MEDICAL ETHICS ADVISOR

YOUR PRACTICAL GUIDE TO ETHICS DECISION-MAKING AND INSTITUTIONAL REVIEW BOARD MANAGEMENT

DECEMBER 2021 Vol. 37, No. 12; p. 149-164

INSIDE

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IRBs Scrutinizing Remote Consent, Screening, and Participation in Study Protocols

IRBs are seeing a surge in study protocols that include remote recruitment, consent, and participation, raising ethical and regulatory considerations for investigators. "We are seeing more requests for remote recruitment and consent to allow for continued enrollment in this new environment," reports **Rhonda Oilepo**, MS, CIP, CHRC, CHPC, assistant vice president for human research administration at UT Southwestern in Dallas.

Previously, study protocols occasionally included remote consent, but it was usually completed via phone or mail. "Now, we are seeing requests for approval of video meetings, electronic consent, and electronic data capture," Oilepo says.

UT Southwestern's IRB asks investigators several questions: How will you confirm the identity of the participant? What system for electronic consent and data capture will you use to ensure your study meets 21 CFR Part 11 compliance for FDA-regulated clinical investigations? How will you confirm children will not be accidentally enrolled when the IRB has not approved the study to enroll children? How will the witness requirement be met (if applicable)?

"Remote recruitment and consent should not be considered as an opportunity for less conversation," Oilepo notes. "Instead, the conversation should still be substantial."

For IRBs, concerns about remote processes are not entirely new; investigators have been using social media for recruitment for years. Recently, this expanded to remote consent processes, electronic signatures, and remote interactions with research subjects. "We've been doing this for years in the context of web-based surveys and the like. But it has only been relatively recently that other types of research have started taking advantage of remote interactions," says **Bruce Gordon**, MD, assistant vice chancellor for regulatory affairs and executive chairman of the IRB at the University of Nebraska Medical Center in Omaha.

To the extent that remote technologies, whether they are web-based, app-based, video-based, or phone-based,

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MEDICAL ETHICS ADVISOR®

Medical Ethics Advisor®, ISSN 0886-0653, is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Medical Ethics Advisor*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

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AUTHOR: Stacey Kusterbeck
EDITOR: Jonathan Springston
EDITOR: Jill Drachenberg
EDITORIAL GROUP MANAGER: Leslie Coplin
ACCREDITATIONS DIRECTOR: Amy M. Johnson, MSN, RN, CPN

can be used to facilitate conversations between researchers and prospective subjects, "we wholeheartedly support them. Anything that facilitates the process of consent is to be encouraged," Gordon offers.

However, it is critical to remember face-to-face contact remains the best way to conduct the process of informed consent. Remote processes should not be used as an alternative if face-to-face contact is safe and practical. Thus, says Gordon, "investigators who want to use remote processes as an alternative, as opposed to use as an adjunct, will need to show why the remote processes are superior to face to face."

One of the big advantages of remote consent is it could open research participation to people who might not otherwise have been able to participate due to inability to travel long distances or competing demands like work or child care. "But the concern is that these potential participants might be exactly the people who don't have the technology or the internet access or bandwidth to fully utilize these technologies," Gordon says.

The person from rural Nebraska with a four-hour drive to Omaha who cannot participate in a clinical trial because of the distance or time is quite possibly the same person who does not have broadband internet to allow for a remote visit.

At Northwestern University, questions are raised as to whether a lot of the research that previously required visits to the medical center could be conducted remotely. "The thought was that remote research could increase participation rates," says **Mary McDermott**, MD, professor of medicine at Northwestern University's Feinberg School of Medicine.

As a physician scientist who conducts research on peripheral artery disease at a medical center, McDermott expressed some concerns about whether remote informed consent could be obtained ethically. She and a colleague authored a paper that offers ethical considerations for scientists and funding organizations.[1]

One important question is whether remote consent can be obtained with the same integrity as it can in person. For example, the investigator cannot be certain the remote participant is fully engaged. It may be more difficult to establish a rapport or assess understanding with a remote participant.

"Establishing rapport is important in informed consent because if a participant feels comfortable with the research staff, they may feel more comfortable asking questions or indicating when something is not clear," McDermott explains.

For both IRBs and investigators, there are advantages and disadvantages of obtaining informed consent remotely. Advantages include the potential for wider accessibility of the research to potential participants. Investigators should consider whether they can as easily establish rapport, whether participants will feel comfortable asking questions, and whether investigators can fully assess understanding of the participant.

Important considerations include the degree of risk of participation and whether the research itself is conducted remotely. "If the participant must attend the medical center to participate, it seems reasonable that investigators would also obtain consent in person," McDermott says.

After they were asked to take face-to-face contact out of studies if at all possible when the COVID-19 pandemic hit, researchers at the University of Illinois Chicago (UIC) came up with many acceptable alternatives. "They did need to come back to the

IRB for approval to make changes, or to change the nature of the study if it presented different risks and benefits," says **Jonathan Klein**, MD, MPH, professor of pediatrics and associate vice chancellor for research.

Researchers came up with all kinds of modified processes. "The IRB worked quite hard to process the modifications that were requested as rapidly as possible," says Klein, noting UIC's colleges maintain hundreds of active protocols at any point in time.

Staff provided guidance for researchers to consider before submitting study protocols to the IRB for review. "Researchers realized that video platforms, both HIPAA-secure and not, could be incorporated into research in ways that weren't thought about previously," Klein says.

The research community now routinely uses hybrid modalities for consent and study procedures. Face-to-face activities sometimes are necessary, as with studies on fall prevention, "but we are not always defaulting to that," Klein notes. "There is no question that it changed the nature of some people's work. They realized they could do more remotely than they thought."

One creative researcher figured out a way to preprogram tablets, which could be mailed or delivered to participants so they could complete follow-up questionnaires at home, with the tablets dropped off or picked up later. "Obviously, the IRB had to review that. But it was a very creative solution, which protected the subjects as well as the research study staff," Klein recalls.

For IRBs, there have been some new considerations with remote processes. If participants arrive on site, there is a way to ensure confidentiality. If study activities are conducted via Zoom, email, or text, it opens the possibility the participant's confidentiality could be compromised. "When you have someone physically in the clinic, you don't have to think about who might be listening to the conversation," Klein observes. "If participants are being asked for sensitive information, protecting the subject's privacy needs to have some extra thought."

