ORPP&E Webinar

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Session: IRB Chairs Series: Conducting Research in the Inpatient Mental Health Unit

Presenter: Stephen Bartlett, RPh, MSPH; Fred Hendler, MD, PhD; Ryan Holliday, PhD

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**Soundia Duche:** How thrilled I am that we’ll be having an opportunity to do this with some exceptional presenters that we have lined up for you. Just as some background, we’ve been working on implementing this series for the past couple of months and our hope is to do it on a quarterly basis, and our goal is really to discuss ethical and regulatory considerations that affect the IRB’s review of human subjects research, okay? This is going to be very, very different than pretty much any of our other webinars because you’re not going to be dealing with a yes or no, black or white in your decision making as to can I do it, you know, in this case it’s research in the inpatient mental health unit. What we hope to do in this series is really explore complex issues. Some of them will be highly contentious topics and we want to, through the discussion between compliance officers, IRB members, investigators who we might invite to present, really talk about the considerations that the IRB would take in reviewing such research. The things that would make it approvable, the things that would not. And so our hope is that when you’re at an IRB meeting and you get a similar proposal that comes in you can think back to this series and think about the thought processes, the deliberation, the considerations that were discussed and then apply them. Obviously each case will be unique and so you may come up with a different decision than what you’ll hear today in some of our cases. Cases are for illustrative purposes only. What we want to make sure is that we think through the ethical considerations of the topic at hand. For our investigators who are participating, our hope is that you too by listening in to some of the considerations that the IRB members discuss, by hearing the issues that the compliance officers will raise, that in designing your protocol you can take these things into consideration. And so either avert potential negative situations and design your protocol so that you can achieve your research goals in an ethically sound way ensuring that our Veteran subjects are adequately protected, okay? Again we’re going to get into some topics that are very, very contentious. I received an e-mail from someone who was not able to attend this training, but she remarked that she’s so happy that we’re doing this and shared with me that she remembered a decade or so ago when she worked in the inpatient mental health unit. I will call it, there were highly spirited discussions on the ward about whether research could be done or not. And so, again, we’ll be talking through these issues. You’re not going to leave with a yay or nay but really just the framework and the considerations to take into account. And so with that, I’m going to turn this over and introduce our first speaker, Ms. Cynthia Kerenyi, who is with the VA’s Office of Research Oversight. And so Cynthia, before you actually start on your slides if you can just give people a little bit of background on you and what you do for ORO that would be very helpful.

**Cynthia Kerenyi:** Thank you Soundia. My name is Cynthia Kerenyi. I joined ORO in late 2006 as a Health Science Specialist. I’ve been with the office since and I’m currently a health science specialist with the Human Research Protections Workgroup. Our workgroup interacts with the facilities for remote compliance cases and also goes onsite for focus reviews as part of our CPR program where we go out to facilities and do multi-subject reviews. We participate in those. And then also as complaints come in from stakeholders or there’s allegations of concern from whistle blowers or other interested parties we also do those investigations.

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**Soundia Duche:** Perfect. Thank you Cynthia.

**Cynthia Kerenyi:** Thank you. So, the presentation today is concerning ethical considerations for research in an inpatient mental health unit. The reason for focusing on this area from our oversight office is that we had an oversight case, a little while ago, that included ethical concerns that revealed some compliance gaps. And so we thought it was a teachable moment that we should share with the field. We had a similar presentation in late 2017 and so we were very pleased to be invited back to continue the conversation with the field. The concerns that were identified in the teachable moment included the appropriateness of including in a study conducting research recruitment activities and obtaining informed consent for study participation from prospective subjects while they were admitted in an in-patient mental health unit that had elopement prevention features, so individuals could not freely come and go. Unfortunately the protocol did not describe recruitment of involuntarily admitted patients or patients on involuntary hold, so the problem was that the IRB had not considered in the informed consent process, had not formalized protections as a result of that lack of awareness. So as part of our oversight of the situation, we sought ethics consults, we reached out to the National Center for Ethics and Healthcare, and the recommendation that, was that the study team and the IRB document the appropriateness of introducing the study, conducting research recruitment activities and then obtaining informed consent for participation from prospective subjects while they were admitted in the inpatient mental health unit. So, I’ll stop here to point out the teachable moment, and the take away on the required action was consider and document. So there wasn’t a pre-judged outcome that we were pushing in any particular direction. The remedy was simply to have a consideration of the ethics and appropriateness and to document that.

So our discussion then is really about, well, how do we do this right? So the inclusion of the subject population requires that investigators and IRBs assure that the protocol and the consent process recognize those real and perceived vulnerability to coercion and undue influence and limitations to autonomy. And the caution here is really to consider that there is variety in perception to information based on vantage points. And so we want to make sure that when this type of study is being considered that that perspective of the differing vantage points is in the thought process and the consideration process. Because something that seems perfectly fine may not be perceived by other stakeholders and so its communication, consideration, and making sure that the process is well documented. So we’re going to go through some ethical principles that guide that discussion, actual informed consent requirements that we’re all aware of, and the need to distinguish between voluntary and involuntary admissions, and we’ll get into the specifics of why that’s important. We’re going to include some case studies, really just to illustrate the thought process and to bring home the point that there is no one right answer, that everything is going to be fact pattern specific. So as Soundia mentioned, somebody who listens into this discussion should not think that if they have a similar set of key facts that there is a pre-determined outcome on what the IRB should do. That’s not the take away. The take away should be to look at the fact pattern and, if necessary, make adjustments to the recruitment process, the informed consent process, or even the protocol to make sure that the ethical considerations are respected but not to pre-determine what the approval outcome should be. And then we’ll have some suggestions for recruitment and informed consent procedures and other safeguards that are intended to minimize and/or mitigate both apparent and actual coercion concerns and undue influence issues for these subjects, and then we’ll have some time for questions and discussion.

So the first starting point, the basic starting point, is the Belmont Report and the basic ethical principles in the Belmont Report. So the expression of basic ethical principals in this context refers to those general judgments that serve a basic justification for the many particular ethical prescriptions and evaluations of human actions. And as outlined in the Belmont Report, the three basic principles among those generally accepted in our cultural tradition are those particularly relevant to ethics of research involving human subjects or the principles of respect for persons, beneficence, and justice. And in the application of these ethical principles we’re going to particularly look at the considerations of the following requirements for informed consent, a risk benefit assessment, and the selection of subjects of research. And so in our discussion we’re going to really hone in on informed consent and selection of subjects.

