Key Informant Interview Guide
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Ethics of Adaptive Designs for Randomized Controlled Trials

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Appendix 1.
Key Informant Interview Guide

Thanks again for agreeing to an interview today. As I mentioned, I am a postdoc fellow at the Johns Hopkins Berman Institute of Bioethics and the School of Public Health, and as part of my practicum I would like to understand how adaptive trial designs affect the ethical character of trials, when compared with traditional trials. I would like to answer two main questions: 1) What ethics-related justifications are provided for the use of adaptive trial designs, and 2) What ethical challenges does the use of adaptive designs present? *I hope to explore the challenges and opportunities associated with adaptive trials.*

For clarity, and to guide our conversation, I want to share a working definition of adaptive trials as ***those clinical trials that allow planned modifications to an ongoing trial, such as change in the hypothesis, treatment arms, dosing regimens, randomization scheme, sample size and recruitment criteria****, as opposed to a traditional trial where most of these attributes largely remain the same throughout the trial.*

I am going to ask you some questions related to both adaptive designs and traditional trials. You are free to answer or not to answer any of the questions.

Respondent characteristics

1. Before we get into the details, can you kindly describe to me your professional background
2. How many years have you been working in this field?
3. What is your area of research interest
4. Please tell me also about your own involvement in adaptive trials? For how long have you worked in this area and can you tell me a bit about the nature of your work in this area?
5. Are you a member of or have you previously served on an IRB?

Involvement in clinical trials and general questions about adaptive trials

I am interested in hearing more about what professionals in the field think both about the validity and methodological rigor of adaptive trials. I would like to start with a general discussion on adaptive trials. After that, I would like to explore your thoughts about the ethical issues…

1. When do you think the current interest in adaptive trials started
    a. What is your understanding of how the interest we are seeing now of adaptive trials started?

2. For how long have you been interested in adaptive trials?
    a. What got you interested in adaptive trials?
3. I'd like to hear what you see as the advantages and disadvantages of adaptive trials, in general.
    a. Could we start with what you think are the advantages?
    b. Now could you tell me what you see as the disadvantages?
4. How has your attitude towards these trials changed over time?
5. When do you think it would make sense to use a traditional RCT design, and when would it make sense to use an adaptive design?

   …why?
6. What do you think are some of the methodologic tradeoffs of adaptive trial designs?

Ethical issues

I now want us to turn to specific ethical issues related to adaptive trials and the implications for trial participants and communities.

7. What do you see as the advantages and disadvantages, generally, of adapting a trial design in terms of the ethics of a study?
    a. Follow up: can you give me more detail? Some examples?
    b. Any specific issues related to communities, rather than individuals
8. In what ways do you think that adaptive trials affect benefits to participants?
    a. If you feel that adaptive trials improve benefits of participants, how is that similar to/different from a traditional RCT?
        a. Please elaborate. Could you give me an example?
    b. If you feel that adaptive trials decrease benefits to participants, how is that similar to/different from a traditional RCT?
        a. Please elaborate. Could you give me an example?
    c. If you feel that there is a decrease in benefits, how can we improve that?
9. What about harm… in what ways can an adaptive trial increase or decrease harm to participants compared to a traditional RCT?
    a. If participants are affected in a negative way, how can we decrease/limit/minimize the harm?
10. What about autonomy of study participants? Or ways in which adaptive trials may increase or decrease respect for study participants? Do you see any implications there?
    a. If negative impact: In what way can this be resolved/mitigated?
11. How do you see adaptive trials affecting justice or fairness (burden carried by participants or communities). Is this a different compared to traditional trials?

12. Randomization is premised on there being significant uncertainty around the relative safety or efficacy of interventions being compared. How do you think **response** adaptive designs maintain or disrupt this principle?
    a. [Mention equipoise if needed]
13. Is there a specific subtype(s) of adaptive trials that you think of as being more ethically helpful, or ethically problematic than others?

Global perspectives

I would now like to get your opinions on adaptive trials when conducted in different environments.

14. In what ways do you think that the ethical issues identified above would be different if the adaptive trial was being done in a high-income country vs a low-income country context?

Questions for a member of an Ethics Committee

(These questions only applicable for researchers who are also members of ethics committees)
I am interested in learning about your experiences with respect to the review of adaptive trials by the IRB on which you serve or have previously served.

