The most recent *National Survey on Drug Use and Health* showed a continuing trend in the non-medical use of prescription medications, notably opioid analgesics, which accounted for 75% of prescription drug non-medical use in 2006\(^1\). In 2006, in response to this growing “pharmacoepidemic,” the Office of National Drug Control Policy set a goal of reducing past month prescription drug abuse by 15% over the next three years\(^2\). The challenges of meeting this mandate to curb the rising tide of prescription drug abuse and diversion are daunting, with the primary policy challenge remaining to reduce drug diversion and drug abuse without creating additional barriers or limiting access by patients with a legitimate need for such medications\(^3\).

The use of state-issued, paper-based prescription forms remains one potential solution.

State-issued prescription forms, also known as “Multiple Copy Prescriptions” or “Trip (Triplicate) Scrips,” were one of the earliest approaches to controlling the abuse and diversion of prescription medications with addiction potential\(^4\). Originally, paper systems monitored the trail of medication prescribing, dispensing, and purchasing by requiring prescribers to use state-issued prescription forms (duplicate, triplicate, and/or serialized single issue) for covered controlled substances. In this system, the prescriber maintains one copy, the remaining two copies follow the patient to the dispensing pharmacy, which then maintains one copy and transmits the third copy to the designated state agency. Now largely outdated by electronic monitoring systems, pharmacies – not prescribers - are responsible for transmission of paper or electronic data, depending on state regulations, to the designated state agency.

Although there have been several movements over the past three decades to implement a national prescription monitoring system, the actual implementation of paper-based approaches have succeeded only at the State level. For this reason, it is difficult to summarize all state activities in this regard over time. Because state-issued prescription forms were implemented in various guises in a multitude of states over the past 70 years, we discuss this approach here generically.

To date, 38 states have established some form of prescription drug monitoring programs in an effort to reduce drug abuse and diversion of controlled substances and illicit use of prescription drugs\(^4\). All of these programs have enacted legislation that primarily relies on electronic monitoring programs. In other words, ‘traditional’ multiple copy programs no longer exist. Three states -- New York, California, and Texas – also supplement electronic transmission with paper, serialized prescription forms\(^4\). All three states originally implemented their PDMPS using a paper-based approach (triplicate prescription programs).

I. The Need for State-Issued Prescription Forms

The need for a paper-based system to monitor abusable prescription medications has generally arisen over States’ perceptions of abuse and/or diversion of potent medications available by prescription for treating medically-sanctioned indications. At its zenith in the mid-1990s, paper-
based prescription drug monitoring programs (PDMPs) included 18 states that accounted for approximately half of total prescription prescribing and dispensing in the nation. It is important to recognize that states vary dramatically in the implementation, schedule coverage, and process of running these programs. For instance, the “tone” established by the program frequently was determined by the State agency or agencies with oversight responsibilities. Many programs resided in State health departments, which thus focused on educational strategies aimed at providers (and sometimes patients) to reduce inappropriate prescription drug use. In other states, the professional boards ran the PDMPs, while in many others law enforcement agencies were responsible for running the PMP.

**California.** The first triplicate prescription program (TPP) was enacted by California in 1940 in response to the growing diversion of opium-based pharmaceuticals abused by its population. They continued with a paper system, in whole or as an overlay with electronic monitoring, for 58 years when, in 1998, they also implemented an electronic program capable of capturing Schedule II drug data, still maintaining the triplicate forms. Then, in 2004, legislation (SB151) was passed in California to replace triplicate prescription forms with a secure, tamper-resistant form for Schedule II through Schedule IV. In the current system, prescribers must obtain and use new tamper-resistant prescription forms from state-approved security printers. The California Health and Safety Code (11162.1) details specific requirements, such as a watermark, for prescription blanks of controlled substances.