Researchers might ask participants to wear headsets when on calls, or ask questions with a "yes/no/maybe" or numeric response. Remote processes "didn't change the nature of protecting research subjects from harm or disclosure or violating confidentiality, it just changes how the modalities would affect those things," Klein explains.

Remote processes have made community outreach and engaging with diverse populations easier. "Some of the things that people learned out of this have definitely made it easier for more people to have access to participation in research," Klein says.

Before the pandemic, recruitment for clinical trials "was traditionally restricted to the four walls of a clinical trial site," says **Harsha Rajasimha**, PhD, founder and CEO of Jeeva Informatics Solutions, a Virginia-based decentralized clinical trials software company. Physician researchers usually explained all aspects of the study to patients during a brief one-on-one consultation. "This consultation usually lasts about 15 minutes, during which the investigator repeats the same explanation to one patient at a time," Rajasimha says.

The risks and benefits of participating in the study, samples or data to be collected, medical procedures, and the travel involved all were covered during the in-person discussion. This process assured IRBs that each participant received personal attention from investigators. "But the process also had its disadvantages. Most patients feel they have limited time to ask questions or seek clarifications," Rajasimha reports.

Even patients who already decided to enroll in the study had to travel to the trial site to complete formalities. Informed consent forms, some dozens of pages long, had to be reviewed and signed during short consultations. "In this traditional paradigm, underrepresented minorities remain disadvantaged, as they are less likely to access the healthcare system due to a variety of issues," Rajasimha notes.

The pandemic forced clinical investigators to do things differently. "Researchers had to open up to the possibility of venturing out on the internet, social media, and other channels such as emails and texts," Rajasimha says.

There were some unexpected positive developments. Asking questions via chat or videoconference gave people the chance to carefully consider the study, at which point they could sign the informed consent electronically. Some IRBs asked researchers to verify patients understood the risks of participation. "This might include a scored online quiz to assess individual patients' comprehension about the study," Rajasimha offers.

IRBs also are asking if software tools or apps are easy for prospective participants to use, and whether the tools support multiple languages and can accommodate participants with disabilities. Rajasimha has seen many IRBs scrutinize remote processes, even though some of the same concerns existed with previous processes. "The same IRBs that did not question the possible illegibility of handwriting or authenticity of time stamps on paper-based processes are now demanding much more for the electronic processes," Rajasimha says.

Even for onsite processes, there always was the possibility of human

errors, fraud, or abuse. The same is true of digital processes. "However, IRBs also need to weigh in on the changing context, times, tech advances, and the greater good," Rajasimha says. Researchers can reach wider populations beyond a 50-mile radius. The work is shifting toward where the patients are located, meaning more participation from rural residents and underrepresented minorities. As a result, says Rajasimha, "this model is sure to improve diversity, equity, and inclusion." ■

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IRBs Face Unique Ethics Questions About Big Data Research

There is a need for ethics review committees to improve oversight capacity for big data research, the authors of a recent paper argued.[1] The authors assessed the weaknesses of ethics review committees, some of which are not specific to big data research but could be exacerbated by it, and some that are specific to big data research.

"First, it is important to understand what big data are. There are many different and disparate types of data," says **Elizabeth A. Buchanan**, PhD, director of the Office of Research Support Services at the Marshfield (WI) Clinic Research Institute and coordinator of medical ethics at Marshfield Clinic Health System.

Social media data, sensors, wearables, consumer data, and medical data all are examples. Researchers analyzed aggregated data with computational methods or tools. "We're often looking for patterns or trends to understand retrospective and prospective behaviors," Buchanan explains.

IRBs must consider consent, use of secondary data, privacy implications, communal harms that might involve people other than the participant, and "downstream" harms that might occur long after the study is completed.

"While these are not unique to big data research, these issues are complicated and/or amplified by the scope and scale of data, and by the distance between the researcher and individuals," Buchanan explains.

It is easy to forget the data are connected to a real person. "A community can be targeted or stereotyped based on data that are collected and combined, and then reused in a context different from their origin," Buchanan notes.

There also is the consideration of how big data can be biased. "There is a lot of discussion around the concept of algorithmic bias and harm," Buchanan says.[2,3]

IRBs always consider risk/benefit analyses for study participants. However, big data research calls for IRBs to think about risk and benefit differently. "We need to think about this in a broader scope and scale. Big data research can have very real consequences beyond the individual level," Buchanan cautions.

Some IRBs lack the expertise to address these complex concerns. "While it has been common practice for many years to augment a board with an expert reviewer, there is just so much to consider, from legal to ethical to technical perspectives, in regard to big data research," Buchanan says.

At Marshfield Clinic Research Institute, investigators follow a multistep process, which may include feasibility review, security review, and legal review, even before a project makes it to the IRB. The health system's chief information security officer serves on the IRB. "That really helps us think through these complex technical issues," Buchanan says.

The possibility of participants being identified remains a central ethical concern. "We've seen over and over the problems when data are mined and matched in ways never intended," Buchanan laments. Sometimes, researchers use market data or health data where at some point people agreed to terms and conditions stating that data would be sold to third parties. Even if researchers are receiving de-identified data, "reidentification is possible," Buchanan warns. "We shouldn't think of de-identification as our panacea in big data research."

Protecting human subjects from someone using data in unanticipated ways "is one of the biggest concerns and biggest challenges with the rise of big data research," says **Michael Zimmer**, PhD, an associate professor at Marquette University's department of computer science. "It is easy to lose sight that much of our 'big data' are actually data about people, and it is often collected without them really knowing it is happening."

Both researchers and IRBs consider comments on Reddit or images on Instagram as inherently public. "Because of this perceived 'publicness,' it is easy for IRBs to provide exemptions to protocols," Zimmer says. Human subjects probably do not fully

understand how content they choose to share on a social media platform can be used by researchers. "These are questions that IRBs and researchers need to engage with, rather than just providing a simple exemption," Zimmer offers.

