Trends in Abuse of OxyContin® and Other Opioid Analgesics in the United States: 2002-2004

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Abstract: **OxyContin® (Purdue Pharma L.P., Stamford, Conn) was approved by the Food and Drug Administration (FDA) in 1995 as a sustained-release preparation of oxycodone hydrochloride and was thought to have much lower abuse potential than immediate-release oxycodone because of its slow-release properties. However, beginning in 2000, widespread reports of OxyContin® abuse surfaced. In response, Purdue Pharma L.P. sponsored the development of a proactive abuse surveillance program, named the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) system. In this paper, we describe results obtained from one aspect of RADARS—the use of drug abuse experts (ie, key informants)—as a source of data on the prevalence and magnitude of abuse of prescription drugs. The results indicate that prescription drug abuse has become prevalent, with cases reported in 60% of the zip codes surveyed. The prevalence of abuse was rank ordered as follows: OxyContin ≥ hydrocodone > other oxycodone > methadone > morphine > hydromorphone > fentanyl > buprenorphine. In terms of the magnitude of abuse (≥5 cases/100,000 persons in a 3-digit zip code), modest growth was seen with all analgesics over the 10 calendar quarters we monitored, but was most pronounced with OxyContin and hydrocodone. These results indicate that OxyContin abuse is a pervasive problem in this country, but that it needs to be considered in the context of a general pattern of increasing prescription drug abuse.**

Perspective: ***Over the past 5 years, there have been reports, frequently anecdotal, that opioid analgesic abuse has evolved into a national epidemic. In this study, we report systematic data to indicate that opioid analgesic abuse has in fact increased among street and recreational drug users, with OxyContin and hydrocodone products the most frequently abused. Steps need to be taken to reduce prescription drug abuse, but very great care needs to be exercised in the nature of these actions so the legitimate and appropriate use of these drugs in the treatment of pain is not compromised as a result.***

Key words: *Opioid analgesic abuse, prescription drug abuse, OxyContin abuse, trends in prescription drug abuse, risk management program, postmarketing surveillance.*

OxyContin® (Purdue Pharma, L.P., Stamford, Conn) is a sustained-release preparation of oxycodone hydrochloride.[28] It was approved in 1995 by the Food and Drug Administration (FDA) for use as an analgesic in individuals with moderate to severe pain requiring relief for several days or more. It was judged at the time of its approval to carry a risk of drug abuse because of its properties as a narcotic, and it was placed in Schedule II of the Controlled Substances Act. Beginning in 2000, Purdue Pharma and the FDA began to receive reports from the media and several state and local regulatory/legal authorities that OxyContin was being abused in several circumscribed areas, such as southern Maine and the Appalachian region. These reports of abuse, even at a regional level, were unexpected. At the time of its release, both the FDA and Purdue Pharma felt that abuse of OxyContin, although probable in some drug abuse-prone individuals, might actually be less than that observed with other oxycodone products because it was an extended-release opioid. In fact, the original package insert and the 1997 Physicians' Desk Reference contained the following statement: "delayed absorption, as provided by OxyContin® tablets, is believed to reduce the abuse liability of a drug." This conclusion was based on preclinical and clinical evidence that drugs with a slow onset of action (ie, delayed reinforcement) are much less abused than more rapidly released ones.[14,20,22,29]

Although the "epidemic" of abuse of OxyContin, and subsequently other opioid analgesics, that began in 2000 was based, for the most part, on extensive media reports of abuse, several federally funded surveys did in fact suggest that prescription drug abuse was a growing prob-

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lem between 2000 and 2004.[15,32,33] Although the reasons for this are unclear, in prior reports[5,30,37] in which the abuse of tramadol was monitored, the reasons most often given were: 1) prescription drugs are relatively easy to obtain as opposed to the great difficulties in obtaining heroin and other illicit drugs in rural and suburban areas; 2) the purchase of illicit drugs on the street, such as heroin, was closely monitored by law enforcement officials and arrests were therefore far more likely for heroin than legal drugs such as opioid analgesics; 3) the use/abuse of prescription drugs was more socially acceptable among peers than heroin or cocaine; and 4) the purity and the dosage of prescription medications were highly predictable and consequently these medications were much safer to use than illicit drugs.

As mentioned above, awareness of OxyContin abuse across the nation was based primarily on media reports, which raises the question: Why was this problem not recognized by existing detection systems? Indeed, the FDA has long recognized the importance of postmarketing surveillance and utilizes a complex set of databases to gather as much information as possible about the use, misuse, and abuse of drugs. There are, however, several limitations with these systems[11,13,25,31] that were clearly documented by an FDA task force that was charged with evaluating postmarketing surveillance of drug safety (Henney Report, 1999).[34] The catalyst for this task force was a 4-fold increase in drug recalls over the period from 1993 to 2001: 1.56% of approved drugs for 1993 to 1996 to 5.35% for 1997 to 2001.[13] The task force concluded that the monitoring systems currently in place failed to identify most adverse events before they evolved into full-blown public health concerns. The most significant aspect of the Henney Report, however, was the mandate that the FDA work with drug sponsors to develop proactive risk management strategies that would better protect the public by obtaining "real-time" evidence of emerging problems.

During 2000 and 2001, the FDA and Purdue Pharma initiated a dialogue in which a mandated proactive risk-management plan was discussed. As the first priority, it was realized that the label or package insert needed to be changed in a number of ways, the most important of which was deletion of all indications that OxyContin might have a lower abuse potential than other oxycodone products. To emphasize this point, Purdue modified the label to include a "black box" warning concerning abuse, making OxyContin the only commonly prescribed opioid analgesic with a "black box" warning.