**Texas.** The triplicate prescription program for Schedule II drugs was established by the Texas legislature in 1982 under the Department of Safety (DPS). This program, now known as the Texas Prescription Program, moved to electronic submission by pharmacies in 1999 and was expanded in September 2008 to include Schedule III – Schedule IV. Prescribers in Texas must use either a single or triplicate, serialized prescription form for Schedule II prescriptions. The single copy, serialized form has been available in Texas since March 1, 2002. The form has a number of security features such as a pantograph thermochromatic link and DPS seal, both used in an effort to assist pharmacies in verifying prescription authenticity. The triplicate form also is still valid for dispensing Schedule II controlled medications. These forms are available for a fee from the Texas Prescription Program.

**New York.** In 1973, New York broke ground by becoming the first state to use a paper-based PDMP to cover lower-scheduled prescription medications. In this year, Schedule III sedative-hypnotics were included. In 1989, the state controversially added Schedule IV benzodiazepines after several State agencies noted trends in the use and likely abuse and diversion of benzodiazepines. All prescriptions, controlled and non-controlled, effective April 2006 must be issued on a single-serialized Official New York State Prescription form. This form also contains security features to prevent alterations and forgeries. The official prescription form is a complement to the electronic monitoring system adopted that year to replace the multiple-copy paper program.

**II. Implementation of State-Issued Prescription Forms**

Many patient advocacy groups and physician were opponents of legislation in the 1990s to implement paper-based PDMPs on a Federal level, considering them burdensome and intrusive. Today many advocacy groups, including the Alliance for State Pain Initiatives (ASPI) and the
American Pain Foundation (APF), still maintain that state-issued forms should be avoided in favor of alternative prescription monitoring methods\textsuperscript{11, 12}. The pharmaceutical industry has generally opposed both paper and electronic monitoring programs.

From their inception in most states, the implementation of paper-based prescription monitoring systems was controversial. Paper-based systems have their proponents and opponents, with those favoring the approach generally acceding that the paper trails of paper-based PDMPs having a significant influence in reducing the availability of abusable prescription drugs in the grey and black markets. Opponents remain primarily concerned that paper-based PDMPs have a deleterious effect on patient access to needed medications.

Physicians did not care to have their prescribing practices scrutinized; indeed, they were quite concerned about the “chilling effect” state scrutiny would have on medical access. It was felt that paper forms, tangible reminders of such scrutiny when handled by the prescribing physician and dispensing pharmacist, would have a greater effect on reduced prescribing and dispensing than would an electronic system that remained largely invisible to health care practitioners. On the other hand, the adoption of special prescription forms was thought to be a deterrent to prescription alterations and forgeries common with ordinary prescription forms. There also is some consensus that theft of special prescription drug forms reduces the capacity for theft of blank prescription drug pads as the serialized forms are easier to spot and trace. Many providers felt the hassle of procuring and safely storing the special prescription pads onerous. Indeed, a primary contention with paper-based programs was the costly and time-consuming task of inputting the physical triplicate scripts into a database, and is a motivating reason why states have embraced electronic strategies.

Patients were similarly concerned about state scrutiny, with various patient advocacy groups testifying on behalf of their constituencies, whom they were afraid would no longer be able to access needed medications. Patient groups have raised concerns about the privacy and confidentiality of paper forms.

Law enforcement agencies are typically the strongest proponents of paper-based PDMPs. They contend that paper trails allow law enforcement to better target their efforts to those providers with questionable prescribing and dispensing practices, as well as identify patients who ‘Doctor shop’ and ‘pharmacy hop’ with fraudulent prescriptions.

\textbf{III. Evaluation of the Paper-Based PDMPs}

There is limited empiric evidence on the intended and unintended consequences of paper-based PDMP programs. To date, there is no study that has specifically evaluated the effectiveness of single, serialized prescription forms, either alone or as a paper overlay to electronic systems. As well, there are no empiric studies that have specifically examined the empiric evidence of electronic PDMPs in reducing prescription drug abuse and diversion and attendant impacts on medically-sanctioned use of targeted pharmaceuticals.

