and *as it should be*. This is a conceptual error. Inferior vena cava filters are supposed to capture embolized clots, decreasing symptomatic PEs, and collect thrombus on the inferior side of the filter, where intrinsic antithrombotic mechanisms should dissolve it. These captured clots should appear in neither the DVT nor PE totals and should constitute net benefit. Thus, if IVC filters are working as intended, DVTs (unembolized clots) should be *unchanged*, PEs should be *diminished*, and total venous thromboembolisms (VTEs) should be *reduced*. The increase in DVTs suggests the prothrombotic effect of IVC filters.

Second, Dr Hoffer[1] notes that we discount the reduction in "symptomatic" PE in the Prevention du Risque d'Embolie Pulmonaire par Interruption Cave (PREPIC) study.[2,3] We do for 2 reasons. First, that the reduction in PE does not translate into any improvement in mortality, and second, PEs in the PREPIC study were not solely clots causing symptoms, but also clots elicited by annual telephone interviews and imaging. It is hard to know what to do with these "screened" PEs, since it is clear that the more you scan, the more incidental clots can be found.

There is no doubt that IVC filters increase DVTs. The PREPIC study, a randomized trial, demonstrates a consistent surplus of DVTs. At 2 years,[2] there were 16 more DVTs in the filter group (37 vs 21). At 8 years, this surplus persists (57 vs 41), though, as half the population had died, the true increased risk of DVT may not be fully captured.[3] Finally, population data repeatedly confirms the increased risk of DVT.[4]

Third, Dr Hoffer[1] cites 2 studies supporting the IVC filter. Neither is adequate. Stein et al,[5] in an inpatient data set, found that among the 3.4% of patients with PE who were unstable (*International Classification of Diseases, Ninth Revision* codes for shock or ventilator use), those who received filters did better than those who did not. The authors made no attempt to correct for baseline differences between these groups. Thus, the more plausible interpretation of their data is that in an era where filter use was widespread, unstable patients with PE, whom physicians elected not to place a filter, were sicker.

The study by Spencer et al[4] is an observational study, from which drawing conclusions regarding benefits is tenuous, though such studies are better at assessing harms. The highlighted difference in PE is likely due to ascertainment bias, since physicians were less likely to scan patients with a known filter. However, if Dr Hoffer[1] believes the reduction in PE is real, does he also believe the 20% increase in all-cause mortality among filter users? Interestingly, Dr Hoffer ignores the increased risk of DVT with IVC filters in this study.[4]

In summary, there remains no good evidence for the benefits of the filter and only clear documentation of harm.

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Disclaimer: The views and opinions of Dr Prasad do not necessarily reflect those of the National Cancer Institute or National Institutes of Health.

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Exercise, Cardiac Rehabilitation, and Post–Acute Coronary Syndrome Depression

To the Editor We congratulate Davidson and colleagues[1] for their randomized clinical trial demonstrating that, compared with usual care controls, an active depression treatment program involving problem solving therapy and/or pharmacotherapy resulted in greater reductions in depressive symptoms in depressed patients with post-acute coronary syndrome (ACS). This work is important in demonstrating that meaningful improvements in depression can be achieved with traditional mental health interventions. However, we were surprised that the potential value of exercise training (ET) in the routine management of depressed patients with ACS was not mentioned.

A high prevalence of adverse behavioral characteristics, including depression, has been observed in patients with coronary heart disease (CHD), particularly post-ACS, with marked benefits in these behaviors following ET-based cardiac rehabilitation (CR).[2,3] In fact, younger patients with CHD (age <55 years) had 50% to 80% reductions in the prevalence of depression, anxiety, and hostility following CR, and older patients had 30% to 70% improvements in the prevalence of these factors.[2] In addition, patients with CHD with symptoms of depression who attend CR have nearly 70% reductions in 3-year mortality compared with those who did not attend CR, and only relatively modest improvements in cardiorespiratory fitness were needed to reduce depressive symptoms and improve depression-related mortality risk.[3] A recent single-site randomized clinical trial demonstrated that ET alone was associated with significant reductions in depressive symptoms and improved CHD biomarkers in patients with stable CHD and elevated depressive symptoms; reduced levels of depression were comparable to antidepressant medications, and both ET and medication use achieved greater reductions in depression compared with placebo.[4] In addition, results from the multisite Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) trial demonstrated

that ET resulted in larger reductions in depressive symptoms relative to usual care in patients with heart failure.[5]

Although referral of patients with ACS to CR programs is recommended by a wide range of organizations, including the American College of Cardiology and the American Heart Association, these programs are significantly underutilized, with less than 20% of eligible patients participating in CR. While cost and accessibility may discourage referrals, the value of ET-based CR remains underrecognized and underappreciated. There now is compelling evidence that ET, especially in the context of CR, should be incorporated routinely in the secondary prevention of CHD, particularly in patients with post-ACS with symptoms of depression.

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In Reply We thank Lavie and colleagues for their interest in the results of our recently published Comparison of Depression Interventions After Acute Coronary Syndrome (CODIACS) Vanguard trial,[1] which showed that depressed patients with acute coronary syndrome (ACS) randomized to centralized, stepped, patient-preference depression treatment (psychotherapy or medication use) had substantially fewer depressive symptoms after 6 months compared with those receiving enhanced usual care. We also demonstrated that we could deliver this depression treatment by telephone and/or by webcast across a number of different health care settings in geographically diverse areas. These elements will be vital design components of a future phase 3 trial of depression treatment for patients with ACS.