So the first ethical principal that we’re going to go through is respect for persons. So respect for persons incorporates at least two ethical convictions. First, is that individuals should be treated as an autonomous agent. And secondly, that persons with diminished autonomy are entitled to protection. So the first one, autonomous agents. Now this gets to the point of allowing individuals to choose for themselves how they are treated and what happens to them. So this goes to the fact that just because somebody is in a particular health treatment status that we should continue to treat them as autonomous agents to the extent possible. And secondly, also recognizing that individuals in certain situations may have and may experience diminished autonomy and that by virtue of that diminished autonomy they are entitled to additional protections. And this is where the distinctions and the admission status and the stay status of an individual in an inpatient mental health unit, this is where it becomes particularly important to know their status. Because an individual can be in one of these units through a voluntary admission where they come in, or they’re brought in either through the ER or some other process, and they agree to be a patient in the inpatient mental health unit. And then there are also those situations where a patient is put into the unit on an involuntary admission. So another individual is making a decision on their behalf but for their own protection and safety and welfare they require an involuntary admission. A sort of related, but somewhat different status, an involuntary hold. So involuntary holds are kind of the intermediary status where somebody may have come in through a voluntary admission, and through some process, and there are a variety of processes, they’re now on an involuntary hold. So their status has changed. And as we’ll go through in a later part of the discussion, it’s important to have the research team understand and communicate with the critical care staff so that they’re aware of the status because these can shift over the course of an admission. And it’s also important for study teams, and especially multi-site study teams, for the study chairs, to understand that there can be variability between states and overall governing the issue of involuntary holds, and there may be jurisdictional provisions to delay discharges for even voluntary patients in one of these units. And these are usually as a consequence of ensuring that somebody is still able to take care of themselves once they leave the unit, and so it involves an assessment. And it’s not intended to be an adversarial process but from the vantage point of the patient, they’re not able to freely leave, or there may be elopement prevention features as part of the unit that may also contribute to lack of mobility for the patient. And it’s also, and as this particular case study highlighted, there are situations where an individual becomes involved in a legal proceeding where there needs to be a court approval to convert a voluntary to an involuntary admission and then to leave an inpatient mental health unit. And even within a particular state a facility can elect to have procedures, or the county that the facility is in may have procedures that will require different steps for an individual to leave an inpatient mental health unit. So as part of the protocol design process and in designing the informed consent process, it’s important for the study teams to communicate with the local study teams, if it’s a multisite study, and then to incorporate that into the protocol and the application for the IRB to understand.

And this is probably a really good point to point out that this case study, this teachable moment emerged in a large multi-study, a multi-site study, that was conducted by a very experienced research team. The study chairs were well recognized in their fields, very senior, and the IRB of record had excellent procedures, was professionally managed, so there was nothing clearly indicative that there was going to be a gap. The gap only became apparent due to other situations that emerged, and a caution is that the gaps are not necessarily avoidable, it’s how to bridge the gaps. And so the considerations and the infrastructure for a study is really in bridging the gaps to make sure that people have a way past these concerns.

So now we come to the informed consent process. And this is a particular area where IRBs struggle. They struggle with how to adequately implement this and with understanding the conditions under which informed consent will be sought. So the basic requirements of respect for person requires that subjects agree that they are capable or given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards of informed consent are satisfied. And then an agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence.

So going back to the vantage points for various participants in the research process. The vantage point for free of coercion and undue influence from somebody in an inpatient mental health unit with physical elopement prevention features, such as double lock doors and other such features, will have a very different vantage point possibly than the study team or an IRB that isn’t aware of these elopement prevention features. So how to facilitate the participants, their perception of free from coercion and undue influence, and we’ll go through some potential mitigating features that can be added to protocols to address those concerns.

So next we have some actual regulatory requirements. The regulatory requirements for us are put into the directives. And the approval criteria, the IRB approval criteria, requires that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with limited decision making capacity or educationally or economically disadvantaged persons, that the protocol method, it include additional safeguards to protect the rights and welfare of these subjects. So in this particular instance, individuals who are in an inpatient mental health unit, and depending on the status of their transition out of the mental health unit, they may perceive coercion or undue influence depending on their overall condition. So if they, for example, have a court order that requires them to comply with the treatment plan, and then they’re approached and it’s not clear to them, to the patient, that their research participation is separate from the treatment plan and completely optional, they may perceive that offer as something that was not intended. So just something to consider that from their vantage point, we need to consider what their vantage point is for things like being approached for participation.

And then the informed consent requirements. An investigator must seek such informed consent only under circumstances that provide the prospective subjects, or the legally authorized representative, sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence. So IRBs sometimes get caught up in how to make these requirements fit in practice. And we have seen some very conservative decisions where IRBs are not comfortable allowing recruitment, informed consent, or even procedures to occur in inpatient mental health units and it’s because of the concern in overcoming these requirements. So we want to talk and have a discussion about how to overcome some of these requirements with either structural or conditions that we can put in that provide the necessary protections that minimize the possibility of coercion and that minimize the possibility of undue influence.

So going back to the inpatient mental health unit. As I mentioned, the inpatient mental health unit patients will experience certain elopement and harm prevention design features regardless of their admission status. So something that may not be known to IRBs, and that sometimes when it becomes known to IRBs, that causes some concern, is that individuals in the same unit, irrespective of whether they came in on a voluntary admission, an involuntary admission, or an involuntary hold, if they’re put into a unit that shares elopement and harm prevention features then in some ways their admission status is irrelevant from the perspective of the vantage point of the patient, because they’re experiencing the same environment as somebody in a different status. So what can we do? Investigators should facilitate IRB understanding through the protocol application for IRB review or rather submission documents of which of these patient types and when these patients would be approached for participation in research. Providing this information to the IRBs should facilitate that communication with the IRB to alleviate some of the ethical concerns that might arise in proposing use of this patient population. And the IRBs should consider autonomy limitations of voluntary mental health inpatients, whether they’re waiting for a medical determination of the eligibility for discharge, whether there’s legal requirements involved in their discharge from the unit. And so in considering the autonomy limitations, that’s not to say they automatically get excluded, but just what additional protection should be implemented, whether additional safeguards should be afforded. And one way to facilitate this entire process is providing the IRBs a full description of how informed consent will be obtained. In our teachable moment the IRB was not informed and so some of the reticence subsequent to being informed from the IRB’s perspective may have been as a result of that. And facilities should consider providing additional education to IRB members on some of these issues, and participation in this series is one way to do that. And then also ensuring appropriate expertise to facilitate IRB review, whether it’s membership composition or ad hoc reviewers or consultants. So that if an IRB either is a multi-site IRB that does not know the specific conditions of a performance site or maybe just doesn’t have a high enough protocol load to have full time members with expertise in these areas that they are able to draw on that expertise when they do need it.

