Reconsidering the Need for Reconsent at 18

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The prevalence of research with biological specimens has led to a debate over what type of consent is needed to obtain biological specimens from minors and store them for future studies. In most cases, parental permission is needed to obtain samples from minors. In addition, almost all commentators and guidelines maintain that researchers need the consent of the donors if they want to continue to store the samples and make them available for future studies after the donors reach the age of majority. In this Ethics Rounds, we argue that this near-consensus view is mistaken on the grounds that the agreement of the parents at the time of obtaining samples provides sufficient permission to store them and use them in research even after the donors turn 18 years old.

Investigators now routinely conduct research on biological samples obtained from children. This practice raises the question of what type of consent process is needed to obtain biological samples from children and store them in repositories for future studies. Researchers typically need authorization from the parents to obtain and store samples from children. Should the researchers also be required to attempt to track down pediatric donors to obtain their consent when they turn 18 years old to continue storing and making their samples available for research? The near-consensus answer in the literature and guidelines is yes: Researchers should obtain the donors' consent at the age of majority for studies that occur after they turn 18 years old.

In this Ethics Rounds, we present a case that highlights the potential challenges and costs of this approach. These costs must be accepted if consent at the age of majority is ethically necessary. However, we argue that the consensus view is mistaken because parents' authority to make decisions on behalf of their children includes the authority to permit future studies on samples obtained from the children. We conclude that reconsent at the age of majority should not be required unless the future studies require interaction with the now adults or pose greater than minimal risk to them.

THE CASE

Little is known about the pharmacokinetics of sedatives in critically ill children. To attempt to address this gap in knowledge, researchers propose obtaining blood samples from young children who are undergoing mechanical ventilation in ICUs. To minimize the risks to the children, the volume of the samples obtained will be low, and the samples will be collected during clinically indicated procedures. The researchers plan to obtain parental permission to obtain the samples and store them indefinitely in a repository for future studies. The samples will be made available to other researchers who have valuable research uses for them. The researchers wonder whether

abstract

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they need to obtain reconsent from the donors when they turn 18 years old and, if so, whether they need to design their research to make that possible. The researchers want to ensure that the study is done ethically. At the same time, they are concerned about the potential challenges and costs. Will they need to set up a system to try to track the children from early childhood until they become adults? Will they need an ongoing process of keeping track of the donors' ages and searching each year for those who turn 18 years old? Will they need to discard valuable samples if the donors cannot be found?

Benjamin E. Berkman, JD, MPH, Comments

The majority position, which is endorsed by research ethics commentators[1] and institutional policies,[2] is that in addition to parental permission and assent (for children who are capable of providing it) at the time of obtaining and storing samples, researchers should obtain the donors' consent at the age of majority for studies that occur after that time. The majority view is described in different ways and is often qualified. Some claim that new consent is ethically desirable and should be obtained when feasible.[3] Others describe getting new consent as a prima facie obligation that can be superseded by other considerations, including excessive burden on the researchers.[4,5] Still others maintain that obtaining consent is an ethical requirement but argue that institutional review boards (IRBs) may waive the requirement in some cases.[6]

Commentators defend this requirement in its various forms by noting that obtaining parental permission is not equivalent to obtaining consent from the donors themselves. They conclude that respect for autonomy implies that there is an obligation to at least attempt to obtain consent from the donors when they reach the age of majority to continue to use their samples for research. The problem with this argument is that parental permission does not need to be equivalent to donor consent for it to serve as an adequate authorization for the research use of the children's biospecimens. Parents have broad authority to make decisions on behalf of their children, provided that they protect their children from significant risks.[7] This suggests that parental permission can be sufficient and, for most studies, obviates the need for reconsent when the donors turn 18 years old. We believe that this position is consistent with a reasonable interpretation of current US regulations protecting human subjects.

Broad Parental Authority

The claim that reconsent is not needed when the donors turn 18 years old is consistent with views of parental authority in other areas. Consider as an example parents who institute a rule that any money given to their school-aged children is divided equally between savings, discretionary spending, and charitable donations. The goal of this rule is to teach their children about the importance of saving and instill a value of helping others even at some cost to oneself. Parents have the authority to make such decisions, although the consequences may continue into the children's adulthood. This authority is evident in the fact that charities are not obligated to obtain the consent of the children at age 18 years to continue to use any unspent money for charitable purposes.

