There is no longer doubt that the misuse, abuse, addiction, and diversion of prescription opioids comprise a national epidemic [1]. A simple solution is unlikely. As HL Mencken stated, “For every complex problem, there is an answer that is clear, simple, and wrong.”

In retrospect, the quandary we are in was predictable. Physicians practicing in the 1990s received minimal education in pain management and almost no training in addiction medicine; they were given a Drug Enforcement Administration (DEA) certification without their having demonstrated any knowledge base of safe opioid prescribing. A few physicians with expertise in managing cancer pain with opioids suggested that a subpopulation of patients with chronic pain of nonmalignant nature might benefit from long-term opioid treatment to decrease pain and improve function. With little evidence base [2], this model became common practice among many physicians. This model was promoted by the pharmaceutical industry, which saw an opportunity to expand its market. Third-party payers and society were seduced by the relatively low cost of opioids as a simple solution to a complex problem. While the cost of opioids is relatively low, managing the adverse effects and the current opioid prescription epidemic is proving to be very costly in lives and treasure.

In view of the alarming rise of emergency department admissions and unintentional overdose deaths due to prescription opioids, the Office of National Drug Control Policy (ONDCP) and the American Society of Addiction Medicine (ASAM) issued statements supporting mandatory education in safe opioid prescribing as a prerequisite for DEA certification. The American Academy of Pain Medicine (AAPM) demonstrated its leadership by developing a comprehensive prescriber education curriculum that provides responsible, multidimensional solutions for prescribers, patients, and society. It offered a 2-day Safe Opioid Prescribing course at its 2012 Annual Meeting [3], cochaired by Drs. Lynn Webster and Sean Mackey. The course included didactic sessions as well as a workshop on urine drug testing.

The current issue of this journal contains two timely articles. The first by Peppin et al. [4] gives recommendations on UDT in chronic pain management with this caveat: their recommendations are based upon weak but evolving evidence. They advocate for research that “quantifies the effects of UDT on opioid management therapy and patient outcomes.” The second article by Pesce et al. [5] concerns interpreting UDT in pain patients. Both articles state potential conflict of interest, as many individual contributors have relationships with the UDT industry.

Although UDT is recommended by AAPM, APS, and ASAM, what evidence do they base their recommendations on?

Only a few studies and weak evidence exist about UDTs’ identification of and impact on misuse, abuse, addiction, diversion, overdose [6], or patient outcomes. In addition, no studies exist that evaluate the potential harm due to misinterpretation of UDT results. We don’t know how many patients have been incorrectly labeled as abusers of opioids and discharged from care or how many have been labeled as compliant, when, in fact, they are abusing and/or diverting opioids.

In forensic drug testing, most results are expected to be negative. There is zero tolerance for illicit and nonprescribed substances, and collection and chain of custody are strictly regulated. The test results are reviewed by a certified, medical review officer (MRO).

In contrast, in clinical UDT, the situation is more complex and unregulated, and a majority of prescribers possess limited knowledge to interpret UDT results [7]. To improve this situation, clinicians must be educated as to what drugs to test for and how to choose the correct methodology. Misinterpretation of results can have profound, negative, medical, ethical, legal, and financial effects on patients, prescribers, and society.

A correctly ordered and interpreted clinical UDT gives only a snapshot that reveals the presence of a prescribed drug and its metabolite, an un-prescribed drug and its metabolite, or an illicit substance at a particular time. Toxicologists can tell us if a drug is present or not. However, because UDT results cannot diagnose abuse, addiction, or diversion, clinicians should make such diagnoses only after carefully taking a history, physically examining the patient, obtaining corroborating evidence from family members, and building a therapeutic relationship with the patient over time. Only then, will it be possible to determine whether aberrant behaviors exist and develop strategies for extinguishing them.
As pointed out in both articles cited above, diagnosing diversion based on the absence of a prescribed drug in the urine is dangerous. A negative result can have many explanations, other than diversion, some simple, others complex.

A urine specimen containing the prescribed drug and metabolite and not containing un-prescribed or illicit drugs is described as consistent. A specimen not containing them is described as inconsistent. A consistent specimen does not document patient compliance with the treatment regimen, as the clinician does not know the dose, dosing interval, frequency of use, or route of administration. Clinicians often see patients with consistent UDTs, who, later in a therapeutic relationship, readily admit snorting opioids with a pint of vodka as a chaser and diverting. A UDT can’t distinguish between social drinking and alcoholism or use of an illicit substance and abuse or addiction to that substance. Therefore, advocating for the patient (often stated as one of the benefits of UDT), based solely on UDT results, may be problematic.

Given the lack of evidence of UDTs’ benefit or potential for harm, a prescribing physician must take into account UDTs’ cost to the physician, patient, and society. For example, given the estimated 100 million individuals affected by chronic pain in America [8], the assumption that only 5% are candidates for long-term opioid therapy as part of a multimodal pain-management approach, combined with current annual costs ranging from $500 to $5,000 per patient, one can conservatively estimate that UDTs will cost society a minimum of $5 billion per annum.

Pesce et al. claim that UDT “has been documented to be cost-effective in reducing healthcare expenditures” based on an industry funded study by Laffer Associates, an economic research and consulting firm [9]. Yet, how can one perform a cost-effectiveness study when only weak evidence based on a few studies suggests UDT’s benefit? Only future, nonindustry, studies can establish if UDT is beneficial and cost effective.

