

## Clinical Research Ethics Question of the Month: Altruism

By Norman M. Goldfarb

You are a physician at a Catholic hospital investigating a new treatment for a women's health condition. This healthy volunteer study requires an unpleasant and somewhat risky procedure, so you do not expect to meet your enrollment target. The first five participants are nuns who say their primary motivation is altruism.

### Results

#### Question 1. Would you promote altruism as a reason to enroll in the study?

Of the 87 respondents, 46% would promote altruism as a reason to enroll in the study and 54% would not.

Respondents made the following statements:

This is a healthy volunteer study, [so] any participation should be due to altruism. The monetary compensation is not mentioned here, but should not be coercive."

I don't think it's up to us as regulatory reviewers to encourage or question why someone chooses to enroll in a study. As long as s/he has been given all of the information about the procedures and the individual is cognitively able, they should be allowed to decide for themselves if they would like to participate."

Many ICF documents in the Benefits section have a statement that [appeals to] a sense of altruism like 'participation in the study may not directly benefit you, but could help others in the future.'"

One respondent expressed concern that promoting altruism as a reason to enroll might reduce enrollment by people not motivated by altruism.

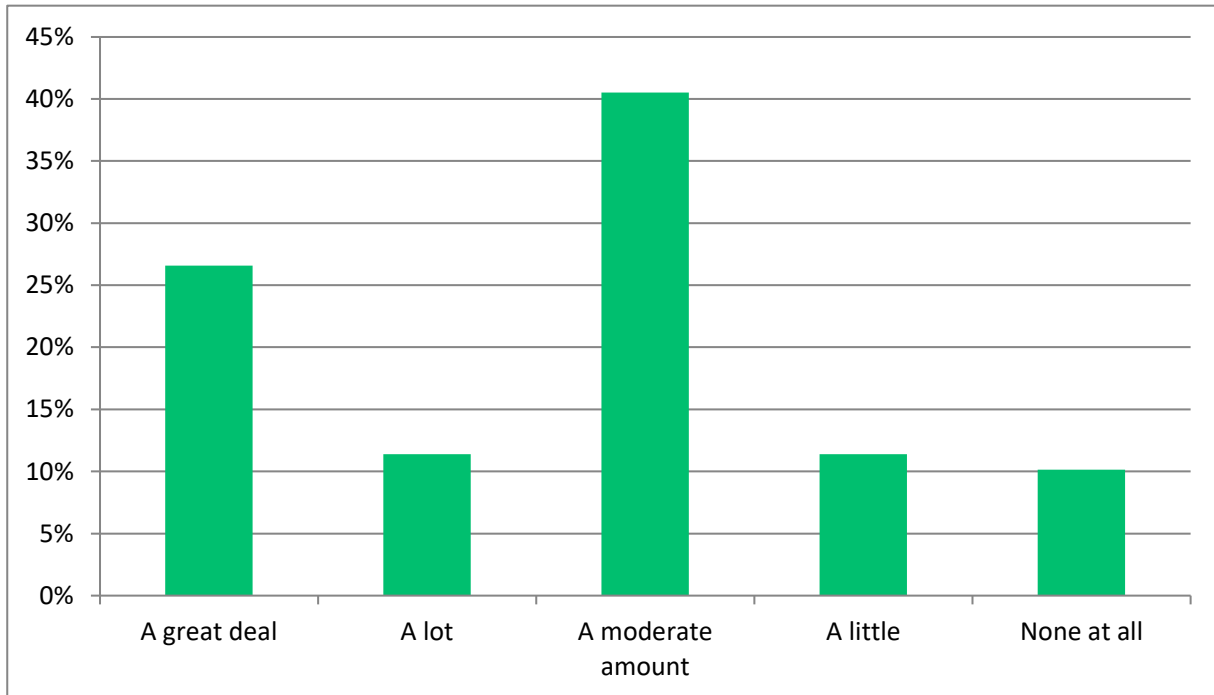
One respondent suggested that the nuns might be enrolling to benefit their institution or under the influence of their superiors.

One respondent questioned whether a study with a "somewhat risky procedure" should be conducted at all.

One respondent pointed out that, since the investigator does expect to achieve the enrollment target, he or she should terminate the study.

One respondent expressed concern that the investigator's actions might be improperly motivated by the enrollment challenge.

**Question 2. How much personal sacrifice (without personal benefit) should study participants be allowed to make?**



Thirty-eight percent of respondents would allow study participants to make a great deal or a lot of personal sacrifice, 52% would allow study participants to make a moderate or a little personal sacrifice, and 10% would allow study participants to make no personal sacrifice at all.