15. In your experience as a member of the ethics committee, have you or did you ever review an adaptive trial?
    a. If yes, In what way did you feel prepared/unprepared to handle the ethical issues surrounding adaptive trials
16. In general, how do you feel about the readiness of the IRB that you have served on in reviewing adaptive trials? Did you feel like they understood the design itself? Did their discussion of the ethics of the trial seem any different than how they discussed a traditional trial?
17. Tell me what you think were/are the main ethical issues highlighted by the IRB when these studies were submitted to the IRB.
18. Could you comment on the adequacy of IRB guidelines for the submission of adaptive trials.
19. Are there any regulatory issues you have dealt with from the FDA or the local regulatory agency with respect to adaptive trials?

Any other comments

20. Is there anything else we have not covered that you think would be useful for us to know about ethics and adaptive clinical trials?

Thank you very much for taking the time to answer my questions today.

Before we end, I would like to get as many opinions on adaptive trials as possible.

21. Are there any researchers, methodologist or ethicists who you might recommend that I try to contact about this topic?

Thank you, once again.

E&HR

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Appendix 2.
Original Quotations from Respondents with Edited Versions and Paraphrases That Appear in the Article[1]

	Original quotations	Edited versions and paraphrases in order of appearance in the article
1	R2: "I think there's a greater potential for confusion [about informed consent] in an adaptive trial because it's more complicated, has additional decision points in it, and I think it is—at a very superficial level, it can sound very attractive, but at a more detailed level, it also has some risks that need to be discussed with the patients and the scientific community that is working on the study."	R2: with adaptive trials, "there's a greater potential for confusion" regarding informed consent due to their complexity and "additional decision points." While they may seem attractive on a "superficial level," the respondent said, there are also "risks that need to be discussed with the patients and the scientific community working on the study."
2	R9: "I suppose that's useful, but that doesn't meet the real problem that—so I'm involved in a trial and all of a sudden, unbeknownst to me, the treatment is changed, the dosage is changed, or whatever. I mean, yeah .... Maybe they warned me about that this could happen, you know, when I got enrolled. Maybe part of the consent was, "Well, you need to be informed that what we are doing is, you know, we may change the design, and we may change it unbeknownst to you." I don't know, does that exonerate you then? Are you now okay? Have you met your commitment to the people you study by, by telling up front? It's sort of like the stuff you get when you go on any of these websites: you have to agree to certain things before you can use the system. Well, I mean it's a little bit of a rich hold, so I, it doesn't make me a lot more comfortable; it maybe makes me a little more comfortable, but it doesn't."	R9: "I suppose that's useful [being able to inform the participant that trial allocations may change, throughout the trial, based on results thus far], but that doesn't meet the real problem," the respondent said, describing the problem by imagining being in a trial: "I'm involved in a trial, and all of a sudden, unbeknownst to me, the treatment is changed, the dosage is changed, or whatever. ... Maybe they warned me ... that this could happen ... when I got enrolled." The respondent questioned whether a participant's consent to such change would "exonerate" the researchers and whether researchers could meet their "commitment to the people [they] study by ... telling [them] up front." The respondent compared providing consent in this context to agreeing to terms and conditions on a website before using it, saying that the prior disclosure may make them a little more comfortable, but not much.

