A SOCIAL, BEHAVIORAL, & EDUCATIONAL RESEARCH (SBER) CASE STUDY OF MEDICATION ADHERENCE AND DESTIGMATIZING OPIOID RECOVERY SERVICES

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OVERVIEW
The social, behavioral, and educational research (SBER) case studies provide education and guidance on how to identify and mitigate risks associated with SBER. These studies may be used by both IRB administrators and investigators when reviewing and designing research studies that involved SBER components.

Case studies follow a standard format that includes: 1) a fact pattern, 2) regulatory, cultural, and ethical issues, and 3) a risk/benefit analysis and risk management options. This format was created to allow for flexibility in applying the case studies.

By identifying common themes, linking them directly to federal regulations and guidance, and outlining risk mitigation options, the case studies can be used in a variety of ways, which include: 1) as an education tool for training individuals in human subjects research, 2) as a basis for developing reviewer checklists/worksheets, and 3) as a tool in designing research projects.

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CASE STUDY
Piloting initiatives to overcome reluctance to utilize group-based recovery services for patients with Hepatitis C (HCV) and opioid use disorder.

SCENARIO/FACT PATTERN
Behavioral health clinicians at Big City Community Health Center (BCCCHC) are trying to improve outcomes for patients with HCV who have joined their addiction recovery and wellness service program. Services for those with substance use issues include: detox; counseling; education and case management; individual and group counseling; and harm reduction/recovery skills groups. While utilization of their detox treatment program has been high, group counseling and harm reduction/recovery skills group sessions have proven difficult to sustain. Engagement in these services by affected individuals and by their support group can be a crucial factor in reducing risk of relapse. Anecdotally, clinicians have noticed that consistent use of the group sessions seems to be associated with medication adherence and improved outcomes for patients with HCV. However, an initial quality improvement assessment revealed that patients found stigma associated with both substance use and HCV to be a barrier to both accessing and continuing to using the group sessions.

The clinicians would now like to further analyze the relationship between stigma, group service utilization, and medication adherence for HCV infected patients. To do this, they propose a two part study. First, they plan to hold a series of 3 focus groups (10 Subjects in each) who self-report HCV and opioid use. The groups will discuss why Subjects do or do not utilize or want to utilize the group services, in an effort to to further identify characteristics of the perceived stigma. They will also discuss what might help encourage
those with HCV who use opioids to use the services, and ask them to help craft targeted affirming messages aimed at reducing stigma. Subjects will be passively recruited using flyers on the addiction recovery and wellness service floor of BCCHC. Eligibility will be confirmed during a screening interview when Subjects call in.

Once the messages are finalized (and IRB approved), they will then enroll 60 adults with treatment naive HCV and documented opioid use disorder in a randomized trial. Investigators will compare service utilization and outcomes of those who receive standard appointment reminders to those who receive enhanced affirming messages and reminders. They plan to recruit from BCCHC’s online patient communication portal, seeking a HIPAA waiver to identify the eligible patient population, and then sending a letter co-signed by the potential subjects’ Primary Care Physician or Addiction and Recovery Specialist. Thirty subjects will receive standard messages, with 12 week course of a single pill/day HCV treatment regimen consistent with standard of care at BCCHC. Thirty Subjects will receive enhanced appt reminders, with the 12 week course of a single pill/day HCV treatment regimen. The pills will be in digital capsules to provide real-time verification of medication ingestion events and can be used to monitor medication adherence.

Digital pills are a radiofrequency emitter combined with a standard gelatin capsule that is compounded with a medication. Upon ingestion of the digital pill, the electro chemical gradient in the stomach will activate the emitter, signaling medication ingestion information to a wearable tech device (reader). The reader then stores encrypted ingestion data and sends it to a smartphone and cloud based server in real time. This data is then available for review by clinicians. The smart phones and readers will be provided by the study. Subjects may keep the smart phones upon completion of the study. The study will also cover the cost of the HCV medication.

In addition to regular care and optional group service utilization, Subjects will come in for 4 study visits (6 weeks, 12 weeks, 6 months, 1 year). Each visit will consist of a brief physical exam, drug test (blood), semi-structured interview, and quality of life survey. Investigators will combine this with review of the Subjects medical record for information regarding group service utilization, medication adherence, liver function, relapse, overdose, and general wellness at these time points.

