Article

Giving Children a Say without Giving Them a Choice: Obtaining Affirmation of a child's Non-dissent to Participation in Nonbeneficial Research

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Abstract: To what extent, if any, should minors have a say about whether they participate in research that offers them no prospect of direct benefit? This article addresses this question as it pertains to minors who cannot understand enough about what their participation would involve to make an autonomous choice, but can comprehend enough to have and express opinions about participating. The first aim is to defend David Wendler and Seema Shah's claim that minors who meet this description should not be offered a choice about whether they participate. The second aim is to show, *contra* Wendler and Shah, that the principle of nonmaleficence requires more with respect to giving these minors a say than merely respecting their dissent. Additionally, it requires that investigators obtain affirmation of their non-dissent. This addresses intuitive concerns about denying children a choice, while steering clear of the problems that arise with allowing them one.

Keywords: Assent; dissent; non-dissent; research involving children; research involving minors; nonbeneficial research; vulnerable subjects; David Wendler; Seema Shah

Introduction

It is uncontroversial that conducting research ethically requires treating subjects with respect. However, it is not always clear what respectful treatment requires in practice. This is especially the case when it comes to research involving individuals who lack the capacity to provide informed consent. Consider the following case.

> *The Dora Case*. Dora is a typical eight-year-old child. She is being considered for enrollment as a healthy volunteer in a research study that offers her no prospect of direct medical benefit. Her participation would require spending a couple of hours in a lab on four successive Saturday afternoons. She will be asked to perform tasks that she would not particularly enjoy, but that are unlikely to cause her more than minimal pain or discomfort.[1] There is good reason to think that the study will be valuable and it cannot be conducted without the participation of minors.

Dora cannot participate in the study unless her parents provide consent.[2] But what sort of voice should Dora, herself, be given with respect to whether she enrolls, or remains enrolled, in the study? A typical eight-year-old lacks the capacity to make an informed decision about whether to participate in research. However, Dora is eight, she is not a toddler; she can understand some of what her participation would involve and may well have something to say about it.

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In this paper, I am concerned with what sort of say, if any, a child like Dora should have concerning whether she enrolls, or stays enrolled (henceforth, 'participates') in research studies that offer no prospect of direct medical benefit to subjects. Call research of this sort *nonbeneficial*. By a child "like Dora," I mean a child who does not understand enough to make an autonomous choice about participating in research, yet understands enough to have and express thoughts about it.[3] Call children who meet this description *intermediate minors*. Intermediate minors are contrasted with those whom I will call *capacitous* minors on one hand, and *very young* minors on the other. Capacitous minors are those who, despite being *legally* incompetent, have the capacity to make an autonomous choice about whether to participate in research. Capacitous minors are typically older children and teenagers. *Very young* minors are children who can understand little or nothing concerning what their participation would involve, and so are unable to form or articulate thoughts about it.[4] As intermediate minors occupy a gray area between capacity and incapacity, they present a particular difficulty when it comes to determining how to take their perspectives into account. With this in mind, the central question I am concerned with can be put as follows:

> **The Input Question:** To what extent, if any, should intermediate minors have a say concerning whether they participate in nonbeneficial research?

An intuitive answer to the Input Question is that Dora *herself* should decide whether she wants to participate in the study, assuming her parents are willing to provide consent. This is the answer suggested by the U.S. Code of Federal Regulations (henceforth, 'the Regulations'). The Regulations require that investigators conducting nonbeneficial research obtain *assent*, defined as "affirmative agreement to participate in research," from all children capable of providing it.[5]

However, numerous commentators have raised difficulties for this answer to the Input Question.[6] In particular, David Wendler and Seema Shah argue that, while the principle of *respect for autonomy* justifies giving capacitous minors a choice about participation, there is no comparable justification for giving intermediate minors (or very young minors) this choice.[7] Appealing to research on child developmental psychology, they suggest that most minors are capacitous by age fourteen. They thus recommend that investigators be required to obtain assent only from minors fourteen years and older. When it comes to intermediate minors, Wendler and Shah argue that *the principle of nonmaleficence* grounds a requirement that investigators *respect their dissent*. Here 'dissent' is understood, roughly, as an expressed objection to what an individual is experiencing, or anticipates she will experience, in response to research participation. (I discuss the dissent requirement in detail later in the paper.)

Few, if any, have endorsed Wendler and Shah's answer to the Input Question. Most of those responding to their paper argued that intermediate minors should have more of a say concerning whether they participate in nonbeneficial research than they would be given under a dissent requirement. However, the problems Wendler and Shah raise for the idea that intermediate minors should be given a choice are serious; and the fact that many are critical of the assent requirement suggests some measure of agreement with this. This leaves the issue raised by the Input Question largely unresolved.

This paper has two main aims. First, I defend Wendler and Shah's claim that intermediate minors should not be given a choice about whether they participate in nonbeneficial research. Second, I argue, contra Wendler and Shah, that the principle of nonmaleficence requires more with respect to giving intermediate minors a say than merely respecting their dissent. In particular, I argue that nonmaleficence additionally requires that investigators obtain what I will call 'affirmation of non-dissent' from intermediate minors. I argue that this additional requirement addresses some of the intuitive concerns about denying intermediate minors a choice, while also avoiding the difficulties that come with giving them a choice.

I limit my discussion to *nonbeneficial* research because I am concerned with the extent to which intermediate minors should have a say when the research in question holds minimal risk, and considerations of their personal medical benefit cannot justify denying them a say. That said, I think that much of what I say applies to research that offers a prospect of direct benefit to subjects.

The paper will proceed as follows: I begin by arguing that 'they should choose' is the wrong answer to the Input Question. Next, I explain why addressing the Input Question is important in the context of recent discussions of the assent requirement. In doing this, I distinguish the Input Question from a more general question about what respectful engagement with intermediate minors requires in the context of research. Following this, I defend an answer to the Input Question. In doing so, I build on Wendler and Shah's position by arguing that nonmaleficence requires more with respect to giving intermediate minors a say than they claim. I conclude by suggesting that my recommendation that investigators obtain affirmation of intermediate minors' non-dissent is best conceptualized as part of a more robustly fleshed out version of the dissent requirement.