Among the small body of research examining paper-based multiple-copy PDMPs, there are no published peer-reviewed papers evaluating the process measures of paper prescription
monitoring programs. Potential process indicators include: number of forms issued; compliance with issued forms; and form uptake by physicians by specialty. Although the Bureau of Justice Assistance has published some process evaluation indicators, these almost all relate to electronic systems. At the State level, most states use a variety of process and outcome measures to evaluate the impact of prescription monitoring systems, both paper-based and electronic. To our knowledge, none of these were ever published in peer-review journals or made widely or publicly available.

Few published well-designed studies have documented the potential impact of PEMPs on patient care. Of these, most focused on triplicate versions of paper-based PDMPs, particularly the benzodiazepine PDMP in New York. In interpreting the results of these studies, it is important to consider the two therapeutic classes. The opioid analgesics, used to control pain, are generally more prone to abuse and thus more highly controlled (Schedule II and Schedule III) than the benzodiazepines (Schedule IV). As a result, the politics around PDMPs for opioids and benzodiazepines tends to be different, with different stakeholders, patient constituencies, and clinical supports.

**PDMPs: Impact on Opioid Analgesics.** Two primary studies evaluated the impact of paper-based systems on opioid analgesics. One is limited to a single hospital in Texas; the second uses a cross-sectional, nationally-representative database of physician office visits. In the first, the authors evaluated the impact of PDMP implementation before and after in Texas on Schedule II prescriptions using data from a 1200 bed teaching hospital. The authors found a 60.4% decrease in Schedule II prescriptions after PDMP implementation.

In the second analysis, the influence of PDMPs on opioid and non-opioid analgesic use was examined using the National Ambulatory Medical Care Survey (NAMCS). In this study, the independent variable was whether the physician office visit occurred in a PDMP state (at the time of this analysis, nineteen states had paper-based PDMPs and none had electronic systems). The authors found that the PDMP variable was statistically significantly associated with a reduced probability of Schedule II opioid receipt relative to non-PDMP state. Further, patients in PDMP states had an increased likelihood of Schedule III analgesic use relative to their non-PDMP peers. These findings suggested that PDMPs exert an inhibitory effect on receiving Schedule II analgesics, as well as a “substitution effect” of receiving a lower scheduled ‘therapeutic alternative’.

**PDMPs: Impact on Benzodiazepines.** Considerably more research has been conducted on the PDMP implementation of benzodiazepines in New York. In a study published by Weintraub and colleagues, the authors used three different databases – New York Medicaid, IMS (National Prescription Audit), and BCBS data from the Rochester region – to compare benzodiazepine and alternative medication use before and after the benzodiazepine PDMP. Briefly, the authors found benzodiazepine prescribing reductions across the three databases ranging from 30% to 60% in the post-PDMP period relative to the pre-PDMP period. The authors also found increases in the use of alternative sedative-hypnotics, such as meprobamate +125%, ethchlorvynol +29%, and chloral hydrate +136% (relative to reductions in use nationally). Reductions in benzodiazepine spending also reduced slightly.
A series of four NIDA-sponsored studies further evaluated the impact of the New York PDMP on benzodiazepine use. Using a segmented time-series with comparison design, the researchers estimated changes in levels (discontinuities) and trends (slope) in the use of benzodiazepines and potential substitute medicines, controlling for possible pre-existing trends, in New York (case) and New Jersey (control) Medicaid populations. During the baseline year (1988), patterns of benzodiazepine use in each state were very similar (20.2% in New York and 19.3% in New Jersey). After the PDMP was implemented in New York, there was a sudden, sustained reduction in benzodiazepine use of 54.8% (95% CI=51.4%, 58.3%) with no change in New Jersey. Controlling for age, sex, eligibility category, race/ethnicity, population density, and poverty level, the overall risk of discontinuation of benzodiazepine therapy was twice as high in New York as in New Jersey. The PDMP also presented a substantial deterrent to new use of benzodiazepines by New York enrollees during the subsequent two years: only 1.2% of unexposed individuals in 1988 in New York had received a benzodiazepine prescription by the end of 1990, compared to 10.4% additional benzodiazepine recipients in New Jersey. Offsetting increases in the use of potential substitute drugs such as buspirone, diphenhydramine, chloral hydrate, and others were modest.