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3	R6: "Just finding a good way to explain it in layman's terms that minimizes the risk that the study design is misunderstood or, you know, that they are failed to be understood, you know, I think you would have to find a good way to communicate. I don't think that's impossible. I think most people would understand if you said, 'Hey, if it looks like it's not working, we might stop early, and, you know, we have some other things on standby that we might try if we have good reason, and you have to trust us on our reason'—something like that."	R6: One respondent recommended finding a way to explain the study design in layman's terms that minimizes the risk that the design will be misunderstood. "I think you would have to find a good way to communicate," the respondent continued. "I don't think it's impossible. I think most people would understand if you said, 'Hey, if it looks like it's not working. We might stop early, and ... we have some other things on standby that we might try if we have good reason, and you have to trust us on our reason'—something like that" (R6).
4	R8: "Adaptations make it more mysterious perhaps, harder to understand, and might make the participant more uncomfortable that way, I guess. I don't think that it's any more different than any sort of even, you know, a fixed design that's kind of complicated can lead to confusion. So, I think it might make it more complicated than a nonadaptive design, but you could have a fixed design trial that is more complicated to understand than an adaptive design; it may make it a little harder, but I don't think it makes it impossible to overcome at all, in terms of explaining it and having people to understand it."	R8: This respondent commented that adaptations can make a study "more mysterious" or "harder to understand and might make the participant more uncomfortable" but said that they did not think that was different from what a participant could experience with "a fixed design that's kind of complicated," as such a design can also "lead to confusion." The respondent went on to say, "You could have a fixed design trial that is more complicated to understand than an adaptive design; it may make it a little harder, but I don't think it makes it impossible to overcome at all, in terms of explaining it and having people understand it."
5	R15: "I like to look at the whole study as the object of the intervention, not the issue of, you know, what the probability of randomization is going to be. I mean, you could get into very complicated territories to even say should you tell them what the randomization probability is that they, you know, they are encountering. I do not think you should—I think you should say, 'You know, it's a study that will try to treat as many people	R15: "I like to look at the whole study as the object of the intervention, not the issue of what the probability of randomization is going to be." This respondent asserted that even discussing whether to tell participants what the randomization probability is could get very complicated. "I do not think you should. I think you should say it's a study that will try to treat as many people as possible the right way, given the knowledge that we have, and

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	as possible the right way, given the knowledge that we have,' and just leave it at that .... I don't believe that's a violation of patient autonomy because they don't know all the logistics you use in any trial .... I mean, to make it successful."	just leave it at that .... I don't believe that's a violation of patient autonomy because they [participants] don't know all the logistics you use in any trial to make it successful."
6	R16: "So, if the goal of informed consent is to make sure that the participants have a really pretty full understanding of what they are consenting to and really understand what's going on, and that's the goal of informed consent, then we should just shut down the entire research enterprise. Because one thing we know empirically is that that is not what we're doing and not what happens. So, people don't have any understanding, even under the optimal circumstances. So, I just don't think that's what informed consent is about."	R16: "If the goal of informed consent is to make sure that the participants have a really pretty full understanding of what they are consenting to and really understand what's going on … , then we should just shut down the entire research enterprise. Because one thing we know empirically is that that is not what we're doing and not what happens. So, people don't have any understanding even under the optimal circumstances. So, I just don't think that's what informed consent is about."
7	R13: "So, I think that the idea is that an adaptive trial would try to help get to [enhancing autonomy] because it allows, . . . you know, sort of learning and evolution of the trial based on earlier participants, and so, … you know, the autonomy of each person is upheld because we're not ignoring, … you know, growing information about a treatment when you're considering whether or not to enroll. So, I think … that is, that's one way that autonomy … is, in adaptive trials, is supposed to be or adaptive trials are supposed to enhance autonomy."	R13: This respondent thought that an adaptive trial would try to enhance autonomy because it would allow for learning and evolution based on earlier participants. "The autonomy of each person is upheld because [researchers are] not ignoring growing information about a treatment when … considering whether or not to enroll."
8	R12: "The potential to increase efficiency, make decisions earlier with fewer patients and resources, the potential to accelerate the drug development timeline for the benefit of companies and patients, the potential to treat patients in a more personalized manner, for example, randomizing with higher probability to a drug that seems to be working better in their particular cohort, as in response-adaptive randomization designs, and the	R12: adaptive trials have "the potential to increase efficiency, make decisions earlier with fewer patients and resources, [and] ... accelerate the drug development timeline for the benefit of companies and patients." This respondent said that such trials also have the potential "to treat patients in a more personalized manner, for example, [by] randomizing with higher probability to a drug that seems to be working better