Why "They Should Choose" is the Wrong Answer to the Input Question

It is intuitive that Dora should be allowed to decide whether to participate in the study, assuming that her parents are willing to provide consent (I will henceforth leave this qualification unstated). The idea is that Dora would be provided with age-appropriate information about what her participation would involve, and then given ample opportunity to discuss her thoughts and ask questions. She would then be allowed to decide whether she wants to participate. She need not make the decision all on her own; she can consult her parents, or decide while talking with them if she wishes. Rather, the idea is that, at the end of the day, it is up to her: She can choose to participate or not participate for any reason at all, and her choice will be honored.

Despite its initial plausibility, there are serious problems with this idea, and I argue that it should be rejected. In this section, I defend this claim. I detail and build on the difficulties raised by Wendler and Shah and explain why, *contra* the contention of many commentators, treating intermediate minors respectfully *does not* require giving them a choice about whether they participate in nonbeneficial research.

Cognitive limitations, choice, and children

To consider the merits of giving intermediate minors a choice about research participation, we need to know exactly what the child would be making a choice *about.* The obvious answer, and the one given by the Regulations, is 'participation in research.' But a little thought reveals that this does not make sense when it comes to intermediate minors. Two general points about making a choice are relevant here. First, when one agrees to participate in an activity, she agrees to participate in that activity *under some description*. For example, I can agree to participate in a recreational soccer game without agreeing to participate in a fundraiser for a political campaign, even if the soccer game *is* a fundraiser. Second, an individual cannot agree to something unless she possesses the concepts required to *mentally represent* that thing as an option.[8] For example, a typical five-year-old cannot agree to participate in a campaign fundraiser at least because she lacks an adequate grasp of the concepts *candidate*, *campaign*, and *political office*. While she might be able to agree to participate in the event *under a different description*—e.g., playing in a soccer game—this would not amount to agreeing to participate in the fundraiser.

As Wendler and Shah discuss, an individual cannot agree to participate in nonbeneficial research unless, at the very least, she has an adequate grasp of the concepts of *research* and *risk.* They point out that in order for a subject to be able to weigh the risks, she must be able to appreciate how those risks are relevant in the context of her life, values, and specific circumstances.[9] Wendler and Shah also argue that when it comes to deciding whether to participate in nonbeneficial research, an individual must possess the concept of *altruism*—acting for the good of others with no promise of personal gain.[10] While many commentators disagreed with Wendler and Shah on this point, I think that it is correct.[11] A child who lacks the concept of *altruism* cannot understand the social significance or value of participating. Thus, she cannot understand that or why there is a nontrivial reason in favor of her participating. This point is especially pertinent in the context of nonbeneficial research. I say more about this below.

The problem with asking intermediate minors to make a choice about participation in nonbeneficial research is that most of them will lack a sufficient grasp of the concepts required to mentally represent this proposition, and so will be unable to genuinely entertain it as an option. Those on the older end of the spectrum may be capable of grasping the requisite concepts to the degree required to *at least entertain* participation as an option and so make a choice about *it*. But this choice will not be meaningful in virtue of being ill-informed.

In sum, many intermediate minors literally cannot choose to participate in research because they lack the concepts required to entertain the relevant propositions, and those who can will be incapable of making an *autonomous* choice, at least in virtue of its not being sufficiently informed.

However, a proponent of 'they should choose' might argue that allowing intermediate minors to choose is valuable, even if that choice is not autonomous. As many of Wendler and Shah's critics pointed out, the idea behind the assent requirement was never to set the bar this high.[12] Rather, the idea is that there is value in allowing a child to decide whether to participate in research *as she understands what it would involve.* So just as a five-year-old can agree to participate in a soccer game, even if not a campaign fundraiser, an intermediate minor might agree to 'staying at the clinic for a few hours, having blood drawn, and answering some questions.'

However, the value of obtaining an intermediate minor's agreement to participate in research *as she understands what it would involve* is dubious. If a child's understanding is sufficiently impoverished or inaccurate, then her decision might not reflect her values, desires, or interests. Consider an analogy. Normally I would not choose to wake up at six a.m. to go to my local coffee shop and get fresh coffee. But suppose I find out that the shop is giving out free coffee this morning, so I decide to wake up early and get some free coffee. I am, however, missing a crucial piece of information: To qualify for the giveaway, I must commit to buying one pound of coffee from them per month for the next six months. If I knew about that qualification, I would not have made the choice I did.

Similarly, suppose an intermediate minor is under the mistaken impression that her participation in a research study will have a particular benefit (e.g., she once saw a television program about a research study that looked fun, and she incorrectly assumes that the study she would participate in involves similar activities). In this case, the child is not misinformed. Rather, she misunderstood the information she received, perhaps in a similar way to how I mistakenly assumed that the free coffee came without strings attached. In that case, her agreement would be no better an indication of her values, desires, or interests than my decision is an indication of my preferences regarding the relative merits of free coffee and sleeping in.

The problem is exacerbated by the practical and epistemic difficulties involved in judging how well a child understands the information she is given. While the investigators can try to gauge the child's understanding, it will not always be possible to tell exactly whether, how, or to what extent her conception of what participation involves is incomplete or inaccurate. Or even if an intermediate minor understands the activities required by participation, lack of experience might render her a poor predictor of how she will react to them. This concern is especially pertinent when it comes to nonbeneficial research with healthy intermediate minors, as it is likely that they will have minimal experience as subjects in a clinical or research setting.

