Comparative effectiveness research has received considerable attention in recent years and has been accompanied by controversy, especially in response to the 2013 Office for Human Research Protections (OHRP) investigation of the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT)—a randomized trial of 2 contrasting oxygen saturation settings in mechanical ventilation of premature infants within the established standard of care. The OHRP convened a public meeting in August 2013 on “Matters Related to Protection of Human Subjects and Research Considering Standard of Care Interventions” and recently issued draft guidance on “Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care.” This guidance has been sharply criticized.

The phrase “research evaluating standards of care” suggests that standard-of-care treatment randomized clinical trials (RCTs) comprise a class of studies with ethically relevant characteristics (ie, testing of standard-of-care interventions) that have specific implications for determining what constitutes risk of research and what risks should be conveyed to participants. Although this assumption seems to be shared by commentators on both sides of the debate, it is problematic. This is because various positions regarding the ethics of standard-of-care treatment RCTs tend to rely on selected specific examples of such RCTs. It is not possible to determine whether such positions are generalizable or whether they reflect the specific risk-benefit and informed consent issues posed by the particular examples used. For instance, varying the time that an antianxiety drug is administered, such as 9 AM or 3 PM, is quite different from varying the amount of oxygen support administered to a newborn in a neonatal intensive care unit.

For instance, varying the time that an antianxiety drug is administered, such as 9 AM or 3 PM, is quite different from varying the amount of oxygen support administered to a newborn in a neonatal intensive care unit.

Some studies involve challenges (of different types) to obtaining traditional written informed consent (studies 2, 6, and perhaps 1); others do not. Most of the studies compare 2 standard-of-care treatments, but one study (study 6) involves only one standard-of-care intervention group and another addresses an area without a clear standard practice (study 7). In some studies, the only research element is the randomization (with an electronic health record as the source of data; study 1). In other studies, other research-specific procedures and data collection are likely. In some studies, the degree of interest in whether costs can be reduced without impairing efficacy or safety is extremely high (studies 2, 5), whereas in others perhaps less so.

Determining the ethical importance of each of these differences among standard-of-care treatment RCTs would require detailed analyses. However, the need for such example-specific ethical analysis should be clear. The fact that a study is comparing 2 widely
accepted treatments for a certain condition seems ethically relevant, but how it is relevant will be different for different studies. The ethics of standard-of-care treatment RCTs as such cannot be determined by a debate over a single type of study and certainly cannot be resolved if debating parties appeal to very different types of standard-of-care treatment RCTs. Even when there is disagreement about the same study—as has been the case with SUPPORT—it will not be clear whether the differing views are generalizable to other types of standard-of-care treatment RCTs. The task of abstracting principles that are specific enough to provide robust ethical guidance (about research risks or the scope of informed consent) and yet are broad enough to apply to standard-of-care treatment RCTs across the board will be a difficult, if not impossible, task. Investigators and ethics review committees should not draw broad ethical conclusions from the fact that studies are comparing standard treatments and instead consider the wide variability of ethically salient features even among standard-of-care RCTs.

**References**


