nauseous, and extremely worried about the well- being of her soon-to-be-born infant. If it is a vaginal delivery, she is also working very hard (literally laboring) to meet her child safely. If there is another legal parent in the room, that person is immediately preoccupied with all of the aforementioned, and additionally worries for the welfare of the delivering mom. Although they are likely not in physical discomfort, both parents would probably agree they are unable to receive information about a research study and are incapable of making a thoughtful split-second decision.

In certain delivery room situations, the time between meeting study criteria and randomization and delivery of the study's intervention can be a matter of seconds. In the proposed study in November's Ethics Rounds, for example, the determination of whether an infant born through meconium-stained amniotic fluid is "vigorous" or not immediately follows intubation for suctioning or no intubation. This is certainly not enough time for the kind of informed consent advocated by the common rule. I agree with these authors of the SAIL study group that not only is the legal decision-maker's "presence" arguable, the time (or lack thereof) makes this an emergency situation.

In November, Dr Wiswell and I argued that consent might be waived with the opportunity for parents to opt out later and with education provided to all laboring moms about the study in case their children were to meet criteria for enrollment at the time of birth. This approach is similar to the approach for which Foglia et al advocate in their "retrospective" consent. The key issue of disagreement we had with Dr Schreiner on the acceptability of waiver of consent was the meaning of "minimal risk." Dr Schreiner maintained that the risks of participating in the study exposed a newborn to risks greater than those found in "daily life," using the example of risks associated with laryngoscopy, an invasive procedure. Dr Wiswell and I argued that "daily life" for a nonvigorous newborn born through meconium-stained fluid, due to unproven "standard care" practice starts with this invasive procedure thanks to an unproven standard care practice.

What qualifies as "minimal risk" is becoming exceedingly important in how comparative effectiveness studies are being regulated. Joffe and Wertheimer[3] contrast interpreting the risks of such studies as "absolute" versus "incremental." If a literal interpretation of the "daily life standard" is maintained, absolute risks (ie, every risk of the study treatment, including the risks a patient is exposed to from the treatment in regular care) will make few comparative effectiveness studies qualify as "minimal risk." Alternatively, if incremental risks (risks unique to participating in the study that do not accompany the same treatments when outside of the study) are considered by an institutional review board, many comparative effectiveness studies might be considered "minimal risk." Unfortunately, the newest directives from the OHRP's "Draft Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care" issued in October appear to be interested in absolute risks. According to this draft guidance, "at a minimum, identified risks associated with a standard of care that are being evaluated as a purpose of research, should certainly be considered 'reasonably foreseeable."[4] This interpretation could make minimal risk determinations nearly impossible for comparative effectiveness research.

The OHRP is currently processing the general public's input on this draft guidance.[5] For the sake of our patients who deserve to receive evidence-based therapies, I hope the OHRP reconsiders their stance on which risks should be considered by institutional review boards. If a patient is harmed as a result of an unproven standard care treatment, and there's no one there to research it, doesn't the patient still suffer?

Dalia M. Feltman
Evanston Hospital, NorthShore University HealthSystem, and Pritzker School of Medicine, University of Chicago
E-mail: dfeltman@northshore.org

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None declared

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Author's Response

Three ethical principles govern research with human subjects: respect for persons, beneficence, and justice. Respect for persons demands that, whenever feasible, we ask parents for permission before

enrolling their infants in research studies. Beneficence requires us to make sure that the potential risks of any study are balanced by the potential benefits. Both principles require interpretation in light of the particular circumstances of particular trials. Our "Ethics Rounds" article presented a situation in which clinical investigators proposed a study of an unforeseen crisis in the delivery room. In such a circumstance, it would be impossible to adequately inform parents of the potential risks and benefits of enrolling in a study. One must, then, choose 1 of 2 troublesome options: either do the study without the permission of fully informed parents, or not do the study and never know which treatment is safest and most effective for infants. I believe that, in such circumstances, the principle of respect for persons is outweighed by beneficence and justice. Beneficence demands that we do what is best for infants. If we do not know what is best, we have an ethical obligation to find out. Justice demands that the research subjects be selected fairly and that the risks of research be minimized by designing the study as rigorously as possible to answer the study question as efficiently as possible. All future infants will benefit as a result. As both Foglia et al and Feltman suggest, such studies require careful oversight with exquisite attention to safety monitoring. Parents should be fully informed about such studies as soon as it is feasible to do so.

John D. Lantos
Children's Mercy Hospital Bioethics Center
E-mail: jlantos@cmh.edu

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John D. Lantos

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