Another difficulty is that children often want to please adults or show that they are mature enough to handle responsibilities. This might lead some intermediate minors to participate only to please their parents (making it unclear that they are empowered by having the choice). Related considerations might make a child who wishes to withdraw from a study reluctant to do so, even though she would have that option (she might think withdrawing would show than she couldn't handle the responsibility of choosing after all).[13]

This last point shows that not only is the value of giving intermediate minors a choice dubious, but that it might be harmful.[14] Another concern along these lines is that giving an intermediate minor a choice might itself be a source of anxiety. The child might well realize that she does not have a sufficient grasp of what participation involves, and so is choosing in the dark. Knowing that one is ill-prepared to make a choice can be stressful. More generally, it is a mistake to think that having a choice about something is always empowering, or otherwise beneficial. As Gerald Dworkin has pointed out, choices come with the burden of being (or at least *feeling*) responsible for the choice and its outcome.[15]

So, one problem for the proposal that intermediate minors should decide whether to participate in nonbeneficial research is that, due to their cognitive limitations and lack of experience, they are not in the right epistemic position to do so autonomously, and the value of making the choice non-autonomously is dubious. Of course, the fact that an individual is not well positioned to make an autonomous choice need not imply she should not be given that choice. A cognitively normal adult might choose to purchase a house without doing adequate research on the area, integrity of the building, or other relevant issues. There is no relevant information that she is cognitively unable to understand; rather, she simply did not do her homework. Even so, it is arguable that the value of autonomy justifies noninterference in this case.[16] But such considerations do not straightforwardly apply when the agents are intermediate minors and not adults, and the decision in question concerns matters that the intermediate minors do not adequately understand.[17]

A related concern is that when an intermediate minor non-autonomously chooses to participate in research, this might seem to provide justification for exposing the child to risks in the same way that a person's providing valid consent does. But if the child's choice is nonautonomous, this appearance is illusory.[18]

Considerations of beneficence

So far, the problems I have raised for the 'they should choose' answer to the Input Question center on considerations about minors' cognitive limitations and lack of experience. However, one might appeal to considerations of *beneficence* in support of giving them a choice. In particular, some have argued that giving intermediate minors a choice is beneficial in virtue of teaching them to make decisions.[19]

But this argument is unconvincing. As Wendler and Shah point out, it is doubtful that giving intermediate minors a choice about something they do not well understand would help them learn to make *good* decisions.[20] After all, part of making a good decision is ensuring that one is sufficiently well informed. When one realizes that she is not sufficiently informed, the right thing to do may well be to defer to someone who is. So, it seems doubtful that giving intermediate minors a choice about whether to participate will improve their decision-making skills. In fact, to the extent that allowing intermediate minors to decide influences their development as decision-makers, it might hinder more than help.

Further, it is unclear that there is any reason to think that giving intermediate minors *this particular choice* would be beneficial to their development as decision-makers. Typically, one has ample opportunities throughout childhood to decide about a wide variety of matters, some of which are likely more momentous than whether to participate in a nonbeneficial research study. To make the beneficence argument work, it would need to be shown that there is something distinctive about the potential benefits of giving intermediate minors this particular choice. It is hard to see what this distinctive feature might be.

But even if we set these doubts aside, beneficence cannot justify allowing intermediate minors to decide unless the potential benefits outweigh the potential harms discussed above. It seems doubtful that this is the case.

Respect for developing autonomy and rational agency

A common argument in favor of giving intermediate minors a choice about participation appeals to respect for their *developing* autonomy or capacity.[21] However, it is unclear how this argument is supposed to go. On one interpretation, it collapses in the argument just discussed—that allowing intermediate minors to decide aids this development by teaching them to make good decisions.

On another, the fact that they *will* be autonomous in the future provides a reason to treat them as if they are autonomous now. But this is clearly wrong. While there may be reason to treat an individual who was previously autonomous and has now lost capacity (e.g., a demented adult) in a way that respects her *past* autonomy, this does not seem apt when it comes to minors with *developing* capacities.

However, the appeal to developing autonomy might be getting at something else. While intermediate minors are not capable of making an autonomous choice about whether to participate in research, they are still *rational agents.* That is, they are individuals who are capable of *self-directed, intentional* action, and are rational in the sense that they are engaged in an active effort to understand the world and make sense of what is happening to and around them. Both rationality and agency are distinct from autonomy. While intermediate minors are not capable of making an autonomous choice about participation in research, they are rational agents, in the sense described.

With this in mind, there is a plausible line of reasoning from the claim that intermediate minors are rational agents to the conclusion that they should be allowed to decide whether to participate in nonbeneficial research. The argument might be put as follows:

> Intermediate minors are rational agents and their agency should be respected in the absence of a reason to override it. The fact that an individual cannot choose autonomously does not always provide such a reason. Respect for an intermediate minor's rational agency provides a reason to let her decide what activities to participate in, other things being equal. This reason can be overridden when it is in the intermediate minor's best interest that her parents choose for her. This might be the case when participation in the study holds a prospect of direct medical benefit. But since participation in nonbeneficial research does not hold any prospect of direct medical benefit, there is no reason that would justify overriding an intermediate minor's agency and making the choice for her.

While there is a lot right in this argument, it relies on the assumption that an intermediate minor's *medical wellbeing* is the only consideration that would justify overriding her agency and choosing for her. I think this assumption is incorrect.

Since nonbeneficial research stands to benefit society in nontrivial ways, participation has moral significance. This means that there is a *moral reason* for intermediate minors to participate in nonbeneficial research. Due to this, not giving an intermediate minor this choice need not be a morally problematic, or unjustified, failure to respect her agency. This point, in conjunction with the arguments that follow, support Wendler and Shah's claim that possessing the concept of *altruism* is relevant to whether a child should be given a choice about whether she participates in nonbeneficial research.

Consider an analogy. Suppose the father of an intermediate minor makes her come with him to help in a soup kitchen. He reasons that her participation in this charity work will further a good cause (i.e., feeding the hungry) and positively influence her moral development. Arguably, parents have an obligation to teach their children to become morally good people. It is also plausible, even if controversial, that children have moral and societal duties, even if fewer than adults.[22] Volunteering at the soup kitchen is one way, but of course not the only way, of fulfilling an imperfect moral duty to society.[23] Plausibly, considerations of this sort justify the father's decision not to give his daughter a choice about whether she helps at the soup kitchen and so, does not constitute a morally problematic failure to respect her agency. It would be such a failure if he never (or only very rarely) allowed her to make choices about what to do. But occasionally failing to give her a choice about whether to participate in morally valuable activities seems unobjectionable.

