

# Serum magnesium and calcium in preeclampsia: a comparative study at the Korle-Bu Teaching Hospital, Ghana

Ebenezer Owusu Darkwa<sup>1</sup>  
 Charles Antwi-Boasiako<sup>2</sup>  
 Robert Djagbletey<sup>1</sup>  
 Christian Owoo<sup>1</sup>  
 Samuel Obed<sup>3,†</sup>  
 Daniel Sottie<sup>4</sup>

<sup>1</sup>Department of Anaesthesia, University of Ghana School of Medicine and Dentistry, <sup>2</sup>Department of Physiology, University of Ghana School of Biomedical and Allied Health Sciences, <sup>3</sup>Department of Obstetrics and Gynaecology, University of Ghana School of Medicine and Dentistry, College of Health Sciences, <sup>4</sup>Department of Anaesthesia, Korle-Bu Teaching Hospital, Accra, Ghana

<sup>†</sup>Samuel Obed passed away on May 12, 2017

**Background:** A large percentage (16% of maternal mortality in developed countries, compared to 9% in developing countries), is due to hypertensive disorders in pregnancy. The etiology of preeclampsia remains unknown, with poorly understood pathophysiology. Magnesium and calcium play an important role in vascular smooth muscle function and therefore a possible role in the development of preeclampsia.

**Aim:** We aimed to compare serum magnesium and total calcium levels of preeclamptic and normal pregnant women at the Korle-Bu Teaching Hospital in Ghana.

**Patients and methods:** A comparative cross-sectional study involving 30 normal pregnant and 30 preeclamptic women with >30 weeks gestation and aged 18–35 years, was conducted at the Korle-Bu Teaching Hospital. Magnesium and calcium were determined using a flame atomic absorption spectrometer.

**Results:** Mean serum magnesium and total calcium levels in preeclamptic women were  $0.70 \pm 0.15$  and  $2.13 \pm 0.30$  mmol/L, respectively. Mean serum magnesium and total calcium levels in normal pregnant women were  $0.76 \pm 0.14$  and  $2.13 \pm 0.35$  mmol/L, respectively. There was a statistically nonsignificant difference in serum magnesium and total calcium in preeclamptic women compared to normal pregnant women, with *p*-values of 0.092 and 0.972, respectively.

**Conclusion:** Serum magnesium and total calcium, therefore, seem not to differ in preeclamptic women compared to normal pregnant women in Ghana.

**Keywords:** electrolytes, maternal deaths, pregnant, hypertension, Ghanaian women

## Introduction

Preeclampsia is one of the commonest etiologies of fetal and maternal mortality and morbidity.<sup>1</sup> The incidence of preeclampsia in developing nations is estimated to be 4–18%.<sup>2</sup> Thus, 16% of all maternal mortality in developed countries and 9% of maternal mortalities in Asia and Africa are said to be due to hypertensive disorders in pregnancy.<sup>3</sup> Moreover, 18% of 724 total maternal deaths at the Korle-Bu Teaching Hospital between 1984 and 1994 were due to hypertensive disorders in pregnancy, including preeclampsia.<sup>4</sup> A worldwide perinatal and neonatal mortality rate of 10% is associated with preeclamptic disorders, with prematurity as the commonest cause of the neonatal deaths.<sup>5</sup> Current evidence suggests that the endothelial dysfunction seen in preeclamptic pregnant women may persist years after the episode, and therefore preeclamptic women may be at high risk of cardiovascular diseases later in life.<sup>6</sup>

Though the etiology of preeclampsia remains unclear, many theories suggest abnormal placental implantation and abnormal trophoblastic invasion as possible causes.<sup>7</sup> The molecular basis of this condition is unresolved in literature.<sup>8</sup> It has been postulated

Correspondence: Ebenezer Owusu Darkwa  
 Department of Anaesthesia, University of Ghana School of Medicine and Dentistry, College of Health Sciences, PO Box 4236, Accra, Ghana  
 Tel +233 24 467 0149  
 Email eoddarquah@yahoo.co.uk

that fluctuations in maternal serum ions may be the precipitating cause of elevated blood pressures in preeclampsia.<sup>9,10</sup> Dietary deficiency of mineral ions has been shown to have a harmful effect on the pregnant mother and growing fetus and possibly complicate preeclampsia.<sup>11</sup> Dietary deficiency of magnesium has been established to play a role in blood pressure regulation and hence development of preeclampsia.<sup>12</sup> Evidence supporting routine magnesium supplementation for all pregnant women has not been substantiated by research, though most studies have reported reduced magnesium levels in pregnancy and worse levels in preeclampsia.<sup>13–18</sup> However, other studies have also reported a nonsignificant change in the serum magnesium levels of preeclamptic women compared to normal pregnant women.<sup>19–21</sup>

