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EDITORIAL

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Implementing supported decision making in clinical research

Key points

- Current practice relies on surrogates to make research decisions for adults who have cognitive or intellectual disabilities.
- A number of commentators argue that this practice should be replaced with 'supported' decision-making.
- The present manuscript considers three way to implement supported decision-making in the context of clinical research.
- We argue that using supported decision-making to enhance authenticity has the greatest potential to respect and protect adults who have cognitive and intellectual disabilities.

1 | INTRODUCTION

The Nuremberg Code famously described informed consent as "essential" to ethical clinical research.[1] This understanding of the ethical importance of informed consent has been codified in essentially all subsequent regulations governing clinical research.[2] To satisfy these regulations, investigators provide potential participants with information regarding the study in question. The potential participants must then understand and appreciate this information, reason on the basis of it, and communicate a voluntary choice whether to participate in the study.[3,4]

These component abilities all come in degrees. Participants can be more or less able to understand, more or less able to reason. While there is no consensus regarding precisely how much of each ability is required for decisional capacity, the standard model maintains that there are thresholds on each of the component abilities.[5] Individuals whose abilities exceed the thresholds have decisional capacity; those whose abilities fall below them lack decisional capacity.

Adults who have decisional capacity are permitted to make their own decisions whether to participate in clinical trials. Those who lack decisional capacity may be enrolled only when there is sufficient justification for their enrollment and special provisions are in place to protect them.[6] This standard approach is intended to respect the autonomy of adults who have decisional capacity while protecting the rights and welfare of those who lack it.[7]

To determine which provisions are needed to protect adults who lack decisional capacity, policy makers frequently look to existing guidance for another group that is unable to give informed consent, namely, children.[8] Based on this model, current practice maintains that adults who do not have decisional capacity may be enrolled in research only with the permission of a legally authorized representative (e.g. an appropriate surrogate), and only when participation offers them a prospect of medical benefit, or it poses low risks.[9] More recently, advocates of supported decision-making have expressed concern that reliance on surrogate decision-makers can discriminate against individuals with cognitive or intellectual disabilities.[10,11] Some even argue that, no matter where one's level of cognitive function falls, all adults, including those with cognitive and intellectual disabilities, have a right to make their own decisions.[12] Clinicians and loved ones may offer assistance and guidance, but the individual themselves should always have the final say.

There is growing interest in supported decision-making.[13] However, the ways in which supported decision-making is being implemented vary widely and, to our knowledge, none have addressed its application to clinical research. The present paper thus asks: How should supported decision-making be implemented within clinical research? In response, we describe three possible approaches. The first– *replacing* surrogate decision-making with supported decision-making– poses significant risks, and should not be implemented in clinical research. A second approach– using supported decision-making to enhance individuals' decisional capacity– has important value, but is already being implemented in clinical research. We then describe a third approach– using supported decision-making to enhance authenticity– which has significant potential to both respect and protect individuals who have cognitive and intellectual disabilities. Future work will be needed to assess how best to incorporate this approach in practice, guidelines, regulations and laws governing clinical research.

2 | SUPPORTED DECISION MAKING AS A REPLACEMENT FOR SURROGATE DECISION-MAKING

The United Nations Committee on the Rights of Persons with Disabilities argues that reliance on surrogate decision-makers violates Article 12 of the Convention on the Rights of Persons with Disabilities and should be replaced with supported decision-making.[10] Family and loved ones, they argue, may offer support and guidance, but the person retains the right to make the final decision. This

proposal to replace surrogate decision making with supported decision making is motivated by a desire to promote the dignity and equality of all human beings, independent of the level of their cognitive abilities. Unfortunately, adoption of this approach in clinical research could dramatically increase the potential for abuse and exploitation of the very individuals it is trying to respect.[14,15]

Consider an individual with severe cognitive impairments due to advanced dementia who is eligible for a clinical trial testing a first in human experimental treatment. On the present proposal, family members and loved ones may offer support, suggestions, and even recommendations regarding whether the individual should enroll in the trial. But, the final decision remains with the individual. If they are eligible, and they agree to enroll, they are enrolled, no matter what their family and loved ones recommend, and independent of whether the individual understands the material facts relevant to the study. Individuals could thus decide to enroll themselves in research, even when they do not understand the risks or the alternatives. This approach would thereby dramatically increase the potential for abuse and exploitation of individuals with cognitive and intellectual disabilities. It should be adopted only if one accepts the extreme view that permitting individuals to make their own decisions always takes precedence over protecting their rights and welfare.