Users might not fully understand or be comfortable with how their social media data could be used for research.[4,5] Informed consent is "largely impossible when dealing with big data," Zimmer says. "This does not need to completely stop research from happening. But we need to ensure processes are in place to ensure researchers have thought about issues of possible harms."

Typically, researchers assert the data are publicly available, and IRBs provide an exemption. One obstacle to closer examination of the way "public" data are used, says Zimmer: "IRBs might lack suitable proficiency to understand the technical nuances of how certain platforms operate that researchers might leverage to create their big data sets." For example, not all IRBs are familiar with how TikTok differs from Instagram. Meanwhile, researchers are finding novel ways to collect data from devices, profiles, and platforms. For IRBs, says Zimmer, "it's easier to fall back on the publicness of data, rather than digging deeper into the affordances of a particular platform and what user expectations might be."

IRBs could strengthen their ability to properly assess these protocols by including scholars with expertise in online research methods on their boards.

Much big data research focuses on vulnerable populations. If researchers obtain data from a Reddit forum dedicated to discussing depression, "reporting back to that community so they know how their data was used is essential," Zimmer says.

Data often are used outside the original context. That is ethically problematic. "If big data are collected and used outside of that context, that must prompt a critical reflection on the ethics of the research — and not just a simple 'but the data were public' stance," Zimmer adds. ■

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Paying Participants? Incentives Should Be Reasonable for Research Activities Involved

The mere fact that study participants are paid "cannot render a study unethical," according to **Holly Fernandez Lynch**, JD, MBe, assistant professor of medical ethics at the University of Pennsylvania Perelman School of Medicine. "We pay people for lots of different reasons: To reimburse their expenses, to compensate their time and effort, and to incentivize their participation above and beyond reimbursement and compensation rates."

There are two central ethical concerns. One is undue inducement, meaning an offer so attractive it leads to bad judgment. "This is typically overblown if the IRB is doing its job of making sure that no research is approved where risks outweigh benefits," Fernandez Lynch argues.

It is not undue inducement for someone to be willing to do something only if they are offered enough payment. "Most of us feel that way about our jobs," Fernandez Lynch offers.

Second is unjust inducement, meaning payment is more attractive to lower-income people, putting too much of the burden of research participation on them. "This is a legitimate ethical concern, but the response should not necessarily be to pay less. It could be to pay more," Fernandez Lynch says.

Offering incentives to research participants did not result in undue or unjust inducement.[1] Researchers randomly assigned patients to incentives of $0, $200, or $500 to participate in an actual smoking cessation trial from 2017-2019 or $0, $100, or $300 to participate in an actual ambulation intervention trial from 2018-2019. The authors compared the percentage of people who decided to consent and found no evidence of undue or unjust inducement.

Fernandez Lynch says IRBs and researchers should be considering

if they are offering participants too little, given what they are asked to contribute. "Payment is often important as a matter of fairness and avoidance of exploitation," Fernandez Lynch says. "Yet attention is typically around whether payment is too high."

Fernandez Lynch and colleagues recently addressed whether and how much participants in COVID-19 human infection challenge studies should be paid. They created a payment worksheet to help researchers and IRBs assess ethically justifiable payment amounts.[2] "The worksheet is not specific to challenge studies, per se," Fernandez Lynch notes. "It should be easily adjusted to serve as a model for all clinical research."

IRBs look carefully at both the amount and the method of payment for research participation, says **Janet Usinger**, PhD, associate professor, state extension specialist emeritus, and IRB co-chair at the University of Nevada, Reno. For IRBs, the most important question is: Is this a fair amount of money (or gift) for the research conducted? An incentive for research that requires a great deal of time and complexity should be higher than for simple procedures of short duration. "The basic principle is that incentives should be fair, but should not be perceived as coercive, particularly for studies that are more than minimal risk," Usinger says.

The method of payment also is a consideration. "Incentives are used to recognize the time and effort for participating in a research study; they are not payment for participation," Usinger notes. In other words, completion of the research activities should not be a criterion for receiving the incentive.

For research that involves a lengthy commitment, payment can be made as the study progresses. "This encourages continued participation and allows participants to receive the incentive for as long as they are active participants in the research," Usinger explains.

Risk usually is the primary consideration of unethical incentives. "There are numerous examples of offering a great deal of money to individuals who have limited resources for participating in biomedical research that involves a great deal of risk," Usinger says. "However, this equally applies to the social sciences."

Giving a young adult who is homeless several hundred dollars to provide data that may put the person at legal risk would be considered unethical. Usinger says IRBs should ask: Is the person's participation voluntary, or is the incentive unduly coercive? "The incentive should reflect a fair and just thank you for their participation," Usinger says. "It is not a hard and fast rule. Rather, an incentive should be reasonable for the research activities involved." ■

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Medical Providers' Views Vary on Refusals of Life-Sustaining Treatment

After a patient attempted suicide by overdosing on prescription medications, the psychiatrist who had assessed him came to discuss the case with **Thomas D. Harter**, PhD, director of the department of bioethics and humanities and chair of the IRB at Gundersen Health System in La Crosse, WI.

"She interviewed the patient and found him to be rational. He was no longer acutely suicidal, but explained that his life lacked value because his damaged hands prevented him from working," Harter recalls.

The patient was otherwise medically stable. In the psychiatrist's view, admission to an inpatient behavioral health hospital did not seem warranted. However, the psychiatrist's colleagues strongly disagreed, arguing that since the patient had recently been suicidal, he lacked decision-making capacity. "Patients who elect to forgo life-sustaining treatment used to be considered suicidal and would not be permitted to stop treatment. But that perception is no longer considered ethically acceptable," Harter reports.

The case brought to light the "philosophically nuanced difference" between patients who make treatment decisions in which they accept death as the outcome vs. decisions that patients hope will end their lives, Harter says. To learn more about what physicians thought about this issue, Harter and colleagues surveyed 714 medical providers about their perspectives on decision-making capacity and moral acceptance in cases of withdrawing or withholding treatment or suicide.[1]

Regardless of whether a medical provider questions a patient's

treatment decision-making capacity depends in part on the type of provider. Behavioral health providers tended to question decision-making capacity to refuse life-sustaining treatment, more than surgeons or other medical providers. "I was expecting behavioral health providers to be more sympathetic to the patient's reasons for refusing surgery. The results showed the opposite," Harter shares.

