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FDA Recalls Not as Alarming as They Seem

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Inverse Association Between Duration of Use of Acid-Suppressive Medications and Fracture Risk

The article by Abrahamsen et al,¹ suggests that our article on proton pump inhibitor (PPI) use and fracture risk,² has “suggested a causal relationship.”

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This is not a correct interpretation of our findings: although we found a small overall association between PPI use and fracture, we emphasized that “there was inverse association between duration of use of acid-suppressive medications and fracture risk, which does not support adverse effects on the bone.”^{2(p1997)}

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1. Abrahamsen B, Eiken P, Eastell R. Proton pump inhibitor use and the anti-fracture efficacy of alendronate [published online February 14, 2011]. *Arch Intern Med*. 2011;171(11):998-1004.
2. de Vries F, Cooper AL, Cockle SM, van Staa TP, Cooper C. Fracture risk in patients receiving acid-suppressant medication alone and in combination with bisphosphonates. *Osteoporos Int*. 2009;20(12):1989-1998.

In reply

My colleagues and I are sorry if the introduction in our article¹ gave the impression that the authors of the 2009 publication by de Vries et al² considered their findings suggestive of causality. This interpretation of their findings was solely our own. The study by de Vries² is referred to in more detail in the “Comment” section, where we note that while the effect could not be shown to persist with longer durations of PPI treatment, most patients were coadministered PPIs for less than 12

months. We are grateful to Dr de Vries for this opportunity to clarify.

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1. Abrahamsen B, Eiken P, Eastell R. Proton pump inhibitor use and the anti-fracture efficacy of alendronate [published online February 14, 2011]. *Arch Intern Med*. 2011;171(11):998-1004.
2. de Vries F, Cooper AL, Cockle SM, van Staa TP, Cooper C. Fracture risk in patients receiving acid-suppressant medication alone and in combination with bisphosphonates. *Osteoporos Int*. 2009;20(12):1989-1998.

HEALTH CARE REFORM

FDA Recalls Not as Alarming as They Seem

The article by Zuckerman et al¹ reported that 80 (71%) of the 113 high-risk medical devices recalled by the US Food and Drug Administration (FDA) between 2005 and 2009 were originally approved via the 510(k) process (§510(k) of the Food, Drug, and Cosmetic Act) rather than the more stringent premarket approval (PMA) application process and concluded that more stringent regulation is required.¹ However, when they evaluated the frequency with which approved devices were recalled, the authors failed to calculate the most appropriate measure, namely the probability that a device approved via either pathway would subsequently be subject to a high-risk recall. Specifically, the authors calculated the proportion of recalled devices that were approved via each pathway rather than calculating the proportion of devices approved via each pathway that were recalled. We provide the pertinent calculation herein.

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From 2005 to 2009, there were 16 522 medical devices approved via the 510(k) pathway and 145 approved via the PMA pathway.² While some of the recalled devices were likely approved prior to this period, these numbers can be used to estimate the relative numbers of devices approved via each mechanism. Thus, devices approved via the 510(k) pathway had an approximate recall rate of 0.48% (80 of 16 522), while those approved via the PMA mechanism had a recall rate of 14.5% (21 of 145). In other words, a premarket-approved device is approximately 30 times more likely to be recalled than a 510(k)-approved device. This suggests, in contrast to the conclusions reached by Zuckerman

et al,¹ that the premarket-approved devices are substantially higher risk.

We believe the FDA should continually reassess and identify the best methods for product review and approval to ensure that only safe and effective devices come to market. This process should be based on a determination of the risk and benefit associated with each device. The risk of a recall for a device is best assessed using the probabilities provided herein rather than those calculated in the article by Zuckerman et al.¹

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In reply

Connor et al conclude that the large percentage of high-risk recalled devices that have been cleared through the FDA's less stringent 510(k) process is acceptable because only 113 of thousands of types of devices were recalled. Their analysis does not take into account the impact of dangerous medical devices on the health of patients or the costs of health care. It also does not consider the importance of federal agencies following the law consistently in their regulation of medical products.

Current law requires the FDA to use their more rigorous review, the PMA process, if a medical device is life sustaining or otherwise high risk.¹ The 510(k) process is intended for devices that are lower or moderate risk.¹ We pointed out that if a medical device can severely injure or kill patients when it fails, then it is not a low- or moderate-risk device and should have been approved through the PMA process. Unfortunately, the FDA designates many new devices as moderate risk and clears them through the 510(k) process but later recalls the devices after they kill or seriously injure patients. Most high-risk recalls are caused by predictable problems (such as implant breakage, deterioration, or manufacturing defects); therefore, there should be few high-risk recalls among devices that are truly low or moderate risk.

The economic and human costs of high-risk recalls are substantial. Our new analysis finds that the 113 high-risk recalls between 2005 and 2009 involved 112.6 million products. In just the first 6 months of 2010, there were more than 437 million high-risk recalled products that were 510(k) devices,² equaling 1.4 high-risk-recalled devices for each person in the United States. Examples in 2010 include millions of inaccurate glucose test strips that could result in death.

Because physician reporting of adverse reactions is voluntary, deaths and injuries related to defective medical devices are severely undercounted.³ Based on data on the FDA Web site, we calculated 4556 deaths associated with medical devices in 2009, a 60% increase compared with 2006.⁴ (Note: Our calculation was based on the 5547 deaths reported to MAUDE [Manufacturer and User Facility Device Experience Database] in 2009, subtracting duplicate death reports.) Almost half (n=2006, or 44%) of the deaths were blamed on devices that had been cleared through the 510(k) process or were exempt from any regulatory review because the FDA considered them very low risk. Two-thirds (n=3040) of the deaths were linked to cardiovascular devices and 12% (n=561) were linked to general hospital devices. Annuloplasty rings, used for valve repair, are a 510(k) device that was associated with 152 deaths in 2009, for example.

Connor et al attempt to calculate the percentage of devices cleared through the 510(k) process that were subsequently high-risk recalls. However, many devices cleared through the 510(k) process are never sold in the United States, some are never sold anywhere, and many sell very few products. As a result, the total number of cleared devices is an inflated denominator that should not be used for evaluating the safety of 510(k) devices.

The US Government Accountability Office (GAO) found that almost 87% of the 3510 recalls from 2005 through 2009 were high or moderate risk. Even using the denominator of 16 667 new devices in the letter by Connor et al, this increases the serious recall rate to 18%. Although not all these recalled devices are potentially fatal, many require surgical removal or present other serious risks, such as the 158 moderate-risk recalls for artificial hips, knees, and joint components.

In conclusion, lives could be saved, patients' quality of life improved, and medical costs would decrease if all potentially high-risk devices were subjected to the more rigorous PMA process, which requires clinical trials and premarket inspections, includes authority for postmarket studies as a condition of approval, and gives the FDA the authority to rescind approval of unsafe devices.

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Images From Our Readers

Harvard Yard, Boston, Massachusetts.

Courtesy of: Guy D. Eslick, PhD, MMedSc(Clin Epi), MMedStat, The Whiteley-Martin Research Centre, Nepean Hospital, The University of Sydney, Sydney, Australia.