Clinicians worry most about the misusers, abusers, addicts, and diverters. The latter two are “professionals,” who can regularly beat, not just opioid risk-assessment tools such as the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), Opioid Risk Tool (ORT), and the Current Opioid Misuse Measure (COMM), but also a clinical UDT program. Testing currently is not truly random as in forensic testing or Physician Health Programs. Recommendations in Peppin et al. [4] as on how to decide when to test at a scheduled visit such as using a coin flip have no evidence base and fundamentally do not take into account the mentality of an addict or diverter.

It is important to note that medication non-adherence to the treatment regimen prescribed in any chronic condition is a well-known public health problem. Rates of non-adherence to any medication range from 15% to 93% [10], even when there are severe consequences to non-adherence [11]. Medication non-adherence in patients with chronic nonmalignant pain is common [12]. The details of non-adherence as to magnitude, overuse, underuse, dosing interval, or route and subpopulations remain poorly defined. Not all non-adherences by pain patients as measured by UDT imply abuse or addiction issues or are done with intent to deceive the clinician.

The decisions guiding whom to test, what drugs to test for, how to test, and how often to test clearly have vast cost implications for society. All costs associated with these decisions should be made clear to all involved in them. Providers need clear recommendations based on current knowledge of urine toxicology guiding panel testing with appropriate methodologies when using UTD in the clinical setting of pain management.

Currently EIAs are reimbursed at $102 in Medicare Fee Schedule (G0431) while confirmations by GC/MS or LC/MS/MS are billed at $100+ per drug class for third-party payers. A single UDT test can cost from $300 to as high as $2,500 for a full 12–16 panel of drug classes. Patients have received balance billing for $400 and higher per UDT.

Pre-employment and forensic testing has been commoditized and costs between $7 and $20, as most tests are negative and do not require confirmation testing. In contrast, a clinical UDT, expected to yield positive on EIA for prescribed drugs, will need frequent confirmations, driving up the cost. One confirmation study generally cost labs less than $2 per drug class. If pricing were commoditized, the total cost of a UDT could average $40–$60, allowing industry a good profit margin. Unreason-able margins will have a negative effect on our efforts to promote clinical UDT testing in a responsible manner that does not adversely impact patients, physicians, and society.

Given that the screening immunoassay using a point-of-care (POC) device drives costly confirmations, what role, if any, should POC devices have?

POC devices provide little useful definitive and actionable information in clinical decision making, and this lack of information usually leads to extensive and costly confirmations. Confirmations should be driven by the more accurate presumptive positive or presumptive negative (for prescribed drugs) EIA results obtained within the confines of a specialized laboratory. There is no evidence that same-day turnaround time is needed in a clinical setting as suggested by Peppin et al. [4]. Placing value on same-day turnaround time implies the importance of utilizing a POC device, when in fact there are severe limitations to POC devices. It is important to point out that a clinician is going to have to purchase and bill for a POC device. Medicare has changed its fee schedule to be a $20.47 (G0434) reimbursement. The POC device costs on average $7, staff time $5, and biller time $10. With these numbers,
clinicians are losing needed revenues on every specimen, hence negatively impacting the use of UDT by prescribers.

In addition, testing specimens with POC devices might be adequate if every doctor prescribed only morphine, but such is not the case. Currently, several prescribed drug classes—Fentanyl, Tramadol, Tapentadol, and Carisoprodol—have a huge potential for abuse, but no POC reagent for them has been manufactured. Furthermore, no manufactured POC device accurately detects low urine concentration levels of hydrocodone, the most prescribed and abused drug in the United States.

The value of validity testing for specific gravity, pH, creatinine, and adulterants performed in a specialized laboratory should not be underestimated, and the consequences for an invalid specimen should be harsher than for an inconsistent UDT.

While we await future, well-designed studies to define the benefits or possible harm of UDT, those in the field, including industry, should minimize UDT costs, so that prescribers, patients, third-party payers, and regulators are not alienated as health care costs are a zero sum game. Already, some physicians and labs “game the system” and create negative publicity for UDT [13]. UDT is but one tool for managing chronic pain with opioids. Misinterpreting or overinterpreting UDT results or claiming benefit or cost effectiveness when no data exist will ultimately harm prescribers, patients, and industry.

I believe that UDT will ultimately result in measurable, beneficial outcomes that will outweigh harm. We need a vibrant and efficient industry that can make a reasonable profit and perform R&D to advance the science. However, when the science does not justify clinical implementation such as industry promoted compliance algorithms that purport to correlate a measured urinary concentration of a prescribed drug with a consumed dose [14], it is important that clinicians and toxicologists reject such tests as they give little valid or useful information and drive up costs.

Before prescribers can receive DEA certification, we urgently need the following three to occur:

- Mandatory education on the safe prescribing, management, and discontinuation of controlled substances.
- By passing a written exam, demonstrated mastery of knowledge base that includes the basics of interpreting clinical UDT [15].
- Agreement on a standardized language between various clinicians and toxicologists on terminology used to describe the results of UDT [16].

Lastly, if one believes in the 80–20 rule and that 80% of problems are caused by 20% of the patients, we need a better model to identify that 20% so as we can spend our precious resources on that 20% rather than on the compliant 80% while keeping in mind that all patients are potentially at risk [17].

I hope that these comments and opinions are controversial enough to spark debate.

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References