Overall, providers questioned decision-making capacity more in cases where patients refused life-saving surgery or requested voluntary starvation than in cases of patients asking to deactivate pacemakers. "I was personally surprised by the general acceptance of the decision [to deactivate a pacemaker], both in terms of moral permissibility and lack of concern about the patient's decisional capacity," Harter observes.

Another surprising finding was on providers' views regarding refusal of life-saving surgery. "I was expecting the surgeons to question the patient's capacity to refuse to a much higher degree than they did," Harter offers.

The study's findings highlight the complexity of providers' assessments of treatment decision-making capacity. "Physicians should be willing to accept that 'capacity' is not singular in terms of decision-making," Harter argues.

Patients may lack capacity in one sense, but have capacity in another. For example, some adult patients struggle with cognitive delays or neurotrauma that prevents them from thinking abstractly about complex medical information, making it impossible for them to make their own complex medical decisions. However, those patients may be able to think concretely about someone whom they love or trust to help them make complex decisions. In such cases, the patient may have the capacity to name a power of attorney for healthcare, but cannot be their own treatment decision-maker.

"The way to limit variability in capacity assessments is to standardize the practice through continuous education of all clinicians involved in direct patient care or as consultants, not just physician-level providers," Harter says.

Ethicists also can help determine how best to proceed with treatment decision-making in cases in which patients lack decisional capacity. "Ethicists can help explain why the tie between treatment decision-making and capacity is morally important and essential for sound ethical medical practice," Harter notes.

Conflicts over refusal of life-sustaining treatment by patients lacking decision-making capacity is a common reason for ethics consults at NewYork-Presbyterian Hospital. "For ethics consults in our hospital, we routinely refer to a paper that suggests the consideration of seven core questions when considering treatment of an incapacitated patient over the patient's objection," says **Lydia Dugdale**, MD, MAR (ethics), associate director of clinical ethics at NewYork-Presbyterian and director of the Columbia Center for Clinical Medical Ethics.[2]

Ethicists should consider the likely severity of harm without intervention, along with how imminent harm might be without an intervention. They should consider the risks of the proposed intervention, not just whether it will work. Consider why the patient is refusing and how might the team carry out treatment over those objections. Finally, consider the potential emotional effect of a coerced intervention.

Remaining mindful of these considerations did help guide one group of clinicians in these complex cases.[3] Researchers retrospectively reviewed ethics consultations from 2017-2020 where adult patients were determined to lack decision-making capacity and were refusing treatment. In most consults, clinicians were given an ethics recommendation to proceed over the patients' objections.

"We found that although all seven questions were important to the ethical analysis of a patient's situation, the presence of logistical barriers to treatment and the imminence of harm without intervention most significantly affected our decision-making," says Dugdale, one of the study's authors.

The implications for clinical ethicists are that if death is imminent and the intervention is rather straightforward, one should proceed over the patient's objection. For example, removing a ruptured appendix could save the patient's life and would be a fairly limited intervention.

"By contrast, sedating and subjecting a patient to thrice-weekly dialysis over his wishes would save his life, yes, but the logistics to sedating and transferring an unwilling patient in perpetuity would render it ultimately impractical and, thus, should not be imposed," Dugdale says.

Despite the fact a large proportion of ethics consults regard treatment over objection, "there is a large gap in the literature about how to handle such questions," notes **Katherine Fischkoff**, MD, MPA, FACS, associate professor of surgery and critical care at Columbia University Medical Center.

Consults for treatment over objection cover a wide variety of medical interventions: General hospital treatment, surgery and other invasive procedures, and discharge planning.

"We published our experience in an attempt to provide a framework

for others to use to help make clear and consistent decisions," Fischkoff says. ■

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Many Ethics Consults Involve 'Unbefriended' Patients

The number of "unbefriended" patients, those who lack decisional capacity and are without surrogates, has surged recently.[1] Researchers conducted a retrospective chart review of 156 patients who petitioned for public guardianship from 2014 to 2019. They found cases rose from eight in 2014 to 44 in 2019. Neurocognitive disorders and psychotic disorders were the most common conditions that impaired capacity.

"Ethics consults in these cases are crucial," says **Amber R. Comer**, PhD, JD, assistant professor of health science at Indiana University in Indianapolis.

Many hospital policies allow the clinical care team to change an incapacitated/unbefriended patient's code status when it is clinically and ethically appropriate to do so. Typically, it requires a consensus among the clinical care team, ethics, the chief medical officer, and the legal department. "The group is tasked with weighing what is in the patient's best interest regarding the patient's code status," Comer says. "Multiple perspectives are important for ensuring that decisions are made in the best interest of the patient."

If the group agrees it is in the patient's best interest to not proceed with a resuscitation in the event the patient's heart stops, then the patient's code status can be changed. "Decisions to change an unbefriended patient's code status can only occur at the hospital level if the situation is urgent," Comer notes.

If the situation is not urgent, it is appropriate to pursue a court-appointed guardian to make medical decisions on behalf of the incapacitated/unbefriended patient. Usually, pursuing a court-appointed guardian is not a quick process. It often takes weeks to apply due diligence in attempting to find a legal surrogate medical decision-maker and to pursue the appropriate legal channels in court. "This time-consuming process has the ability to delay treatment," Comer says.

If a patient lacks decision-making capacity and has a clear medical emergency, hospitals have protocols in place to proceed with treatment. "However, medical teams often encounter situations that are non-emergent but still important and very difficult to navigate without decision-makers," says **Erika Leemann Price**, MD, MPH, an associate clinical professor at the University of California, San Francisco and hospitalist at the San Francisco VA Medical Center.

Examples of these less-urgent cases include initiation or continuation of dialysis treatments; initiation of chemotherapy or radiation therapy for newly diagnosed malignancy; and nonemergent surgical treatments, such as spine surgery for stabilization in patients with spinal cord compression and repeated falls. The treatments in question are important, but patients might reasonably choose to forgo treatment after consideration of the risks and benefits and their own care goals. "In these situations, an ethics consultation can be helpful," Price says.