So again, the admission types, voluntarily admitted is for acute care in a unit with elopement prevention features and Providers determine if a subject is eligible for discharge. As many of us became aware through this teachable moment, involuntary holds and involuntary holds have the same features except that for voluntarily admitted individuals in some states relief from inpatient care may also involve a legal process. And that’s something that the local study team should be expected to provide their study chairs and the IRB. They should facilitate that knowledge transfer.

So research consideration. So again, individuals should be treated as autonomous agents. And to the degree that they are capable, individuals should be given the opportunity to choose whether or not they participate in a research study. So if they are capable of participating in that decision process, that should be facilitated. However, persons with diminished autonomy which, depending on the status may apply to inpatient mental health unit individuals, they’re entitled to additional protections. And then for the protocol concerns, it’s important to ensure that patients are being approached for participation because they’re needed to answer the research question. And the study team should consider whether the research is being conducted, whether they can conduct the study without including them. And if they are needed to answer the research questions, they should propose additional safeguards to protect the rights and welfare of these subjects.

So for the informed consent process, one of the questions is what has been included in the consent process to ensure informed consent only under circumstances that provide the prospective subject with sufficient opportunity to consider whether or not to participate and to minimize the possibility of coercion and undue influence. And so some protections here might be clearly distinguishing that they’re being approached by somebody who is not making decisions regarding their care. Or providing information and assurances that minimizes the concerns or possible perceptions about coercion or undue influence that the person being approached might have. So it’s just that vantage point. And then just considering does your IRB have the expertise to address these concerns? Is a consultant needed? And if you don‘t have a consultant that you need right now, because you don’t have one of these studies, if a study is proposed to your IRB, does your IRB have a process for identifying an appropriate consultant?

So our first case study. A research team proposes to enroll involuntarily admitted patients from the inpatient mental health unit because they are aware that these subjects can’t leave and would be able to complete all the study procedures while they’re in the unit. The study is on obesity and hypertension in Veterans, and involves a survey and a onetime blood draw for research purposes that will be coded and linked to identifiers. The study team is aware that prospective subjects could adequately be recruited from elsewhere in the facility but could lead to two visits instead of one. So what are some things to consider? One, well, the subjects are involuntarily held. So if it’s appropriate to recruit them, do they require additional protection? Probably. And then does the study question involve a disease or condition that affects this population? Well, they might have these concerns as well but can subjects be adequately recruited from elsewhere? It seems like they could be. So the IRB might question whether or not this population should be recruited at this time. If there’s some additional protections that should be afforded to them if the study team feels that they are a particularly good fit for the study design. Maybe they are. Maybe their circumstance is that, that the study would not be privy to if they excluded this particular patient class. So just some, some issues for consideration. It’s just important to tie the ethical and regulatory concerns for informed consent protection of subjects, the additional protections, to the particular study theme proposed. Sometimes something looks like it’s on the surface quite inappropriate but with consideration, with a proposal that lays out the strategy for recruitment and the appropriateness of the patient type, maybe it’s okay. We just can’t prejudge, shouldn’t prejudge.

And our second case study. We have a research team that proposes to enroll voluntarily admitted patients into a study on joblessness and depression in Veterans. The study also involves a survey and a onetime blood draw for research purposes that will be coded and linked to identifiers. The protocol includes supporting evidence of the incidence of Veterans who are jobless and suffer from depression is higher in patients admitted into the inpatient mental health unit than elsewhere in the facility. The team still acknowledges that they may be able to complete all study procedures while the patient is admitted. So the concerns, issues, should this patient population be recruited at this time? Well it sounds like by excluding them, they might not be able to get information about individuals who are particularly affected. So maybe the subject type is okay. That’s something to consider. And then could the study team also enroll involuntarily admitted patients? If yes, under what conditions? So if the patient type is appropriate then the status of the individual, so the condition, maybe it is a little bit different for involuntarily admitted patients. So maybe the burden then is just on ensuring that the recruitment, enrollment process is under conditions that don’t seem coercive, that afford individuals the opportunity to consider without undue influence whether or not their participation is appropriate for them. So autonomy, respecting autonomy but also the ethical considerations for affording them those protections. And then also about subjects on involuntary hold. So if somebody is on an involuntary hold just being aware, having communication with the study teams or with the clinical teams about the status of this individual. They may just be in a unit, but unless there’s communication with the clinical team, the research team wouldn’t necessarily know that this person is waiting on this particular item before they can leave and they’ll do anything to get out of the unit. They wouldn’t know that. So it’s important to have that communication with the clinical teams.

And so our takeaways from this, oh, I went one too far, sorry. So our takeaway. Prospective subjects recruited and enrolled from the inpatient mental health unit, should be afforded the opportunity to decide to participate, to the extent that they are capable. But it’s also important to recognize that subjects may have diminished autonomy and they should be provided and afforded additional protection. And how do you do that? How do you afford additional protections? Well, the protocol and the informed consent process should describe the additional protections. It shouldn’t just be assumed that it’s going to happen. And the IRB should have the expertise to adequately evaluate whether the subjects should be recruited and enrolled, and if yes, what protections are needed. And if they don’t have the expertise, seek consultation. And then lastly, the IRB and the study team should work collaboratively in developing a protocol and informed consent process to ensure that respect for persons is adhered to. And this is not to say that IRBs need to redesign a study or that IRBs need to write the informed consent or anything like that. It’s just that if they receive something and they have concerns, to articulate those to the study teams so that the study team can propose something. And that’s it. If we have questions?