Current approaches do better in this regard. They rely on a process of shared decision-making in which researchers explain the proposed study to adults who lack decisional capacity, to the extent and in a way they can understand it, and also to the adult's legally authorized representative. The individual and the legally authorized representative then discuss the proposal and make a decision together.[16] If they elect to enroll, the investigators obtain the permission of the legally authorized representative and the positive agreement (assent) of the individual. Finally, the objections of adults who lack decisional capacity are taken seriously, and objections that cannot be addressed result in the individual being removed from the study. By keeping individuals involved in the decision-making process, and also requiring the agreement of a loved one, this approach offers a better way to respect individuals who lack decisional capacity, while also protecting them from abuse and exploitation.

3 | SUPPORTED DECISION MAKING AS ENHANCING INDIVIDUALS' DECISIONAL CAPACITY

A second approach would be to use supported decision making to enhance individuals' decisional capacity and enable those who initially lack capacity to make their own decisions.[17] For example, on this second approach, individuals who initially fail to understand how the research differs from standard clinical care would not be deemed incapable of giving informed consent. Instead, the researchers would first assess whether they can explain the differences in a way that enables the individual to understand them. If they can, the individual would be permitted to consent for themselves rather than having to involve a surrogate decision-maker.

Granting the value of this approach, it is already being implemented in clinical research.[18] Essentially all the decisions we make involve some input from others.[19] This is especially true in clinical research. Clinical trials are complicated and very few people understand them without any assistance at all. Standard practice thus requires investigators to provide participants with a consent form which explains the study. In addition, investigators discuss the trial with potential participants, answer their questions, and offer them time to discuss it with their clinicians and loved ones.

Undoubtedly, current practice could be improved in this respect. Consent forms remain too long and too complicated. And researchers need to more effect address shortcomings in individuals' understanding before deeming them incapable of giving consent. For example, studies find that individuals with schizophrenia are often not able to understand enough to give informed consent after a single meeting. This finding, together with the individuals' diagnosis, may sometimes result in their being deemed incapable of giving consent. Yet, educational interventions which target the specific aspects of the study the individual did not understand the first time frequently result in their being able to understand and make their own decisions.[20]

Recognizing that there is room for improvement, the solution to existing deficiencies is not to replace current practice with supported decision-making. It is to implement current practice more consistently and effectively. This leaves the question of whether supported decision making might be useful in cases where individuals are not able to consent for themselves, even following targeted assistance.

4 | SUPPORTED DECISION MAKING AS A MEANS TO PROMOTING AUTHENTICITY

The first approach, replacing surrogate decision-making with supported decision making, is intended to maximize the extent to which individuals make their own decisions. However, this approach would threaten the interests of individuals with cognitive and intellectual disabilities, and expose them to potential abuse and exploitation. Moreover, when individuals do not understand a study, permitting them to decide whether to participate can significantly increase the chances that the resulting decisions conflict with their own values and goals. For example, an individual with Alzheimer's disease who does not understand that a clinical trial has significant potential to help identify possible treatments is not in a position to make decisions in a way that promotes their own goal of helping others with the disease. This concern with the first approach suggests a third possibility: incorporate supported decision-making in a way that increases, rather than decreases, the extent to which research decisions are consistent with and promote the individual's own values and goals.

To implement this third approach, family, loved ones and researchers would work with the individual to promote authenticity in the sense of increasing the extent to which decisions regarding research participation accord with the individual's own "distinctive beliefs and values."[21,22] To see how this approach might be implemented, imagine an individual who, after developing mild cognitive

impairment, documents their wishes regarding research participation in an advance directive. The individual reaffirms these wishes over the following years while their condition progresses to moderate Alzheimer's disease, at which point they lose the capacity to consent. When that happens, current practice, as noted earlier, appeals to the norms for parental decision-making. However, there are several ways in which making decisions for adults who have lost decisional capacity is ethically different from making decisions for children.