Similar considerations apply to the case of intermediate minors and nonbeneficial research. Choosing for an intermediate minor is not a morally problematic failure to respect her agency if she is allowed to exercise her agency sufficiently often in other aspects of life, and there are significant moral reasons in favor of her participation.[24]

Arguably, underlying the argument from agency is the worry that depriving intermediate minors of the choice concerning their participation in nonbeneficial research studies is akin to treating them like lab rats. In other words, depriving them of a choice amounts to treating them as mere means to some end (albeit, a socially worthy one) rather than as ends in themselves. This worry underlies the objection, raised by many commentators, that failing to give intermediate minors a choice fails to respect them *as persons*, or as *beings with moral value*, or as *nonobjects*.[25] The soup kitchen analogy shows that such worries are misplaced. Good (or at least morally permissible) parenting involves making some choices for one's children. Doing so is sometimes justified by moral reasons that might not benefit the child directly. If these moral reasons are good enough, then choosing for the child is consistent with treating her respectfully.

One way to bring out the force of the above points is to consider the following (imagined) exchange between a twenty-year old and her parent:

> **Parent:** When you were seven, you almost enrolled as a healthy volunteer in a research study on childhood leukemia. You didn't participate because when we told you about what participation would involve—being at the hospital for half a day, have blood drawn, and answering some questions from doctors—you decided that you preferred to play computer games.
> **Child:** Was I scared to participate? Or did I just want to play computer games?
> **Parent:** You didn't seem scared or anxious. But we gave you a choice, and you preferred to go home and play computer games.
> **Child:** Wait, why did you let me decide? I didn't understand what I was doing! I had ample time to play computer games in my childhood and you gave me the opportunity to make all sorts of other choices. Participating in that study would have been socially valuable and important. I didn't understand that when I made the choice to play computer games.

If the twenty-year-old has a strong sense of social responsibility and an appreciation for the value of medical research, she might well see the choice of her younger self as a bad one and wish she had chosen differently—or wish that she had not been allowed to make this particular choice.[26] While not every child would react in this way, the point is that this reaction seems *reasonable.* The above discussion explains why it is reasonable.

In this section I have argued that 'they should choose' is the wrong answer to the Input Question, and that rejecting this answer is consistent with treating intermediate minors respectfully. Before defending an answer to the Input Question, I explain why the question matters, and must be addressed in discussions of the assent requirement.

Why addressing the Input Question matters in discussions of the assent requirement

While few, if any, have expressed agreement with Wendler and Shah's rejection of 'they should choose' as an answer to the Input Question, many have raised concerns about the idea that investigators should 'obtain affirmative agreement' from capable minors (per the Regulations' definition of 'obtain assent'). These concerns have led some to propose alternative ways of understanding the assent requirement. In this section I discuss one such proposal, and argue that while it contains many good recommendations, thinking of assent in this way neither addresses the Input Question nor obviates the need to do so. Following this, I consider what question or issue is being addressed by those who have proposed alternative ways of understanding the assent requirement. In doing this, I distinguish the Input Question from a more general question about what respectful engagement with intermediate minors requires in the context of research.

In 2015, the Nuffield Council on Bioethics issued a report on ethical issues concerning children and clinical research. They put forth the following proposal concerning how the requirement to 'obtain assent' should be understood when it comes to intermediate minors (whom they call 'Case Two' minors).[27] The Nuffield Council's proposal is as follows:

> We recommend that requirements in guidance and regulation to 'seek' or 'obtain' assent from children who are being invited to take part in research should be understood as requirements to *involve* children, as much as they wish and are able, in the decision about participation. In devising assent processes, researchers should primarily be concerned with how best to develop trusting relationships with children and communicate information appropriately throughout the research.[28]

While the Nuffield Council on Bioethics (henceforth, 'Nuffield') is, to my knowledge, alone in *formally* proposing that 'assent' be understood along these lines, the ideas in their proposal and general way of thinking about the requirement are broadly representative of the ideas that have been discussed in the assent literature. In particular, numerous commentators have suggested that 'obtaining assent' should be understood holistically, as one aspect of a larger process aimed at ensuring that intermediate minors are treated respectfully in the context of research participation. The idea is that the process consists of many interconnected practices, providing intermediate minors with information and engaging them in discussion, and obtaining parental consent.[29] As such, while the following comments focus on the Nuffield proposal, they apply more broadly to many of the suggestions made by those writing on the assent requirement in recent years.

The Nuffield proposal is very plausible. In fact, much of what it suggests seems clearly correct and is, I expect, uncontroversial. For example, it is clear that investigators should provide intermediate minors with information, engage them in discussion, and work to develop trusting relationships with them. However, notice that these practices do not concern 'obtaining assent' as Wendler and Shah were thinking of it, or as it is understood in the Regulations.[30] Nor do they concern the Input Question. Of course, Nuffield also suggests that intermediate minors should be 'involved' in the decision about their participation—this suggestion *does* concern the Input Question. However, nowhere in the recommendation do they flesh out what they mean by this. There are many ways one can be involved in a decision. For example, one could have a vote, or one could have an opportunity to contribute thoughts without any guarantee they will be given weight, or one's preferences might be honored only to the extent that they are plausible (or she can convince others that they are justified), or one might have the final say without having to explain her reasons.[31] The problem is that the Nuffield proposal does not make it clear what sort of involvement they have in mind. Notice that if the child's expressed choice will ultimately be honored, regardless of her reasons for that choice, this amounts to endorsing the 'they should choose' answer to the Input Question. If this is the idea, then the Nuffield proposal is helpful as far as it draws attention to the fact that the choice should be situated in the context of many other important practices and goals. However, it also is not clear how the proposal differs substantively from the assent requirement as it is set out in the Regulations. Presumably, the writers of the Regulations did not intend that 'obtaining assent' should take place in a vacuum, or that a child must make the decision about participation alone, without discussion or input from her parents.

Nuffield explicitly acknowledges that the recommendations are open-ended, noting that this is because it allows it to apply to a wide range of cases and be tailored to specific children, research, cultures, etc.[32] This makes sense: An overly specific requirement will not work in all cases, so some flexibility must be built in. However, a guideline can be general while providing enough information to make it clear how to apply it in different cases. The problem with the Nuffield proposal is that this information is lacking. We need a clear answer to the Input Question in order to know how to understand and apply this recommendation in practice. Moreover, we need a clear answer to the Input Question in order to know exactly how to apply the other aspects of the Nuffield proposal. Exactly how investigators and parents should present information about the study to the child, explain what her participation would involve, solicit concerns, and talk with the child, quite generally depends on what sort of say the child has concerning whether she participates.