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	general ability to remain flexible enough to answer the scientific questions of interest in a setting where an off-the-shelf traditional design would be inefficient or impractical."	in their particular cohort, as in response-adaptive randomization designs, and the general ability to remain flexible enough to answer the scientific questions of interest in a setting where a ... traditional design would be inefficient or impractical."
9	R17: "[Y]ou know, you might want to say this not an ethical issue, but I think it is—the efficiency of the trial, how long does it take, how many participants—because doing adaptive design means that you, at the end of the day, after you enroll 30% more participants in order to get to the same level of statistical confidence, and would you be better off doing the shorter trial and getting the answer more quickly?"	R17: "You might want to say this not an ethical issue, but I think it is," a respondent asserted, noting that a trial's efficiency, how long it takes, and how many participants are involved are all important factors. Using an adaptive design means, this respondent explained, that you may need to enroll 30% more participants to achieve the same level of statistical confidence. "Would [researchers] be better off doing a shorter trial and getting the answer more quickly?"
10	R6: "I mean, because if you're a participant, well, I mean, the benefit of a participant to an adaptive design is that, if there is a underperforming arm that can be dropped, trial participants are less likely to be enrolled in an arm that is ineffective, right?"	R6: One respondent (R6) observed that the benefit of an adaptive design for participants is that, if there is an underperforming arm, it can be dropped, and trial participants are less likely to be enrolled in an arm that is ineffective.
11	R15: "So, all these things go in the mix, but if there's a therapy that doesn't work, the ethical pressure is a lot less, I believe. Yes, more people are exposed to the therapy that doesn't work, but unless it actually kills, I mean, unless the therapy kills, I don't get as worked up about a situation where more people are in the trial and nothing is working because that is the same as the situation outside unless the therapy itself is quite toxic, which is another situation. So, my main concern—although maybe if you convince me otherwise—is for those situations where the therapy does work, not where it	R15: "All these factors go in the mix, but if there's a therapy that doesn't work, the ethical pressure is a lot less, I believe." He said, that, "yes, more people are exposed to the therapy that doesn't work," but that "unless it actually kills" or is "quite toxic," he doesn't "get as worked up about a situation where more people are in the trial and nothing is working" because that is comparable to the situation outside the trial. So, my main concern . . . is for those situations where the therapy does work, not where it doesn't work."

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	doesn't work. If it doesn't work, you know, it doesn't matter whether you're in or out again if it's not overly toxic."	
12	R10: "I mean, I've seen this again with statisticians giving talks about this where they sort of say adaptive trials are more ethical because more people end up in a better-performing arm, and so, you know. It's like maybe, maybe in some circumstance like that it makes sense …. [Y]ou know, I'm not, we have to be careful about trying to sell trials as therapy. There are contexts under which, like a clinical equipoise, where I think it's reasonable to say things like that, but then again, I think we have to be careful about how we communicate, what exactly it is that we're doing in trials.… I'm skeptical that they are more ethical, but I could see there's really interest in them because that perception that is out there."	R10: "I've seen … statisticians giving talks … where they sort of say adaptive trials are more ethical because more people end up in a better-performing arm." The respondent said that that might make sense in some circumstances but that "we have to be careful about trying to sell trials as therapy." This respondent thought that in contexts "like … clinical equipoise … it's reasonable to say things like that, but then again, … we have to be careful about how we communicate what exactly it is that we're doing in trials." "I'm skeptical," the respondent stated, "that [adaptive trials] are more ethical, but I could see why there's really interest in them because that perception is out there."
13	R14: "So, would rather say that, yah, except if some decision [about adaptations] can be made that make design changes that are wrong because you don't have enough data, but if you're able to have somebody with, like, smart enough that you don't make decisions [about adaptations] that changes the design based on data that are insufficient to make the decision-making. You know, if it's done with people who are properly trained and, I don't really see how we could harm participants, and we need to think more about that except if you change the design in the wrong way, but this would happen if you have people who are not skilled enough that they change things when it's not relevant, you know."	R14: This respondent stated that they would rather say that if decisions about adaptations are made by someone who is smart enough not to make changes to the design based on insufficient data, then they (the respondent) could not see how participants would be harmed. This respondent expressed that it was necessary to think more about this problem but that harm would result only if a design was changed "in the wrong way," which would happen if researchers were "not skilled enough" and made changes that were "not relevant."
14	R10: "I mean. there is the sort of, I think, there is a sort of basic concern in adaptive trials that it potentially disadvantages patients who are in a more desperate situation, like if you're really self-	R10: One of the respondents (R10) had concerns about the possibility that some participants may disadvantage other participants who are in a more desperate situation by waiting until the trial is near

