

Supplemental Material: Additional Illustrative Quotes

A. INITIAL CONTACT

Through Physicians	
Advantages for researchers	
MD as authoritative advocate for study	<p>The ‘pros,’ of course, are the involvement of the provider. You have somebody that’s on board that’s engaged in the study and is a partner with you to get it done. (24, IRB)</p> <p>If the letter comes from the physician’s office, it’s more effective. People pay more attention to such a letter... As letter from a physician would be, probably in most cases, more effective than the letter from the researcher. (31, Researcher)</p> <p>Patient recruitment is higher if a physician the person trusts asks the patient to participate in the study. (39, Researcher)</p>
MD knowledge of patients’ lives, health	<p>Another benefit to the researcher is, I’m only going to be offering this to people that I think can actually do that. If I know that my patient doesn’t have a working phone or cuts all their calls short because they’re using a flip phone ... I’m not going to mention this to those people. If I know that they only work nights and they can barely sleep between their night job and taking care of their kids, I might not remember to bring it up because I’m not sure if it would be useful. You might get a more appropriate, more activated ... you know, if this person is suicidal and drinking every day, and I kind of have bigger fish to fry right now with this patient, I’m not really probably going to remember this either. (02, PCP)</p> <p>I can say, “These patients, while they qualify, they never show to their appointments” or “they live too far away to take part in this on a regular basis.” So that means we can narrow down who we first reach out to, to try and get the best possible people for the study. (17, PCP)</p> <p>The provider may say, “Look guys. I know this patient. They’re going through hell. They’re going through all sorts of difficult issues. This is not the time to contact them.” There’s absolute validity of that. (23, PCP)</p>
Advantages for patients	
Established relationships, trust	<p>The pros would be the subject is hearing first from somebody they would hopefully recognize, somebody they would accept has access to their medical information. (01, IRB)</p> <p>[The physician] is someone who the patient already knows, so they’re already familiar and probably more comfortable to receive that information. (21, Researcher)</p> <p>A ‘pro’ is ... to not freak out the patient because somebody who’s not their clinician is looking at their medical record. (21, Researcher)</p>

Relationship to healthcare	It can cause confusion in the medical care with the physician or other healthcare provider not knowing what their patients are being approached about and potentially participating in. (24, IRB)
Disadvantages for researchers	
MD as bottleneck	<p>Just thinking about my own practice, it is ... quite possible that it would be lost in the shuffle. Knowing myself and my colleagues, there's just so many pieces of paper, and emails, and messages that you're probably not gonna get the same amount of attention than if it was addressed to the patients directly. (19, PCP)</p> <p>Presenting me with a letter that I can review and sign is not a bad one. It just has to be the least painful possible. If you say "here's another [task] to add to the mix," I'm going to say I'm not going to do it... I'm not against research. I'm just against me spending a lot of time giving away my time for free... I'm fully employed, and I don't need more work. (37, PCP)</p> <p>I know in my practice now, if I got a letter asking me to enroll patients in a research study, I honestly would probably put it to the side just because I'm so busy right now. (41, PCP)</p>
Recruitment challenges	<p>Having the letter come through the primary care provider, in my experience, absolutely is a major obstacle—just from a time and effort perspective, it's just a major obstacle to recruitment. Recruitment is prolonged and more expensive when you have to involve the primary care provider. (04, Researcher)</p> <p>Basically, the fewer intermediaries you can insert in that process, the better in a sense because if the primary care doctor is busy or doesn't perceive it as urgent, then that's potentially not going to get done in an expeditious fashion, and the patient might not end up getting contacted. (06, Researcher)</p> <p>The cons would be that it may take a while to get the patients enrolled if you're waiting on the physician to contact them. (36, PCP)</p>
Disadvantages for patients	
Decreased autonomy	<p>If it's just to give the information to physicians and then they only relay the possibility of the research if they agree, that gets back to that paternalistic scenario that I referenced before, where I think people are asking why does the physician get to decide for everybody? There are some concerns, I think, about that approach. (01, IRB)</p> <p>First of all, many primary care providers will just simply refuse to be involved in those activities because they don't have the time or interest. That completely deprives the patient of the opportunity to participate. You're essentially making a decision for the patient if you're a primary care provider who decides that. Or, let's say, the patients in my clinic if I don't agree to participate in that activity I've decided that none of my patients can be involved, which is not fair and maybe not representative of the individual patient's interests. (04, Researcher)</p>