In sum, my main concern about the Nuffield proposal, and any other proposal for reconceiving of assent along similar lines, is that it neither addresses, nor obviates the need to address, the Input Question.

Notably, the assent requirement, as set out in the Regulations, takes the form of *an answer to the Input Question*: namely, the child is supposed to provide *assent,* or *affirmative agreement,* as a condition of enrollment, where her agreement expresses her choice to participate. 'Assent' proposals like Nuffield's seem to be addressing a different, and much broader, question.[33] This question seems to be something like, "what practices are required for respectful engagement with intermediate minors and investigators in the context of research?" While the *Respectful Engagement Question*, as I will call it, technically subsumes the Input Question (as the Input Question concerns one aspect of respectful engagement), the Input Question is clearly not the question that Nuffield, or many others writing in the literature, is concerned to address. This is problematic for two reasons. The first is because, as I have argued, it is important to address the Input Question. The second is because the ambiguity concerning what question is being addressed in discussions of 'the assent requirement' has made it difficult to distinguish substantive from semantic disagreement in the literature. For example, when Wendler and Shah denied that investigators should obtain 'assent' from intermediate minors, they were *not* denying that investigators should provide intermediate minors with information and explanation, engage them in discussion about their participation, develop trusting relationships with them, etc.[34] Rather, they were arguing that neither intermediate minors nor very young minors should be given a choice about whether to participate in nonbeneficial research.

An answer to the Input Question: Respecting dissent and obtaining affirmation of non-dissent

In this section I argue that intermediate minors should have a say concerning whether they participate in research to the extent that investigators should respect their dissent and obtain what I will call 'affirmation of their non-dissent.' I begin by explaining how both requirements are grounded by considerations of nonmaleficence, and then explain each requirement and how it should be implemented. In doing this, I explain how respecting an individual's dissent and obtaining affirmation of an individual's non-dissent both differ from giving her a choice. I hope to show that obtaining affirmation of intermediate minors' non-dissent addresses some of the intuitive concerns that arise about denying them a choice, while also avoiding the difficulties that come with giving them a choice.

What nonmaleficence requires when it comes to giving intermediate minors a say

Earlier, I argued that nonmaleficence does not justify giving intermediate minors a choice about whether to participate in nonbeneficial research. However, I think that it does justify giving them a say of some sort. While I do not claim that nonmaleficence is the *only* consideration that justifies giving intermediate minors a say, I argue that to the extent that there are additional such considerations, they do not require anything more in practice than what is already required by nonmaleficence. I return to this point after I present and defend my answer to the Input Question.

I claim that nonmaleficence requires giving intermediate minors a say for two distinct reasons. The first is that an individual's perspective can often be a guide to whether or how she might be harmed by participation. I argue that this provides a reason not only for investigators to respect intermediate minors' dissent, but also to obtain affirmation of their non-dissent to participation. The second is that failing to *actively solicit* affirmation of an individual's non-dissent to participation can itself be harmful. This provides an additional reason for obtaining affirmation of intermediate minors' non-dissent. In the following two subsections, I explain each of these ideas.

Respecting dissent

Many commentators have proposed that regulatory and guidance documents require that investigators respect the dissent of all minors involved in research.

In the context of research participation, I understand 'dissent' as an expressed objection, either verbal or behavioral, to what an individual is experiencing, or anticipates that she will experience, in response to a research procedure.[35] Here I understand 'objection' and 'object' in an atypically broad way that departs from normal usage. For example, objections might take the form of refusing to stay still or crying out. Notably, this makes it possible for an individual to express dissent without intending to do so. It also makes it possible for an individual to dissent without understanding anything about the research procedure, or even that she is participating in research. This is important because it makes it possible to apply the dissent requirement to very young minors, individuals with severe cognitive impairments, and nonhuman animals.[36]

To implement the dissent requirement with intermediate minors, the child should be provided with age-appropriate information and explanation concerning the study and what participation would require of her. She should be engaged in discussion and given ample opportunity to express thoughts and ask questions. However, at no point should she be told or given the impression that it is 'up to her' whether she participates, or that she should participate only if she *wants* to. Rather, the investigators should frame the situation in a way that makes it clear that she is expected to participate unless participation is causing her to experience what I will henceforth refer to as 'discontent.' One experiences *discontent* when she experiences more-than-minimal pain, discomfort, anxiety, or distress of any sort.[37]

It is important that investigators do not put undue pressure on an intermediate minor to participate—it must be clear that no one wants her to participate if she is discontented. However, at the same time, the range of legitimate reasons for objecting must be clear. In particular, only reasons that are indicative of discontent are legitimate. For example, boredom, a desire to rebel, or the fact that research participation is not as much fun as playing computer games, are not legitimate reasons for objecting.[38] The balance is delicate, and investigators should be trained in talking with intermediate minors to ensure that they do not convey mixed messages with respect to whether the child is being given a choice about participating.

Putting a limit on the range of legitimate reasons for objection does not guarantee, of course, that the child will not object for reasons that she is not supposed to consider relevant. Indeed, a child might well realize that she can avoid participating by telling the investigator that she is scared when, in fact, she is bored, wanting to go home and play computer games, or just rebelling. Doing this will get her what she wants; and to this extent, she can choose to take action that will lead to her nonparticipation. But this does not mean that she was *given* a choice. Just as a child can malinger to avoid going to school or throw a noisy tantrum to force her parent to take her out of the library, a child can take action that will guarantee her nonparticipation in a research study. But this does not mean that she was given a choice any more than children are typically given a choice about going to school or staying in the library with their parents.

In response to any indication that an intermediate minor is dissenting, the investigator should pause (or delay beginning) the relevant procedure and check in with her. While an intermediate minor's dissent will often take the form of a verbally articulated objection, investigators should also respond to any behavioral indication of discontent even absent a verbally articulated objection.