**Soundia Duche:** Wonderful. Thank you, Cynthia. That was very informative. We do have one question in the box. And it’s related to the second case study. I think the individual was curious to know why a study on joblessness and depression would need to have a blood draw included?

**Cynthia Kerenyi:** So we threw in that case study just to draw attention. There might actually be a perfectly reasonable justification for that. That was just to make sure people were reading it.

**Soundia Duche:** Exactly. And it could be maybe they’re looking at\_

**Cynthia Kerenyi:** So, that was a fictional case study.

**Soundia Duche:** Maybe they’re looking at biomarkers associated with depression. You know?

**Cynthia Kerenyi:** Yeah.

**Soundia Duche:** Who knows?

**Cynthia Kerenyi:** Could be. Could be. Yes.

**Soundia Duche:** All right, so thank you. I don’t see any other questions in the chat box right now. I’ll give it a minute while we load the presentation, the next presentation. And if not, we’ll just continue on and then we’ll have a second question and answer session at the end, which will be open for all presenters, so you can throw in your questions. And if you have a presenter in particular, once we get to the second Q&A, just write who you would like your question directed at. Okay? And so now, building on the excellent foundation that Cynthia laid, what we’re going to do in the second part of the webinar we have representatives from the VA Central IRB. We have the two co-chairs of the VA Central IRB as well as an IRB member who’s also a clinical psychologist researcher. And so what we’re going to do is we’re going to talk through a case that’s been designed, again, to illustrate certain key points, and we’re going to, this part will be moderated by Dr. Ryan Holliday, our IRB member and a researcher. And we’re going to really try to tease out some of these varied considerations that Cynthia has already brought up, and we’re going to delve into it further by a very, very unique case that’s been designed specifically for this purpose. Before we go on, let me, perfect, if we can have our panelists on this next case introduce themselves and tell us a little bit about what you do. Maybe we can start with you Steve?

**Stephen Bartlett:** Yeah. Could you start with somebody else? They decided to do construction on the other side of my wall just as you asked me.

**Soundia Duche:** Okay. All right. We’re moving on to Fred.

**Stephen Bartlett:** Let me go talk to them real quick, okay?

**Soundia Duche:** That sounds good. Okay. Dr. Hendler, you’re up.

**Dr. Fred Hendler:** Yeah. This is Fred Hendler. I’m an oncologist in Louisville and I’m chair of the local IRB as well as one of the co-chairs of the Central IRB. And I’ve been a participant with the Central IRB I think since 2005 when we started putting it together and since it’s been operating.

**Soundia Duche:** Excellent. Thank you Dr. Hendler. Dr. Holliday.

**Dr. Ryan Holliday:** Hi. So my name’s Ryan. I’m a, a clinical research psychologist out here at the Denver VA. I’m really excited to be a part of this presentation as the majority of my research does focus on suicide prevention, and we end up doing a lot of research including within inpatient settings, so I think we are really excited to discuss this with the panel, and I’m a recent joinee of the Central Office IRB.

**Soundia Duche:** Excellent. Thank you, Ryan. We’ll see if Steve’s back and if not, we’ll move on. But Steve Bartlett is the other co-chair of the VA Central IRB and he’s been on the IRB since its inception. I do believe he’s also chair of his local IRB, is that correct Dr. Hendler, in Denver?

**Dr. Fred Hendler:** Yes. Yeah.

**Soundia Duche:** Yes he is. Right. Perfect. So when he joins us again we’ll get him to say a little spiel about himself.

**Dr. Fred Hendler:** And he’s also been co-chair of the Central IRB since its inception as well.

**Soundia Duche:** Excellent. Indeed. So our objectives, we’ve already stated them. We’re going to use this case to illustrate some of the ethical considerations that the IRB should take into account when they’re reviewing this type of research that involves enrollment of patients in the inpatient mental health setting. I will alert you that the case that’s been designed does include patients who are involuntarily committed to treatment. So we’re really going to be able to delve into some of the issues that Cynthia mentioned during our discussion. But before we get started, I did want to point out that one of the handouts that we provided you with was the American Psychiatric Association’s position statement on research with involuntary psychiatric patients. That’s included in your handout. [Cough] Excuse me. I’m not going to go over the points of their position because we are not at this point endorsing, or otherwise, their statement. But I think it’s important to present all the information that’s applicable to this situation, and that is publicly available information. I do want to, though, talk about, according to them at least in their issue brief, what led them to this potion, to feeling the need to disseminate this position statement. And I’m going to take us right down to the fourth bullet point whereby they found and discovered that recently some jurisdictions were placing categorical restrictions on research involving involuntarily committed patients, okay? And so by categorically excluding these individuals from participation in research you hit right into the issue that Cynthia mentioned about respect for persons and autonomy. By creating, by excluding them you’ve created the presumption that all such patients are unable to give adequate consent to research and, therefore, should be excluded from participation. And we know one of the tenants of the Belmont Report is that you want to treat people as individuals, as autonomous agents, but at the same time, yes, you still want to protect those with diminished autonomy. And so that’s what we’re really going to be talking about. We’re going to be weaving this throughout the case. How does the IRB ensure that patients, in this case, who are potentially vulnerable to undue influence, coercion, confusion in terms of is this is a research study or is this clinical care? If I agree to this, you know, will it affect my ability to leave, my admission status? All of these things. But, at the same time, the APA states that there really is an ongoing and urgent need for clinical research on serious mental disorders, including the treatment of acute episodes. And many times these acute episodes are presented in the inpatient setting. And again, the case that Dr. Holliday is going to go over really touches on this issue. Issues about perhaps this is the only time we will have access to these patients in order to provide them this, in order to gather this research. The APA states that psychiatric patients who are involuntarily committed to treatment are an important population for such research, and they agree it is important to safeguard the integrity of the informed consent process, but state that the law presumes that all patients do have adequate capacity to consent involuntariness unless there is evidence to the contrary, okay?

