

### Notice of retraction

The study<sup>1</sup> that served as the basis for the PURL entitled, "Ramipril for claudication?" (*J Fam Pract.* 2013;62:579-580), has been retracted from the *Journal of the American Medical Association*.<sup>2</sup> Therefore we, on behalf of all of the authors of the PURL, are retracting the PURL, as well.

According to *JAMA*'s retraction statement, the first author of the article admitted to data fabrication following an internal investigation.<sup>2</sup> The source article does not provide subgroup analysis to determine how much of an effect the fabricated data may have had on the final reported outcome. However, a separately reported (and also retracted) sub-analysis of this study indicates that 165/212 (77.8%) patients were enrolled from the site of the first author.<sup>3</sup>

The question remains: Does ramipril work for symptoms of claudication? A completely separate group of researchers conducted a similar, but smaller, randomized clinical trial of ramipril in patients with intermittent claudication.<sup>4</sup> In this study, 33 patients were randomized to ramipril or placebo for a 24-week trial. The ramipril group (n=14) improved maximum treadmill walking distance by an adjusted mean of 131 meters (m) (95% confidence interval [CI], 62-199;  $P=.001$ ), improved treadmill intermittent claudication distance by 122 m (95% CI, 56-188;  $P=.001$ ), and improved patient-reported walking distance by 159 m (95% CI, 66-313;  $P=.043$ ).

The 2004 Heart Outcomes Prevention Evaluation (HOPE) study indicates that ramipril maintains a mortality benefit for patients with intermittent claudication.<sup>5</sup> A subgroup of this study included 1725 patients with baseline peripheral artery disease who were randomized to ramipril at 10 mg, which yielded a relative risk (RR) of 0.75 (95% CI, 0.61-0.92) for the primary outcome (cardiovascular mortality, myocardial infarction, stroke). This alone validates the use of



ramipril in patients with intermittent claudication. But with the retraction of the large randomized controlled trial, we are not sure how much it may improve walk distances. Further studies might better clarify if ramipril provides symptomatic benefit by reducing claudication symptoms, in addition to the known cardiovascular mortality benefit.

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> The question remains: Does ramipril work for symptoms of claudication?

1. Ahimastos AA, Walker PJ, Askew C, et al. Effect of ramipril on walking times and quality of life among patients with peripheral artery disease and intermittent claudication: a randomized controlled trial. *JAMA.* 2013;309:453-460.
2. Notice of Retraction: Ahimastos AA, et al. Effect of Ramipril on Walking Times and Quality of Life Among Patients with Peripheral Artery Disease and Intermittent Claudication: A Randomized Controlled Trial. *JAMA.* 2013;309(5):453-460. *JAMA.* 2015;314:1520-1521.
3. Notice of Retraction: Potential vascular mechanisms of ramipril induced increases in walking ability in patients with intermittent claudication. *Circ Res.* 2014. *Circ Res.* 2015;117:e64.
4. Shahin Y, Cockcroft JR, Chetter IC. Randomized clinical trial of angiotensin-converting enzyme inhibitor, ramipril, in patients with intermittent claudication. *Br J Surg.* 2013;100:1154-1163.
5. Ostergren J, Sleight P, Dagenais G, et al. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J.* 2004;25:17-24.

### ERRATUM

The article, "Bone disease in patients with kidney disease: A tricky interplay" (*J Fam Pract.* 2016;65:606-612), incorrectly stated: "Elevations of both fibroblast growth factor 23 (FGF23) and parathyroid hormone (PTH) lead to hyperphosphatemia and hypocalcemia because of decreased urinary excretion of phosphorus." In fact, FGF23 normally acts to lower blood phosphate levels. Furthermore, an elevated phosphorus level causes an increase in serum calcium levels and not hypocalcemia. This sentence, and the 2 that followed it, should have read:

"Elevations of FGF23 lower blood phosphate levels by inhibiting phosphate reabsorption in the kidneys, thus increasing urinary excretion of phosphorus. Secondary hyperparathyroidism, driven by hypocalce-

mia, responds to normalize serum calcium levels by increasing the number and size of osteoclasts actively breaking down bone matrix. This increased level of bone breakdown escalates fracture risk.”

This information has been corrected in the online version of the article.

### A tricky interplay, indeed

Bone disease in patients with kidney disease is indeed a tricky interplay, as the article by Nyman et al (*J Fam Pract.* 2016;65:606-612) aptly states in its title.

The author made incorrect statements on page 607 regarding hyperphosphatemia and hypocalcemia and the escalation of fracture risk. (Editor's Note: See erratum, above.)

