

The ethics of studying subjects in non-ideal circumstances

David Wendler

Clinical investigators frequently study individuals who are in less than ideal circumstances. Oncologists study individuals with brain tumours; psychiatrists study individuals who have undergone traumatic experiences. There is little these investigators can do to improve the circumstances of their subjects, short of finding new treatments for the conditions that affect them. In other cases, investigators study individuals who are in less than ideal, but remediable circumstances. These studies press the question of when it is acceptable for investigators to study, rather than assist individuals.

The literature on this question has focused on clinical trials in which patients who do not have access to the best treatments are given placebos, or a second-best treatment.¹ Research on the effects of secondhand smoke (SHS) similarly involves individuals who are in less than ideal, but potentially remediable circumstances. To assess the impact of SHS on sleep bruxism in children, Montaldo *et al* randomised parents who were known to smoke in the presence of their children into two groups. Parents in Group 1 were instructed to stop smoking in the presence of their children, whereas parents in Group 2 were instructed to not change their smoking habits.²

One might assume that clinical investigators may collect data only when doing so is consistent with protecting research subjects and promoting their clinical interests. This view suggests that research on individuals who are in less than ideal, but remediable circumstances, violates investigators' obligations. Rather than conduct a study in which patients who lack access to the best treatments are given placebos, researchers should give their subjects the best treatments available. Rather than study the effects of SHS, researchers should protect individuals from SHS.

While this characterisation of investigators' obligations makes sense, and is well intentioned, it is inconsistent with a good deal of acceptable research. Investigators fail to protect subjects' clinical interests whenever they perform procedures, such as blood draws, biopsies or imaging scans, purely for research purposes. Guidelines and regulations around the world allow investigators to perform these procedures when they have the potential to collect socially valuable information, the risks to subjects are not excessive and there is no less risky way to obtain the information. The first step in evaluating the ethical acceptability of research on SHS exposure is to assess whether it satisfies these conditions.

We know a good deal about the negative effects of exposure to SHS. It is associated with an increased risk of pneumonia, bronchitis, respiratory illness, wheezing, cardiovascular damage, cancer and heart disease. Given this wealth of information, investigators should propose, and review committees should approve, new studies on the effects of SHS only when they offer the potential to collect additional valuable information. In the present case: is there added social value to determining the impact of SHS on sleep bruxism in children?

Assuming these data are valuable, the next step is to ensure that the risks to subjects are acceptable. Most regulations allow children to be enrolled in research only when it offers the potential for clinical benefit, or the risks are very low. Enrolment in the Montaldo study offered the potential to reduce participating children's exposure to SHS if they were randomised into Group 1. In addition, at the end of the study, participating families received lessons on the risks of SHS. The potential benefits of these interventions may have outweighed the risks of the study, suggesting that the study offered participating children a favourable risk-benefit profile. This is important, and given the importance of protecting research subjects from excessive risks, it might seem to follow that the study was necessarily acceptable.

Research on individuals who are in less than ideal, but remediable circumstances, highlights the fact that the ethics of clinical research are not limited to collecting valuable information and protecting participants from excessive risks. Whether clinical research is acceptable also depends on whether investigators act in accord with relevant norms on human behaviour. Two norms in particular merit brief mention in the present context.

We have a moral obligation not to impose risks on others. We also have duties to assist those in need, including a duty of rescue, which implies that we are morally obligated to assist others in urgent need, at least when doing so poses minimal burden and risk on us. Notice two things about these norms. First, they apply to all of us. They do not depend on one's having agreed to take them on, nor on one's having acted in ways that imply such agreement. Second, the duties implied by these norms are *pro tanto*: we are morally obligated to act in the manner specified by the norm unless there is compelling reason to act otherwise in a specific case.

Research in which investigators decline to help those in need violates the norm on providing assistance to others and, therefore, requires greater justification than research in which investigators assist those in need. Research in which investigators perform risky procedures on subjects violates an even stronger norm on not exposing others to risks, and requires compelling justification. Does research on SHS offer the necessary justifications?