Direct Contact	
Advantages for researchers	
Efficiency	<p>Another 'pro' is that keeping as few parties out of it as possible keeps things easier, so you're not relying on other people... You're the one that's actually doing it. You know it's done in an appropriate way. (08, Researcher)</p> <p>One advantage is that it's easier, it involves one less person. (15, PCP)</p> <p>Sending a letter directly to patients appears to be a little bit more efficient, so I don't have to get permission from other layers, so to speak. (32, Researcher)</p>
Advantages for patients	
Increased autonomy	<p>My view of it is it's the patient's life, it's the patient's right to decide what they want to do. Nobody owns them, their primary care doctor ... or whoever. (07, Researcher)</p> <p>It provides [patients] the most direct chance to make their own independent decision. I would think, for probably better or worse, they could be swayed by the physician, if [he or she] were involved. If the patient got communicated with directly, they probably would have it to sit with and figure out what they wanted to do based on their own perspectives. (19, PCP)</p> <p>There's value in contacting the patient directly because that way people can make their own choice. I think most patients are capable of deciding whether or not they want to be involved in research... The pros of that is that people are independent. They can make their own decisions. (41, PCP)</p>
Disadvantages for researchers	
Recruitment challenges	<p>The cons of directly would be having the patient question what's happening, and question research, and that sort of thing. Because the patient doesn't know you, they may be less likely to agree to participate. (08, Researcher)</p> <p>A patient might be less likely to enroll in the study if their physician didn't recommend it or propose it to them. If the patient didn't have a relationship with this third party maybe they'd be a little bit more wary of enrolling in a study versus if their doctor had asked them about it. (13, PCP)</p> <p>The researcher would not have an ongoing relationship with the patient, and would have, I think, a lot harder time getting any level of support or trust that would need to be a part of that relationship. Getting that initiated would be harder for the researcher going directly to the patient. (26, Researcher)</p> <p>If you put in a cold call on virtually anything, buying stocks, buying insurance, or participating in a research study, you're not going to get nearly as high an uptake as if a trusted person is recommending the procedure or whatever. (37, PCP)</p>

Disrupt MD-researcher relationships	Let's assume physicians don't even get a heads up that their patient's in a trial, and in that case I think that can lead to bad relationships... I think that cutting out a physician entirely can lead to some bad feelings. (14, PCP)
Disadvantages for patients	
Privacy concerns	<p>The patient would [be] uncomfortable knowing that someone else was peeking through their medical records. (21, Researcher)</p> <p>Occasionally somebody is irritated that somebody there knows their diagnosis. (09, Researcher)</p> <p>If the patient was not familiar with the organization doing the research, they might not want to have someone reach out to them directly or they might feel like it's a violation of their privacy rights. (13, PCP)</p>
Disrupt MD-patient relationships	The question there would be clinician-patient confidentiality. "Are they sharing my information when they're not supposed to be, outside the scope of the clinical practice?" ... As a patient, I would be like, "why are you sharing my information?" (05, Researcher)

B. RESPONSE REQUESTED

Opt In	
Advantages for researchers	
Motivated participant pool	<p>With an opt-in approach, you're going to end up with a population that really wants to participate in the study. If they take the time to read the letter and call you to express interest in the study and say they want to participate, that's a motivated patient who's interested in participating and they're going to stick with the study program most likely. You'll wind up with a group of patients that's really invested in the study. (06, Researcher)</p> <p>[Researchers] are going to have more engagement with somebody who says, "Yes, I'm interested. Let's talk about this." If that patient ultimately enrolls in their study, they're going to have a better, more involved, engaged participant in their study and probably a better chance of somebody who adheres to the study procedures and completes the study than if there's not even a starting point of them reaching back out to the researchers to say, "Yes, I'm interested." (24, IRB)</p>
Advantages for patients	
Respect for privacy	<p>It keeps the subject in the driver's seat. The opt-in approach, where they have to actively follow up on it ... would maximize the respect for their privacy. (01, IRB)</p> <p>That's most respectful to the time, privacy, and interest of the patient. That's the most protective of the patient's just day-to-day life. (04, Researcher)</p>