**DISCUSSION**

**Questions/Comments for the researcher:**

- How will individuals be consented for participation in the focus groups?
- Considering that inclusion criteria for this group is opioid use disorder, how will you determine if a subject is able to consent to participate? Might the capacity for consent change over time? How should continued consent be assured and documented?
- Will the focus groups be audio recorded? When will audio recordings be transcribed? When will they be destroyed?
- Is information in the cloud and on the reader secure?
- What would happen if the reader or phone are hacked or stolen?
- Given the sensitive intersection of identities, and the understanding that they carry stigma, could a more private method of discussion achieve the same/similar aims without risk of outing?
- What are the protections for the electronic information as it is stored and analyzed on the cloud?
- If stigma is preventing this patient population from accessing group services, will passive recruitment be sufficient to get focus group Subjects?
- Is a letter in the patient portal the right way to make first contact?
- Who will be conducting the focus groups and/or study visits?
- Will monitoring adherence impact adherence in the control group?
- Will the content of the enhanced messages place subjects at risk?
REGULATORY, ETHICAL, AND CULTURAL ISSUES

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research Subjects in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to Subjects.

Waiver of Documentation of Consent (45 CFR 46.117) is permissible when:

- The signature on the informed consent document would be the only record linking the subject to the research and the principal risk of harm to the subject would be a breach of confidentiality. For example, for research on sensitive topics, such as domestic violence or illegal activities; OR
- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context. For example, minimal risk research that involves surveys/interviews conducted via telephone or online.
- Under the 2018 Common Rule, there is an additional requirement for the IRB approval of an informed consent documentation waiver request: Where the Subjects are members of a cultural group in which signing forms is not a normal/acceptable practice.

Questions for the IRB:

- What are the security/HIPAA concerns related to digital pill use?
- Does the institution need a BAA with the digital pill/cloud server/phone app company?
- Should age inclusion criteria be added?
- Should the study seek a Certificate of Confidentiality from the NIH (not an NIH funded study)?
- Should written consent for participation in the focus group be waived?
- Is provision of a smart phone and/or payment for this extremely expensive medication an undue inducement to participation?
- How might alterations to the study design lower risk to subjects?
- What are the procedural risks of this study?
- While the HCV medication is approved and standard of care, does combining with the digital pill make this an FDA regulated study? Are additional determinations required (e.g., non-significant risk)?
- What training should be required for the study staff responsible for facilitating the focus groups?
- What are the physical security details associated with the study smart phone and reader (e.g., storage of the device, access to it)?

RESOLUTION AND DISCUSSIONS

Risk/Benefit Analysis:

- What special challenges does this research pose for this population? Consider specifically: loss of confidentiality, disclosure of substance use disover, disclosure of HCV, disclosure of seeking treatment, risk to insurability.
- Does the recruitment process pose unnecessary risks?

Mitigation/Management of Risks:

- Focus groups sessions should begin with a confidentiality reminder to all Subjects.
- Information provided to volunteers during recruitment, pre-screening, and enrollment should describe the nature of the questions that will be included in the semi-structured interview, quality of live survey, and asked in the focus group. Given the sensitivity of questions, Subjects must be free
to skip questions on the survey, refuse to answer questions during the focus group, and may terminate participation at any time.

- Data must be collected through a HIPAA compliant web server then securely relayed to a cloud-based program. The cloud-based database must be hosted behind the secure firewall and accessed through BCCHC secure computers. Identifiers should not be linked to ingestion data captured by web server or the cloud-based program.
- Subjects may be having liver function and drug testing blood draws for clinical care at similar time points. Can this data be drawn from the medical record to prevent re-sticking/superfluous draws?

**ALTERNATE DETAILS:**

**Other Events:**
A recording device with the audio interviews is stolen.
Subject loses their phone.

**New Recruitment Strategy:**
Passive recruitment is insufficient, so the investigator submits an amendment seeking to give $5 gift cards to enrolled subjects who refer a potential Subject who completes screening (snowball/chain-recruitment).

**REFERENCE(S):**

45 CFR 46.117(c) [http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.117](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.117)