Various studies have also reported reduced serum calcium levels in preeclampsia compared to normal pregnant women.<sup>18,20–24</sup> Calcium supplementation has been reported to half the risk of development of preeclampsia.<sup>25</sup> Kanagal et al,<sup>25</sup> in their study on calcium supplementation in pregnancy, recognized that daily calcium supplementation of 1.5–2 g reduced the blood pressure, prevented the development of preeclampsia in normotensive pregnant women as well as reduced morbidity and mortality, a finding supported by Hofmeyr et al<sup>26</sup> in their systematic review on calcium supplementation in pregnant women at the community level. Other studies, however, noted a nonsignificant difference in serum levels of calcium in preeclampsia compared to normotensive pregnant women.<sup>19,27–29</sup> In a prospective study, Levine et al<sup>30</sup> also observed that calcium supplementation during pregnancy does not prevent the development of preeclampsia in healthy nulliparous women.

The serum calcium and magnesium picture in preeclampsia remains uncertain. We therefore sought to compare serum total calcium and magnesium levels of preeclamptic and normal pregnant women at the Korle-Bu Teaching Hospital in Ghana.

## Patients and methods

### Study design

A comparative cross-sectional study was undertaken from March to June 2016 at the Korle-Bu Teaching Hospital, Ghana.

### Study site

The Korle-Bu Teaching Hospital is the largest tertiary referral hospital in Ghana with 17 clinical and diagnostic departments and a total bed capacity of 2,000, out of which 350 are in the Department of Gynaecology and Obstetrics. The hospital has a daily outpatient attendance of ~1,500 patients, out of

whom ~100 are antenatal patients. About 10,000 to 12,000 deliveries are conducted per year at the hospital.

### Study population

All normal pregnant and preeclamptic women with gestations >30 weeks and aged between 18 and 35 years inclusive, visiting the antenatal clinic at the Department of Obstetrics and Gynaecology, constituted the target population, except pregnant women with renal disorders, chronic hypertension, gestational or preexisting diabetes mellitus, and those on magnesium and/or calcium therapy. Preeclampsia was diagnosed using a systolic blood pressure  $\geq 140$  mmHg and a diastolic blood pressure  $\geq 90$  mmHg plus a random urine sample proteinuria  $\geq 1+$  on dipstick.<sup>31</sup>

### Sample size and recruitment

The sample size was determined based on a formula by Charan and Biswas<sup>32</sup> considering a mean serum magnesium level of 0.58 mmol/L in preeclamptic women compared to 0.73 mmol/L in normal pregnant women<sup>33</sup> at a power of 80% and a 5% significance level.

Sixty pregnant women comprising 30 normal pregnant and 30 preeclamptic women with >30 weeks of gestation and between the ages of 18 and 35 years inclusive, who met the inclusion criteria were recruited consecutively and included in the study after obtaining written informed consent.

### Procedures

After obtaining an informed consent, participants' demographic characteristics (age, weight and height) were recorded on a structured data collection sheet. The blood pressure of the participants was measured using a mercury sphygmomanometer, twice in each participant 20 minutes apart and averaged, noting the systolic and diastolic blood pressures, from which the mean arterial pressure was calculated using the following formula:

$$\text{Mean arterial pressure} = \text{Diastolic blood pressure} + \frac{1}{3} (\text{Pulse pressure}) \quad (1)$$

where Pulse pressure = systolic blood pressure – diastolic blood pressure

Using a 5 mL syringe on a 19G hypodermic needle, 4 mL of venous blood was obtained from participants' cubital vein under aseptic conditions. For most serum ions, samples are to be separated within 2 hours as recommended by the Clinical and Laboratory Standards Institute.<sup>34</sup> Blood samples drawn were immediately placed in a plain test tube and sent to the laboratory for analysis. At the laboratory, the blood samples

were centrifuged at 4,000 rpm for ~10 minutes to obtain the serum within 2 hours of sample collection, and subsequently stored at  $-20^{\circ}\text{C}$  prior to analysis within 24 hours of sample collection. Serum magnesium and total serum calcium were determined using an atomic absorption spectrometer in an acetylene–air flame (Variant 240FS; Varian Australia Pty Ltd, VIC, Australia) with reference ranges of 0.74–1.03 mmol/L and 2.12–2.62 mmol/L, respectively.