Purdue Pharma also proposed educational efforts, sales force retraining, and, most importantly, the establishment of a proactive surveillance program to monitor and characterize abuse, named the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) system. The main goal of the RADARS® system was to develop proactive, timely, and sensitive methods to assess the abuse and diversion of OxyContin and a number of other abused Schedule II and III opioids. The intent was to stratify the information by all of the 973 3-digit zip codes in the United States to better understand the degree to which abuse was a nationwide problem or was found mainly in areas with a known proclivity for prescription substance abuse. Once an indication of abuse or diversion was detected, it would be verified and amplified by obtaining as much information as possible so that appropriate intervention strategies could be developed. It was also important to determine its longevity because there is prior evidence of transient and geographically confined outbreaks of drug abuse, such as those which occurred with Robitussin® (Wyeth Consumer Healthcare, Madison, NJ) abuse and "Ts and Blues" (triptelenamine and pentazocine) several decades ago.[16,21,30,38]

Table 1. Schedule II and III Opiate Analgesics Evaluated by RADARS®

Buprenorphine
Fentanyl
Hydrocodone
Hydromorphone
Morphine
OxyContin®
Other oxycodone products (*not* OxyContin)
Methadone (added in June 2002)

As its base, RADARS used 3 systems to detect and characterize abuse: first, surveys of drug abuse experts about abuse of prescription opioids in their catchment areas; second, surveys of police agencies for diversion of these drugs; and, third, monitoring Poison Control Centers for calls regarding intentional misuse or abuse of prescription medications. To place abuse of OxyContin in an appropriate context, the abuse of a number of other Schedule II and III opioids (Table 1) was also monitored to determine whether the trends in the relative rates of OxyContin abuse were steeper than those of other prescription opioid analgesics.

In this paper, we describe one important aspect of the RADARS signal detection studies: the use of "key informants" or drug abuse experts as a rich source of data on the emergence of abuse of prescription drugs at a local, community level. The term "key informants"[1] refers to clinicians, epidemiologists, treatment counselors, and other observers who are well-recognized experts in the field of substance abuse and who are in a position to know about new and emerging drug problems in their areas. The concept of utilizing key informants was to include in the surveillance program individuals who would be in a strong position to assess, at the very earliest possible time, whether prescription drugs were being abused in their communities and why. Furthermore, a drug informant network was used effectively in a prior postmarketing surveillance program to detect, in a time-sensitive fashion, regional outbreaks of Ultram (Ortho-McNeil, Raritan, NJ), generic tramadol and Ultracet abuse,[5,6] which then led to intervention strategies (ie, a risk-management program). Thus, the key informant program seemed to provide an excellent part of a system to determine the extent of OxyContin abuse in the coun-

try and the characteristics of those abusing it, serving as a guide for the development of appropriate prevention and intervention strategies.

Materials and Methods

Key Informant Selection

A number of populations were identified as groups that needed to be monitored for prescription analgesic abuse in RADARS.

Health Care Professionals

Historically, health care professionals have reflected high rates of drug abuse and recidivism occurs quite often even in those enrolled in special drug abuse treatment programs. They were one of the earliest populations detected abusing both pentazocine and fentanyl.[4,9,19] They have very easy access to prescription drugs, and they are keenly aware of their euphorigenic properties and, hence, programs designed for treatment of this vulnerable group needed to be monitored.

Methadone Patients

These individuals represent a population that would reflect diversion of prescription drugs to the street. It is a logical population to examine for abuse liability and dependence potential because its members are highly vulnerable to experimenting with all drugs, particularly opioids.

Patients in Private Substance Abuse Treatment Programs

This population was essential because these programs normally consist of individuals who can pay for appropriate medical care. Thus, this population often is Caucasian and relatively affluent compared to most street addicts, which makes them prime targets for prescription drug abuse based upon earlier studies.[5,6]

Pain Patients

The group with by far the most exposure to the comparative drugs listed in Table 1 are, of course, legitimate pain patients. Because it was felt that the fear of iatrogenic abuse was so large,[3,8,26] we concluded that patients should be monitored for abuse of their pain medicines. Therefore, very high prescribing physicians and pain clinics (identified by Purdue Pharma) who use the drugs listed in Table 1 with much greater frequency than the national average, were added to the key informant network.

National Institute on Drug Abuse

The National Institute on Drug Abuse (NIDA) supports a number of comprehensive epidemiological studies of drug abuse populations. The purpose of these studies is to detect the emergence of drug abuse, including that of newly available medications, in their catchment areas and, hence, the grant PI's were logical choices for inclusion as key informants.

Table 2. Areas of Specialty of Key Informants

Impaired health professional programs	17
Pain management specialists	48
Addiction treatment specialists	148
Adult treatment programs	105
Adolescent treatment programs	55
University/research/prevention centers	34
Hospitals	30
Methadone specialists	23
Drug/family courts/other	12

Enlistment of Key Informants

Over 2500 letters were sent to representatives of the nation's methadone programs, treatment centers, impaired health care professional programs, NIDA grantees and high-prescribing physicians. The sample was not random, but rather individual programs, physicians, and drug abuse experts were selected from national databases based upon their qualifications and experience with recognizing problematic substance use or abuse. The only other selection criterion was that informants be recruited not only from large urban areas with significant opioid abuse problems, but from as many rural and small- to medium-sized urban areas as possible to provide extensive coverage of the entire country. Of the 2500 letters sent, there was an initial base of slightly more than 200 informants, but with additional recruitment efforts, the total in the third quarter of 2004 rose to 338 individuals in 208 (21.4%) of the nation's 973 3-digit zip codes. Perhaps the high rejection rate was due to the commitment of effort required for this somewhat time-intensive activity. The disciplines covered by the key informants are shown in Table 2 and the national distribution of the key informants who agreed to participate is shown in Figure 1.

A quarterly questionnaire posed several basic questions regarding whether the informant had direct, first-hand knowledge and evidence of abuse of OxyContin and the other drugs listed in Table 1 in that quarter. For purposes of these studies we used 1 of 4 criteria to define a case of drug abuse: 1) use to get high; 2) use in combination with other drugs to get high; 3) use as a substitute for other euphorogenic drugs of abuse; and/or 4) use of the drugs to treat opioid withdrawal. A valid case was defined as one in which the informant had first-hand knowledge of the case histories of those individuals using the drugs in question. In order to get the greatest amount of information, each informant was requested to provide as much information as they could, including age, sex, and reasons for use. To be included in this study, each informant had to have responded to at least 6 of the 10 quarterly questionnaires.