First, parents have significant leeway to make decisions for their children. They have the leeway to make decisions aimed at shaping their children and inculcating values the parents endorse, even when the child objects. Surrogates, in contrast, do not have the authority to shape the course of their charge's life based on their own preferences and values. Instead, surrogates should make decisions that are consistent with and promote the individual's values and goals.[23,24] Second, surrogates may sometimes have substantial evidence regarding the individual's distinctive beliefs and values. This evidence might come from a formal advance directive, conversations with the patient, or decisions the patient made themselves. For example, the fact that an individual chose to enroll in a study while they had decisional capacity provides evidence that participation is consistent with their values. This evidence provides some reason to keep the individual in the study after they lose decisional capacity. Of course, the researchers and surrogate should also consider whether the development of decisional incapacity provides a reason to withdraw them.

These differences between parental decision-making and decision-making for adults with decisional incapacity suggest that current practice, which is based on existing safeguards for minors, may be underprotective in some cases and overprotective in others. With respect to underprotection, current guidelines and regulations permit legally authorized representatives to enroll adults who lack decisional capacity in research that does not offer them the potential for benefit when it poses low risks. This attention to the study's risk-benefit profile is important for protecting the individual's welfare. Yet, exclusive focus on a study's risk-benefit profile fails to consider whether participation is consistent, or inconsistent, with the individual's values.

Current practice tries to address this concern by requiring researchers to obtain the assent of individuals who are capable of providing it, and to respect their dissent. However, adults who have lost decisional capacity may, as a result of their cognitive impairments, not understand the research well enough to determine whether it accords with their values, with the unfortunate result that adults who lack decisional capacity may be enrolled in studies that conflict with their values. For example, a study of adults who completed a research advance directive found that 13% were not willing to participate in research should they become unable to consent for themselves.[25] These data suggest that, even when a study poses minimal risk, enrolling individuals who lack decisional capacity may sometimes conflict with their values. This concern is reinforced by findings that, although many people want their surrogates to have leeway when making decisions, approximately one in four adults state that their surrogates should not be permitted to make decisions that conflict with the individual's own preferences and values.[26] Importantly, those who do not want to participate in research are less likely to grant leeway to their surrogates.[27] The data thus suggest that a small but significant proportion of adults do not want to participate in research in the event they lose decisional capacity, even when it poses very low risks.

Current practice has the potential to be overly protective as well. Imagine an individual who documented in their advance directive a strong interest in supporting research on Alzheimer's disease and a willingness to participate in research, even when it poses greater than minimal risk and offers no potential for participant benefit. Assuming the study is valuable, and needs to enroll adults who cannot consent, blocking their enrollment may fail to respect the individual and also unnecessarily impede valuable research.

To address the potential for under and over protection, supported decision making might be used to supplement current practice in a way that helps to promote the authenticity of decisions regarding whether individuals with decisional incapacity participate in clinical research. This approach could provide a means to both respect and protect adults who cannot consent. To achieve these goals, revisions to current practice should take into account the nature of the trial in question, as well as the nature and extent of the individual's decisional impairments.

5 | IMPLEMENTATION

Individuals' values tend to be expressed for at least a period of time after they lose decisional capacity.[28] Current requirements to obtain the assent and respect the dissent of adults who lack decisional capacity thus provide some assurance that participation in research is consistent with their values. But, sooner or later, individuals' cognitive deficits may result in their failing to understand the research and, thereby, failing to appreciate whether it is consistent with their values. Individuals may, as a result of their cognitive deficits, object to research that is consistent with their values, or assent to research that isn't. Revising research regulations, laws, and guidelines to stipulate that decisions regarding the enrollment of individuals with decisional incapacity must take into account their preferences and values offers a way to address this possibility.

When the individual retains the capacity to express their values, this process could involve the surrogate and individual discussing the individual's values and helping to realize them.[29] In some cases, this may involve redirecting the individual:

> ...from unattainable goals to more realistic ones that align with their values, helping a beneficiary to more fully imagine and assess possible outcomes according to their impact on what the beneficiary values.[30]

When the individual retains the capacity to understand important aspects of the study, but does not have clear preferences regarding it, the surrogate should work with them to determine what makes the most sense given their current preferences and values, and the preferences and values they endorsed when capacitated. The surrogate can make suggestions and encourage the individual, but the goal is to ensure that decisions are based on the values and goals of the individual, not the surrogate.[31]

When individuals lose the capacity to understand the study, surrogates should consider any evidence of the individual's preferences and values as expressed in discussions or an advance directive, or based on the surrogate's knowledge of the individual. For example, the fact that a study offers the potential to treat the individual's condition may provide evidence that they would want to be enrolled. If the evidence suggests that participation is not consistent with the individual's values, the legally authorized representative should not enroll them, even if the study offers the potential for benefit or poses low risks.

