC PI recently learned that she is the prime awardee of a new R01. This grant will fund study activities in South Africa conducted by collaborators at the University of Witswatersand (Wits). The Wits IRB will review and provide IRB oversight for the local South African study team. Subjects will be enrolled and consented by Wits study staff. Blood will be drawn at 5 timepoints, and subjects will also fill out questionnaires. De-identified blood samples and de-identified questionnaires will be shipped from South Africa to the BMC PI in the USA for analysis.
- 1- BMC is engaged in human subjects research
- 2- BMC is not-engaged in human subjects research

Scenario 9:

+A BU-CRC student is joining a BU SPH study staff in order to help support the conduct of a focus group study. This BU-CRC student is excited about the opportunity as she will both gain experience in research and also will be obtaining academic credit for her work on the project. She will be helping to facilitate the focus groups.

+- BU-CRC is engaged in the research

+- BU-CRC is not-engaged in the research

Scenario 10:

- A BMC PI is collaborating under a subaward on a multi-site clinical trial that is a evaluating a new type of cognitive-behavioral therapy (CBT). Subjects will be identified and consented at UMass Chan Medical School, and the UMass team will randomize subjects to one of two study arms; (1) usual care + CBT, or (2) usual care alone. For subjects randomized to the usual care + CBT arm, BMC co-investigators will administer the CBT at regular study visits using a telehealth platform hosted by UMass.
- 1- BMC is engaged in human subjects research
- 2- BMC is not-engaged in human subjects research

Scenario 11:

- A study team decides to try community-based participatory research. They will recruit leaders of a local church to help them with the study. These community members will participate in the design of the study. They will also pass out study flyers to other attendees of their church, and they will allow the study team set up a recruitment booth at upcoming events.
- 1- The community members are engaged
- 2- The community members are not-engaged

Scenario 12:

- A study team decides to try community-based participatory research. They will recruit residents of a local housing complex to help them with the study. These residents will pass out flyers to their neighbors and will also be trained to explain the study and answer questions. Interested individuals will be asked to call the study team to go over the consent form and the study team will conduct the consent process. The residents will also be trained to help conduct interviews and focus groups with individuals who decide to participate.
- 1- The community members are engaged and a reliance agreement is needed to cover their IRB oversight
- 2- The community members are not-engaged and no reliance agreement is needed