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Letter to the Editor

The difference between withdrawal and refusal of consent in trials

To the Editor,

The recent paper by Nichol and colleagues[1] draws on data across five Resuscitation Outcomes Consortium trials using waivers of prospective consent under the US Exception from Informed Consent rules.[2] The authors report low average rates of withdrawal from studies (0.3% in cardiac arrest, and 7.7% in traumatic injury). The authors draw the conclusion that low withdrawal rates "suggest" or "infer" that trial inclusion without consent is acceptable to cardiac arrest patients and trauma victims. However, withdrawal is not the same as prospective refusal to consent. Patients' decisions to withdraw are inherently biased by hindsight, resignation, and perhaps a healthy dose of fatalism to accept what has happened to them. Withdrawal is also a statement of defiance and conflict, reflecting at some level displeasure or hostility to the actions of the researchers, which may be difficult or uncomfortable for patients to express in a clinical setting.

Demonstrating the difference between withdrawal and refusal are trials that attempt to secure consent from some subjects while also waiving consent from other subjects, often at different trial sites.[3–8] One clear example was the Nice-Sugar trial.[9] As summarized elsewhere,The Normoglycemia in Intensive Care Evaluation - Survival Using Glucose Algorithm Regulation (NICE- SUGAR) trial, run in Canada, Australia, and New Zealand, involved tight versus loose control of blood glucose levels in intensive care patients and was stopped early due to high mortality in the former arm. Consent was required in Canada, while a form of waiver—delayed consent—was permitted in Australia and New Zealand. The refusal or failure to affirm enrollment in the latter countries was 9%, while the refusal rate by capable patients or surrogates in Canada was 41% (S Finfer, personal communication, 2012).[10]

That difference cannot reasonably be attributed to cultural differences between Canadians and Australians and New Zealanders.

Which perspective and set of preferences will we most value in setting policies for and assessing the appropriateness of waivers of informed consent? Decisions to withdraw are flawed, as noted above, but are "informed" by lived experiences of patients and their families and caregivers. Informed consent, while also flawed, values autonomy and the rights of people to determine what will be done to them, values that are undermined by waivers. The duty to secure informed consent from research subjects should not be diminished or undermined by the inapposite assertion that people from whom no consent was sought will likely affirm their participation or at least not complain.

Conflict of Interest Statement

Since 1997, JFM has been a paid expert witness in 3 civil cases involving the adequacy of informed consent and IRB review in research, twice for defense and once for plaintiff, as well as a 4th case involving the definition of human subjects research. In the last 3 years, JFM has received financial compensation for service on several Data and Safety Monitoring Boards for the NIH and the American College of Radiology Imaging Network, and for service on a pharmacogenomics ethics advisory board for Merck. JFM received partial salary support as moderator of the IRBForum (https://community.primr.org/home) by a grant from Public Responsibility in Medicine & Research (PRIMR) from 2012 through 2020.

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