All of the data in this paper are stratified by the 3-digit zip codes of the mailing address of each informant. We realize that most informants have contact with subjects from adjacent zip codes and, hence, their catchment area would be much more extensive than just their own zip codes. For example, a single treatment specialist in St.

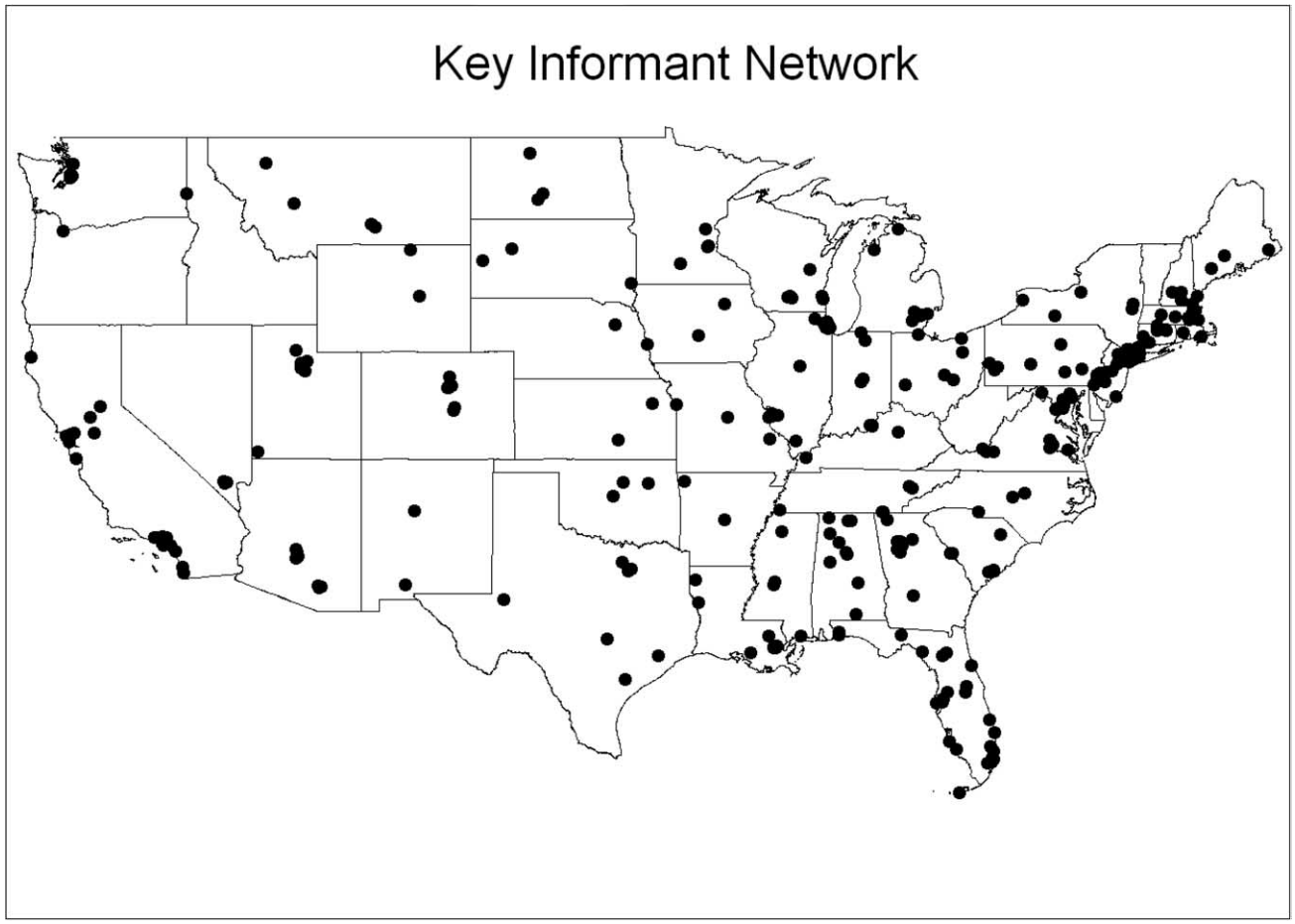

Figure 1. Location by 3-digit zip codes of the key informants.

Louis may routinely see individuals from 8 to 10 3-digit zip codes. It would be difficult for this specialist to provide the exact zip code for each abuse case reported. Consequently, we used the zip code of the informant as the geographical location of all cases of abuse, recognizing that this probably underestimated the coverage area of the informant and attributed cases to a more narrow, geographical locus than might be the case.

Geographical Prevalence of Abuse

An overall measure of the prevalence of prescription drug abuse was provided by the proportion of the reporting key informants in each quarter who reported at least 1 case of abuse of any of the drugs in their 3-digit zip code. We used the total number of the 3-digit zip codes from which positive or negative reports of abuse were received as the denominator of interest. To compare the geographical spread of abuse of opioid analgesics and in order to adjust for the variable number of 3-digit zip codes with reports from key informants each quarter, we calculated the percentages of 3-digit zip codes reporting at least 1 case of abuse for each drug in each quarter. We determined statistically significant changes in trends over time for each drug by regressing the logarithm of the odds of at least 1 case of abuse (ie, $\log(p/[1-p])$ where $p = \%$ of 3-digit zip codes reporting abuse) on calendar time starting with 0 for quarter 2 of 2002, 1 for quarter 3 of 2002, and so forth, up to 10 for quarter 4 of 2004. The results from the first quarter of 2002 when the study was initiated were not included because it is well known that there is often an overrepresentation of reports at the initiation of a study, reflecting historical perspectives rather than information only on the quarter for which data had been requested.

