Study examines high-risk therapeutic medical devices receiving FDA premarket approval

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Of high-risk therapeutic devices approved via the Food and Drug Administration (FDA) Premarket Approval (PMA) pathway between 2010 and 2011, there has been wide variation in both the number and quality of premarket and postmarket studies, with approximately 13 percent of initiated postmarket studies completed between 3 and 5 years after FDA approval, according to a study in the August 11 issue of *JAMA*.

In the United States, the FDA predominantly grants marketing approval through the PMA pathway for high-risk medical devices, which are defined as those that support or sustain human life, prevent illness, or present potential, unreasonable risk to patients. The PMA pathway requires premarket clinical evidence providing reasonable assurance of device safety and effectiveness and permits supplemental applications whenever postapproval changes are made to the device. Recently, concerns have been raised that the clinical studies supporting FDA approval of these devices lack adequate rigor and are prone to bias, according to background information in the article.

Joseph S. Ross, M.D., M.H.S., of the Yale University School of Medicine, New Haven, Conn., and colleagues examined the clinical evidence generated for high-risk therapeutic devices over the total product life cycle (premarket and postmarket). The analysis included all clinical studies of high-risk therapeutic devices receiving initial market

approval via the PMA pathway in 2010 and 2011 identified through ClinicalTrials.gov and publicly available FDA documents as of October 2014. Studies were characterized by type (pivotal, studies that served as the basis of FDA approval; FDA-required postapproval studies [PAS]; or manufacturer/investigator-initiated); premarket or postmarket; status (completed, ongoing, or terminated/unknown); and design features, including enrollment, comparator, and longest duration of primary effectiveness end point follow-up.

In 2010 and 2011, 28 high-risk therapeutic devices received initial marketing approval via the PMA pathway. The researchers identified 286 clinical studies of these devices: 82 (29 percent) premarket and 204 (71 percent) postmarket, among which 18 percent were nonpivotal premarket studies, 10.5 percent pivotal premarket studies, 11.5 percent FDA-required PAS, and 60 percent manufacturer/investigator-initiated postmarket studies. Six of 33 (18 percent) PAS and 12 percent of manufacturer/investigator-initiated postmarket studies were reported as completed. No postmarket studies were identified for 18 percent of devices; 3 or fewer were identified for 46 percent of devices overall.

Premarket clinical studies of high-risk therapeutic devices were limited in number and quality. Nearly all devices were cleared on the basis of 2 studies: 1 nonpivotal and 1 pivotal study.

Approximately half of all studies used no comparator. Median duration of primary effectiveness end point follow-up was 3 months, 9 months, and 12 months for pivotal, completed postmarket, and ongoing postmarket studies, respectively.

"Our characterization of the clinical studies examining high-risk therapeutic medical devices initially approved via the FDA PMA pathway between 2010 and 2011 demonstrates that the amount and quality of evidence generated over the total product life cycle varies

widely. Some devices are currently being evaluated through ongoing studies that, if completed, will provide evidence on clinical outcomes for large numbers of patients with planned follow-up of a year or longer. However, most devices have been or will be evaluated through only a few studies, which often focus on surrogate markers of disease in small numbers of patients followed up over short periods of time and study indications that differ from the original FDA-approved indication," the authors write.

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