## Statistical analysis

Data obtained were stored in Microsoft® Access database 2010 and analyzed with SPSS® software version 20. The age, parity, body mass index (BMI), systolic blood pressure, diastolic blood pressure and mean arterial pressure of the participants are presented as mean values  $\pm$  SDs. The mean serum magnesium and total calcium levels of normal pregnant women and preeclamptic women were compared using an independent *t*-test and are presented in a bar chart. Pearson correlation coefficient was used to determine the association between mean arterial pressure and serum calcium and magnesium levels. A *p*-value  $<0.05$  was considered statistically significant.

## Ethical issues

The Ethical and Protocol Review Committee of the University of Ghana School of Medicine and Dentistry, which is affiliated to the Korle-Bu Teaching Hospital approved the study (protocol identification number: CHS-Et/M.4-P4.5/2015-2016).

## Results

Thirty normal pregnant and 30 preeclamptic women with  $>30$  weeks of gestation and between the ages of 18 and 35 years were recruited into the study. Table 1 summarizes the characteristics of the pregnant women recruited. In this study, the mean arterial pressure ( $p<0.001$ ), systolic blood pressure ( $p<0.001$ ) and diastolic blood pressure ( $p<0.001$ )

of preeclamptic women were significantly higher compared to normal pregnant women.

## Mean serum magnesium levels of the study participants

There was no significant difference ( $p=0.092$ ) in the mean serum magnesium levels between preeclamptic ( $0.70\pm 0.15$  mmol/L) and normal pregnant women ( $0.76\pm 0.14$  mmol/L), as shown in Figure 1.

A nonsignificant weak negative correlation was found between mean arterial pressure and serum magnesium levels in preeclamptic women (Pearson correlation coefficient  $r=-0.089$ ;  $p=0.639$ ), as shown in Figure 2.

## Mean total serum calcium levels of the study participants

There was no statistically significant difference ( $p=0.972$ ) in the mean total serum calcium levels between preeclamptic ( $2.13\pm 0.30$  mmol/L) and normal pregnant women ( $2.13\pm 0.35$  mmol/L), as shown in Figure 3.

A nonsignificant weak positive correlation was found between mean arterial pressure and serum total calcium levels in preeclamptic women (Pearson correlation coefficient  $r=0.047$ ;  $p=0.806$ ), as shown in Figure 4.

There was a nonsignificant negative correlation between serum total calcium and serum magnesium levels in preeclamptic women (Pearson correlation coefficient  $r=-0.328$ ;  $p=0.077$ ), as shown in Figure 5.

## Discussion

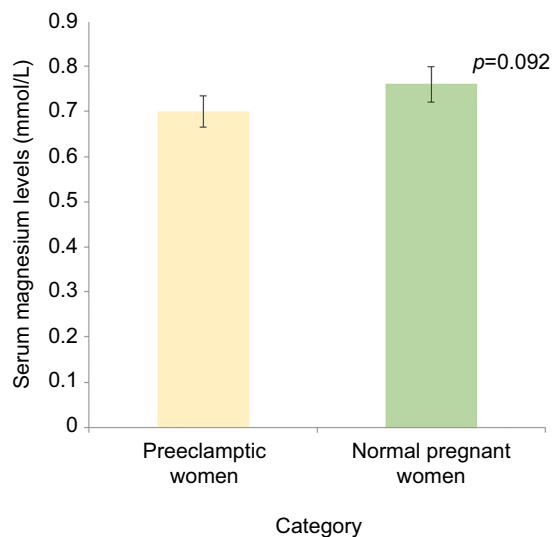
Similar to the findings in other studies,<sup>35,36</sup> our study showed no statistically significant relationship between maternal age and preeclampsia ( $p=0.358$ ). However, this contrasts with the results of the study by Macdonald-Wallis et al,<sup>37</sup> which was a very large longitudinal cohort study with a sample size of ~11,651 women living in a higher income region (Avon,

