operating on one Medicaid patient every 1 to 2 weeks.

The model for a 5% commitment proposal could come from the Choosing Wisely campaign, an initiative of the American Board of Internal Medicine (ABIM) Foundation. To date, 54 specialty societies participating in this campaign have released lists of more than 150 potentially unnecessary tests and treatments that physicians may want to avoid except in unusual clinical circumstances. Perhaps the ABIM Foundation and other specialty societies could consider making the case for caring for Medicaid patients and asking their members to voluntarily commit to accepting a minimum of 5% (or even 3%?) of Medicaid patients into their practices.

We live in an era in which, for better or for worse, market-based solutions are dominant and policymakers tend to view physicians as self-interested actors. Little or no attention is paid to physician professionalism or to the possible effects of policies on professionalism. Policies that are based on this view may be justifiable if many physicians are indeed seeking to maximize their incomes and refusing to accept even a slight reduction in income as the price for helping to provide care to the most vulnerable patients in our society. A 5%-commitment campaign would be a meaningful, highly visible demonstration of physician professionalism — of putting patients first.

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The Word That Shall Not Be Spoken

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During the years when I worked in an academic integrated delivery system, my colleagues and I would frequently discuss patients' experiences and ways to improve our management of their pain and reduce their confusion as they navigated our complex organization. We knew that anxiety is inevitable for patients facing health issues, but we also knew that there is anxiety, and there is *unnecessary* anxiety — caused, for example, by the uncertainty that weighs on patients and their families while they await a consultation for a potentially serious diagnosis, or the confusion induced when clinicians give conflicting information. We worked hard to reduce these problems. From a business perspective, it was a smart strategy; from a clinician's perspective, it was obviously the right thing to do.

So it was a pleasant surprise when I studied the business strategy of a company that assesses patients' experiences and found that it was based on "helping health care providers reduce suffering." This strategic framework divided suffering into three types: suffering from disease (e.g., pain), suffering from treatment (e.g., complications), and suffering induced by dysfunction of the delivery system (e.g., chaos, confusion, delays). The company was recruiting me for a senior management role, and my first reaction was that they were interested in the same things as my colleagues and I were.

My second reaction was that the word "suffering" would take some getting used to. I couldn't remember the last time that my colleagues and I had used that word. "Suffering" made me uncomfortable. I wondered whether it was a tad sensational, a bit too emotional. But on reflection, how could I object to its use? After all, from the perspective of patients, that is what's going on.

I soon learned that my colleagues and I were not the only ones who avoided the word. As a matter of policy, it doesn't often appear in our academic journals or textbooks, at least in reference to particular patients. The widely used *AMA Manual of Style* says, "Avoid describing persons as victims or with other emotional terms that suggest helplessness (afflicted with, suffering from,

stricken with, maimed)."[1] Public health programs can suffer from lack of funding, and human suffering can be considered (and preferably averted) in the abstract, but patients must generally simply "have" a disease or complications or side effects rather than "suffer" or "suffer from" them.

I asked some colleagues why we tiptoe around this term, which captures so completely what patients endure, and I got a range of responses. One theme was that "suffering" was not "actionable" for clinicians, especially physicians. "Suffering" is too heterogeneous, too complicated. Aware of the irony, one colleague pointed out that too much talk about patients' suffering might distract clinicians from doing what they could to relieve it.

Physicians need to analyze patients' problems and address what can be addressed. Thus, there is an ICD-9 (*International Classification of Diseases, Ninth Revision*) code for anxiety (300.0); you can bill for visits under it, and we have pills that help, too. Most hospitals have a pain service (ICD-9 code 338). We have an increasing number of care coordinators, we have palliative care consultation teams, and there are CPT (Current Procedural Terminology) codes under which their work can be reimbursed. I turn to these services for my own patients when my ability to reduce their suffering is exhausted. But there's no obvious referral or reimbursement code for alleviating suffering itself.

A second, darker theme was raised by several colleagues: the word "suffering" makes us feel bad. It reminds us that we are powerless against so many of our patients' problems. And it makes us feel guilty. Suffering demands empathy and response at a level beyond that required by "anxiety," "confusion," or even "pain." None of us see ourselves as people who would stand by while someone is suffering. None of us can imagine ourselves as parts of organizations that tolerate or even inflict suffering in systematic ways.

I hope this doesn't sound sanctimonious; in fact, I hope it sounds coldly clinical. Our diagnosis was that we avoid the word "suffering" even though we know it is real for our patients because the idea of taking responsibility for it overwhelms us as individuals — and we are already overwhelmed by our other duties and obligations.

