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Editorial

Peer review in the reporting of clinical trials in *Arthroplasty Today*

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As *Arthroplasty Today* enters its 5th year, the Editorial Board remains mindful of its duty to ensure the integrity of peer review, a foundational element of our publication. Research is critical to advancing our specialty, and peer review is essential toward improving, validating, and corroborating that research, and communicating results to our readers.

We address here the subject of human research trials, with a brief historical overview, and discussion of current practices in medical research using human subjects. In clinical trials, patient benefit and safety must come first. The orthopaedic device industry may sponsor clinical trials, raising the question of investigator bias. As such, the peer review process must be rigorous and transparent. *Arthroplasty Today* has instituted policies and protocols that ensure patient protections and research integrity during review of submitted manuscripts.

Human subject research is necessary to determine the efficacy of innovative interventions, such as new devices and operations in orthopaedic surgery. The protection of human research subjects was codified by the Nuremberg Code of 1947, in the Helsinki Declaration of 1964, and most recently in the Belmont Report [1]. The latter captures the findings of the 1974 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This commission, formed in the aftermath of the Tuskegee experiment scandal, was charged with shaping bioethics policy. Toward that end, the commission was asked to identify the boundary between research and accepted medical standards, assess the risk-benefit ratio of research, determine the appropriate guidelines for human subject selection, and define the nature and definition of informed consent. The guiding principles issued by the commission are still helpful in minimizing patient risk, while ensuring the maximum potential benefit in human trials. Human trials today require oversight, with patient protections monitored and enforced by a local or external Institutional Review Board (IRB).

On occasion, it is necessary to stop a human trial prematurely, in the interest of patient safety. For example, in 2002 MacDonald et al [2] stopped an approved, randomized controlled trial comparing metal-on-metal to metal-on-polyethylene total hip bearings, when early data showed a concerning rise in serum cobalt and chromium ions. One of this editorial's authors (T.J.B.) has written about the first recalled orthopaedic product in the United States [3]. Well-known arthroplasty surgeon Lawrence Dorr openly cautioned his colleagues in 2008 about premature failures of a specific hip implant, and urged discontinuation of the device; those concerns were subsequently validated [4]. In each of these instances, orthopaedic investigators took proactive steps to mitigate risk, and protect patients, exemplifying the concept of beneficence.

Industry-supported research may be important, but it raises concerns related to investigator bias. This bias can manifest in favorable patient selection, interpretation, presentation, and publication of data. Investigators may have financial incentives toward publishing only positive findings for favored products, and negative findings for competing products. Externally funded research must acknowledge the funding source, and strive to maintain objectivity with regard to data analysis and conclusions. As an example, at the 2018 American Association of Hip and Knee Surgeons Annual Meeting, a researcher acknowledged that a product did not show the expected benefit, even though he was a paid consultant for the manufacturer [5].

Peer review is essential in scholarly publication, in ensuring relevance of the research question, appropriateness of the methodology, and validity of the conclusions. The reviewer is tasked with judging the merits and quality of the submission, relying on the IRB and other regulatory mechanisms to ensure that human subjects were properly counseled, gave informed consent, and were sufficiently protected throughout the trial. *Arthroplasty Today* has measures in place that require affirmation from the corresponding author that proper IRB approval is in place.

Human subjects research may be prospective or retrospective, and may involve a single center or multiple centers. Subjects can be enrolled in an observational study, or in prospective randomized trials. In some cases, trial participants and/or the investigators may be blinded to the treatment arm. Some studies simply involve

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analysis of data acquired to test a research hypothesis. In multicenter studies, enrollment of patients requires IRB approval at each participating institution. A distinct kind of clinical trial is the seeding trial, which does not require informed consent. Some patients who have participated in a trial of a device or drug prior to 510K-market approval may be added to the data set of the seeding trial; only these specific patients will have undergone informed consent. In the medical arena, these trials usually involve approved drugs [6].

A 2-decade old article in the New England Journal of Medicine reported that seeding trials were relevant to product marketing, rather than product evaluation; significant funding to the investigators was involved [7]. In seeding trials in arthroplasty surgery, the trial sponsor may pay surgeons to enroll patients and collect data on an approved device, sometimes in order to establish the surgeon as a key opinion leader. The trial sponsor typically does not provide the product for free, and in fact may charge more for the technology being investigated, while claiming equivalence to an existing product. In such instances, informed consent may not be required.

Arthroplasty Today requires confirmation of IRB approval and informed consent for all manuscripts involving human subjects. Informed consent must include relevant financial disclosures, and the relationship of the surgeon to the manufacturer. In addition, conflict of interest forms are completed by all authors for disclosure of external funding so that readers are aware of potential bias. These standards help ensure the integrity of the collected data, and its subsequent analysis. Reviewers are asked to focus on the importance of the research question, the novelty of the hypothesis tested, and the absence of ethical concerns with the submission. Next, the reviewers assess the scientific merit of the investigation, the ability of the data to prove or disprove the hypothesis, and the validity of the results shown. Finally, the discussion must represent valid conclusions based on the data presented, without overstating the implications of the results or editorializing in favor of a product.

Once the peer reviewers are done with the above tasks, the Editor-in-Chief or Deputy Editor assesses and scores the quality of the reviews, makes additional comments or suggestions for potential changes to the manuscript, then submits an initial decision. For most submissions that are successfully published, one or more revisions to the submission are required. These revisions are often necessary to clarify the methods and the conclusions, and ensure adherence to the publication standards outlined above.

The Editorial Board of *Arthroplasty Today* is committed to the ethical evaluation and publication of relevant and timely submissions that relate to the science and practice of hip and knee arthroplasty. We understand the need for human subject research, and value the peer review process toward a quality control tool in communicating research findings to our readers. We are grateful to, and proud of our outstanding peer reviewers, and will continue to support their generous volunteer work for the advancement of our specialty and association.

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