**Table 1** Summary of participants' characteristics

| Parameter              | Preeclamptic women    | Normal pregnant women | <i>p</i> -value |
|------------------------|-----------------------|-----------------------|-----------------|
|                        | Mean $\pm$ SD<br>n=30 | Mean $\pm$ SD<br>n=30 |                 |
| Age, years             | 30.97 $\pm$ 5.51      | 29.93 $\pm$ 2.60      | 0.358           |
| Parity                 | 1.70 $\pm$ 1.42       | 1.13 $\pm$ 1.41       | 0.567           |
| BMI, kg/m <sup>2</sup> | 32.03 $\pm$ 7.52      | 30.50 $\pm$ 5.50      | 0.374           |
| SBP, mmHg              | 170.13 $\pm$ 23.69    | 116.47 $\pm$ 13.38    | 0.000*          |
| DBP, mmHg              | 106.30 $\pm$ 18.79    | 67.57 $\pm$ 8.54      | 0.000*          |
| MAP, mmHg              | 126.20 $\pm$ 20.86    | 83.87 $\pm$ 8.85      | 0.000*          |

**Note:** \*Significant at  $p<0.05$ .

**Abbreviations:** BMI, body mass index; DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.



**Figure 1** Mean serum magnesium levels of preeclamptic and normal pregnant women.

England), as compared to our sample population. Additionally, they considered the number of fetuses and the sex of the fetuses being carried by the women, as well as the educational status of the women, factors we did not consider in our study. Therefore, differences in the study design and the characteristics of the patient population studied may possibly account for the differences in the results.

We also noted a nonsignificant relation between preeclampsia and BMI ( $p=0.374$ ), as noted by Onyegbule et al,<sup>38</sup> even though other studies have shown a strong association between BMI and preeclampsia.<sup>39–41</sup> The findings of Poorolajal and Jenabi<sup>39</sup> were derived from a meta-analysis, while ours is a case–control cross-sectional study, and this may therefore account for the differences in results. In contrast to our study, Hauger et al<sup>41</sup> conducted a large-sample-size multicenter study with possible confounding factors such

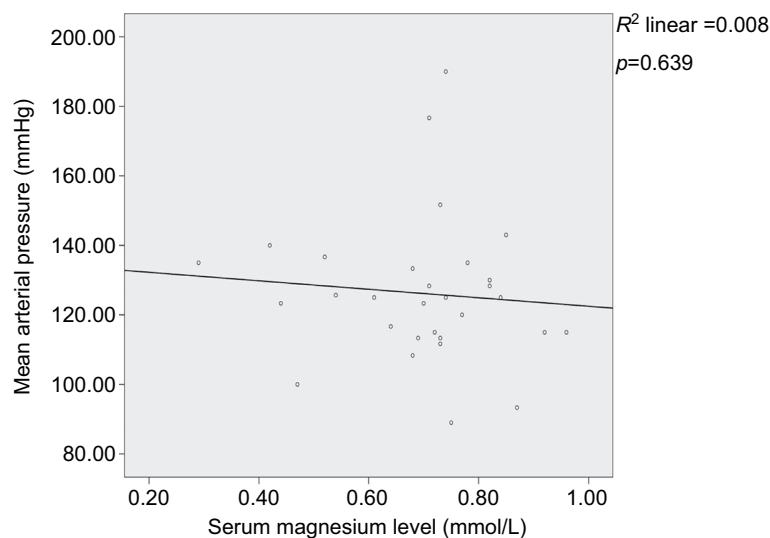
as inclusion of women with known diabetes, known chronic hypertension and gestational diabetes. The BMI calculation in their study was also based on self-reported recall information of prepregnancy weight and therefore there is a possibility of information bias. There also could be differences in the diet of the studied population. These factors may account for the differences in their findings compared to ours.