We agree with Lavie and colleagues that exercise can be useful as a primary or adjunctive treatment for depression in patients with ACS. Indeed, Lavie and colleagues have been leaders in studying exercise as a treatment for depression, and they are to be commended for their rigorous work in this area.[2,3] Moreover, a recent Cochrane systematic review of randomized clinical trials in a variety of patient groups showed that exercise programs are superior to no treatment or to placebo control conditions for treating depression.[4] Nevertheless, we also agree with Lavie and colleagues that more randomized clinical trials of exercise as a treatment for depression after ACS are needed.

We did not discuss exercise training in the context of the CODIACS Vanguard trial for several reasons. First, we enrolled patients with elevated depressive symptoms 2 to 6 months after their ACS, a period when cardiac rehabilitation, which includes exercise, has already been offered. Second, we were focused on evaluating a comprehensive depression treatment that could be delivered in diverse settings, easily, and at modest cost, and that had previously been found highly acceptable to post-ACS patients, thus making it readily adoptable for subsequent testing in a large, multicenter clinical trial.

To our knowledge, there have not been any cost-effectiveness analyses of exercise for treating depression. The Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) trial, which the letter by Lavie and colleagues referred to, offered supervised exercise along with intensive education and support and then provided a home treadmill, all without charge to either the health care system or the patient.[5] Despite these multiple and costly facilitators of continuing exercise engagement for patients with heart failure, adherence to exercise was marginal; at 1 year, only 38% of patients in the exercise group were fully adherent.[6] Furthermore, as noted by the letter authors, cardiac rehabilitation, which has exercise as a core component, is used by less than 20% of eligible post-ACS patients. For these reasons, we did not include exercise as one of the treatments offered in our study. Different patients respond to different depression treatments, so clinicians must be prepared to offer a variety of evidence-based treatments for depression after ACS. Exercise training is indeed a promising candidate, as is the depression treatment approach tested in the CODIACS Vanguard trial.

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Phenytoin Toxicity Unlikely to Result in Arrhythmias

To the Editor We read with interest the Challenges in Clinical Electrocardiography case by Johnson et al[1] discussing a wide QRS following liver transplant. The authors concluded that this was a wide complex tachycardia related to fluconazole and phenytoin toxicity. However, we disagree with the assertion that the phenytoin contributed to this patient's arrhythmia. The clinical course and electrocardiogram are not consistent with phenytoin toxicity. Intravenous phenytoin has been known to produce cardiovascular collapse when administered too quickly; however, this is thought to be related to toxicity from its diluent propylene glycol. In these cases, patients developed hypotension and bradyarrhythmias.[2] Similarly, fosphenytoin use has been described as resulting in hypotension, bradyarrhythmias and asystole.[3] To our knowledge, wide complex tachycardias have not been described. Two previous studies of phenytoin toxicity (with levels as high as 76 µg/mL) did not report any wide complex tachycardias or prolongation of the QRS or QT intervals.[4,5] Although phenytoin is a Vaughn-Williams Class 1B antiarrhythmic, it displays quick on-off kinetics at the sodium channel, thus making it less arrhythmogenic when compared with agents with slow on-off kinetics such as the class IC agents. Furthermore, the authors state that "the free fraction of phenytoin may have been considerably higher"[1(p955)] but report a corrected phenytoin concentration of 26 µg/mL. This correction estimates the free (pharmacologically active) phenytoin concentration after adjusting it for the serum albumin concentration. The level reported is only slightly above the therapeutic range. Thus, we believe that phenytoin was unlikely responsible for producing this arrhythmia. The exact etiology for the arrhythmias is not apparent. This was a complex patient with multiple medical problems and complications. Seizures, however, have also been known to produce numerous arrhythmias. The follow up electrocardiogram provided appears to demonstrate a prolonged QT interval. Although the initial arrhythmia was not characteristic of torsades de pointes, it is possible that fluconazole (or a number of other medications) or comorbidities could have produced an arrhythmia. Monomorphic wide complex tachycardia related to fluconazole has not been described but is an intriguing thought, given that the patient improved with dialysis. Neither phenytoin nor tacrolimus have pharmacokinetics that would make them amenable to hemodialysis. Thus, even though phenytoin is classified as both an anticonvulsant and an antiarrhythmic, its sodium channel kinetics and various studies over several decades have shown that phenytoin (parent compound) is unlikely to produce cardiac arrhythmias even in the setting of severe toxicity.

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In Reply We appreciate the comments provided by Algren and Christian, who contend that phenytoin did not contribute to our presented clinical findings.[1]

We disagree and are certain that phenytoin use was a major contributor. The classic findings of high-dose, rapid phenytoin administration that they describe are inapplicable to our patient, who was a complex patient with recent liver transplant, status epilepticus, and renal failure, in whom polypharmacy resulted in the electrocardiographic (ECG) changes.

For example, although bradyarrhythmias have been reported with phenytoin toxicity, this patient was also receiving dopamine. Second, although our patient's clinical course did include hypotension, we chose not to speculate about causality from phenytoin in a patient with other potential causes including infection.

The patient most likely had sinus tachycardia. The prolongation of the QRS duration was caused by derangement of ventricular depolarization and repolarization of the heart due to polypharmacy, including the use of high doses of intravenous phenytoin. Although Algren and Christian cite 2 older articles[2,3] that contend that phenytoin overdose does not cause QRS and QT prolongation, both articles refer specifically to oral, not intravenous, overdose. For a variety of reasons, the effect of an antiarrhythmic agent administered intravenously may not be the same as the effect of a drug given orally, even if serum levels are comparable.[4] In addi-