For some patients with whom we really identify, of course, we will not rest until we have done all we can to alleviate their suffering. We make the extra phone calls, have the extra meetings, and do whatever it takes to make the system work for them. Those extra efforts define our self-perceptions. But we also know that we don't do that, and don't believe we can do that, for all patients. To make alleviation of suffering our job for *all* our patients feels like trying to fill a bottomless pit.

But what about the organizations for which we work? I was relieved to find that alleviation of suffering is part of the mission statement for the medical school where I teach — and in fact relief of suffering is prominent in the commitments of many health care delivery organizations. That seems right to me. Relief of suffering may be a task too vast to seem real for most people — something on the order of achieving "world peace." On the other hand, organizations need goals around which to build their strategies; they need clarity about the direction in which they are trying to go. Good organizations have ambitious goals, what would be considered "shared purpose" in sociologist Max Weber's framework of motives for social action. If an organization has consensus on its overall goal, even if that goal can never be fully achieved, then other incentives (financial and otherwise) can be developed to drive progress in the right direction.[2]

If good organizations have ambitious goals, great organizations are effective in pursuing them. They close the gap between their mission statements and their operations. They find ways to measure what matters and organize themselves to improve their performance. They track and manage their progress toward those goals with the same discipline that they apply to their financial performance.

In truth, I'm less interested in

Relief of suffering may be a task too vast to seem real for most people — something on the order of achieving "world peace" — but organizations need goals around which to build their strategies.

the words we use than in what we actually do, and what we organize ourselves to do. Collectively, we should not shy away from work that can never be completed. For our organizations, relief of suffering does seem like the right goal, endless though the work might be.

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Cancer-Drug Discovery and Cardiovascular Surveillance

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Targeted BCR-ABL protein kinase inhibitors have revolutionized the treatment of chronic myeloid leukemia (CML) and have established tyrosine kinase inhibition as a model for cancer-drug discovery and therapy in general. In 2001, imatinib became the first such tyrosine kinase inhibitor therapy to be approved by the Food and Drug Administration (FDA). Initially developed as part of a series of compounds that inhibit the platelet-derived growth factor receptor, imatinib was also shown to have potency against ABL and KIT kinases. Despite imatinib's breakthrough success, more than 20% of patients are resistant to the drug. Therefore, second- and third-generation inhibitors — dasatinib, nilotinib, bosutinib, and ponatinib — were developed to overcome imatinib resistance. Among these newer agents, ponatinib stands out as the only approved tyrosine kinase inhibitor with activity against the "gatekeeper" T315I mutation in BCR-ABL. This mutation, which involves a replacement of threonine with isoleucine at ABL residue 315, has been shown to preclude inhibition by other tyrosine kinase inhibitors and is present in as many as 20% of patients with CML who have disease progression while being treated with other agents.

Newer tyrosine kinase inhibitors are increasingly being considered as first-line therapy for CML. Dasatinib and nilotinib have been approved for first-line treatment of CML on the basis of evidence of increased molecular response as compared with imatinib. The randomized trial of ponatinib versus imatinib in patients with newly diagnosed CML (the Ponatinib in Newly Diagnosed Chronic Myeloid Leukemia, or EPIC, trial [ClinicalTrials.gov number, NCT01650805]) sought to investigate whether ponatinib also has greater molecular efficacy than imatinib. Although there are no long-term data to suggest that using the newer agents up front has any effect on survival, there has been an increasing push to use these agents as first-line therapy, based on the rationale that more potent BCR-ABL inhibition would translate to deeper and more sustained molecular remissions. Thus, the recent evolution in CML treatment epitomizes many aspects of the ideal bench-to-bedside investigation and is perhaps the ultimate success story in oncology.

On October 8, 2013, the story took an unexpected turn. Ariad Pharmaceuticals, which manufactures ponatinib, announced major changes to its clinical development program. The announcement followed an analysis of data being collected in a trial of ponatinib in patients identified as resistant to or intolerant of dasatinib or nilotinib or patients identified as carriers of the T315I mutation — the Ponatinib for CML Evaluation and Philadelphia Chromosome–Positive Acute Lymphoblastic Leukemia, or PACE, trial (NCT01207440). Over a follow-up period of 24 months, 11.8% of the patients had serious arterial thrombotic events.[1] After consultation with the FDA, the company placed a hold on enrollment of new patients in clinical studies of ponatinib. The FDA subsequently announced an investigation into the frequency of "serious and life-threatening blood clots and severe narrowing of blood vessels" among patients taking ponatinib.[2] On October 9, Ariad's stock price plummeted. On October 18, the company announced the discontinuation of the EPIC trial in the interest of patient safety. These ponatinib-related events follow numerous recent reports of peripheral vascular events and accelerated atherosclerosis in patients treated with nilotinib.[3] In light of these