Ethicists can articulate the ethical principles at stake with treatment decisions by asking these questions: What preferences has the patient expressed in the past? To what extent is the patient expressing a preference, even if he or she lacks full decisional capacity? Would the treatment itself cause distress or harm to the patient in their current state in a way that could outweigh the benefit?

Since it is not a medical emergency, clinicians often do not request help from ethics. "The temptation is to avoid making the decision, push it down the road until the medical condition progresses and the situation reaches more of a crisis point, which is not the ideal approach," Price observes.

An added concern is that in these nonurgent cases, patients probably do not meet criteria for inpatient stays.

"But medical teams struggle with the knowledge that if they do not advocate for inpatient treatment, or at least for a clear decision to be made, these patients are at extremely high risk for loss to follow-up," Price

reports. These challenging cases pose some ethical concerns:

• **The process for public guardianship can take a long time.** When clinicians make the decision to keep unrepresented patients in the hospital while awaiting guardianship, they are committing those patients to prolonged (months to years) hospital stays. "They are then exposed to the usual hazards of prolonged hospitalization — deconditioning, infection, blood clots, and all of the detrimental mental and physical effects of being in a confined indoor space," Price says.

• **In most states, there is no clear legal framework for keeping medically stable unrepresented patients in the hospital while awaiting guardianship.** If patients are impaired but physically attempt to leave, hospital care teams often lack guidance on how to respond. "This scenario leads to moral distress, confusion, and conflict among team members," Price says.

• **Guardianship does not facilitate the establishment of long-term care options.** For patients who are unrepresented, require long-term care, and have no financial resources, discharge options in the community are going to be extremely limited. "In these cases, patients may remain in the hospital for prolonged periods, even after having guardianship established," Price adds.

Considering all these ethical concerns, Price says "it's critical for hospitals to think about how they are approaching guardianship for patients."

Ideally, clinicians identify surrogate medical decision-makers and establish financial surrogates before a crisis happens. The San Francisco VA Medical Center clinicians work with an attorney to help assess patients' capacity to assign financial decision-makers and identify and complete applications for other sources of support. The attorney also provides assistance in cases of attempted "eviction by hospitalization."

"Often, these proactive measures can help preserve patients' autonomy and avoid the need for formal guardianship," Price says.

In several cases, a patient's landlord sent the patient in reporting a fall injury, and then said the patient could not return home. "Medical teams aren't trained in eviction law, so they don't necessarily know that is not legal," Price says.

However, the lawyer can engage with the patient pro bono, and help the patient pursue legal action, if needed, when these unlawful eviction attempts are made.

For patients who do need guardianship, it is helpful to recognize that medical teams do not have the training required to complete a capacity declaration. In California, the paperwork requires the person filling out the form to have at least two years diagnosing and treating major neurocognitive disorders. "A standard pathway can be useful for going through the process in the inpatient setting," Price offers. "It is a stretch to say the interns just out of medical school have this degree of expertise. But geriatricians certainly qualify."

The inpatient geriatrics consultant team might take responsibility for conducting the formal assessment and completing the paperwork. Ethics does not need to be involved every time guardianship is appropriate. "But it is important to have an open line of communication in those situations where their expertise and input are helpful," Price says.

Most unrepresented patients are living with marginal housing and psychiatric comorbidity in addition to cognitive decline and medical illness. It also is helpful to engage in dialogue among inpatient clinicians and outpatient providers, case managers, and social workers. Working together, these groups can facilitate a transition from inpatient care to the community and provide input on options for housing. "For us, that dialogue is formalized in a weekly interprofessional team meeting," Price says.[2]

Ethicists at Marietta, GA-based Wellstar Health System try to be involved with all unbefriended patients. "These patients' vulnerable nature leads to numerous ethical dilemmas, particularly around medical decision-making and questions regarding these patients' best interests," says **Jordan Potter**, PhD, HEC-C, supervisor of the Wellstar Fellowship in Clinical Ethics.

Recent ethics consults have examined whether it is ethically permissible to change the patient's code status and whether to provide burdensome medical interventions with questionable benefit. Other recent consults concerned whether it is ethically appropriate to withdraw a life-sustaining treatment from an unbefriended patient and discharge issues if the patient is homeless.

Public guardianship itself does not solve all these problems. "Some guardianship organizations limit the medical decisions they are willing to make for unbefriended patients," Potter notes.

Even with a public guardian in place, financial resources are needed. "Without these kinds of resources, hospitals still face significant ethical dilemmas when attempting to adequately care for unbefriended patients," Potter explains.

It is not ideal to have individual physicians make ethically complex decisions at the bedside. "This is inherently problematic, given concerns

surrounding potential biases and a lack of objectivity," Potter says.

It is important to ask a more impartial third party to assist. Most protocols and policies for decision-making for unbefriended patients require some level of ethics consultation service or ethics committee involvement. "Usually, these combine ethics support with two physicians' attestation that the requested medical intervention, treatment, or decision is medically appropriate and in the patient's best interests," Potter reports. ■

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Decisional Capacity Is Most Common Issue in Neuro-Oncologic Ethical Consults

During ethics consults for neuro-oncologic patients, the biggest ethical challenge is decisional capacity at end of life, according to the authors of a recent study.[1] "Patients with incurable brain cancer are a vulnerable patient population from an emotional standpoint due to the gravity of the cancer diagnosis and prognosis, as well as from a physical/cognitive standpoint, given that the cancer can impair normal brain function in these realms," says **Elizabeth Neil**, MD, a neuro-oncologist at the University of Minnesota Medical School and Minnesota Health Fairview.

Researchers retrospectively reviewed 50 ethics consultations involving patients with brain tumors. At the time of the ethics consults, 82% of the patients lacked decisional capacity. Almost all (96%) had a surrogate decision-maker. In the setting of a terminal condition, goals of care need to be identified so that they can be honored. "Unfortunately, in some instances, decline of a patient's well-being can be rapid and unexpected," Neil laments.

If discussions do not happen early, when the patient likely is at his or her peak functional status, it leaves caregivers, families, and physicians with little guidance. These issues came up most often during the ethics consults: Confusion over the patient's Do Not Attempt Resuscitation status, how to respond to requests for non-beneficial treatment, and issues with surrogate decision-making. "Review of these ethics consultations affirmed the difficult nature of patient care for physicians and the lack of reassurance on behalf of caregivers or family that can stem from a lack of knowledge or acceptance of a patient's end-of-life plan," Neil says.