Rates of Abuse

To place into context the raw numbers of any adverse event, including abuse, a rate of its occurrence needs to be determined. Obviously, the only acceptable rate of abuse is defined as the number of individuals abusing the drug divided by the total number of people exposed to it either legitimately or illegitimately by diversion of some sort. The latter can never be ascertained with certainty. As discussed previously,[6] the best proxy for this denominator would be the number of patients for whom the drug was prescribed. Unfortunately, obtaining the inputs necessary to calculate the number of people prescribed each of 8 drugs in 973 3-digit zip codes by calendar quarter is enormously complex and, therefore, this denominator is not available at this time. We concluded, as an interim measure, that a rate of abuse should be calculated using the number of abuse cases

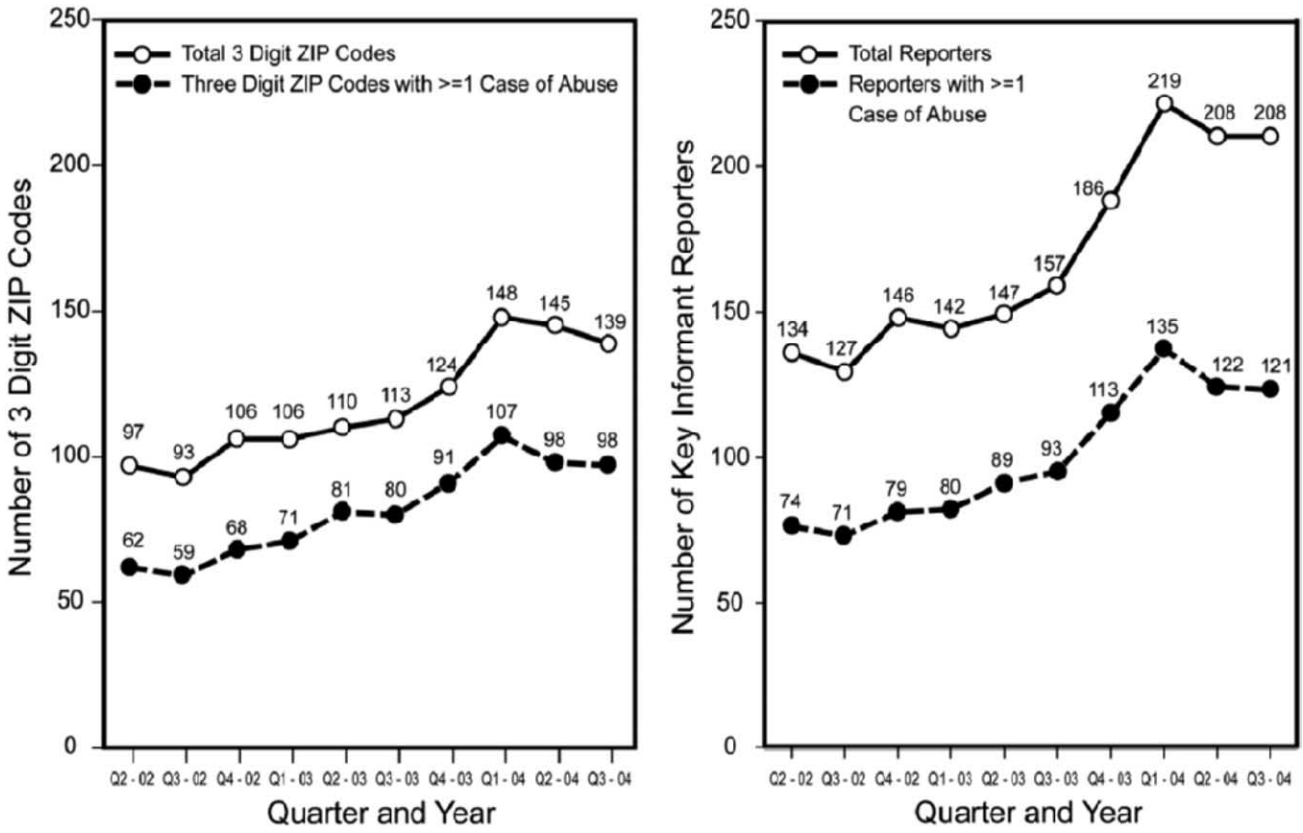

Figure 2. Shows the number of zip codes from which questionnaires were received and the number of zip codes in which any case of abuse was found (left panel). The right panel shows the number of informants completing a questionnaire each quarter and those reporting any cases of abuse of the 8 drugs monitored.

(for multiple informants in the same zip code, we used an average) divided by the 2000 Census-derived population numbers in 3-digit zip codes. The rationale for this approach was simple. We reasoned that 5 cases of OxyContin abuse in the New York City area with 8 to 10 million people might be considered a relatively modest rate of abuse, whereas if this same number of cases were observed in a city of 18,000, this rate would be viewed with considerably more gravity. To define a signal that an area had disproportionately high levels of abuse, we used a level of $\geq$5 cases/100,000 population, which seemed to provide a reasonable and manageable signal of abuse that would trigger more focused studies and the development of intervention strategies.

All drug definitions remained the same over the study period except for OxyContin. OxyContin's patent was considered invalid by a federal judge early in 2004, resulting in the launching of a generic 80 mg oxycodone extended release tablet in the second quarter of 2004. Thus, after this date, OxyContin and all the generics are labeled as "sustained-release oxycodone products."

Patient/Subject Confidentiality

The questionnaire did *not* elicit any individual information that could identify the drug users. The protocol was approved by the Washington University Institutional Review Board (IRB).

Results

Prevalence of Prescription Drug Abuse

Figure 2, left panel, shows the number of zip codes from which questionnaires were received and the number in which any abuse was detected. The right panel in Figure 2 shows the total number of informants who completed the questionnaire each quarter and those who reported at least 1 case of abuse of any of the 8 prescription opioid drugs we assessed (Table 1). The upward trends reflect additional recruitment efforts. From the data shown in Figure 2, it is evident that most informants reported at least some prescription drug abuse in their catchment areas, but there are clearly zip codes in which prescription drug abuse is frequently not a problem in any given quarter (ie, 0 cases reported), and in over 20% of the zip codes there was no abuse reported in any of the 10 quarters covered by this report.