Disadvantages for researchers	
Inefficiency	<p>I think it's ethical, but from a study design standpoint, it's probably not the most efficient way to do that. (15, PCP)</p> <p>You have to wait on the patients and it's harder to get your recruitment. (21, Researcher)</p>
Opt Out	
Advantages for researchers	
Efficiency	<p>The pros would be that you're likely to increase your participation rate. By not just counting on the opt in, you're maximizing or at least increasing your chance that people will actually hear about the study and have a chance to think about it. (01, IRB)</p> <p>Another pro is that it's likely going to be a more representative population. So your study population you end up will be more representative of the general populous because you're less aggressively selecting a population that really wants to participate in the study... An opt-out approach is certainly more feasible and leads to a more representative population, (06, Researcher)</p> <p>You're probably going to get a chance to get more doors open. (21, Researcher)</p> <p>The enrollment is likely to be higher. (30, IRB)</p>
Contact with patients otherwise missed	<p>You'd probably speak directly to move a lot more people that way, because letters sometimes get thrown out without being read, they don't reach the intended person. (18, PCP)</p> <p>The advantage of that is that there's an opportunity to give them more information with the phone call, and people who are indecisive or procrastinate might be persuaded to participate. (35, PCP)</p> <p>It could potentially recruit more patients and it gives the patient the option, without relying on the patient's initiative or memory to contact the researcher and say that they would like to participate. (36, PCP)</p> <p>The pros of that is that your research pool will be larger. Because if a patient actively has to do something, they're probably not as likely to do it. (41, PCP)</p>
Advantages for patients	
Opportunity to hear about research (don't miss out)	<p>It helps to ensure adequate coverage and opportunity for individuals that might be benefiting from the work and from the engagement, whereas basically the opt-in approach kind of presupposes a level of interest that may not be there. (26, Researcher)</p>

<p>Informed decision making</p>	<p>If they forget [to opt out], there will be a call, so the researcher will connect and there will be that opportunity to ... maybe answer some questions about it before they decide, “Am I going to continue with this conversation and then be recruited or not?” It actually gives a little more information to the person ... about the study and some clarifications of things. (12, PCP)</p> <p>At least patients would get a person on the phone to hear more about it, a little bit more context, a little bit more understanding of what [researchers] are actually looking for, that person on the phone to really explain that. They might appreciate that. (14, PCP)</p>
<p>Disadvantages for researchers</p>	
<p>Many phone calls with low rate of return</p>	<p>Patients might not pick up the phone for these phone calls. (06, Researcher)</p> <p>Disadvantage to opt-out is some people don’t really want to be contacted. At least my perception of that is that they don’t answer their phone or they say, “Don’t call me again,” or they don’t answer the letter. (07, Researcher)</p>
<p>Disadvantages for patients</p>	
<p>Privacy concerns</p>	<p>Even though you say “I’m going to call next week,” the patient may still get upset, like, “Why are you bothering me? You just wrote me a letter, I don’t want to hear from you.” (15, PCP)</p> <p>We’re living in an era when people are bombarded with offers, requests, and invasions of their privacy. I think we have to be respectful of that. (35, PCP)</p> <p>If I don’t say anything and I just get these phone calls until I say, “Hey, please stop, what’s going on, why you calling me...?” I think that would just cause a lot of unnecessary bother to the participants for research that shouldn’t really be bothersome... It’s just very annoying and it’s not the right way to do it. (38, IRB)</p>
<p>Burden of having to opt out</p>	<p>The cons are, obviously from the participant’s perspective is that they actually now have to do something to actually not be contacted. It puts in a sense more burden on the potential participant. (25, Researcher)</p> <p>It’s annoying, it puts a burden on the patient to have to do something to not be annoyed. (27, PCP)</p>