Respondents made the following statements:

Assuming the IRB has evaluated the risk-benefit ratio and found it to appropriate, it's up to the participants to evaluate their own level of personal sacrifice, which is inherently subjective.

As much as they want after being fully informed, as long as the study has been approved under standard ethical principles (i.e., a balanced risk/benefit ratio). Anything else is unacceptable paternalism.

As the risks go up and benefits down, you have to wonder why someone would participate if they or a family member didn't have the condition under study. I might wonder about their state of mental health and not allow them to participate.

To interfere denies personal autonomy.

If the participant has been correctly consented, then the level of personal sacrifice required needs to be their decision. However, if the person taking consent believes that it will negatively impact the participant, then this needs to be considered when enrolling the participant.

**Question 3. If it concerns you that people are volunteering because of too much altruism, what are the relevant ethical principles?**

Respondents mentioned the following principles: beneficence, autonomy, justice, respect for persons, nonmaleficence (try spelling that one), informed consent, risk-to-benefit ratio, paternalism, human dignity, and lack of coercion.

**Question 4. Should enrollment be limited to people or their relatives who are prone to the condition?**

Twenty-five percent of respondents would limit enrollment to people or their relatives who are prone to the condition, and 75% would not.

Respondents made the following statements:

Justice as an ethical principle dictates that those who will benefit from the research should be the ones who undertake the risk. If the research were to specifically target enrollment to individuals who are NOT prone to the condition under study, that might be a cause for concern or reevaluation.

The study as described is for 'healthy volunteers' and involves an 'unpleasant and somewhat risky procedure.' That makes me concerned about the risk/benefit ratio of the study. There would have to be a good justification for targeting healthy volunteers, and absent that, it should be limited to participants with a reasonable expectation of benefit to offset the risks.

Taking away a person's choice just because they may not receive a benefit seems sort of punitive.

Relatives prone to the condition are not truly healthy volunteers.

If a person is volunteering to help a relative, that may increase the likelihood they are volunteering purely for altruistic reasons, and may dismiss the risks of the study.

**Question 5. When obtaining consent, should you attempt to determine the contribution of altruism to the potential study subjects' motivation?**

Twenty-nine percent of respondents would attempt to determine the contribution of altruism to the potential study subjects' motivation, and 79% would not.

Respondents made the following statements:

If the study runs the risk of enrolling subjects with 'too much altruism,' then it's probably the protocol that needs to be changed.

If the volunteer is dismissive of the risks of the study that are 'unpleasant and risky,' then that is a 'red flag' that they may not be a good candidate for the study, either because they don't fully comprehend the risks or they engage in risky behavior without thought to self-preservation.

It's irrelevant. Determining the participants' level of understanding of the discomforts/risks is exponentially more important.

As long as the subject is well informed of the procedure and its possible side effects, we cannot ask their motivation.

No. If we do not attempt to determine the contribution of altruism to the potential study subject's motivation for other studies, we should not do it for this study. What if the primary motivation were money instead of altruism? Is that better?

It is important to understand the reason a subject might participate so that you can be aware if the subject might choose to discontinue participation and even if discontinuation might be encouraged.

**Question 6. Should the consent form explicitly caution against an excessive sense of altruism?**

Eleven percent of respondents said the consent form should explicitly caution against an excessive sense of altruism, 63% said it should not, and 26% made comments.

Respondents made the following statements:

If the IRB or other study oversight thinks that it may be beneficial for the study and design, it could be included. Depending on patient population, it may be very relevant to discuss and have consent list this as a factor to consider.

Altruism is already a part of most research studies' participation rates and should be mentioned in the usual way.

No. How do you measure altruism?

No! We should not be dictating to patients how they [should] 'feel' about participating in a study.

Definitely not. This is silly. The risks and potential benefits should be clearly presented. There is no such thing as a 'risk of too much altruism.' How would this even be included in a consent form?

Definitely not! Research over the years has tended to get carried away with itself with over-explanations in the consent form about simple concepts, further confusing patients. We certainly do not need to also define excessive altruism and its risks. Our goal is to simplify the consent process, not complicate it.

**Question 7. If you are concerned that people are volunteering because of too much altruism, what other steps, if any, would you take to mitigate the issue?**

Respondents made the following statements:

Include these questions when considering if the participant is eligible for the study or modify the study design so that participants with too much altruism are excluded.

We would do what we always do. If we felt a patient was there for the wrong reasons (any wrong reason), we would proceed with caution in consenting and enrolling the patient and apply good ethics and judgment. This has happened in the past, when, for example, a patient came in with family members who were coercing the patient to participate in the study (for the money). We did not enroll that patient because it was not in the best interest of the patient to be in the study. We would apply that standard to any patient.

