ing information about baseline functional status and skeletal-muscle mass is important when addressing ICU-acquired weakness. Previous medical records, a physical examination, and discussions with family members can help to identify patients who are likely to have preexisting sarcopenia.

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Treating Our "Situations" with Science, Not Shame

TO THE EDITOR: I agree with Record's assertion, in her Perspective article in the April 24 issue,[1] that we need to strengthen the ability of our health system to care for patients with mental health disorders. However, she has unfairly targeted primary care physicians (PCPs) as the problem. In fact, much of our practice and training is focused on diagnosing and treating patients with mental health conditions such as depression. Our ability to care for these patients is usually not limited by an absence of knowledge or evidence-based screening tests,[2] but rather by a lack of systems that enable us to carefully manage the care of these patients and by insufficient access to experts to assist in managing the care of patients with the most severe symptoms.

New advances in primary care, such as the patient-centered medical home, are enabling primary care practices to integrate mental health workers and population managers to monitor our patients over time.[3] We should work together to increase the resources available to primary care practices so that we can do the work for which we train, caring for both the physical and psychological health of our patients.

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THE AUTHOR REPLIES: Phillips accurately emphasizes the systemic barriers that patients face in obtaining comprehensive treatment in our current health care system. As he eloquently agrees, increased collaboration is critical to allow PCPs to address both physical and psychological health. PCPs are certainly not the only part of the problem; we must all do more — legislators, scientists, psychiatrists, and attorneys, to name a few, share the burden of increasing access to comprehensive and effective mental health care. However, the idea that depression is the archetypal mental illness is emblematic of deep-rooted biases against psychological health. I hope that one day all PCPs — not just a few — will be comfortable discussing the broad range of mental illnesses and treatment options, so that when the system is improved to facilitate more timely referrals and better access to care, they will be able to identify all patients in need, regardless of the root of the disease.

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Safety Profile of Extended-Release Niacin in the AIM-HIGH Trial

TO THE EDITOR: The results of the Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) trial were published in the *Journal* in 2011.[1] This study showed no incremental clinical benefit from the addition

Table 1. Serious Adverse Events.*

MedDRA System Organ Class	Extended-Release Niacin plus Statin (N=1718)	Placebo plus Statin (N=1696)	P Value
	no. (%)		
Any adverse event	587 (34.2)	551 (32.5)	0.30
Blood and lymphatic system disorders	24 (1.4)	18 (1.1)	0.37
Cardiac disorders†	175 (10.2)	190 (11.2)	0.34
Gastrointestinal disorders	127 (7.4)	93 (5.5)	0.02
Abdominal pain	22 (1.3)	10 (0.6)	0.04
Gastroesophageal reflux disease	0	5 (0.3)	0.03
Rectal hemorrhage	11 (0.6)	3 (0.2)	0.06
Vomiting	20 (1.2)	9 (0.5)	0.04
General disorders and administration-site conditions	58 (3.4)	56 (3.3)	0.90
Hemorrhagic events‡	59 (3.4)	49 (2.9)	0.36
Hepatobiliary disorders	24 (1.4)	17 (1.0)	0.29
Infections and infestations	139 (8.1)	98 (5.8)	0.008
Appendicitis	8 (0.5)	1 (0.1)	0.04
Bronchitis	7 (0.4)	1 (0.1)	0.07
Cellulitis	26 (1.5)	13 (0.8)	0.04
Injury, poisoning, and procedural complications	55 (3.2)	50 (2.9)	0.67
Clinical investigations	23 (1.3)	16 (0.9)	0.28
Metabolic and nutrition disorders	39 (2.3)	28 (1.7)	0.19
Musculoskeletal and connective-tissue disorders	78 (4.5)	91 (5.4)	0.27
Neoplasms benign, malignant, and unspecified, including cysts and polyps	72 (4.2)	73 (4.3)	0.87
Non–small-cell lung cancer	0	4 (0.2)	0.06
Nervous system disorders	63 (3.7)	70 (4.1)	0.49
Paresthesia	0	5 (0.3)	0.03
Psychiatric disorders	26 (1.5)	21 (1.2)	0.49
Renal and urinary disorders	44 (2.6)	46 (2.7)	0.78
Reproductive system and breast disorders	9 (0.5)	5 (0.3)	0.42
Respiratory, thoracic, and mediastinal disorders	51 (3.0)	49 (2.9)	0.89
Skin and subcutaneous-tissue disorders	10 (0.6)	16 (0.9)	0.23
Surgical and medical procedures	6 (0.3)	5 (0.3)	0.78
Vascular disorders	59 (3.4)	62 (3.7)	0.73