Similarly, the American Academy of Pediatrics recommends storing and making publicly available newborns' stem cells that are collected from the blood in the umbilical cord unless an infant has an older sibling who could benefit from them.[8] Consider parents who donate a newborn's stem cells to be stored and used to benefit unrelated children. This decision poses a small risk to the child because his or her own stem cells will not be available as so-called biological insurance if they ever need them. Moreover, once donated, retrieving the stem cells from public banks is prohibitively expensive. Nonetheless, if the risk to the newborn is minimal and the potential benefit to others is important, parents have the authority to make this binding decision for their children.

These 2 examples are analogous to donating children's biological samples for future research. In all 3 situations, the parents make a decision that imposes some risk or cost on the children in the interest of helping others. The fact that parental permission is sufficient to continue to use children's money and stem cells even after they turn 18 years old suggests that there is no need for researchers to obtain consent from the children for research uses of their biological samples after they turn 18 years old. Here, too, parental permission is sufficient.

David Wendler, PhD, Comments

One might object that research is different; donors are subjects of the future studies conducted on their samples, and parents do not have authority to bind their children to participate in research into adulthood. US regulations define a research subject as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.[9] If the investigators of future studies obtain follow-up samples from the now adults or collect identifiable, private information as part of their research, the now-adult donors would qualify as subjects, and investigators should

obtain their consent. In contrast, in many cases, the samples and data are frozen at the time of the original study. In the PICU example, although the initial collection and storage of samples constituted human subjects research, investigators who are using the collected samples for later studies are not interacting with the donors. Thus, the donors do not qualify as subjects of these secondary studies under the first clause of the regulatory definition. In addition, if the samples provided to the secondary investigators do not include any private, identifiable information and the secondary investigators do not obtain such information, the donors shouldn't qualify as subjects of their studies under the second clause either.

A different and more difficult case under US regulations is one in which the secondary investigators make use of the private, identifiable information about the donors stored in the repository. Because the investigators are making use of private, identifiable information, one might conclude that the donors qualify as subjects of the secondary studies in these cases. However, even in this case, the secondary investigators are not obtaining the information from the donors. Instead, they are relying on information that was previously obtained by the investigators of the pharmacokinetic study. Therefore, under US regulations, the donors need not qualify as subjects of these studies either. It is the act of obtaining biospecimens and identifiable, private information from donors for research purposes that makes them subjects of one's research. The later use of the samples and identifiable, private information that were previously obtained by other researchers does not, under US regulations, imply that the donors are subjects of the secondary studies. Thus, technical requirements of the US regulations do not apply to them in those cases. Of course, our view that donors are not subjects of secondary studies does not imply that these secondary studies may be conducted without regard or protections for the donors' interests. Secondary studies should nonetheless undergo review to ensure that they are valuable and appropriate, and biorepositories should ensure that donor samples and information are stored with appropriate privacy protections.

Although potentially counterintuitive, the conclusion that the donors are not subjects of future studies that use their previously obtained and stored samples actually resolves an apparent contradiction in the majority view. Proponents of the majority view claim that reconsent should be obtained when pediatric donors reach the age of majority. However, as far as we are aware, proponents do not argue that the assent of children should be obtained for studies on stored samples that occur after they reach the age of assent, and the vast majority of researchers have not adopted this practice. The way to justify this latter view is to assume that parental authorization constitutes sufficient permission to continue to use children's biological samples for research. This suggests that reconsent is not necessary at the age of majority, either, unless something dramatically changes in terms of the research when the children reach the age of majority.

Moreover, although easy to miss, our claim that parental permission constitutes valid authorization for future sample use is at least implicitly endorsed by proponents of the majority view. Specifically, most commentators do not mandate that investigators track donors over time, and they endorse IRBs routinely waiving the requirement for pediatric reconsent. Thus, in the present case, they would address the researchers' worries about the potential costs of tracking down the donors at 18 years old or discarding the valuable samples by recommending that the reviewing IRB waive the need for consent when it arises.