Similar findings were found in clinically and economically vulnerable populations, namely eligibles with serious mental illness (e.g., who had at least one inpatient or two outpatient diagnoses of schizophrenia, bipolar disorder, panic disorder, or seizure disorder for which benzodiazepines have been documented to be important mainstay or adjunct therapy), racial/ethnic minorities residing in impoverished urban areas, and newly-discharged hospitalized patients. The researchers found significant benzodiazepine reductions in these seriously mentally ill patients in New York, ranging from 36.8% in bipolar patients (95% CI=32.5%, 41.2%) to 54.2% in seizure disorder patients (95% CI=48.1%, 60.3%), with no change in New Jersey trends. While these benzodiazepine use reductions are comparable to that seen in the general population of New York State, they suggest the possibility of a serious compromise in the quality of care received by these particularly vulnerable individuals. Similar findings were found in a study examining post-hospitalization patients needing benzodiazepines. Finally, an untoward consequence of the benzodiazepine PDMP in New York was the further widening of disparities in benzodiazepine access in urban neighborhoods with proportionately greater racial/ethnic populations and lower income.

**Paper versus Electronic PDMPs.** Only one paper to date has compared paper-based PDMPs to electronic programs. This study reviewed the known literature evaluating Multiple Copy Prescription Programs (MCPPs) with the then two electronic systems implemented in Massachusetts and Oklahoma, focusing on the effectiveness of the systems in reducing abuse and diversion, as well as the effect of these two drug control mechanisms on legitimate medical access to restricted drugs. The study suggests that when diversion control programs are implemented, reductions in prescription drug use are due to decreases in diversion and inappropriate use, as well as to decreases in medically necessary care. Of the two types of approaches, however, those using a paper-based prescription form may be the most intrusive due to the continual reminder to providers and patients that their prescribing, dispensing, and procuring patterns are being monitored. On the other hand, this same quality makes paper-based programs more effective in reducing diversion.
Conclusions
A recent report from the Office of National Drug Control Policy (ONDCP) maintains that PDMPs have been effective in reducing drug diversion and misuse. We believe a better statement is that the body of evidence, though sparse, is robust in that it clearly demonstrates that the use of paper monitoring systems results in reducing both prevalent and incident use of targeted medications and increases in the use of ‘therapeutic alternatives’ which, in some cases, may be less safe and/or less clinically appropriate. What this research fails to demonstrate are the downstream consequences of paper monitoring programs on patient outcomes, quality of care, patient satisfaction with disease management, and patient and program costs. Furthermore, the research fails to definitively find that paper programs limit inappropriate use, abuse, and diversion without influencing the use of medically-sanctioned use. This difficult balance is the bane of all prescription drug monitoring programs, be they paper-based or digital-based.

With state and any future Federal programs likely taking an electronic approach to monitoring abusable prescription drugs, it is important to consider the effectiveness of paper overlays in reducing use. Indeed, under the Deficit Reduction Act passed last year in an effort to stem fraud and abuse, state Medicaid programs are now required to use special prescription forms for all medications prescribed to enrollees. Future research to evaluate the impact of PDMPs on medical use and access, abuse and diversion, and clinical and economic outcomes are imperative. PDMP outcome measures are needed to fully evaluate the impact on patients along with drug abuse and diversion. The goal of balancing appropriate treatment with reduction in prescription drug abuse and diversion should remain in the forefront of new and alternative drug policy strategies.

References

1. SAMHSA. Results from the 2007 National Survey on Drug Use and Health: National Findings. Substance Abuse and Mental Health Services Administration; 2008.
8. NYSDOH. What every practitioner needs to know about controlled substance prescribing: New York State Department of Health; 2008.
11. APF. American Pain Foundation (APF) position statement on H.R. 3015 the National All Schedules Prescription Electronic Reporting Act of 2004 (NASPER); 2005.