FOUR OPTIONS FOR STUDYING EXPOSURE TO SHS

There are at least four possible designs for studying the effects of SHS on children. *Active Exposure* involves investigators actively exposing children to SHS. For example, under this design, investigators might bring subjects into the laboratory and have machines blow smoke on them. *Encouraged Exposure* involves investigators encouraging parents to smoke in the presence of their children. *Observation* involves investigators studying the effects of SHS on children without attempting to reduce parents' smoking or children's exposure to SHS. *Discouraged Observation* involves investigators taking steps to reduce parents' smoking and/or to reduce children's exposure to SHS, and then studying those children who are, nonetheless, exposed to SHS.

Studies with multiple arms may fall into multiple categories. Consider a study

Correspondence to Dr David Wendler, Department of Bioethics, NIH Clinical Center, Building 10, Room 1C118, Bethesda, Maryland 20892-1156, USA; dwendler@nih.gov

that randomises children into two groups. The first group includes children whose parents are given medication to help them stop smoking. The second group involves a control in which the investigators neither attempt to reduce the parents' smoking nor the children's exposure to SHS. The first arm of this study qualifies as Discouraged Observation, the second arm qualifies as Observation. Studies that fall into more than one category are not acceptable unless the more problematic arm is justified.

Active Exposure violates the strong norm against exposing others to risks. This design is acceptable, if at all, only when it has the potential to gather clearly and sufficiently valuable information, which cannot be collected in a less problematic way. Given that we already know a good deal about the negative effects of SHS, and the possibility of using observational designs, Active Exposure seems unethical.

Encouraged Exposure seems unacceptable for similar reasons. Although investigators are not themselves exposing children to SHS, they are encouraging parents to do so. This design indirectly violates the strong norm against exposing others to risks.

Observation does not involve investigators actively exposing children to SHS, nor does it involve investigators encouraging parents to do so. This makes Observation preferable to Active Exposure and Encouraged Exposure. At the same time, Observation does involve investigators failing to discourage parents from smoking, at least in the presence of their children. Hence, Observation should be used only when it has the potential to collect valuable information that cannot be collected using Discouraged Observation.

APPLICATION TO THE MONTALDO STUDY

The Montaldo manuscript states that parents randomised to the second group 'were asked not to change their smoking habits'. The authors might have assumed that this approach rendered the second arm a form of Observation: the investigators were simply observing families without intervening in the parents' smoking behaviour, or in the children's exposure to SHS. Yet, as Barrientos-Gutierrez *et al* point out, asking parents who are known to smoke in the presence of their children to 'not change their smoking habits' might have had the effect, if not the intent, of making the second arm an instance of Encouraged Exposure.³ Parents who enrolled and later wanted to stop smoking in the presence of their children might have continued because they told the investigators they would not change their smoking habits.

In response to this possibility, the letter from Montaldo states that participating 'parents were all informed about the risks of SHS', and the parents in Group 2 were those who reported 'not being able to reduce' their children's exposure to SHS. This additional information suggests that the second arm might have included elements of Discouraged Observation. If so, whether the study was appropriate depends on whether the data being collected were socially valuable, and how forcefully parents were discouraged from smoking, at least in the presence of their children. Discouraged Observation, typically, should include at least strong warnings about the dangers of smoking, and strong warnings about the dangers of SHS, with occasional warnings over time for longitudinal studies.

Finally, the study by Montaldo *et al* highlights a point rarely discussed in the research ethics literature, namely, the importance of including in manuscripts a description of the ethical considerations raised by the study and the safeguards it employed. This is especially important for controversial research, such as research on the effects of SHS in children. Explicit description of the ethical considerations raised, and the safeguards employed, helps to make clear studies that are acceptable, ensure public accountability and protect against possible modelling of unethical research.⁴ The present discussion represents a commendable example of this approach, one in which investigators describe and attempt to address the ethical challenges raised by research on the effects of exposure to SHS.

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