The first problem with this approach is that the investigators cannot know at the time the study is initiated whether, in 15 years or so, the IRB will agree to waive the need for consent. In addition, if respect for autonomy implies a need to obtain reconsent, allowing IRBs to routinely waive the reconsent requirement does not respect the autonomy of the donors. Furthermore, if IRB members believe that there is an important reason to obtain consent from pediatric donors at 18 years old, then they should stipulate that investigators put in place measures to track the donors over time and attempt to contact them when they become adults. It seems odd at best to claim that reconsent at 18 years old is ethically important but that investigators do not need to do anything to put themselves in a position to obtain reconsent.

Dana Howard, PhD, Comments

In the way of possible critiques to this position, commentators point out that many stored samples will be used for genomic research. Furthermore, genomic data are impossible to truly deidentify, thus suggesting that the now-adult donors should have the opportunity to assess whether they are comfortable with the privacy risks incurred from the ongoing use of their samples.[10]

We are not claiming that parents can provide authorization for future studies that pose significant risks to their children (absent the potential for clinical benefit). However, although it may be impossible to promise absolute privacy protection for donors of biospecimens, the chance of an actual breech remains exceedingly low. As of yet, there have been no documented cases of individuals being reidentified for

nefarious purposes. There is a chance that breaches have occurred and have not been reported, although this possibility is remote given the attention and care that the research enterprise gives to the protection of genomic data. Furthermore, even if the risk of reidentification were higher, there is scant evidence that such exposure would lead to tangible harms.[11] This is not to dismiss privacy concerns as unimportant but rather to suggest the need for a clearheaded assessment of privacy risks when they are the basis for requiring pediatric reconsent.

Moreover, our conclusion that the now-adult donors are not subjects of future studies conducted on their pediatric samples does not imply that their interests should be ignored with respect to these studies. Donors with significant personal concerns could be permitted to request the withdrawal of their samples when they become adults; they just needn't be asked for consent or assiduously tracked.

Second, recent controversy over research with newborn screening bloodspots has raised a concern about possible loss in trust for research with biospecimens.[12] Notably, cases about newborn bloodspot research brought in Texas and Minnesota resulted in the destruction of millions of samples. However, these controversies arose because parental permission for the use of samples in research was not obtained. We advocate for obtaining parental permission and assent of the child when appropriate. This should substantially reduce the potential for distrust. Nonetheless, one may worry that failure to obtain donors' consent at adulthood may still have a deleterious impact on the public's perception of research, especially when parents provide broad consent for a wide range of future studies.

To assess whether this is a significant concern, more empirical research is needed.[13] Some studies found that the public supports broad parental authorization for the future research use of children's biospecimens.[14] Other studies suggest that individuals may prefer limiting parental authority to more specific consent.[15] Given the lack of clarity on what type of parental authorization is most appropriate in this context, the most important step to protect public trust may be to make sure parents are aware of the scope of the future studies for which they are consenting and the limited risks that their permission confers onto their children.

Benjamin E. Berkman, JD, MPH, David Wendler, PhD, and Dana Howard, PhD, Comment

We have presented a controversial view about pediatric reconsent that may seem counterintuitive in a field where autonomy is sacrosanct. Although our intention is not to undermine respect for persons, nor is it to undermine protections for pediatric donors, it is important to periodically question what respect and protection require of researchers in practice. The broad support for an obligation to obtain new consent at the age of majority is understandable but ripe for a challenge. Intuitively, it seems odd that a one-time sample donor remains a subject indefinitely. Given the burdens that such a requirement places on researchers (requiring them to track down past donors for additional consent or destroying valuable data and biospecimens when such consent is not possible), there should be an important ethical justification for imposing it. We see no such justification forthcoming. Rather than focusing on the gap between parental permission and individual consent, the relevant ethical question is whether parental permission is sufficient in the case of using stored samples in future studies that pose minimal risk. We believe it is. It is widely accepted that parents possess a broad authority to make decisions on behalf of their children, which can legitimately extend into adulthood. Such is the case with the collection of samples for future research; when parents permit their children's samples to be stored, they have given sufficient authorization for the ongoing use of those samples, obviating the need for additional consent when the children reach adulthood unless the future studies require interaction with the donors or pose greater than minimal risk to them.

All of the cases in Ethics Rounds are based on real events. Some incorporate elements of a number of different cases in order to better highlight a specific ethical dilemma.

ABBREVIATION

IRB: institutional review board

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