To provide a measure of the prevalence of prescription drug abuse, Figure 3 shows the percentage of zip codes reporting at least 1 case of abuse of each of the study prescription drugs in each quarter, from the second quarter of 2002 through the fourth quarter of 2004 (second quarter of 2003 for methadone). As can be seen, OxyContin was mentioned most frequently in approximately 60% of all reporting zip codes, with hydrocodone

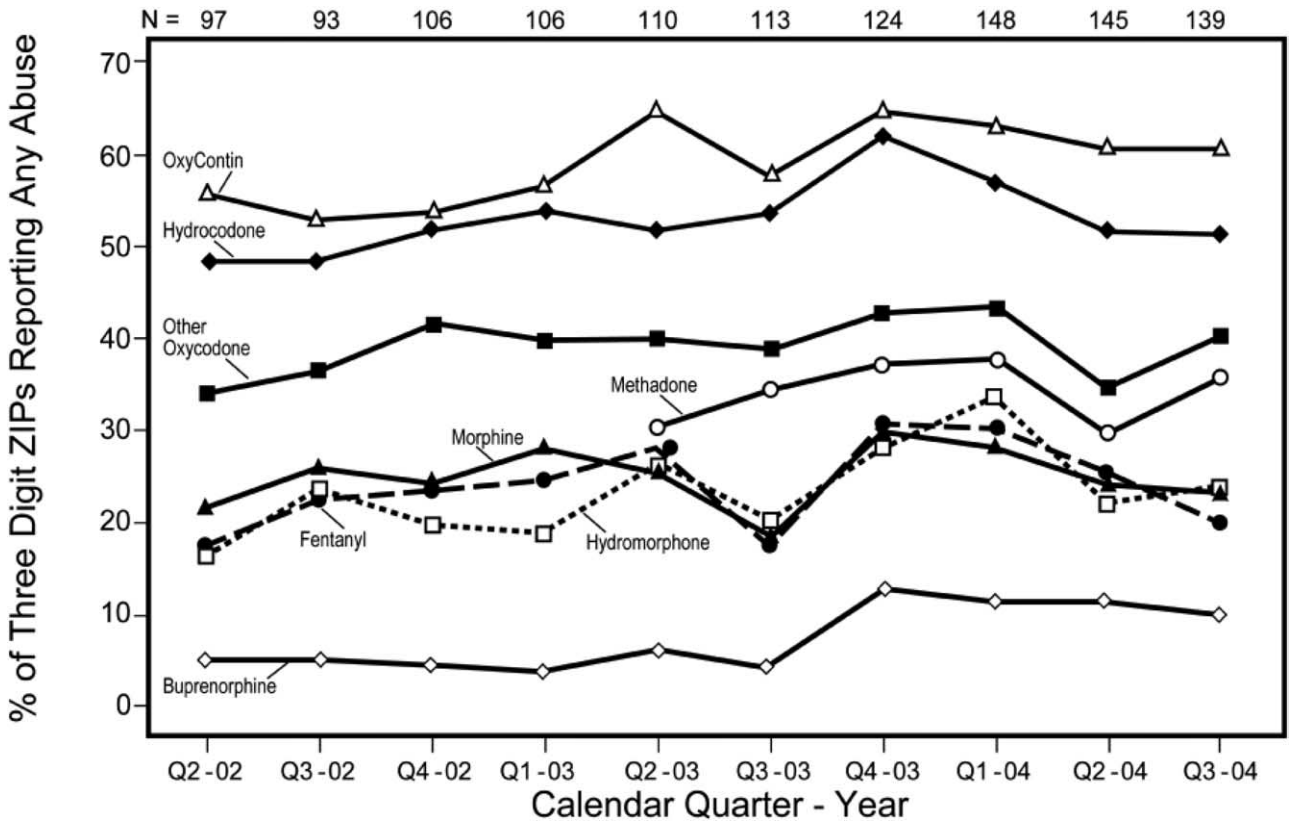

Figure 3. Percentage of zip codes reporting at least 1 case of abuse for each of the 8 study drugs by quarter. The number of zip codes from which reports were received is listed at the top.

a close second. The remaining drugs were observed with much less frequency, in descending order: other oxycodone products > methadone > morphine > hydromorphone > fentanyl > buprenorphine. In terms of trends over time, all of the drugs showed increase with buprenorphine being statistically significant ($P = .021$) and OxyContin and hydromorphone trends marginally significant ($P = .056$ and $P = .067$ respectively).

Occurrence of Signals of Abuse

To quantify the magnitude of abuse, Figure 4 shows the percentage of zip codes with at least 5 cases of abuse/100,000 people or greater for each of the 8 comparative drugs. In this case, hydrocodone and OxyContin signal sites were essentially equal with some variation in first and second place over the course of the study. The rank order of signal sites for other drugs yielded a similar pattern as that seen in Figure 3. In terms of trends over time, all drugs showed small to modest increases with morphine's and OxyContin's trends being statistically significant ($P = .010$ and .036, respectively).

Regional Distribution of Abuse

The regional distributions of zip codes in which a signal of abuse (≥5 cases/100,000) of any of the 7 comparative drugs (not OxyContin), signals of abuse of OxyContin alone, or both OxyContin and other drugs are shown in Figure 5, for the years 2002 (3 quarters), 2003 and 2004 (3 quarters). As is evident in Figure 5, prescription drug abuse in general, and OxyContin abuse specifically, is prevalent in all areas of the country but seems to be unevenly concentrated in the eastern and southeastern part of the United States. It is also evident in Figure 5 that: 1) prescription drug abuse seems to have spread geographically over time with a tendency to migrate from the Northeast and Appalachia to the Southeast and West; 2) OxyContin was rarely the sole prescription drug abused in any zip code, but rather, it was most frequently associated with polysubstance abuse; 3) in some areas, drug abuse problems other that OxyContin were observed; and 4) the abuse of prescription drugs seems very highly concentrated in rural, suburban, and small- to medium-sized urban areas. Notably, despite very concentrated numbers of informants in the nation's largest cities (Fig 1), we found very little abuse of prescription drugs in large metropolitan areas in which heroin use is endemic (Table 3).