In addition, on page 610, the article mentions that 1,25-(OH)<sub>2</sub> vitamin D may help prevent hypertension, myocardial infarction, and stroke in patients without chronic kidney disease. This is not supported by the literature and even the reference cited states that fact.

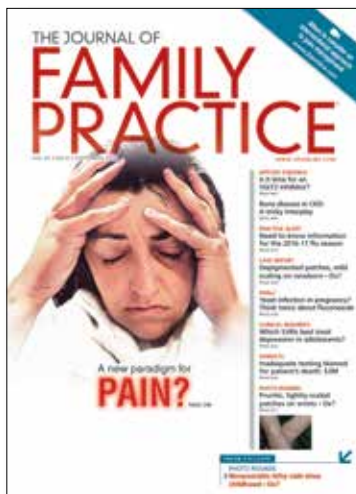
Roy N. Morcos, MD, FAAFP  
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### Author's response:

Thank you, Dr. Morcos, for your careful read of our article.

Regarding the discussion of 1,25-(OH)<sub>2</sub> vitamin D, we are in agreement. In fact, the last sentence of our paragraph reads: “There are no data, however, confirming that 25(OH) D supplementation mitigates these outcomes.” We were simply calling attention to the fact that despite the lack of evidence, some providers are still prescribing native vitamin D for their patients with chronic kidney disease for reasons unrelated to parathyroid hormone suppression.

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on behalf of co-authors Heather Nyman,  
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### What can we do about the Zika virus in the United States?

Since Florida has seen several new cases of local mosquito-borne infection, controlling and preventing Zika infection has great urgency. Zika virus involves an arthropod-borne infection transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. Other modes of transmission include the maternal-fetal route, any sexual contact, blood trans-

fusions, organ or tissue transplantation, and laboratory exposure.<sup>1</sup>

The first case of Zika infection in the United States and its territories occurred through international travel. According to the Centers for Disease Control and Prevention, as of October 12, 2016, there were 3807 travel-associated cases of Zika infection in the United States and 84 instances in its territories.<sup>2</sup> As for local transmission, there were 128 people evidencing a Zika infection in the United States and 25,871 in US territories.<sup>2</sup> Regions between Texas and Florida are at high risk because *Aedes* mosquitoes primarily inhabit the gulf coast.<sup>3</sup> Many cases have occurred despite repellent use and eradication efforts, possibly due to resistance acquired by these mosquitoes.<sup>1</sup>

Control measures include using insect repellents, aerial spraying of insecticides, eliminating mosquito breeding sites, covering water tanks, and using mosquito nets or door and window screens. Infection during pregnancy is the greatest concern because of congenital anomalies (including microcephaly) that negatively affect brain development.<sup>4</sup>

Before a possible conception or any sexual contact, women exposed to Zika—with or without symptoms—must wait at least 8 weeks; men with or without symptoms should abstain for 6 months.<sup>4</sup> Individuals should avoid traveling to areas with Zika infestation, wear long-sleeved clothing treated with permethrin, and minimize outside exposure, especially in evening hours.<sup>4</sup>

➤ Despite the lack of evidence, some providers are still prescribing native vitamin D for their patients with chronic kidney disease for reasons unrelated to parathyroid hormone suppression.

The World Health Organization is utilizing genetically modified mosquitoes to diminish *Aedes* populations; trials conducted in affected areas of Brazil revealed that the number of *Aedes* mosquitoes was reduced by 90%.<sup>5</sup> This method of mosquito control is currently being studied in the United States.<sup>6</sup> Vaccinations to prevent Zika infection are also under investigation.

Physicians should educate patients regarding the clinical manifestations and complications of Zika virus infection; people need to know that the Zika virus can be sexually transmitted. Doctors should also counsel patients to curtail travel to areas that have Zika infestations, or to at least wear protective clothing while in such areas to minimize mosquito bite risk. Educating travelers about appropriate postponement of sexual contact

after any exposure to the Zika virus is also essential.<sup>4</sup>

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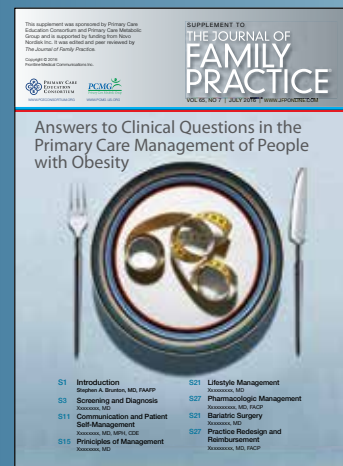
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