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	interested and you're thinking about enrolling in an adaptive trial, your first question should be, how close is this study to finishing, right? And that, you know, you basically want to be the last patient who enrolled if what you're after is benefit."	the end to join, giving themselves a higher chance of getting in a more favorable arm.
15	R12: "Usually, much more intensive development of design features and operating characteristics, power, type-I error, may only be useful in a limited setting, may turn out not to do what it is supposed to do, or the results of the trial may be such that an adaptive trial [and all the work that went into setting it up] really wasn't necessary, can be a harder sell to investigators and regulatory authorities and other stakeholders who are more accustomed to thinking about traditional designs and, in some cases, may actually perform worse than traditional designs or preclude one from answering questions that could have been answered by a traditional design."	R12: One participant pointed out that adaptive trials usually require much more intensive development of design features and operating characteristics, such as power and type-1 errors. Such trials, the respondent stated, may be useful only in a limited setting and may not do what they're supposed to do. The respondent also said that the results of the trial may even show that an adaptive trial and all the work that went into setting it up really wasn't necessary. They can also "be a harder sell to investigators and regulatory authorities and other stakeholders who are more accustomed to thinking about traditional [fixed] designs …. In some cases, [adaptive designs] [CORRECT?] may actually perform worse than traditional designs or preclude [researchers] from answering questions that could have been answered by a traditional design."
16	R1: "I was giving an example for, you know, you're adapting by changing the allocation ratio in a nonblind trial you need to be very conscious that you … may be introducing, you know, investigators will keep aware that you might alter the state of equipoise."	R1: One respondent (R1) stated that this is especially so when the study is not blinded, because the accumulating data may alter the state of equipoise for the investigators.
17	R6: "I am going to assume that, and maybe this is a bad assumption, that if we go into this with an understanding that there's equipoise for, I mean, presumably that exists at the outset of the trial before you've adapted it, that equipoise may be	R6: "I'm going to assume …, and maybe this is a bad assumption, that if we go into [a trial] with an understanding that there's equipoise" at the outset, before any adaptations are made, "that equipoise may be disrupted by the information gained

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	disrupted by the information you gain early on, right? This is why you throw things overboard so, you know, again, if you lose that position, you take action, right? You throw things overboard that underperform. Presumably they would be replaced with things for which there is a similar amount of uncertainty, right?"	early on." The respondent explained that this is why underperforming arms are thrown overboard. "If you lose that position" of equipoise, "you take action" and replace the underperforming arms with ones "for which there is a similar amount of uncertainty."
18	R17: "If equipoise means we haven't yet met the standard of evidence to close the trial and make a decision about which treatment we should use and patients in the future, then you can deviate from 50-50 pretty far before you reach that point, and the question is, what's your breaking point for saying, no, we shouldn't continue the trial because we're already getting a pretty good sense of the answer and people have different values? ... [T]here's different views about that."	R17: "If equipoise means we haven't yet met the standard of evidence to close the trial and make a decision about which treatment we should use … [for future patients], then you can deviate from 50-50 [that is, 1:1 randomization] pretty far before you reach that point, and the question is, what's your breaking point for saying, no, we shouldn't continue the trial because we're already getting a pretty good sense of the answer?" The respondent stated that people have different values and views concerning that.
19	R11: "This is to say that those who represent equipoise as a balanced system ignore or see an ideal world where you can gather all the 'experts'—and I put experts in the quotes—that has something to say about that and when the fatality is very, very high, it's extremely difficult to compute the potential risk benefits of the given intervention."	R11: "This is to say," they explained, "that those who represent equipoise as a balanced system ... see an ideal world where you can gather all the 'experts' ... that [have]something to say about that .... When the fatality is very, very high, it's extremely difficult to compute the potential risk [and] benefits of the given intervention."
20	R10: "[I]t's like when we start the study we have sufficient uncertainty that all of these, you know, arms [A, B, C and D] can be considered kind of rivals for each other. As you go on, that starts to look kind of less and less likely, you know, in theory. And you can imagine that, like, accordingly, there would be fewer sort of experts willing to assign patients to the sort of, you know, arms B, C and D."	R10: "When we start the study, we have sufficient uncertainty that all of these arms [A, B, C, and D] can be considered rivals for each other. As [the study progresses], that starts to look less and less likely in theory .... Accordingly, there would be fewer experts willing to assign patients to arms B, C, and D."