Do not soften language related to risks, benefits and alternatives in the consent process.

It may be a good discussion point during the consent discussion.

Make [it] very clear that their participation will be anonymous and will not result in individual public accolades or praise.

In this particular case, is there pressure within the religious order to participate, which the study staff or the IRB may not be aware of?

If I were truly concerned that people were volunteering for the wrong reasons, I'd need to look more closely at the study procedures to understand why I felt the need to protect a particular subset of people (those motivated by altruism) from participating.

## Discussion

Before getting into the ethical question at hand, it should be mentioned that ethical questions inherently deal with shades of gray — if the answers were obvious, we would not need ethicists. For example, take informed consent. The regulatory requirement is that study participants be *informed*, not that they *understand*. That's fortunate, since every study of informed consent effectiveness has found that many people do not understand and cannot recollect significant consent information. Nevertheless, we enroll them in studies. One of the functions of an institutional review board is to ensure that studies are ethical, so it's not the end of the world if someone enrolls in a study without full understanding. In other words, in the absence of a perfect solution, we have found one that works reasonably well.

People participate in clinical studies for various reasons. Because most healthy volunteer studies do not offer a health benefit to study participants, it is common to pay a "reasonable amount" for participation. While a reasonable payment is considered ethical, the practice has resulted in a community of "professional guinea pigs," who are prone to noncompliance with study requirements. It feels unsavory to pay people to participate in clinical studies, but that seems to be the only option for many early stage drug development programs.

Many later-stage studies provide "stipends" to study participants. These payments are supposed to be too small to cause people to enroll in studies "against their own best interests," which is a strange concept in a country like the United States that celebrates the right of every person of sound mind to make his or her own decisions.

There is thus a general preference in the clinical research community that people enroll in studies (a) to benefit their own health, provided this is a realistic expectation, or (b) to benefit the health of their friends, relatives or community, or future patients, i.e., the public at large.

As the direct benefit to the study participant decreases, we assume that their motivation becomes more altruistic. At the extreme of altruism is the study participant who willingly risks his or her health for the possibility of creating generalizable knowledge that will not specifically benefit that person or his or her friends, relatives or community.

At the extreme, we need to ask whether a person's sense of altruism is so powerful that it would cause him or her to enroll in a study "against their own best interests." (For example, a strong sense of altruism might cause a person to discount the risks in a study.) If so, encouraging that person's sense of altruism could be considered undue influence. We consider it unethical to pay money to an impoverished person in to participate in a study, so how is it ethical to pay an altruistic person in the currency of altruism?

To answer this question, we must first answer a more fundamental question: To what extent do acts of altruism benefit the altruistic person? Looking only at the direct effects of a purely altruistic act, the answer must be "none," since that is the definition of altruism. However, altruism can generate powerful *indirect* benefits to the altruistic person, namely an increase in self-esteem and esteem within the person's community. These indirect benefits increase as the purity of the altruistic act increases. Considering these indirect benefits might be considered cynical, but they cannot be ignored when we are talking about interfering with a person's autonomy.

In the case at hand, we are considering whether this study is taking unfair advantage of nuns, a notoriously altruistic lot. We have no actual evidence that altruism is even their motivation — they might correctly believe that this women’s health study will provide them with personal health benefits.

As several respondents stated, the investigator’s responsibility is to fully inform potential study participants, not to interfere with their autonomous decisions. However, if the investigator believes that the nuns might be enrolling “against their own best interests” *for any reason*, it seems reasonable to investigate the question and, if a problem is found, discuss it with the IRB and take corrective action. For example, perhaps the riskiness of the procedure needs to be clarified in the consent form. Or, perhaps there might be some other reason, e.g., peer pressure, for the nuns’ enrollment. In some cases, it might make sense to decline to enroll a person in a study, in the full knowledge that the principal of beneficence is being given precedence over the principal of autonomy.

### **Next Month’s Question**

You are a member of an IRB reviewing a study with an unusual feature: Because the study population will be very diverse economically, the investigator wants to vary the stipend based on each study participant’s financial situation. Her reasoning is that a fixed stipend for everybody would exploit high-income people but unduly influence low-income people. Will you vote to approve this approach to stipends? Read the full question and give us *your* answer at <https://www.surveymonkey.com/r/2LRL22P>.

### **Author**

Norman M. Goldfarb is Managing Director of First Clinical Research LLC, a provider of clinical research best practices information services. Contact him at 1.650.465.0119 or [ngoldfarb@firstclinical.com](mailto:ngoldfarb@firstclinical.com).