In terms of being able to assess their capacity to consent, I’m not going to go over all this slide, but I did want to point out that the VA is working with the DoD on creating a guidance document on recruiting and consenting individuals who are in the inpatient setting for mental health research. So that’s something, that the guidance document is in the final stages of review. It still may take a couple of months to come out, but it’s going to talk about some of these very issues of assessing capacity to consent. We may be more familiar with doing that when you’re dealing with people with diminished capacity, but some of these same tests that you use where you’re confirming that the individual understands that it’s research, they understand what the research entails. Some of these same types of assessments can be used to make sure that when you’re dealing with someone who’s involuntarily admitted that they understand that this is research. That their admission status will not be changed if they decide to participate or not or if they decide to change their mind in the midst of participating. Some of the points that Cynthia mentioned, making sure that they understand that just because they have to, as part of their legal agreement, they have to participate in all the clinical requirements and clinical procedures, that this is not a clinical procedure, this is research. And making sure that that differentiation is very clear to subjects.

So I wanted to give you a sense of that. That guidance document is actively being worked on and we hope in the next few months to be able to share that with you. The one thing that is important that, again, I do not want to review the points of the APA position statement because, you know, I don’t want to go there. But there is one thing that they say that is a perfect segue into our case. And that is that IRBs are best situated to make case by case determinations about and consider the need for additional safeguards for each study’s risk and benefits, including the potential vulnerability of subjects due to impaired consent capacity for voluntariness. So again, that it shouldn’t be carte blanche whereby these patients are categorically excluded but that the IRB is charged and is capable, with appropriate expertise in making the, a decision and assessment of whether and how patients that are involved in the mental health unit should be approached and should be enrolled. And so with that, I’m going to pass it on to our IRB member, Dr. Ryan Holliday, who is going to moderate this case for us.

**Dr. Ryan Holliday:** Great! Thank you so much. Okay. So just to kind of give a brief background, obviously this entire call could be spent discussing the interrelationship between Veteran status and suicide risk as well as underlying subsets of the Veteran population at heightened risk including those who are experiencing or at risk for housing instability. But to kind of give a crash course, we know compared to the general adult, non-Veteran population, Veterans are at heightened risk for suicide. And that risk is about 1-1/2 times greater. However, we also know from a public health perspective that there’s some subsets of the Veteran population that are at even greater risk for suicide. I’m sure several of you have heard things like depression, bipolar disorder, PTSD. And in addition to those psychiatric diagnoses, we know that there’s certain events that can happen in a Veteran’s life that predispose them to greater risk, including homelessness. In particular, when we look at the rates, we know that per 100,000 individuals, which is a fancy statistical way of talking about it, it’s about 81 in comparison to 39.

And in order to prevent suicide the VA has rolled out a lot of initiatives that are both upstream and downstream. When we look at the clinical practice guidelines by VA DoD, which came out a few months ago, we know that there’s a lot of evidence-based strategies including things like evidenced based psychotherapy, such as cognitive behavioral therapy, and safety planning. However, when we’re discussing a lot of those things, they typically are occurring on an outpatient basis. And when we’re talking about what we consider to be acute suicide risk, we know that there can be elevations in that risk that can warrant hospitalization. And I know in the presentation before this, we talked a little bit about this but just to kind of rehash it a little bit, when an individual presents to an emergency department and they’re discussing things like thoughts about suicide or a suicide plan they can either be what we call voluntarily admitted, so that means that they talk with the provider and the provider says, hey, you know what? It might be really good for you to come to the inpatient unit, and they agree. Or they might be deemed to be a danger to themselves and be involuntarily committed if they’re unwilling to consent to hospitalization. Which I think is a really important nuance when we’re thinking about things like ethics because when we’re talking about suicide risk, we also know that individuals who are involuntarily committed are at greater risk for self-directed violence in the future.

In terms of how this interplays with research, we know that unfortunately, and fortunately, suicide is a low-based rate event. And so what I mean by that is that suicide rarely occurs. Rather, we typically see a lot of what we consider to be, quote, unquote, risk factors for suicide occurring before. So things like depressive symptoms, housing instability, interpersonal conflict. And because of that, a lot of our research really has to look at several factors when we’re doing suicide focused research in addition to things like just purely talking about suicide attempts or suicidal ideation. However, when we’re talking about these really high risk subsets of the population, we often as individuals who are in IRB capacities as well as researchers have to weigh what is the risk to the patient in participating in this research against the utility of these findings in preventing suicide amongst a larger population. And I think one thing that really hits this home is when we’re talking about a population like homeless Veterans. We know that unfortunately, this is a population that is not only likely not going to access VA care, they’re going to be extremely unlikely to come back in for follow up following an inpatient hospitalization, which really suggests the importance of targeting this population while they’re available, to prevent suicidal self-directed violence in the future. And how we kind of thought about this is, in addition to presenting some of the data we’re talking about here, we thought it might be really important for Fred and Steve to kind of share some of their expertise, as well as for those who are in attendance on this presentation to kind of think about what are their reactions to what we’re talking about? So before we even jump into the scenarios, I thought it might be really useful just to throw in a few questions to kind of do an a priori test. Because I think when we talk about suicide it elicits a lot of emotions within individuals that sometimes can be really helpful in clinical care and research and sometimes can actually get in the way. And so I think one of the first things is, if we change this study to focus on substance use, rather than explicitly suicide, how might that change some of the opinions we’re having? Similarly, if we were looking at Veterans as a whole versus just homeless Veterans, again, how might that change how we’re approaching this and what factors might come to our mind about being important in terms of that balance of ethics? Another thing that comes up very commonly when we’re talking about research is compensation. You know, are we compensating the individual and is that potentially impacting their openness to this research? And I think that’s especially important when we’re thinking about Veterans who are experiencing a lot of these psychosocial factors, like homelessness, or under and unemployment, as that might cause undue influence. And finally, kind of bringing it full circle, if the Veteran were voluntarily versus not voluntarily hospitalized, how might that further impact things?

And to kind of kick it off we have this initial scenario we put together where we’re thinking about just doing a survey with homeless Veterans who are currently hospitalized at a VA medical center. And the purpose of this survey is to really better understand factors that led up to this recent admission in order to identify how these factors can potentially be targeted in the future to prevent those admissions. And as we kind of think about it, we think it’s really important to kind of hone in on how different factors such as inclusion of suicide focus measures, homelessness, and compensation as we kind of talked about earlier as well as additional considerations might be at play.

And now what I’m going to kind of do to transition this is kind of open this up to Fred and Steve to talk about kind of what are their initial thoughts when they’re thinking about this initial scenario in terms of ethics.