Ethics consultants resolved the conflicts by facilitating communication, re-articulating patients' previously stated wishes, and facilitating decision-making for incapacitated patients. The study's findings support the need for outpatient palliative care and primary neuro-oncology involvement early in the treatment course. "From there, excellent communication between the patient and their physician and caregivers/family regarding updated goals of care is critical," Neil says. ■

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Moral Distress When Caring for Patients on Mechanical Circulatory Support

As part of a quality improvement initiative in the cardiothoracic ICU at Columbia University Medical Center in New York City, clinicians convened a multidisciplinary group of surgeons, ICU nurses, and ICU attendings to discuss the possibility of implementing palliative care triggers. During these meetings, it became clear the surgeons better understood the need for palliative care involvement after hearing how ICU staff struggle with moral distress and moral injury when caring for some patients undergoing mechanical circulatory support. "I was somewhat surprised, and realized that we needed to raise attention to this problem," says **May Hua**, MD, an assistant professor of anesthesiology at Columbia University Medical Center.

Hua and colleagues surveyed 102 ICU clinicians (67 nurses, 28 physicians, seven advanced practice providers) and found those caring for patients receiving mechanical circulatory support reported high levels of moral distress.[1] "Levels of moral distress reported by clinicians in our study was quite high overall," Hua says.

However, clinicians did not report experiencing frequent moral distress when caring for patients undergoing mechanical circulatory support in comparison to other types of critically ill patients requiring life-sustaining therapies (e.g., chronic critically ill patients or patients with multisystem organ failure). "This is a hypothesis-generating result that needs further examination to better understand if it is a true finding," Hua reports.

Clinicians were most likely to report frequent moral distress when caring for patients with chronic illness or multisystem organ failure, but were more likely to report frequent moral distress when caring for patients receiving mechanical circulatory support (26.5%) than when caring for patients needing routine care (10.8%). Moral distress was significantly higher among registered nurses (vs. physicians or advanced practice providers), clinicians reporting burnout (vs. those who did not), and clinicians considering leaving (vs. those who were not).

Clinicians pointed to palliative care and ethics consults as ways to mitigate moral distress. "We need to better understand how to support and help clinicians who experience moral distress," Hua says.

During the COVID-19 pandemic, there was a surge in the application of extracorporeal membrane oxygenation (ECMO) for younger patients in acute respiratory failure caused by COVID-19 viral pneumonia, reports **Edward Dunn**, MD, medical director of palliative care for Louisville, KY-based Norton Healthcare.

In the first wave of the pandemic, some patients in acute respiratory distress were placed on ECMO in the later stages of their acute illness. These patients often failed to improve on ECMO support and expired. "We have learned that ECMO must be applied to these patients within one week from the onset of their symptoms to achieve clinical improvement and a higher likelihood for their survival," Dunn observes.

However, even under ideal conditions, COVID-19 patients on ECMO recorded a high mortality rate. "The moral distress for ICU nurses occurs when the patient fails to improve on ECMO and continues to have complications like bleeding from a tracheostomy site or GI tract, inability to ventilate the patient, and progressive central nervous system deterioration," Dunn says.

From experience, the nurse knows the patient likely will not survive. A disconnect in expectations of patient outcome between the medical teams caring for the patient and family members exacerbates this stress.

Despite the best efforts in communicating the realities of the patient's critical condition by medical teams and nursing staff, the message may not be getting through to family members due to their grief state from anticipatory loss of their loved one. "The ethics consultant, if requested to become involved with such a patient, has the difficult task of bridging this communication divide among all parties who are witnessing the patient's clinical deterioration," Dunn says. ■

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Data Show Larger-Than-Expected Market for Ethics Consultation Training

Training approaches for ethics consultation vary across hospitals, including multiple days of intensive training, online courses, case simulation videos, podcasts, and standardized curricula, according to the authors of a recent study.[1] To learn some specifics about ethics consultation training needs, researchers surveyed individuals involved in ethics consultation or healthcare ethics at 600 U.S. hospitals.[2] "One of the surprising findings of our study is the size of the potential market for ethics consultation training," says **Ellen Fox**, MD, president of Fox Ethics Consulting.

Based on the survey responses, Fox and colleagues estimated approximately 62,000 individuals at U.S. hospitals would benefit from basic-level training on how to perform ethics consultation, and 37,000 would benefit from advanced-level training. "These numbers seem high in relation to the total number of individuals who perform ethics consultation in U.S. hospitals each year, which we estimate to be 27,000," Fox says.

Fox and colleagues interpreted this to mean survey respondents thought there were many individuals who

were not currently performing ethics consultation who would benefit from ethics consultation training, especially at a basic level. "When considering the market for ethics consultation training, it's important to note that likelihood of participation is dependent not only on price, but also on the desirability of the training in terms of its content, format, and other characteristics," Fox notes.

Training needs assessments can be useful in this regard to help educators specifically tailor training programs to match identified needs of their target audience. "This extends the reach and, ultimately, the impact of their training," Fox says.

Most respondents indicated if they were to participate in ethics consultation training, it would be important for them to be able to interact with instructors, receive a certificate showing ethics consultation training was finished, complete the training during work hours, and practice ethics consultation skills. "Taken together, our results suggest that ethics consultation educators in hospitals might want to consider offering basic-level training that focuses on common ethical issues using case examples, that offers a certificate for completion, and that can be taken during work hours through distance learning at the learner's own pace," Fox offers.

At 19.1% of hospitals, respondents said their hospital would be unwilling to pay anything for ethics consultation training in the next two years. Willingness to pay for ethics consultation training did not vary based on hospital characteristics. "Administrators might be unwilling to pay for ethics consultation training for several reasons," Fox observes.

For example, they might think training is not needed because the people who perform ethics consultation are adequately trained, or they might think ethics consultants should be responsible for their own training.

Preferences regarding ethics consultation training vary based on hospitals characteristics. Academic medical centers often employ one or more professionally trained ethicists, but these facilities make up only a small fraction of hospitals in the United States. "Most hospitals do not have any academic affiliations at all, and about half have fewer than 100 beds. These hospitals perform very few consults each year, and their consults tend to be of lower complexity," Fox explains.