Importantly, respecting dissent does not necessarily require investigators to terminate an individual's participation or decide that she should not be enrolled (in the case that dissent is expressed prior to enrollment) at the first indication of dissent. Rather, when an intermediate minor dissents, the investigator should begin by talking with the child to determine the source of her discontent and see whether it can be addressed. For example, perhaps reexplaining something will quell the child's anxiety. Or, if it turns out that an intermediate minor is bothered by very bright lights in the exam room, then it might be possible to dim them (unless their brightness is essential to conducting the research). In some cases, the child might just need a break.[39] However, investigators should take care that they do not pressure an intermediate minor to continue if her discontent is not eased.

If it is not possible to make modifications that will appease an intermediate minor without compromising the research, participation should be terminated. In cases where the child dissents prior to enrollment, she should not be enrolled unless the source of her unwillingness can be adequately addressed.

In sum, respecting dissent requires that an investigator honor an intermediate minor's *sustained,* or *unresolvable,* objection to participation that indicates more than minor discontent. With respect to the Input Question, this gives her a say to the extent that she can *object to,* or *veto,* participation. However, the fact that she cannot object for just any reason at all, and that the range of legitimate reasons for objecting *is not circumscribed by the intermediate minor herself*, distinguishes respecting an individual's dissent from giving her a choice.

Obtaining affirmation of an individual's non-dissent to participation

The dissent requirement is motivated by the fact that an individual's perspective can be a guide to whether or how she might be harmed by participation in research. This fact implies that investigators should do what they can, within reason, to obtain adequate evidence that the individual is not discontented, and that beginning or continuing participation will not cause her to become discontented.

The fact that an intermediate minor does not *volunteer* an objection (or give a behavioral indication that she is discontented) will not always suffice to provide investigators with adequate evidence in this respect.[40] On the contrary, many intermediate minors, even those on the older end of the spectrum, may be hesitant to express their reluctance or raise a concern for fear of being 'difficult,' admitting weakness, or disappointing their parents or the investigators. For these reasons the dissent requirement, as described above, is insufficient to ensure that investigators have adequate evidence of an intermediate minor's *non-dissent*. I understand 'non-dissent' as a state that is characterized by the *absence* of certain beliefs, thoughts, and qualitative experiences. Namely, those that would make dissent appropriate.[41] More precisely,

> In the context of participation in research, an individual is in a state *non-dissent* at a time *t* if and only if (a) she is not discontented, and (b) is not concerned that she will become discontented if participation begins or continues.

The motivation for (b) is that an intermediate minor who is mildly concerned about beginning or continuing participation is not discontented, but her concern might make dissent appropriate.

There are two distinct reasons that nonmaleficence requires that investigators obtain affirmation of an intermediate minor's non-dissent. First is the reason already discussed: obtaining affirmation of non-dissent is sometimes necessary in order for an investigator to obtain adequate evidence that the research is not causing, nor will cause, discontent.

The second reason is that failing to *actively solicit* affirmation of an intermediate minor's non-dissent can itself be harmful. If an investigator initiates or continues a procedure without soliciting affirmation of an intermediate minor's non-dissent, this might well might cause anxiety, frustration, or fear. The child might feel as if she is being shuffled around without sufficient concern for her thoughts or feelings, or as if she lacks control over what is happening to her. Further, while the investigator will have told the intermediate minor that she should not hesitate to speak up if she has concerns or is feeling discontented, this might seem insincere if the investigator then plows forward with the procedures without checking in. In other words, the intermediate minor might interpret the investigator's failure to solicit affirmation of her non-dissent as suggesting that the investigator does not really care about what she is thinking or feeling, and just wants to get on with things.

How to solicit affirmation of an intermediate minor's non-dissent without giving her a choice

Earlier, I explained that one important difference between allowing intermediate minors to object to or veto participation on one hand, and giving them a choice about participating on the other, is that in the former case the child cannot object for just any reason. Rather, there is a limited range of legitimate reasons for objection, and the child has no say in determining what those reasons are. A second important difference is that in obtaining affirmation of non-dissent, the intermediate minor is being asked to confirm that she is neither discontented nor concerned that participation will cause her to become discontented. She is not being asked to *positively endorse* proceeding with participation.

As with implementing the dissent requirement, soliciting affirmation of non-dissent requires care. In soliciting affirmation of non-dissent, the investigator must ensure that she does not make it sound as if the intermediate minor is being offered a choice. For example, an investigator should *not* say, prior to enrollment, "Would you *like* to proceed?" or, "Does this sound like something you *want* to do?" Rather, she should say things like, "How are you feeling? Are you worried about anything we've talked about? Does anything sound scary? If not, are you ready to start?" After participation is underway, the investigator should regularly check in by saying things like, "Has everything felt okay so far? Are you ready to continue?" The intent is to firmly, but gently, make it clear that the *default* is that she participate, but that the investigators really want to know if she has concerns or is discontented.

In sum, soliciting affirmation of an intermediate minor's non-dissent to participation differs substantively, and in a way that is ethically and practically significant, from giving intermediate minors a choice about participation in nonbeneficial research. In soliciting affirmation of non-dissent, the investigator is basically seeking confirmation that she is *okay*. In giving the child a choice, the investigator is telling the child that it is *up to her* whether she participates (assuming that parental consent has been provided); the child can decline to participate for any reason and her choice will be honored.[42]

Back to nonmaleficence as the basis for giving intermediate minors a say

One might suggest that nonmaleficence alone cannot ground the requirement to obtain affirmation of non-dissent, or that there are additional all-things-considered reasons that require giving intermediate minors a say. With respect to the former, I think this concern derives from an overly narrow understanding of nonmaleficence—as though the nonmaleficence requires only that investigators avoid causing participants *physical* pain. In fact, nonmaleficence also requires that investigator avoid causing *psychological* harm. This includes trying to avoid causing the sort of emotional distress that can result if a child believes that her perspective is not valued, or that she lacks control over the pace at which the investigator is proceeding. Giving the child more of a say can help researchers achieve that goal, along with the goal of discovering other ways that participating might harm the child.

My response to the latter point is related: Nonmaleficence, in fact, requires quite a lot. While it is plausible that considerations such as *beneficence*, *respect for dignity* (understood as *respect for personal and bodily integrity*), and *respect for rational agency* may provide additional all-things-considered reasons for soliciting or obtaining affirmation of intermediate minors' non-dissent in the way I describe, it is hard to see how they could require something more without requiring that intermediate minors be given a choice about whether they participate. I have already argued that these considerations do not justify giving intermediate minors a choice.