* Adverse events are listed according to the system organ classes and the preferred terms in the *Medical Dictionary for Regulatory Activities* (MedDRA), version 15.0. All system organ class categories are listed for which at least five events were recorded in either trial group. For any system organ class category in which a significant between-group difference was detected, individual preferred terms are listed; these terms are restricted to those with a P value of less than 0.10 for the between-group difference.

† This category does not include efficacy end points as defined in the protocol.

‡ This category was identified by means of the standardized MedDRA query for hemorrhagic adverse events.

of high-dose extended-release niacin (Niaspan, AbbVie) to statin therapy during a 36-month mean follow-up period in 3414 patients who had stable atherosclerotic disease, low baseline levels of high-density lipoprotein (HDL) cholesterol, and elevated triglyceride levels. In that article, we provided data on adverse events resulting in a reduction in the dose or discontinuation of the study drug. These results were largely consistent with the previously established side-effect profile of niacin (e.g., itching, flushing, gastrointestinal symptoms, and increased blood glucose levels). Less common adverse events, including abnormal liver-function tests and myopathy, were also reported.

Because of an excess in certain serious adverse events observed in the Heart Protection Study 2: Treatment of HDL to Reduce the Inci-

dence of Vascular Events (HPS2-THRIVE),[2,3] including unanticipated increases in infections and bleeding, there has been interest in whether similar patterns of serious adverse events were observed in the AIM-HIGH trial.[4] It is important to note that in HPS2-THRIVE, a different study drug (Tredaptive, Merck), a proprietary extended-release niacin preparation combined with laropiprant, a prostaglandin D_2 receptor-1 antagonist, was used to retard cutaneous flushing. Here we describe the rates of serious adverse events in the AIM-HIGH trial. Additional information regarding all adverse events (including both serious and nonserious adverse events) is provided in the Supplementary Appendix (available with the full text of this letter at NEJM.org).

All serious adverse events were recorded on standard case-report forms. Terms were coded with the use of the *Medical Dictionary for Regulatory Activities* (MedDRA), version 15.0, and classified according to the System Organ Class categorization and MedDRA preferred term. A standardized MedDRA query[5] was used to identify serious hemorrhagic adverse events.

Overall, 34.2% of patients who received extended-release niacin and 32.5% of patients who received placebo had serious adverse events during follow-up (P=0.30). There were significant between-group differences in the numbers of serious adverse events in the System Organ Class categories of gastrointestinal disorders (7.4% vs. 5.5%, P=0.02) and infections and infestations (8.1% vs. 5.8%, P=0.008). The overall observed rate of serious hemorrhagic adverse events was low, with no significant difference between the two groups in the trial (3.4% vs. 2.9%, P=0.36) (Table 1).

Although the full list of serious adverse events suggests certain similarities with the data from HPS2-THRIVE, particularly regarding serious adverse infectious events, the nonsignificant numerical excess in adverse bleeding events with niacin cannot be considered definitive. Accordingly, there are compelling reasons to interpret these data with caution. The data, and the relevant considerations, are discussed in the Supplementary Appendix.

In summary, in the AIM-HIGH trial, treatment with extended-release niacin was associated with significantly increased rates of certain serious adverse events, as well as increased rates of dose reductions or drug discontinuation related in most cases to known side effects of niacin. Examination of the entire record of all adverse events suggests other possible side effects of this proprietary extended-release formulation. The findings concerning certain serious adverse infectious events associated with niacin have not been previously reported. However, lacking additional clinical and scientific confirmation, we believe that they should be considered to be provisional and exploratory.

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