Thus, the training needs of these hospitals are likely to be different from those of academic medical centers. "It's important that educators be clear about the target audience for their training and tailor the content and format of their training accordingly," Fox adds. ■

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Positive STI Test Results Not Always Shared with Study Participants

More than half of studies on sexually transmitted infections (STIs) did not specify if participants ever were notified of test results, according to a recent analysis of 80 studies on prevalence of STIs.[1] "Left untreated, some of these infections contribute to poor health outcomes for participants and their partners," says **Joshua Grubbs**, the study's lead author and a research assistant and MD/MPH candidate at Tufts University School of Medicine.

Grubbs and colleagues were surprised to find so many articles did not include language about returning positive test results to participants. "Even though the investigators associated with the studies may have informed participants of their results, there was no documentation to let readers know," Grubbs reports.

If investigators do try to recontact the study participants about test results, they might encounter logistical constraints. "Participants can be difficult to contact, especially in situations where sample processing occurs at another site separate from sample collection," Grubbs laments.

For instance, in some large studies, participants may provide samples in one country, after which the samples are mailed to a laboratory in another country for bulk testing. "Investigators need to plan ahead to communicate these results back to the original sites and establish a method for getting these results to the participants themselves," Grubbs suggests.

One tactic is to mail results to patients. Other sites might prefer to compile a report of test results and ask participants to return to their physician's office to be informed. "Investigators that do not physically remain on site will need to maintain connections with local partners to

disseminate results themselves," Grubbs notes.

Early communication on how results will be returned can prevent investigators from running into this question for the first time in the field. "Potential obstacles to contacting participants include not having their preferred contact information, and participants themselves not knowing who to contact for follow-up," Grubbs says.

Typically, journals do not require reporting of treatment status of study participants in the results. "We are not aware of journals that explicitly require documentation of return of results, although individual peer reviewers may raise this point themselves," Grubbs observes.

Grubbs says investigators should develop a plan to return test results to participants, and document their actions in protocols and manuscripts. IRBs should require researchers to include these details in their proposals. "Planning entails a few critical steps. Interruption along any point can prevent results from reaching participants," Grubbs says. Additionally, researchers need to collect appropriate contact information and link it to samples in a secure manner that protects the privacy of study participants. Those results must be communicated from the laboratory to on-site investigators or healthcare personnel involved in conducting the study. Researchers must contact participants (or possibly have already given them notice when and how to collect their results). "We hope the study findings will be a catalyst for ensuring that all clinically relevant positive test results are returned to patients and their providers for treatment," Grubbs says. ■

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Novel Ethics Curriculum for Neonatal-Perinatal Medicine

At three academic institutions, faculty members recently piloted 13 ethics modules for neonatology fellows.[1]

Of the 44 neonatology fellows who participated, baseline ethics knowledge and confidence in addressing ethical dilemmas improved significantly.

"It is critical for clinicians to be able to navigate challenging ethical dilemmas and communicate effectively and compassionately with patients and their families," says **Christy L. Cummings**, MD, one of the study's authors and director of medical ethics & humanities for newborn medicine at Boston Children's Hospital.

This study builds on prior work. "Given a lack of established curricula in ethics and professionalism for neonatology trainees, we conducted a national needs assessment to determine adequacy of current ethics training during neonatal-perinatal medicine fellowship," Cummings says.[2]

Based on these data, Cummings and colleagues developed and published a peer-reviewed curriculum, a hybrid of educational methods, including simulation, enacted role-play with professional actors, and in-depth discussion.[3] Modules can be completed in order or asynchronously, depending on the needs and interests of learners. The curriculum also can be completed remotely or in person. "We hope that this curriculum is helpful for interprofessional trainees [and] faculty and staff in pediatrics, neonatology, and ethics," Cummings says. ■

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COMING IN FUTURE MONTHS

- Implications if patients are the ones calling ethics consults
- Complex ethics of research exclusion for serious mental illness
- Unexpected informed consent challenges with high-risk surgery
- Insight on prevalence of IRB violations

IRBs Often Reluctant to Approve Inclusion of Pregnant Participants in Research

Even when research poses minimal risk of harm to the fetus, pregnancy often results in exclusion from research — sometimes, without clear justification. "As an obstetrician-gynecologist, I have seen how the reluctance to include pregnant participants in research has resulted in profound gaps in our knowledge of the safety, efficacy, and proper dosing of drugs for use in pregnancy and lactation," says **Amina White**, MD, MA, clinical associate professor in the department of obstetrics & gynecology at the University of North Carolina at Chapel Hill. "These evidence gaps have been especially problematic in HIV research on new antiretroviral therapies, from which pregnant individuals are often excluded."

To learn more about decisions regarding whether to include pregnant participants, White and colleagues surveyed 93 IRB members and 39 IRB administrators.[1] The study stemmed from a larger project, Pregnancy and HIV/AIDS: Seeking Equitable Study (PHASES), the authors of which developed concrete guidance for responsibly including pregnant participants in HIV research.[2] "We conducted this survey of IRB members to better understand what they would consider minimal-risk research, and their willingness to approve such research with pregnant participants even outside of the HIV research context," White explains.

Even when IRB members deemed a study to be minimal risk and determined the inclusion of pregnant participants would be ethically and legally permissible under current federal regulations, many remained reluctant to approve enrollment. Some IRB members cited uncertainty on whether inclusion of pregnant participants could affect the study's scientific validity. Others acknowledged they were relying on the common, default practice of excluding pregnant individuals without requiring justification for their exclusion. "Guidance is needed to assist researchers and IRB members in characterizing the risk level of research procedures in the context of pregnancy," White suggests.

IRBs should require researchers to provide clear and compelling justification for excluding pregnant individuals from enrollment (or continuation in a trial, if pregnancy occurs after enrollment). "We need to continue to shift the paradigm from a presumption of excluding pregnant individuals to one of responsibly including them in clinical research, especially minimal risk research," White says.