Conclusion: Dissent, assent, or neither?

I have argued that intermediate minors should not be given a choice about whether they participate in nonbeneficial research, and that treating them respectfully does not require giving them this choice. To this end, I agree with Wendler and Shah's claim that investigators should not be required to obtain assent from intermediate minors—at least if 'obtaining assent' is understood in a way that requires giving the child a choice. In response to the Input Question, I have argued that intermediate minors should have a say to the extent that their dissent should be respected and affirmation of their non-dissent should be obtained. I claim that respecting dissent and obtaining affirmation of non-dissent are both justified by the principle of nonmaleficence.

How should my recommendation that investigators be required to obtain affirmation of intermediate minors' non-dissent be understood in relation to the requirement to obtain assent and respect dissent? I suggest that it is best conceived as part of the requirement to respect dissent, when this requirement is fully and robustly fleshed out. The *robust* version of the dissent requirement would then consist of both the requirement to respect dissent, and my proposed requirement to obtain affirmation of non-dissent. This makes sense because, as I have argued, the considerations that motivate the requirement that investigators respect an individual's dissent also motivate a requirement that they obtain affirmation of an individual's non-dissent whenever it is possible to do so.

Notes

1. The United States Code of Federal Regulations (henceforth, the *Regulations*) requires that research conducted with minors be *minimal risk* unless participation offers a prospect of direct medical benefit to the child. According to the Regulations, research qualifies as *minimal risk* when "…the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." As such, the minimal risk standard is consistent with the possibility that a child experience *minor* pain or discomfort, for example the minor pain felt from venipuncture. However, whether a procedure poses only minimal risk to a child depends on facts about that particular child. For example, if a child is very afraid of needles, this constitutes a reason not to enroll her in a study that requires venipuncture, even if the study is generally considered to be minimal risk. See the Department of Health and Human Services: Protection of human subjects. Washington: US Government Printing Office; 1991: 45 CFR 46 Subparts A and D.
2. This is per the Regulations. See note 1, Department of Health and Human Services 1991.
3. Herein I am concerned with whether a choice is made autonomously and not with whether the agent making the choice is autonomous, full stop. Following Tom Beauchamp, I understand an autonomous action as an action that is, (1) intentional, (2) adequately informed (made with sufficient understanding), and voluntary (free of controlling influences). See Beauchamp T L. Who deserves autonomy and whose autonomy deserves respect? In: Taylor J, ed. *Personal Autonomy: New Essays in Personal Autonomy and its Role in Contemporary Moral Philosophy*. Cambridge: Cambridge University Press; 2005, at 310–29. In the second section of the paper I discuss what an individual must understand to make an autonomous choice about enrolling, or staying enrolled, in research.
4. I distinguish these classes of minors based on capacity, not age. I will not address the question of how investigators should determine what class a particular child belongs in.
5. See note 1, Department of Health and Human Services 1991.
6. For example, see Wendler D, Shah S. Should children decide whether they are enrolled in nonbeneficial research? *American Journal of Bioethics* 2003;3(4):1–7, and Baines P. Assent for children's participation in research is incoherent and wrong. *Archives of Diseases in Childhood* 2011;96:960–2.
7. See note 6, Wendler and Shah 2003, at 1.
8. This view is widely accepted in the philosophical literature on action theory. The *locus classicus* here is *Intention,* by G.E.M Anscombe. Anscombe GEM. *Intention*. Cambridge, MA: Harvard University Press; 1957.
9. See note 6, Wendler, Shah 2003, at 2.
10. Wendler and Shah explicitly qualify that they are not requiring that the child be *altruistically motivated,* only that she possess the concept of altruism. See Wendler D, Shah S. A response to commentators on "Should children decide whether they are enrolled in nonbeneficial research?" *American Journal of Bioethics* 2003;3(4):37–8, at W37.
11. Critics of Wendler and Shah's suggestion that possessing the concept of *altruism* is necessary to make an autonomous choice about participation in nonbeneficial research include: Baylis F, Downie J. The limits of altruism and arbitrary age limits. *American Journal of Bioethics* 2003;3(4): 19–21; Diekema DS. Taking children seriously: What's so important about assent? *American Journal of Bioethics* 2003;3(4):25–6; Fisher C. A goodness-of-fit ethic for child assent to nonbeneficial research. *American Journal of Bioethics* 2003;3(4):27–8; Halila R, Lotjonen S. Why shouldn't children decide whether they are enrolled in nonbeneficial medical research. *American Journal of Bioethics* 2003;3(4):35–6; and Robinson WM. What's altruism got to do with it? *American Journal of Bioethics* 2003; 3(4):23–4.
12. This is clear from how the assent requirement is discussed in the National Commission Report. The report suggests that assent should be obtained from "any child capable of some degree of understanding" and it is suggested that minors as young as seven-years-old can give assent. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Report and Recommendations: Research Involving Children* 1978, at 129.
13. Wendler and Shah also make this point. See note 6, Wendler, Shah 2003, at 5.
14. Wendler and Shah also argue that allowing intermediate minors to choose may well do more harm than good. See note 6, Wendler, Shah 2003, at 3.
15. See Dworkin G. Is more choice better than less? *Midwest Studies in Philosophy* 1982;7(1):47–56.
16. For a classic defense of this view, see Mill JS. *On Liberty*. Cambridge: Cambridge University Press; 2011.