**Dr. Fred Hendler:** Okay. I guess the first thing is we’re going to focus on homeless Veterans who have this high rate of suicide and the, this is, in the first scenario we really, we’re doing only a survey. So the survey is only going to be a onetime only event. So many issues that might come up in the second and third surveys, excuse me, scenarios, are not relevant here because the, it’s really only going to take a short amount of time to go through this. And the real concerns are what, what are the questions that are going to be asked of these individuals? And how does this affect the participation of those individuals? And so we need to know why, you know, exactly what the survey’s going to ask and how this might affect the individuals in the, in this particular setting. And that’s the real risk that’s involved. I don’t think this is going to impact necessarily their treatment. It needs to be planned in such a way that it will not affect their treatment while they’re being hospitalized. But again, the issue is how does this affect the individuals who are taking the survey? And will they have, feel comfortable in not answering the questions if the questions are stressful to them?

**Stephen Bartlett:** Yeah, and so I really [unintelligible 52:56]

**Dr. Ryan Holliday:** So I really loved what, oh sorry Steve, go for it.

**Stephen Bartlett:** Yeah, I was just going to say and, you know, one of the things going back to the principles of autonomy, you know, certainly just the fact that this is a survey they can, you know, they can even start the survey and, you know, stop at any time they want. So, you know, they have a lot more autonomy in this kind of scenario where we’re not introducing kind of an intervention that we might see in some other types of clinical trials.

**Dr. Ryan Holliday:** I really love that you guys both brought up that this is definitely something that’s doable. I know as a individual who does a lot of suicide focused research, I think it can give a lot of methodologists a lot of anxiety to think about well how can I ask someone about that? Or how might that increase risk? So really knowing that we really do need this type of research to be able to inform suicide prevention I think it’s great to hear that. Fred, I know you, you mentioned something about the types of questions being asked. And I wonder if you could tell me a little more about, are there certain questions that if you saw them come through, they might give you pause or you might want more information about or things along those lines?

**Dr. Fred Hendler:** Well I was thinking about really questions that the individual might not be comfortable answering. Whether they have a history of drug abuse, their sexual orientation, things in that order, their relationships with others. Things that really might be trigger events for them in answering. And that, again, this needs to be spelled out by the individuals who are doing the survey to make sure that the individuals feel, that are taking the survey, feel comfortable and they know that there’s no coercion for them to answer these questions that they feel uncomfortable.

**Dr. Ryan Holliday:** Right. And even if the, you know, the questions kind of do go over to those kind of somewhat triggering, what might be considered triggering type questions, that there’s the right support system there for the patient, you know, being inpatient actually in this case is probably a benefit to maybe asking that same kind of question in the outpatient setting. Because hopefully they’d have more support in an inpatient setting.

**Stephen Bartlett:** Great. So like it sounds like I’m kind of hearing this, the really important thing is to ensure that both the potential participant understands that they can say no or stop as well as that it won’t impact their care. One final thing I think that’s important, [clears throat] excuse me, to kind of touch upon is this concept of compensation while someone’s on an inpatient unit or in an inpatient setting. I was wondering if you could talk a little more about that?

**Dr. Fred Hendler:** Yeah. We typically do not think of compensation for someone who’s already hospitalized. So I’m not sure exactly how relevant this is. For filling out a survey while you’re in the hospital, it just doesn’t seem to me that that would be something that you be compensated for. It would make things very complicated.

**Stephen Bartlett:** Yeah. You’d have to be thinking about, you know, what are you compensating for? I mean generally we try not to use compensation as kind of an influencing factor, especially when, in this kind of setting, it’s usually more to accommodate for time and travel of somebody that’s going out of their way to help you. So I think if an investigator wanted to compensate an inpatient population for filling out a survey, I think they’d have to try to make a strong case for that that showed to IRB that, you know, there wasn’t some kind of undue influence of, you know, trying to pay people off to, you know, to answer their question, so.

**Dr. Ryan Holliday:** Great. I think that’s a really important point and I’m glad you guys were able to talk to it. I do see a point that was brought up in chat that I think is important to touch upon before we move over to scenario two. I definitely agree, and I think both of the co-presenters with me would as well, that it’s really important to consider the types of measures you’re using when you’re doing survey research to ensure that they’re appropriate and valid for the populations you’re discussing. So I think that that’s definitely an important point and thanks for bringing it up. In terms of scenario two, you’re going to notice that the methodology has changed a little. So in addition to the survey we talked about in scenario one, the researchers now want to conduct an intervention. So kind of like we were talking about earlier, we know what some of these risk factors are and now we want to figure out how we can prevent them. And to do that they wanted to do an initial feasibility study where they added three sessions of, quote, unquote, enhanced treatment. So in addition to the treatment they’re receiving they added something on top of it. And the intervention was offered free of charge while they were admitted and would continue to be offered once they had been discharged. The purpose of this intervention was to decrease thoughts about suicide as well as future risk for suicide related hospitalization. And in addition to participating in this intervention, participants were monitored during the hospitalization and up to three months post discharge. And what we mean by that is kind of staying in contact with them to follow up and gather data in terms of the suicide related hospitalization.

So now when we think about how kind of this scenario has changed, how might the ethicality of this come more into play versus that initial scenario one? I’m wondering if, Fred and Steve, if you can speak a little to that?

**Stephen Bartlett:** Well I think the first thing that you want to consider is that you have an adequate separation between the care provider and the researcher. Because if the research intervention is also being administered by the clinician, that brings about some questions that, you know, we’re going to have to address at the IRB level in terms of conflict of interest for that investigator. So you want to make sure that the research intervention, it won’t impact something that they should be getting otherwise. And then, I think as Cynthia mentioned as well, you know, what if it’s, you know, court ordered treatment in some way, you know, is that something that you’re going to have to consider? Is this within the same realm of that kind of court ordered or required treatment based on some kind of admission requirement? Fred?