Currently, assessments of decision making in clinical research tend to be limited to the individual participant. However, to implement the present approach, it will be important to assess individuals' surrogates to ensure they understand the research and they are making decisions consistent with the preferences and values of the individual themselves.

If the individual is not able to understand the study, and there is no evidence that participation is contrary to their preferences and values, the legally authorized representative should be permitted to enroll them in research that offers a prospect of participant benefit and research that poses minimal risk. If the research does not offer a prospect of participant benefit and poses a minor increase over minimal risk, the legally authorized representative should be permitted to enroll them when there is positive evidence that participation is consistent with their preferences and values, as might be gained from conversations with the individual or significant knowledge of them as a person.

Most guidelines and regulations prohibit surrogates from enrolling adults who lack decisional capacity in research that does not offer a prospect of participant benefit and poses more than a minor increase over minimal risk. This makes sense to the extent that safeguards focus on protecting individuals' welfare. However, recognition of the importance of promoting authenticity suggests that exceptions might be appropriate when there is compelling evidence that participation promotes the values and goals of the individual.[32] General knowledge of the individual or general conversations about helping others would not be sufficient in these cases. Instead, there should be compelling evidence that the individual was willing to face the level of risks in question to benefit others. This level of evidence might be available, for example, for an individual who completed a research advance directive while they had mild cognitive impairment.

To address the potential for abuse, research in this category should undergo additional review beyond standard IRB approval to confirm that it meets at least the following four requirements: 1 Significant social value; 2. Cannot be conducted in a less risky way; 3. Must enroll individuals who cannot give informed consent; and 4. There is compelling, explicit evidence that the individual's own values endorse participation in the study.[33]

In addition to respecting individuals' values when it comes to research participation, it is also important to assess whether the individual has preferences or values related to the decision-making process itself. Some individuals have strong preferences regarding who serves as their surrogate, and the extent to which they want their surrogate to strictly follow their preferences and values versus having leeway when making decisions. Since it is difficult to predict the exact contours of future research studies, it may be important to know whether the individual authorized their future surrogate to exercise leeway for studies that pose greater risks.

Finally, in addition to promoting authenticity, it is important to protect individuals' well-being. Independent assessment of the study's risk-benefit profile by the IRB provides an important way to implement this protection. However, IRB risk-benefit assessments are necessarily made for populations of individuals. A study that is acceptable generally may turn out to be frightening or anxiety provoking for specific individuals. Given the range of cognitive impairments, it is not possible to make this determination prospectively. Instead, there should be a requirement to respect the dissent of individuals, even in research that is consistent with their values. Expressions of dissent should be assessed and, if they cannot be addressed, the individual should be removed from the study. This requirement helps to ensure that adults who cannot consent are protected from excessive risks or harms.

6 | SUMMARY

Over the past 10 years, there has been increased interest in supported decision making. This work raises the question of how supported decision making might be best implemented within clinical research. We have considered three possibilities: 1. Replace surrogate decision-making with supported decision-making; 2. Use supported decision-making to enhance individuals' decisional capacity; and 3. Use supported decision-making to enhance authenticity in the sense of increasing the chances that decisions regarding research participation are consistent with and promote the values and goals of adults who lack decisional capacity. We have argued that the first approach threatens adults with cognitive and intellectual disabilities. The second approach has value, but is already endorsed in the context of clinical research. The third approach has significant potential. We thus briefly considered how this approach might be implemented in practice. Future research will be needed to refine this approach and incorporate it into practice, guidelines, regulations and laws governing clinical research to ensure that decisions regarding research participation both protect and respect adults who lack decisional capacity.

KEYWORDS
clinical research, decisional capacity, supported decision making

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CONFLICTS OF INTEREST
No, there is no conflict of interest.

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This paper does not include any data.

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