Pamela Payne, D.Bioethics, MSN, NP, says COVID-19 vaccine research brought the issue of including pregnant research participants to the forefront. "Initially, pregnant women were excluded from trials, but organizations like ACOG pushed to have them included, which did happen," says Payne, an instructor at the Patricia A. Chin School of Nursing at Cal State Los Angeles.

Payne says there is a pressing need to know about the safety or efficacy of medications taken during pregnancy. "What happens if a woman needs medication for a seizure disorder, and we are not certain if it's safe to continue or if we need to adjust the dosages for the metabolic changes of pregnancy?" Payne asks.

Mostly, clinicians are forced to rely on anecdotal evidence, such as reports of outcomes of women taking medications before realizing they are pregnant.

"With so many new medications coming out rapidly, it's important for us to know whether they are safe during pregnancy," Payne says.

Often, "the automatic, knee-jerk reaction of IRBs" is to exclude pregnant participants, Payne notes. By doing so, IRBs do not have to worry about adverse outcomes in this population.

The same is true for pharmaceutical companies. IRBs could ask researchers if they have considered inclusion of pregnant participants. If not, why not? "Some IRBs are beginning to ask the question more routinely, largely due to advocacy by ACOG and other professional organization," Payne notes.

In general, IRBs tend to call in experts for consultation about medications during pregnancy. "But what they need to do is call in maternal/fetal experts routinely for IRB evaluations," Payne asserts.

This allows experts to become more familiar with IRBs and allows IRBs to receive input on other research proposals that could safely include pregnant participants. It might require additional precautions, such as more frequent reports to the safety review board.

"But there are ways of protecting women and their fetus in pregnancy while still allowing them to be part of a trial," Payne says.

Katrina Heyrana, MD, PhD, a fellow in family planning at Los Angeles County and University of Southern California Medical Center, notes women experience physiological changes in pregnancy that could change the dose or route

of administration needed to make a treatment efficacious or safe. "When pregnant people are excluded from clinical trials, we are just guessing at the safety and efficacy of the medications we give them because those variables have not been assessed in a pregnant population in a clinical trial setting," Heyrana says.

For example, a higher dose of a drug may be needed for it to be efficacious due to changes in plasma distribution or metabolism. A higher dose may be toxic, leading to complications that could affect both mother and fetus.

"We don't know these things if we don't study them in a controlled setting. Pregnant patients live in a limbo where we are offering them treatments based on our best guesses of their efficacy based on historical experience or clinical consensus," Heyrana laments.

This also raises the ethical principle of justice. "We ask pregnant patients to make clinical decisions all the time based on the best evidence available, which is frequently not high-quality evidence," Heyrana says.

This is because the continued understanding of pregnant women as a "vulnerable population," despite the fact the FDA has removed this categorization, becomes a justification to exclude them from clinical trials.

"Pregnancy doesn't change a person's ability to weigh risks and benefits or their autonomy over their own bodies. They should have the opportunity to use the same kind of decision-making they're using to navigate prenatal care and pregnancy complications to decide whether they accept the risks of entering an experimental study," Heyrana offers.

IRBs and researchers face the same ethical imperative.

"They should be looking for protocols to include pregnant people," Heyrana says. "If they aren't being explicitly recruited into the study, at least have a plan for their enrollment rather than blanket exclusion of this population." ■

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CME/CE INSTRUCTIONS

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CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Discuss new developments in clinical ethics and research regulation and their implications in healthcare systems for patient care, healthcare delivery, and research;
- Discuss the implications of developments in clinical ethics for patients, families, physicians, other healthcare professionals, and society;
- Review and apply principles of human subject protection in clinical trial programs, including compliance with mandated regulatory safeguards and educational requirements for human subject research.

CME/CE QUESTIONS

1. **Which is true regarding remote consent for research?**

   a. Evidence shows remote consent is superior to face-to-face consent.
   b. Obtaining informed consent remotely offers the advantages of reaching wider geographic populations.
   c. Remote consent makes sense only if participants must go on site for other research activities.
   d. Remote processes are limiting participation of underrepresented minority groups.

2. **Which is true regarding IRB approval of big data research?**

   a. IRBs are barred from considering communal harms that might involve people other than the participant.
   b. IRBs should not routinely

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consider "downstream" consequences of studies.
c. The possibility of participants being identified remains a central ethical concern, even if de-identified data are used.
d. Evidence indicating data are publicly accessible should mean an automatic exemption from the IRB.

3. **Which did a recent study reveal regarding payment for research participation?**

a. Payment itself generally renders even low-risk studies unethical because there is ample evidence of undue coercion.
b. Offering incentives to research participants did not result in undue inducement.
c. Offering payments as the study progresses is unethical.
d. Offering any amount of money to low-income people is unethical, regardless of the amount of risk involved.

4. **Which is true regarding patients without surrogates who lack decisional capacity?**

a. Neurocognitive disorders and psychotic disorders were the most common conditions that impaired capacity.
b. Hospital policies forbid the clinical care team to change an unbefriended patient's code status, even when it is clinically and ethically appropriate to do so.
c. Pursuing a court-appointed surrogate usually is an expedited process that can rapidly facilitate treatment.
d. Clinical outcomes of unbefriended patients are best if individual physicians handle decision-making.

5. **Which is true regarding ethics consults for neuro-oncologic patients?**

a. Most patients lacked decisional capacity.
b. Most patients had no surrogate decision-maker.
c. Goals of care discussions were happening too early.
d. Outpatient palliative care was offered before patients and family were ready for it.

6. **Which did a survey demonstrate regarding ethics consultation training?**

a. There were many individuals who were not currently performing ethics consultations who would benefit from ethics consultation training, especially at a basic level.
b. Training should be conducted strictly through online courses.
c. Most hospitals were planning to invest in training.
d. Hospitals can reliably assume ethics consultants were adequately trained.

7. **Which did a recent study reveal regarding pregnant research participants?**

a. Pregnancy only resulted in exclusion from research if there was clear risk of harm to the fetus.
b. Some IRB members cited uncertainty on whether inclusion of pregnant participants could affect the study's scientific validity.
c. Current regulations require IRBs to rely on a default practice of excluding pregnant individuals without requiring justification for their exclusion.
d. IRBs no longer require researchers to provide clear and compelling justification for excluding pregnant individuals from enrollment.