TO THE EDITOR: Drs. Lundberg, Larsen, and Weitzberg’s (9a) comments provide useful information on the potential dangers of uncontrolled uses of nitrates and nitrites. It is important to remember that with most substances that are taken with the express purpose of affecting the structure or function of the body, the dosage and formulation often determine if the effects are beneficial or detrimental. Inorganic nitrate and nitrite can both be classified as either a drug or a food depending on how they are administered. It is also clear that our understanding of both is evolving rapidly. There are currently several published reviews of this topic (2, 4–6, 8, 12).

We understand that nitrate, when consumed, is easily absorbed into the plasma, concentrated in salivary glands (10), reduced to nitrite by symbiotic oral bacteria (9, 11), swallowed and absorbed into the blood. Increased plasma nitrite is capable, under the correct conditions, of producing nitric oxide and nitrosothiols and has been shown to produce a variety of beneficial effects for both athletic performance and vascular health in humans (outlined in the accompanying letter, Ref. 9a). What we are somewhat unsure of is nitrate consumption as a cause of methemoglobinemia (1, 3) and/or the formation of N-nitrosoamines in the stomach (4, 12–14) and the subsequent (albeit weak) association with an increased incidence of cancer (4, 12).

For populations with cardiovascular disease (CVD) such as peripheral arterial disease [in our original article (7)], the issue may be more complicated. This population may receive a greater benefit from supplementation of plasma nitrite to possibly replenish reduced endothelial production of nitric oxide. In fact, diets high in nitrate are associated with reduced blood pressures and decreased incidence of CVD (2, 4). Unfortunately, concomitant conditions or medications in this population may require more careful administration. For example, it may be problematic to consume doses of nitrite in conjunction with PDE-5 inhibitors (Viagra, Cialis), organic nitrates, or xanthine oxidase inhibitors (Allopurinol). In our study, we excluded any PAD subject with a history of renal insufficiency due to the high concentrations of potassium and phosphorus (1.697 and 170 mg, respectively) in beetroot juice.

Overall the current balance of evidence would suggest that for moderate increases in nitrite in our circulation, the health benefits outweigh the risks. The issue at hand is optimal dosage and method of administration. We currently do not know if it is better to increase nitrite intake directly provided it is precisely controlled, or if it is better to consume products and foods high in inorganic nitrate and let our bodies control the conversion rate to nitrite (which may vary by individual). Optimal amounts, methods of consumption, and indications for use will likely become clearer with time and study. In the mean time it is better to err on the side of caution and we advise anyone with risk factors for or diagnosed CVD to consult with their physician before consuming nitrate or nitrite supplements. However, we are in agreement with Dr Lundberg et al. that consuming a good amount of whole vegetables and vegetable juices is probably good for you!

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author.

REFERENCES