Characteristics of Those Abusing OxyContin

In subsequent papers, we will present systematic data on the demographics of prescription drug abusers. However, in our preliminary data with 978 cases of OxyContin abuse, we can draw several tentative conclusions. It needs to be stressed that data were collected only for OxyContin and even the provision of these data was op-

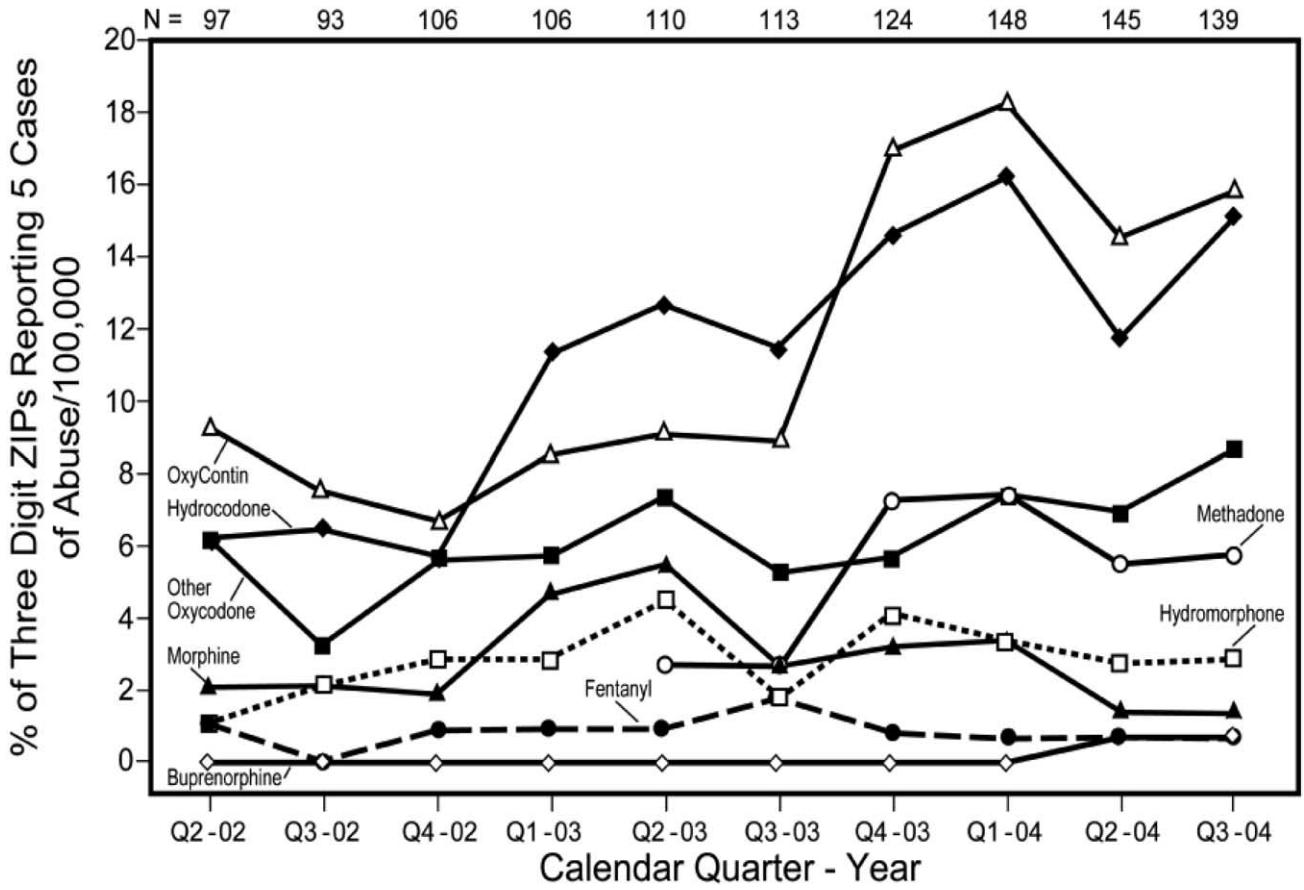

Figure 4. Percentage of zip codes (listed at top) in which at least 5 cases of abuse/100,000 persons (2000 Census figures) were detected for each drug by quarter. The 3 symbols represent abuse of any drug, abuse of OxyContin, and other drugs.

tional because many informants refused to participate if detailed information was required for each drug. These factors reinforce that our results are, at this stage, quite preliminary. Nevertheless, the average age of the individuals was 34.0 with a range of 12-75, with men far more likely (>65%) to abuse OxyContin than women. Over 91% of all individuals who abused OxyContin classified themselves as Caucasian with very small numbers of African Americans (<5%), Hispanics (<3%), and others. Over 87% of OxyContin abusers also had past and current histories of multiple drug abuse and use, and 70% of the OxyContin users listed a physician's prescription as the major source of OxyContin.

Discussion

The results of these studies indicate that prescription drug abuse has become prevalent in the United States and, unlike the pattern of abuse observed with illicit drugs such as heroin, which is heavily localized to the inner cities of very large metropolitan areas, it is most prevalent in rural, suburban, and small- to medium-sized urban areas. In terms of drug preferences amongst the 8 drugs we examined, it appears that the abuse of OxyContin and hydrocodone products is by far the most prevalent and wide spread. In terms of signal sites (ie, ≥5 cases/100,000 people in a zip code in a quarter), we found modest increases for most drugs over time, but these trends were significant only for OxyContin and hydrocodone. Collectively, these data suggest that both the prevalence (ie, zip codes with any abuse) and magnitude (ie, ≥5 cases/100,000 or more) of OxyContin abuse have increased during the course of this study and that abuse of the drug is now ubiquitous in this country with an upward trend that needs to be carefully monitored.