The blood pressures (mean systolic, mean diastolic and mean arterial pressures) of the preeclamptic women were significantly elevated compared to the normal pregnant women ( $p<0.001$ ), as expected per the case definition. Mean arterial pressure has been observed to be predictive of preeclampsia, even though other studies have reported otherwise.<sup>42</sup>

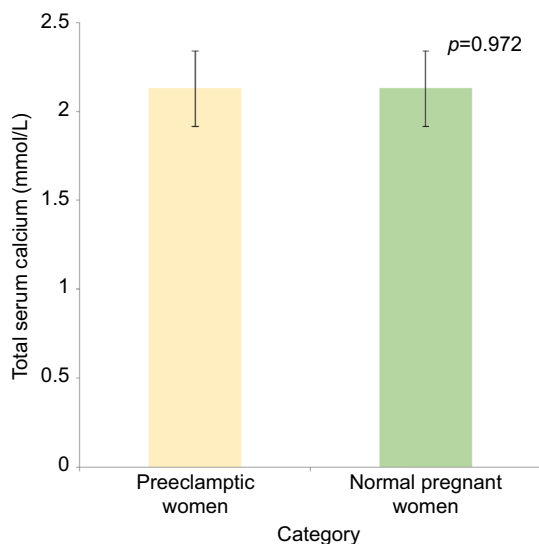
Magnesium and calcium are important cofactors for various enzymatic processes and water balance in cells.<sup>43</sup> These trace elements play an essential role in vascular smooth muscle tone and contraction, and hence they are vital in blood pressure regulation.<sup>44</sup>

Various studies have reported a decrease in serum magnesium levels as a possible etiology of preeclampsia.<sup>13,14,16–18</sup> This evidence is supported by the usefulness of magnesium sulfate therapy for prophylaxis and treatment of seizures associated with preeclampsia/eclampsia.<sup>45</sup> However, this view is not universally accepted, as a Cochrane review involving 2,689 women from seven selected randomized and quasi-randomized trials found no high-quality evidence to support the beneficial effect of dietary magnesium supplementation in preventing the development of preeclampsia in pregnant women.<sup>46</sup>

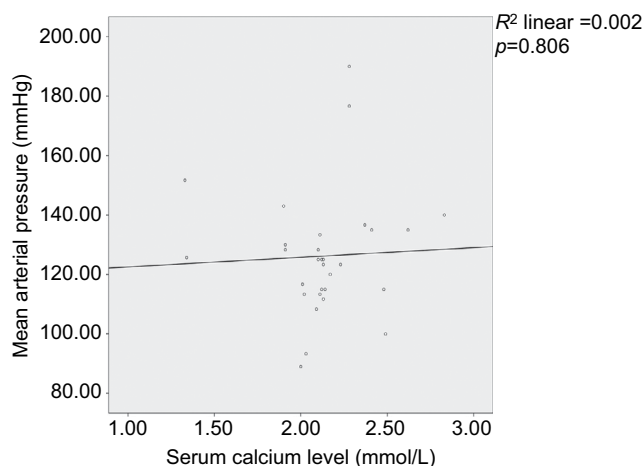
Dietary deficiency of calcium, with consequent reduced serum calcium levels, has been implicated as a cause of preeclampsia in some studies.<sup>18,25,26,47,48</sup> This has been explained



**Figure 2** Correlation between serum magnesium levels and mean arterial pressure in preeclamptic women.



**Figure 3** Mean total serum calcium levels of preeclamptic and normal pregnant women. **Note:** Error bars indicate the confidence interval of the mean of serum calcium levels.