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21	R10: "Now, the challenging bit, I think, comes in is when you sort of think, okay, but look, what exactly is the threshold where we say, kind of, okay now, it's no longer acceptable to randomize people, right?, you know?"	R10: One participant was of the opinion that the challenging part comes when thinking about the threshold where one says that "it's no longer acceptable to randomize people."
22	R10: "[B]ut, like, those people who are getting allocated to B, C, and D … , like, are they going to be—should they be happy with this? Surely, if we gave them the choice, they would all pick A right? So, why is it okay, right? So, I think that's really interesting, and I think, you know, … it really does force us to take seriously the kind of, it forces us to, you know, those of us who are sort of in favor of equipoise, like, we really have, I think, like, kind of bite a bullet there and say, look the whole point is that, like, is actually, we still don't yet know, right? Kind of that nobody should be getting B, C and D, right? Even though A looks much better in the context of this study, we set our thresholds right if you design the study right, … [I]t should, like, it's not, we're not harming people by giving them B, C, or D. It's not inconsistent with competent care to do that, not yet because we haven't yet answered the question to the level of certainty that we agreed from the onset, right?"	R10: This respondent went further to look at this from the participant's perspective, stating that when it is obvious that one arm, say, A, is doing better than the others, all participants would choose that arm, when given a choice. The respondent questioned why it is supposedly okay that participants are kept in other arms. For this respondent, this was a "very interesting" problem that forces those of us who are in favor of equipoise to take seriously the idea that we still don't know whether "nobody should be getting B, C, or D." "Even though A looks much better in the context of this study," the respondent said, if we set our thresholds right and design the study correctly, "we're not harming people by giving them B, C, or D. It's not inconsistent with competent care to do that … because we haven't yet answered the question to the level of certainty that we agreed on from the onset."
23	R3: "So, again, I would say the adaptation itself doesn't raise problems of justice. What raises problems of justice is, are you attending to the underlying uncertainty, and are you ensuring that you're not allocating people to forms of care that no one would recommend for them? ... I think they (people who object to continuing adaptations) [AUS: is this your insertion?] think, oh, if you're adapting, you're depriving somebody of something. I think that presumes that there's a single agent whose uncertainty	R3: adapting, you're depriving someone of something. That presumes there's a single agent whose uncertainty you care about. But maybe there is no such single agent; there's just a diversity of opinions from lots of experts who may disagree with each other. The point of the study is to resolve that disagreement. "I would say the adaptation itself doesn't raise problems of justice. What raises problems of justice is, are you attending to the underlying uncertainty, and are you ensuring that you're not allocating people

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	you care about, you know. And maybe there is no such single agent; there's just a diversity of opinions from lots of experts who may have views that disagree with each other, and the point of study is to resolve that disagreement."	to forms of care that no one would recommend for them?" In this respondent's view, those who object to continuing adaptations believe that if you're adapting, "you're depriving somebody of something.… That presumes there's a single agent whose uncertainty you care about.… [But] maybe there is no such single agent; there's just a diversity of opinions from lots of experts, who may … disagree with each other, and the point of study is to resolve that disagreement."
24	R13: "[E]ven if you're changing the randomization frequency or something or, you know, adding in another arm at some point down the road, I mean, you're doing that still with the general sense of equipoise about the outcome. So, I think that equipoise still has to be the, you know, a guiding ethical principle around adaptive trials, but, you know, given the, you know, the changes to the trial and the complexities of adaptive trials, then I think that you also—you need to be extra certain that you know that there is still contributions that are being made to a general feeling of equipoise until the trial is complete."	R13: "Even if you're changing the randomization frequency or adding in another arm at some point down the road," the respondent stated, "you're still doing that with a general sense of equipoise about the outcome. So, I think that equipoise still has to be a guiding ethical principle around adaptive trials. Given the changes to the trial and the complexities of adaptive trials, you need to be extra certain that there are still contributions being made to a general feeling of equipoise until the trial is complete."
25	R14: "Well, equipoise is not about, equipoise for me, my definition of equipoise, so, this one, you know, is very complex because it's a complex concept, but for me, equipoise requires that we have uncertainty. Like, whenever we are sure that something is better than the other, it's not equipoise, and we need to give the better option to patients, but we're in uncertainty, and like, and we need more evidence to get out of the uncertainty zone, we're in equipoise. So, equipoise doesn't mean like 50-50."	R14: "Equipoise is a complex concept. For me, equipoise requires that we have uncertainty. Whenever we are sure that one option is better than the other, it's not equipoise, and we need to give the better option to patients. But when we're uncertain and need more evidence to get out of the uncertainty zone, we're in equipoise. So equipoise doesn't mean 50-50."

[1] Quotations that were not edited or paraphrased are not included in this table.