**Dr. Fred Hendler:** Yeah. And then I think the other thing is that if we’re talking about three sessions, you know, what exactly is the treatment that’s not spelled out in this? And I realize that’s left open intentionally but something that the IRB really needs to know. And the second thing is since some of this presumably will be done as an inpatient and some will be done as an outpatient, because individuals are not typically kept in a, in a unit for a very long period of time, should, is it really relevant that everything be done in the inpatient unit, and if it is, will that keep the individual longer than they might have been kept if they were, weren’t on the unit? So I think those are really very important questions that have to be answered for the IRB in order to justify this type of scenario as whether the inpatient, outpatient, or a combination of the two. And as Ryan has discussed, we’re dealing with homeless individuals who they’re, they’re not as compliant as the normal individual in keeping their appointments. And if you need to do the study truly on homeless individuals how do you maintain them in the study? And that’s all very important questions for the IRB as well as the study team to deal with.

**Dr. Ryan Holliday:** Yeah. I think you brought up a couple of really great points and I’m wondering, because, you know, you brought up that we left this intervention intentionally vague. And I wonder if you both could speak to a little bit how, what might go through the IRB’s mind if, let’s say especially knowing that on inpatient units and when working with homeless Veterans, a lot of times it can be about titrating up medication that this Veteran might not be taking that they’re supposed to be. How might this, the IRB consider ethics if it was a medication trial versus maybe if it were a therapy trial or kind of more of a smart phone application trial?

**Stephen Bartlett:** Well I think if you’re talking about homeless Veterans, I mean you have to ask if they do have smartphone access, you know, for your latter scenario. And, you know, whether that would be something actually provided to them as part of a trial. Whether that’s, you know, is that a coercive factor but it also might help you stay in contact. As far as the medication trial, you know, if they need to be titrated and monitored you really need to be careful with a population that may not come back as readily as other populations. You know, I think we’ve seen that in a couple of different scenarios of different studies, you know, I’ve dealt with where the Veteran not coming back into the clinic or into the hospital for monitoring posed a potential risk to that individual. And you have to be sure that you’re not setting them up for failure by starting them in house and then discharging them and hoping that they come back. And then, you know, whether they continue on that medication, whether maybe you do get them titrated up maybe there’s an issue with rapid withdrawal if they just stop taking the drug itself. So you need to, I think, you know, something with like medication therapy you need to think about the long term whether you can maintain that, you know, in a longer term manner.

**Dr. Fred Hendler:** And then the other issue that’s also related, if you’re going to have to titrate somebody while they’re in the hospital, how’s that prolonging their stay and how’s that going to affect your study? If these individuals want to get out and you tell them that they’re going to have to stay another week or so to get their drug levels titrated.

**Stephen Bartlett:** Yeah. There’s probably operational issues from the hospital on the other side of that as well, to keeping somebody longer just in order to titrate them off on a medication that’s currently not approved or approved for that indication.

**Dr. Ryan Holliday:** I really like that you’re both bringing up how important it is on the front end to consider that this intervention doesn’t result in individuals having to have an extended length of stay, or that’s something that’s really strongly considered and discussed because I think, especially on outpatient trials, that’s not really something we deal with a lot of times. So I think that’s an unique consideration that some of these methodologists might not be considering. I wonder if you both could speak to, because I think this is going to be relevant for both scenario two and three, does anything go through your mind if these participants were voluntarily versus involuntarily hospitalized or on a hold on the unit in terms of recruitment?

**Stephen Bartlett:** Well I certainly think, you know, involuntarily brings up, you know, a whole host of bad gut reactions of what do you do with, you know, how can you do that and maintain patient autonomy? You would really have to bring some procedures into play that assured that autonomy. And I think there are ways to do that. Certainly you don’t want the clinician/ researcher approaching that, the potential participant with a conflict of interest. You would want to include maybe somebody else seeing these scenarios and in other settings that you might use, you know, an observer for the consent process. But you know, you really, they need to make sure that they have capacity, which, I think in large part, a lot of these patients would. But do they have the autonomy and feel that it’s okay for them to say no if they really, that’s what they feel they want to do is not participate in the study. That they’re not feeling that because they’re inpatient and kind of part of the system right now that they have to participate and make sure that’s 100% clear to the individual that they have choice.

**Dr. Fred Hendler:** Ryan, I think this whole scenario really points out the sophistication that’s needed on the part of the investigators as well as the IRB to work together to develop a protocol that meets the needs of the researchers but more primarily meets the needs of the participants.

**Dr. Ryan Holliday:** Great. I think that’s, that’s a great point too where I think it would be so easy to have these clear black and white answers and sometimes it’s not that clear. Sometimes it’s about, like you said, balancing these different factors and considering them and holding them steady. And I think that’s a really great transition to our third scenario. So in this scenario kind of, we’re kind of thinking about it almost like a stairwell; one led to two, now two leads to three. So scenario two allowed for the feasibility and acceptability to be established for this intervention and now the researchers really want to do a pure efficacy trial. So they want to do a randomized controlled trial where they compare this intervention, used in scenario two, alone to the usual care. And then for those Veterans that are randomized to the interventional arm, they will be offered the option to recommence usual care following completion of the research study, and we’re putting that at three month’s post discharge. So to put it plainly, we’re talking about a scenario in which these individuals are placed to only receive the enhanced treatment and not their treatment as usual, and then comparing treatment as usual to this treatment to determine the efficacy. And so to kind of transition this, Steve and Fred, what sort of ethical considerations come to mind and how might those differ from what we were talking about in scenario two?

**Dr. Fred Hendler:** Well, I think that the question of voluntary versus involuntary becomes a much more important question at this point. Because the, with the randomization, the involuntary individual might feel more coerced to participate than a voluntary individual. Because the voluntary individual would presumably be able to leave more readily. So that, I think that’s number one. And the other issue is a question of this delay of care. If the delay of care requires inpatient hospitalization again then I think that’s a major issue that has to be dealt with. If it can be done as outpatient after completion of the study then that’s not part of the issue. But if it requires hospitalization then that’s something that really needs to be explained in detail during the randomization process.

**Stephen Bartlett:** Right and, yeah, and you know, I think always the primary question, whether it’s in any of these scenarios or just any randomized study is that, you know, is usual care and the investigational care equivalent, you know, do we not know that they’re different enough that it, we still have clinic equipoise. So, you know, that’s a primary question and then given that, you know, I ask them does this really need to start as inpatient? What do you gain by doing this, starting this as an inpatient? Is it something that needs to be titrated as we talked about before under supervision? What happens, you know, post discharge if they, you know, how do they continue? What kind of adherence is needed? Or is this something acute enough in terms of a treatment scenario that this could be done in an inpatient setting? And then once they’re discharged, everything that, you know, the treatment intervention is over. So there’s, you know, a lot of aspects to the trial design that really weigh on the IRB’s considerations for how we’d look at the study. But you know, my question is always if it’s going to be a chronic treatment situation do you gain anything by doing it inpatient first?