**Figure 4** Correlation between total serum calcium levels and mean arterial pressure in preeclamptic women.

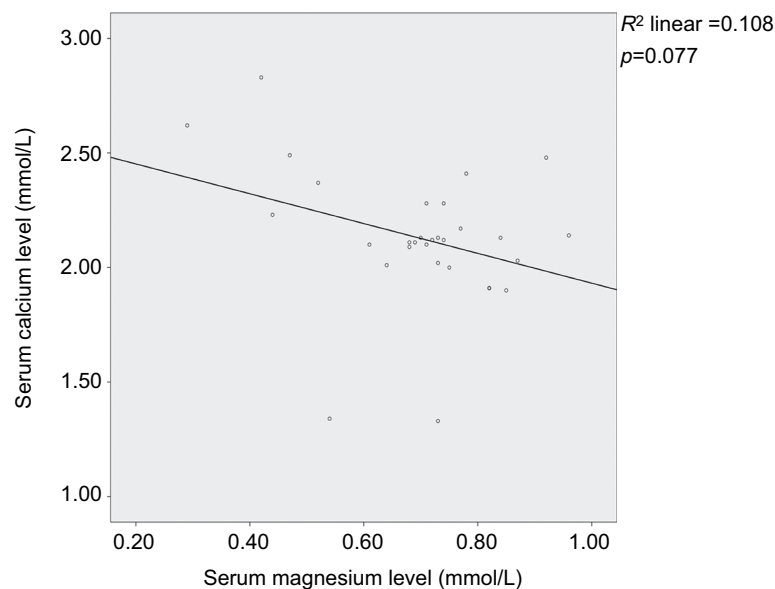
by the vasoconstrictive effect caused by reduced serum calcium levels.<sup>1,20–24</sup> Stimulation of 1,25-dihydroxycholecalciferol has been implicated in this vasoconstrictive mechanism.<sup>18</sup> This concept of a reduced serum calcium level in preeclampsia is not accepted universally.<sup>19,27,29,30,49</sup> This is because other studies in preeclamptic women have noted relatively reduced 1,25-dihydroxycholecalciferol levels compared to normal pregnant women,<sup>50</sup> with consequent increase in parathyroid hormone levels,<sup>1,20</sup> causing reabsorption of calcium from the distal renal tubules and the intestines<sup>51–53</sup> and therefore causing no significant change in the serum calcium levels. Parathyroid hormone also causes renin release with subsequent vasoconstriction and sodium retention in preeclamptic women.<sup>54</sup>

Therefore, hypomagnesemia and hypocalcemia as etio-pathologic factors in the development of preeclampsia are not

a universal finding in literature.<sup>1,20,21,55</sup> Various studies from different regions worldwide have reported varying results concerning the role of these trace elements in the etiology of preeclampsia.<sup>17,18,56,57</sup> In this study, we observed no statistically significant difference in mean total serum calcium and magnesium levels of preeclamptic women compared to normal pregnant women ( $p=0.092$ ), as found in a study by Magri et al.<sup>57</sup> Similar studies conducted, including those done in sub-Saharan Africa using the same method of assay (atomic absorption spectrophotometry), in determining serum calcium and magnesium levels also show varying results.<sup>38,58,59</sup> Ugwuja et al.,<sup>58</sup> in a study conducted among Nigerian women using atomic absorption spectrophotometry for assaying serum calcium and magnesium, found no significant difference in serum calcium but significantly reduced serum magnesium in preeclamptic women as compared to normal pregnant women. Another study conducted among Sudanese women using atomic absorption spectrophotometry for assaying serum calcium and magnesium found a decreased serum calcium level and an increased serum magnesium level<sup>59</sup> in preeclamptic women as compared to normal pregnant women. These studies, including ours, were conducted in sub-Saharan Africa using the same method of assay for both ions, but the findings were different.

It is therefore possible that the differences in the findings may be attributed to not only differences in the method of assay of serum ions but also differences in dietary habits, genetic pools, as well as the social and economic lifestyle factors of the populations studied. The dietary history and socioeconomic status of the participants in this study were, however, not elucidated. Additionally, differences in sample size may also account for the observed differences in findings.

A nonsignificant negative correlation was observed between serum total calcium and serum magnesium levels in preeclamptic women (Pearson correlation coefficient  $r=-0.328$ ;  $p=0.077$ ) in contrast to the findings of Ephraim et al.,<sup>60</sup> who noted a nonsignificant positive correlation between serum calcium and serum magnesium levels. A nonsignificant weak negative correlation was observed between mean arterial pressure and serum magnesium levels in preeclamptic women (Pearson correlation coefficient  $r=-0.089$ ;  $p=0.639$ ). A nonsignificant weak positive correlation was observed between mean arterial pressure and serum total calcium levels in preeclamptic women (Pearson correlation coefficient  $r=0.047$ ;  $p=0.806$ ). Therefore, total serum calcium and serum magnesium may be weak predictors of mean arterial pressure in preeclamptic women.



**Figure 5** Correlation between serum magnesium levels and total serum calcium levels in preeclamptic women.

## Conclusion

There was no significant difference in the mean serum levels of magnesium and total calcium between preeclamptic and normal pregnant women.

Total serum magnesium and calcium therefore seem not to differ in preeclamptic women in comparison with normal pregnant Ghanaian women.

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## Disclosure

The authors report no conflicts of interest in this work.

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