ficity of PSA. We agree that these methods may enhance our ability to distinguish indolent cancers from aggressive ones. However, none of these methods have sufficient evidence to change current screening practice and prostate cancer management. Our study[4] quantified the downstream impact of overdiagnosis and overtreatment at a population based level. A sizeable proportion of older men with low-risk cancer underwent aggressive treatment, and a lot of men who started with conservative management later received androgen deprivation therapy within a few years after cancer diagnosis. The prerequisite of a screening program is effective treatment; however, no prostate cancer treatment has been shown to improve prostate cancer-specific survival among older men.[5] We could prevent a lot of older men from treatment complications and psychological stress by limiting PSA screening to those who are more likely to benefit from cancer treatment.

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Buprenorphine as a Safety Net for Opioid Treatment of Nonmalignant Pain

Dr Katz[1] persuasively articulates what many physicians are now thinking as they witness the casualties of chronic noncancer pain (CNCP) opioid therapy first hand and also comments on well-designed studies of adverse consequences now regularly appearing in the pain, pharmacology, and internal medicine literature.

Believers in opioid therapy for CNCP were influenced by a noble impulse to right a series of wrongs. Following decades of opioid excesses, the federal government seized control of opioid prescribing between 1915 and 1920 and severe opiophobia ensued, leading to the neglect of patients, the criminalization of addiction, and the prosecution of physicians. Even as the undertreatment of pain still persists for many populations throughout the world, the pendulum is now swinging back to fears of opioid's hazards in CNCP, particularly when a morphine equivalent dose exceeds a threshold of 100 to 200 mg.

To formulate new understanding, 20 of the nation's top pain researchers met at the University of Utah in 2008 and recently published a research guideline for opioid pharmacology in CNCP.[2] Theirs is a call to arms about the primitive state of our knowledge and the need to move beyond " . . . past narrow vision and industry-driven incentives."[2(p812)] Might sublingual buprenorphine, addiction medicine's most promising new pharmacotherapy, be an essential tool with which pain researchers and clinicians can widen this vision?

A potent, high-affinity, but partial μ-opioid agonist analgesic, buprenorphine is less euphoric than other opioids and is associated with much less respiratory depression, abuse, tolerance, and overdose.[3] While using buprenorphine requires special training, pharmacologic procedures, and certification, it can become a safety net for opioid-dependent patients with CNCP facing the difficulty of coming off of high doses. Over the last decade, in our practice[4] and elsewhere,[5] many opioid-dependent patients with CNCP were successfully rotated to buprenorphine and then stabilized or tapered. Since 2001, in Europe, transdermal buprenorphine has been associated with unexpected efficacy in both neuropathic and cancer pain and also in reversing opioid-induced hyperalgesia.[3] Its use in human immunodeficiency virus clinic settings is growing. Indeed, the Food and Drug Administration just approved a new low-dose form of transdermal buprenorphine (Butrans; Purdue Pharma LP, Stamford, Connecticut) for chronic pain.

Public health and research initiatives in the United States should be encouraged to further develop buprenorphine as an analgesic. This may be modern pharmacology's best bet for avoiding harms like those that emerged in an earlier era of opioid regulation. Believers need not lose faith.

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Correcting Several Oversimplifications of Chronic Opioid Therapy

Braden et al[1] appropriately reported chronic opioid therapy risk stratification with prescription minimization recommendations but erroneously oversimplified hazard attribution to "high-potency" schedule II opioids and the generic term *schedule II long-acting opioids*.

Hydrocodone's class III Drug Enforcement Administration (DEA) regulatory designation permits clinicians convenient telephone prescriptions on behalf of patient care, but hydrocodone is roughly equianalgesic with oxycodone, a class II opioid. Clearly, it is erroneous to reproach schedule II over III opioids by inaccurately correlating potency to legislative scheduling. Schedule V liquid codeine is class III as tablets. Ingesting additional tabs of schedule III opioids effectively enhances potency. Oxymorphone is class II but is 10 times more potent than morphine,[2] also class II.

Braden et al[1] also vastly oversimplify long vs short-lasting opioid iatrogenic risks. OxyContin (Purdue Pharma LP, Stamford, Connecticut) is 40% short-acting and 60% long-lasting oxycodone in one product, and it is thus concerning that the authors failed to denote that which they declared "long lasting," an impossible task with OxyContin tablets.

Abusers crush opioids to rapidly effect euphoria, unintentionally compromising ventilatory centers, prompting emergency department visitation. Capsulated long-lasting morphine formulations considerably minimize abuse potential relative to tablets of short- and long-lasting opioids. It is inappropriate to aggregate conclusions regarding long-duration capsulated and tablet opioids as abuse is mitigated by inability to crush morphine capsules for insufflation or injection.

Nocturnal ingestion of class III hydrocodone induces 100% to 70% oxygen desaturation within less than 30 minutes secondary to central sleep apnea hypoventilation,[3] impairing cellular respiration, causing end-organ hypoxemia, and exposing the misconception by Braden et al[1] of the safety of short-duration class III opioids. It also reinforces the value of early morning ingestion of 12-hour half-life morphine opioid relative to 18- to 29-hour–longer formulations that persist nocturnally. Again, combining discussion of different long-duration agents is misleading, and the authors are encouraged to report risk stratification with each medication.

Not just long-lasting status, but also opioid source is critical. Addiction center methadone-treated patients may be vastly more prone to dose-dependent QTc interval prolongation–induced torsades de pointes, prompting ED presentation. This is apparent given high recidivism to cocaine cardiotoxic ingestion among addicts, frequently vastly higher QTc interval–prolonging methadone dosing in addicts relative to chronic pain clinics, and higher opioid dose-dependent hypogonadism in addicts with lower testosterone levels lengthening ventricular repolarization duration to potentially dangerous levels.[4] Addicts are also at higher risk for comorbid hepatitis C infection–induced hepatic dysfunction[5] with impaired methadone clearance to dangerously prolong QTc intervals.

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In reply

We appreciate Dr Geller's comments on the complexities of prescription opioid pharmacology and additional factors of consideration in the safety and abuse of these medications. We believe he has a valid point in noting that the DEA schedules concern abuse potential and this only approximates to potency. However, most opioid-dosing tables and calculators consider oxycodone to be 1.5 times the potency of hydrocodone.[1] Our choice of categorization by DEA schedule is consistent with the terminology used by practicing physicians, in current and proposed state and federal regulations,[2,3] and in clinical guidelines.[4] The specific medications categorized as schedule II short acting, schedule II long acting, and non–schedule II are listed in a table in our prior article.[5]

We acknowledge that there are risks associated with use of any prescription opioids, and hence, schedule III-IV medications are not without risk. There were fewer emergency department visits and alcohol-drug encounters among those receiving only schedule III-IV drugs in our study compared with those receiving any schedule II drugs, but overall risk is determined by many factors. We examined several of these factors in our regression models, but there are likely to be other unmeasured factors such as source of opioids and use of illicit drugs as Dr Geller points out. We agree that examining risks associated with specific medications and how they were actually used would help to shed additional light on our findings and should be incorporated into future studies.

It is important to remain focused on the big picture. In our article, we cite a Centers for Disease Control study demonstrating marked increases from 2004 to 2008 in emergency department visits for nonmedical use of opioids.[6] Ac-