**Dr. Ryan Holliday:** So it sounds like I’m hearing two major points. I think the first is that there’s a lot of ethical consideration surrounding what care we are reducing for this individual, which I think is really important from a clinical perspective, right? If we’re talking about restricting access to these first line treatments, that might be really important, that’s something that’s really important to consider. Or I know you both were kind of talking about titrating a medication, and looking at those levels, and what it would mean to take those away from an individual and kind of potential harm associated with that. I think there’s also a second really important thing I heard you both talking about, which is how and why the treatment is delivered in this setting. So really having that justification of why it must be inpatient, and if not, providing it as an outpatient. As well as thinking about can this be provided in a really brief time frame, so it actually wouldn’t impact care all together, which I think is a really interesting point that might not come to people’s initial thought of, okay, we could do this with one time session thing, it actually wouldn’t impact care while they were in it or things like that. And I think that kind of really addresses a lot of the things we’re talking about in terms of issues and questions raised as well as potential methods of redefining the study. I’m wondering is there anything else that you both feel is really important to kind of elucidate or discuss now before we move on to kind of questions at the end?

**Dr. Fred Hendler:** Well the other thing was that in scenario two, the intervention was overlaid on standard of care. And in scenario three we’re dissociating the intervention from standard of care for a period of time. And that in itself it might be more appropriate if you really wanted do this intervention separately to do a three-arm study where you have an overlay, you have standard of care, and then you have the intervention by itself.

**Stephen Bartlett:** And I would just re-emphasize one of Fred’s points earlier that, you know, it’s really important to have experienced investigators talk with the IRB and figure out the best way approach for this, you know, that particular scenario. Like I think Soundia said earlier, like every one of these scenarios is going to be a little bit different. There’s going to be different aspects to consider. And the only way to, you know, really work this out is to sit down and talk it through and consider all the stakeholder’s perspectives as you go forward to make sure, you know, that you meet all the aspects of the Belmont Report as well as all the scientific design issues and the medical treatment issues to be able to, you know, bring these new treatments to Veterans and hopefully have a positive impact on reducing suicidal ideation and suicide.

**Dr. Ryan Holliday:** Great. I love that you both brought up kind of this really important point of having that open line of communication and considering how best to tailor the methodology to be both ethical as well as robust in terms of answering the initial research question. So I kind of want to transition here to leave a bit of time for any questions we might have. But just to summarize, I think this was a really great discussion of kind of how we, even though we’re talking about a high risk population and, as well as a high risk behavior, we’re talking about a lot of methods by which this research can be done including in inpatient settings and, in fact, needs to be done to prevent suicide because it’s an unfortunate event that is happening with increased propensity over the last decade. So with that, I kind of want to transition and open it up to potential questions we might have so that we can kind of continue the discussion.

**Soundia Duche:** Excellent. Thank you so much Ryan and Steve and Fred. That was definitely a very, very interesting and illuminating discussion. We’ll give it a second to see if there’s any questions that come in the chat box. And remember, we have four presenters here who are willing to take your questions. In the meantime, though, I’m going to go one by one and ask if there’s any points you want to kind of summarize or, you know, as we’ve heard, you know, from so many, we’ve heard from all of you and you shared such good and interesting perspectives. Cynthia, is there anything you want to add in closing?

**Cynthia Kerenyi:** Thank you, Soundia. Just a reminder that as an agency we have stakeholders that are in addition to our Veteran population and so communicating, communicating, and communicating and making the process as transparent as possible can go a long way towards minimizing misconceptions as to the relative risk of participating in a research study. You may have a situation where it’s a comparison of two standard of care procedures and the impression from the Veterans’ loved ones may be that there was a significant research risk from being randomized into either of the two appropriate standard of care procedures. So being able to highlight some of these things in the informed consent process and just overall in the information that’s provided to the research participant it becomes important for building trust.

**Soundia Duche:** Excellent. Great point Cynthia. Fred, any close remarks?

**Dr. Fred Hendler:** Yeah. No, I think that one of the things that you really have seen if you’re paying attention to what’s, how Steve and I have interacted with Ryan, is that this is the way we, at the Central IRB, interact on our studies. Not just the problem studies like this but on all our studies. And I think that it’s very important that in any scientific research that involves human subjects, and probably even that doesn’t involve human subjects, there has to be a dialogue between the IRB and the investigators to assure that the participants have complete autonomy and risks are reduced as much as possible.

**Soundia Duche:** Absolutely. Absolutely. Steve, any closing thoughts?

**Stephen Bartlett:** No. Not really. I think Fred said all that, you know. I, I totally agree with that, and Cynthia as well. It’s all about the conversation and making sure that all the voices are heard, coming up with the best possible way forward for, so that these studies can be done and we can find a way to alleviate these kind of issues.

**Soundia Duche:** Thank you. And then lastly, Ryan, the researcher and IRB member, what say you?

**Dr. Ryan Holliday:** So I think my final point is just, you know, as a person who originally didn’t start in suicide focused research I think I had a lot of preconceived notions and anxieties in approaching asking about suicide and kind of, because of that, I think a lot of researchers have had similar beliefs and it’s really restricted the amount of data we have. And now we’re having to play catch up and so I think presentations like this and really just starting these discussions about this can happen and needs to happen is just something I’m very passionate about and I’m glad that we were able to have this today.

**Soundia Duche:** Excellent. Thank you all. Thank you to all our presenters. Really appreciate you being a part of this. For our audience, do not be surprised if you hear from me in another month as I start soliciting presenters for the next topic. I don’t have a topic in mind so if someone has something they’d like to bring up and share with their fellow VA colleagues, contact me. Lori and Lauren, thank you so much for your support in making this happen. We really appreciate it. It’s been a seamless process and I really like this Adobe Connect system. So thank you.

**Dr. Ryan Holliday:** Great and then I will say there’s our contact info. Meant to put that up there.

**Soundia Duche:** There you go. Thank you, Ryan. All right. Thank you everybody and have a\_

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