Although these results seem to support preliminary findings in federally supported surveys and extensive media coverage[15,23,28,32,33] that OxyContin abuse is substantial, it needs to be emphasized that this abuse seems to be just part of a general pattern of increasing prescription drug abuse because we found no zip code in which OxyContin was the sole drug abused and nearly all drugs showed upward trends of abuse over time. We hypothesize that OxyContin may simply be the current drug of choice among recreational drug users and street addicts and that this preference will dissipate over time. Ongoing surveillance by the key informant network and other parts of the RADARS system will either support or refute this assertion.

The sharp increase in the prevalence of buprenorphine abuse in the last 5 quarters of this study coincides with the release of Subutex® and Suboxone® (Reckitt Benckiser, Berkshire, UK) for the treatment of opioid addic-

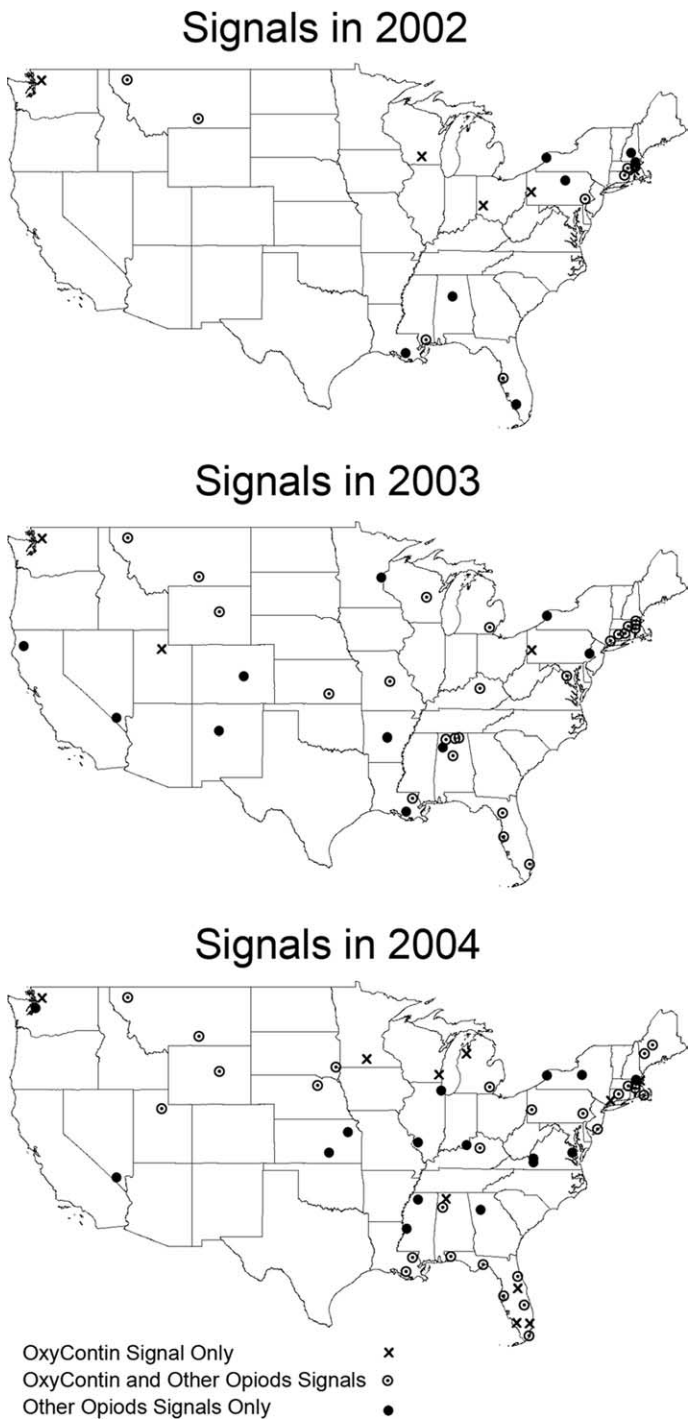

Figure 5. The regional distribution of zip codes in which a signal of abuse (5 cases/ 100,000 population) of any of the 8 comparative drugs (not OxyContin), a signal of abuse of OxyContin (>5 cases/100,000), and a signal for both are shown for the years 2002 (3 quarters), 2003, and 2004 (3 quarters).

tion. It should be stressed that the actual number of zip codes in which any abuse was detected was very small at only 10% of all zip codes monitored. Nevertheless, it appears that the increase in exposure resulting from its availability as new product lines led to an almost immediate increase in buprenorphine use for nontherapeutic purposes. This is not an unexpected finding because prior studies have shown that a period of experimentation with new drugs often occurs,[5,6] which dissipates quite quickly. Obviously, this needs to be carefully monitored, particularly in view of the use of buprenorphine in the highly vulnerable population of opioid abusers. In this connection, as shown in this and a prior study,[7] we have also documented significant and growing levels of methadone abuse which, of course, is used in these same populations.[7] Trends in the abuse of both methadone

Table 3. OxyContin® Cases/100,000 Population in 7 Major Metropolitan Areas in the Last Year of the Study

City	State	Qrtr 4 - 2003	Qrtr 1 - 2004	Qrtr 2 - 2004	Qrtr 3 - 2004
Boston	MA	0.00	0.00	0.00	0.00
New York City	NY	0.06	0.02	0.00	0.09
Philadelphia	PA	No data	0.00	No data	0.07
Baltimore	MD	0.31	0.00	0.00	0.00
Washington	DC	2.27	0.70	0.52	0.35
Miami	FL	.55	3.59	1.10	0.00
Chicago	IL	0.00	0.00	0.03	0.00

and buprenorphine are continuing to be monitored in our key informant network.

The abuse of OxyContin was found almost exclusively in Caucasian individuals (>91%), which is in marked contrast to the over-representation of blacks and Hispanics amongst illicit opioid (heroin) abusers. Given the tendency for prescription drug abusers to live in suburban and rural areas, this racial disparity may be understandable. Perhaps of equal importance, it may be that greater relative wealth exists in suburban and rural areas than in most inner cities, which may make expensive prescription drugs and treatment facilities more readily available.