17. This addresses the concern that by denying children a choice about participation on the basis that they cannot make an autonomous choice, we are holding them to higher standards than we sometimes hold adults. This concern is raised by Botkin JR. Preventing exploitation in pediatric research. *American Journal of Bioethics* 2003;3(4):31–2, at 31.
18. Thanks to David Wendler for pointing to this additional concern.
19. For example, Bartholome WG. Informed consent, parental permission, and assent in pediatric practice. *Pediatrics* 1995;96:981–2; Diekema (see note 11, Diekema 2003); King NMP, Cross AW. Children as decision makers: Guidelines for pediatrics. *Journal of Pediatrics* 1989;115(10:10–6).
20. See note 6, Wendler, Shah 2003, at 3, and Wendler D. Assent in paediatric research: Theoretical and practical considerations. *Journal of Medical Ethics* 2006;32(4):229–34.
21. Some examples include Bartholome (See note 18, Bartholome 1995); Baylis and Downie (See note 10, Baylis, Downie 2003, at 20); Diekema (See note 10, Diekema 2003); and King and Cross (See note 19, King, Cross 1989).
22. For a defense of this idea, see Millum J. *The Moral Foundations of Parenthood*. Oxford: Oxford University Press; 2017, at chapter 6.
23. For a defense of the idea that participation in nonbeneficial research is an *imperfect* duty, see Shapshay S, Pimple K. Participation in biomedical research is an imperfect moral duty: A response to Harris John. *Journal of Medical Ethics* 2007;(33)414–7; and Millum (see note 22, Millum 2017, at chapter 6).
24. As Wendler and Shah point out, there are many other opportunities for children to exercise agency by making choices. See note 6, Wendler, Shah 2003, at 5–6.
25. Those who have argued in this vein include Diekema (see note 11, Diekema 2003); McGee E. Altruism, children, and nonbeneficial research. *American Journal of Bioethics* 2003;3(4):21–2; Nelson RM, Reynolds WW. We should reject passive resignation in favor of requiring the assent of younger children for participation in nonbeneficial research. *American Journal of Bioethics* 2003;3(4):11–3; and Sibley A, Pollard AJ, Fitzpatrick R, Sheehan M. Developing a new justification for assent. *BMC Medical Ethics* 2016;17(1):1–9.
26. Wendler argues that participation in nonbeneficial research is likely to (indirectly) benefit children. See Wendler D. A new justification for pediatric research without the potential for clinical benefit. *American Journal of Bioethics* 2012;12(1):23–31.
27. See Nuffield Council on Bioethics. *Children and Clinical Research: Ethical Issues* 2015.
28. See note 27, Nuffield Council on Bioethics 2015, at recommendation 14. See also note 25, Sibley, *et al*. 2016, for a defense of Nuffield's proposal concerning intermediate minors and assent.
29. For example, Diekema writes, "At its best, assent is an interactive, instructional process that includes the investigator, the parents, and the child with the goal of assuring the child has at least a simple understanding of the study purpose, the procedures, that will directly involve the child, and the possible harms and benefits of participation." See note 11, Diekema 2003, at 26. Numerous commentators have suggested that the parental consent process should not be entirely separate from the assent process. For example, see Joffe S. Rethink "affirmative agreement," but abandon "assent". *American Journal of Bioethics*;2003.3(4):9–11; Nelson and Reynolds (see note 25, Nelson, Reynolds 2003); and Sibley, Pollard, Fitzpatrick, and Sheehan (see note 25, Sibley *et al.* 2016).
30. Sibley, Pollard, Fitzpatrick, and Sheehan,. explicitly note this and use "assent*" to refer to the assent requirement as proposed by Nuffield. In their paper they defend Nuffield's "assent*" requirement. They explicitly reject the idea that assent should be understood as "obtaining affirmative agreement." See note 25, Sibley *et al*. 2016.
31. Notably, Joffe emphasizes that the *reason* a child does not want to participate should bear on whether she gets her way. See note 29, Joffe 2003, at 10.
32. See note 27, Nuffield Council on Bioethics 2015, at 155.
33. Again, Sibley, Pollard, Fitzpatrick, and Sheehan are explicit about this. See notes 25 and 30, Sibley *et al*. 2016.
34. In fact, Wendler and Shah explicitly state that some children who are not capable of making an autonomous choice should still be given age-appropriate information and explanation about the study (perhaps written as well as verbal, when appropriate), that should be allowed to make small decisions that arise during their participation, if appropriate (e.g., which elevator to take, what to wear, which task to do first, etc.), and that, in general, researchers should work to make the child's experience as beneficial and enjoyable as possible. See note 6, Wendler, Shah 2003, at 5–6.
35. Dissent is sometimes understood as an objection to what one is *presently* experiencing only. However, it seems that it can also be anticipatory without blurring the line between

assent and dissent. This should be clear in what follows. Thanks to Jane Johnson for drawing my attention to this point.

36. For discussions of whether or why investigators should respect the dissent of animals used in research, see Fenton A. Can a chimp say "no"? Reenvisioning chimpanzee dissent in harmful research. *Cambridge Quarterly of Healthcare Ethics* 2014;23(2):130–9; Kantin H, Wendler D. Is there a role for assent or dissent in animal research? *Cambridge Quarterly Healthcare Ethics* 2015;24(4):459–72; and Johnson J. Animal dissent in research: What then must we do? (unpublished manuscript).
37. I assume that it is permissible to expose minors to minimal harm or distress in the context of participation in nonbeneficial research, consistent with the minimal risk standard set by the Regulations. See note 1, Department of Health and Human Services 1991, at 45 CFR 46, Subpart A.
38. Joffe also makes this point. See note 29, Joffe 2003, at 10.
39. I understand *dissent* in a way such that not every indication of discontent constitutes *genuine* dissent. Genuine dissent is expressed in response to what the individual is experiencing, or anticipates she might experience, due to her participation, or possible participation, in research. The idea is, roughly, that she would not experience the discontent if she were not participating. For example, some very young children (e.g., a one-year-old) cry all the time. If such a child is crying during a research procedure, this might not constitute genuine dissent to the research procedure.
40. Fisher explicitly raises this concern in response to Wendler and Shah. See note 11, Fisher 2003, at 27.
41. In a brief response to Baines (see note 6, Baines 2011) Wilkinson suggests that assent is perhaps usefully understood as non-dissent. See Wilkinson D. Dissent about assent in paediatric research. *The Journal of Medical Ethics* 2012;(38)1:2.
42. Notice that if a child's parents can override her choice, then it is unclear that she has been given a choice in any meaningful sense. Further, telling the child she has a choice and then failing to honor it, or even to express reluctance to honor it, would be disempowering and undermine trust. Paul Baines makes a similar point. See note 6, Baines 2011, at 961.