Our finding that nearly all of the OxyContin abusers (>87%) had extensive current and past histories of substance abuse, much like that previously documented for another opioid analgesic, tramadol,[5,6] suggests that few legitimate, drug-naïve patients become addicted as a result of the intended use of OxyContin as an analgesic. However, our data cannot be considered definitive because reports of little abuse from pain clinics and other physicians dealing with pain may indicate either that there are very few patients in which abuse occurs or that the physicians were simply unaware of addiction issues in their patients. Moreover, the issue of whether iatrogenic dependence is an important factor in substance abuse has not been addressed in patients maintained on opioids for long periods of time. Thus, although many studies have concluded that the rate of abuse in pain patients ranges from very low to moderate,[2,12,24,26,27,36] there really is very little systematic data relevant to this point. Although this issue needs to be resolved in definitive studies, there is little question that the abuse of prescription opioids seems to be substantially confined to the illicit use of these drugs by recreational users and street addicts.

The regions with the greatest problems with OxyContin abuse were expected to be areas in which illicit opioid (heroin) abuse was prevalent, but this prediction was almost entirely wrong. Rather, abuse was concentrated in small- to medium-sized urban, suburban, and rural areas. The reasons for this are unclear, but several prominent possibilities exist, as suggested in earlier studies[5,6] and from direct feedback from our informants in these studies: first, very cheap heroin is often not readily available in nonurban areas; second, prescription drug abuse has been indigenous for decades,[17,18,35,38] with OxyContin simply being the latest drug of choice; third, OxyContin can be obtained relatively easily in much safer locations (eg, school or friends) than heroin; and finally, as alluded to above, the cost of OxyContin at $1 to $2/mg may be less of an obstacle to its use in suburban and small urban areas than it is in the inner cities, where very cheap heroin is available and financial resources are otherwise limited.

The authors appreciate the fact that, in many earlier surveys, hydrocodone products were by far the most abused analgesics in this country,[10,15,21,32,37] and our data for the first 18 months of this program confirms that finding. However, our observation that OxyContin now apparently ranks the same, or higher, than hydrocodone products in the last 9 months can be explained in 1 of 2 ways. First, our data collection system provides very timely information about the incidence of abuse in specific loci, as opposed to the more passive and somewhat "historical" data collection systems currently used in most systems, such as the Drug Abuse Warning Network (DAWN) or the FDA's MedWatch program. Thus, our data may indicate that OxyContin abuse has become more prevalent while other less proactive systems have not yet detected this trend. Second, it is conceivable that the key informants were aware that we were collecting data on OxyContin abuse and, hence, tended to overestimate the actual number of abuse cases of OxyContin, or conversely, underestimate the occurrence of abuse of other drugs.

There is another limitation to our approach that needs to be recognized: the geographical location and the diversity of specialties of our key informants could have influenced the magnitude and loci of abuse that we observed. That is, if we have informants in a given area and abuse occurs, we are likely to detect it. On the other hand, without an informant present, an absence of reported cases in a zip code does not mean that abuse was absent. Hence, one may not be able to conclude that drug abuse is regionally specific unless all regions are monitored. However, it should be noted that we frequently found zero abuse cases in 20% to 30% of all of the zip codes each quarter in which we had an informant, indicating that, at least in many regions, prescription drug abuse was not a problem. Thus, although we cannot claim that we have detected all zip codes that were positive and/or negative for abuse, our heavy sampling certainly suggests that our conclusions are valid.

The possibility that the specialty of the informants (eg, methadone clinic director) might lead to more or fewer cases because abuse is over-represented in their population is precisely why we selected a broad range of specialties in each zip code. Unfortunately, at the present time, we do not have the statistical power to draw any definitive conclusions about which of the large number of subdisciplines represented by our informants generated the most cases.

As mentioned above, the federally based tracking systems for abuse are largely passive registers and lack timeliness. Nevertheless, it is instructive to compare our results to 2 of the better systems currently in place: the Treatment Episode Data Set (TEDS) and the Community Epidemiology Work Group (CEWG). The TEDS system requires reporting on all clients admitted to treatment in clinics receiving any funding from state agencies, including funds from the Substance Abuse Prevention and Treatment block grants. The CEWG has been operated by the National Institute on Drug Abuse since 1976. In essence it is a "key informant" model in which epidemiologists and researchers from 21 cities convene twice yearly to discuss trends in drug abuse. Data from a variety of sources including DAWN, TEDS, the Arrestee Drug Abuse Monitoring program (ADAM), the System to Retrieve Identified Drug Evidence (STRIDE), the National Forensic Laboratory Information System (NFLIS), the National Household Survey on Drug Use and Health (NHSDUH), Monitoring the Future (MTF), and the Toxic Exposure Surveillance System (TESS) are used. Data from ethnographic studies may also be available.

The data from TEDS show a clear increasing trend in the proportion of admissions to treatment associated with opiates other than heroin. Admissions for prescription opioid abuse increased from 0.8% in 1992 to 2.3% in 2002, the most recent year for which data are available, but the rate of increase was much greater 1999 through 2002. In the last several years, increases have been noted for methadone, oxycodone, and other opiates (eg, hydrocodone). Although the CEWG only began to include a focus on prescription drugs in 2000, there was a substantial increase in prescription drug abuse from 2000 to 2002 that seems to have been driven by hydrocodone and oxycodone. Thus, both TEDS and CWEG, despite their obvious limitations, in general support the proactive and timely results reported in this paper that prescription drug abuse is a growing national problem.

On the basis of the studies described in this paper, it is clear that a number of signal sites have been identified with problematic use of OxyContin (eg, Table 2). Now that these sites have been identified, which was the goal of the key informant network, more focused efforts are underway to definitively examine the characteristics of the abuse. Through these efforts we hope to develop effective intervention and prevention strategies to reduce the abuse of OxyContin or "manage" the risk of abuse, which is in fact the sole purpose of all risk-management programs now mandated by the FDA.[34]

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