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# The Epidemiologic Association Between Opioid Prescribing, Non-Medical Use, and Emergency Department Visits

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**ABSTRACT.** *Introduction:* Since the 1990s prescriptions for and the non-medical use of opioids have increased. This study examines associations between opioid prescribing, non-medical use, and emergency department (ED) visits.

*Methods:* Data were abstracted from four federally sponsored, nationally representative, annual surveys (National Hospital Ambulatory Medical Care Survey, National Ambulatory Medical Care Survey, National Survey on Drug Use and Health, and Drug Abuse Warning Network).

*Results:* For hydrocodone and oxycodone, associations between prescribing and non-medical use, and prescribing and ED visits were statistically significant (p-values < 0.04) and strongly associated (correlation coefficient range 0.73 to 0.87). Male gender, White race, and age  $\geq 35$  were all statistically significant (p-values < 0.0001) predictors of receiving a hydrocodone or oxycodone-containing prescription.

*Conclusion:* The increased number of prescriptions written for hydrocodone and oxycodone between 1995 and 2004 was associated with similar increases in non-medical use and the number of ED visits during this time period. doi:10.1300/J069v27n01\_01 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2008 by The Haworth Press. All rights reserved.]

**KEYWORDS.** Opioid prescription, non-medical use, emergency department visits, hydrocodone, oxycodone

## INTRODUCTION

Data suggest that since the early 1990s there has been an increase in the medical use of a variety of opioid analgesics.<sup>1-3</sup> In 2005, more prescriptions were written for hydrocodone/

acetaminophen combination products than any other medication.<sup>4</sup> This was at a rate almost twice that of the second most prescribed generic or the most prescribed brand name medications, amoxicillin and atorvastatin (Lipitor; Pfizer Inc., New York, NY), respectively.<sup>4,5</sup> In

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addition, oxycodone/acetaminophen was the most frequently prescribed schedule II medication.<sup>4</sup>

In the early 1990s there was an indication that there was little change or actually a decline in the abuse of opioid analgesics.<sup>1</sup> However, since the late 1990s there has been evidence of increasing non-medical use and abuse of many prescription opioids.<sup>2,6,7</sup> In 2004 it was estimated 2.4 million individuals 12-years old or older initiated non-medical use of prescription pain relievers within the prior year.<sup>8</sup> Most of this non-medical use was associated with hydrocodone, codeine, propoxyphene, and oxycodone-containing products. The director of the National Institute of Drug Abuse (NIDA) has attributed this increase in prescription drug abuse, in part, to five factors: “significant increases in the number of prescriptions, significant increases in drug availability, aggressive marketing by the pharmaceutical industry, the proliferation of illegal Internet pharmacies that dispense these medications without proper prescriptions and surveillance, and a greater social acceptability of medicating a growing number of conditions.”<sup>9</sup>

Less information is available in the literature regarding the population-level impact of opioid analgesic abuse. Data collected as part of the Drug Abuse Warning Network demonstrate that from 1994-2002 there was a 2.7 fold increase in emergency department (ED) visits related, at least in part, to opioid analgesic abuse.<sup>10</sup> In addition, deaths attributable to opioid analgesic abuse increased almost 100% over the time period 1997-2002.<sup>11</sup>

The purpose of this study is to further explore the relationship between prescribing trends for hydrocodone, oxycodone, and morphine and aggregate indicators of non-medical use and potential consequences, specifically drug-induced and drug-related ED visits, from the mid-1990s to early 2000s.

## METHODS

### Study Design

This exploratory study utilizes four national data sets to examine correlations between pre-

scribing, self-reported non-medical use, and drug-induced and drug-related ED visits for hydrocodone, oxycodone, and morphine.

### Databases

#### *The NHAMCS/NAMCS Data Sets*

The National Hospital Ambulatory Medical Care Survey (NHAMCS) and National Ambulatory Medical Care Survey (NAMCS) include ambulatory care visits to hospital outpatient departments and nonfederally employed office-based physicians, respectively.<sup>12,13</sup> These surveys gather data on a sample of patient encounters and provide information relevant to prescribing practices.<sup>14,15</sup> Data on prescribing of hydrocodone, oxycodone, and morphine-containing prescription products were utilized.

#### *The DAWN Data Set*

The Drug Abuse Warning Network (DAWN), which collects medical record and toxicology screening data from a nationally representative hospital sample, was the source of information on drug-induced and drug-related ED visits.<sup>16,17</sup>

#### *The NSDUH Data Set*

The National Survey on Drug Use and Health (NSDUH, formerly the National Household Survey on Drug Abuse [NHSDA]) directly assesses the use and abuse of a variety of illicit and licit substances, including non-medical use of prescription drugs, based upon responses from a sample of the non-institutionalized civilian population.<sup>18,19</sup> Non-medical use is defined as use of a prescription pain reliever by an individual for whom it was not prescribed or use only for the experience or feeling that is produced.<sup>19</sup>

### Data Collected

Table 1 provides demographic characteristics obtained from the databases.

#### *The NHAMCS/NAMCS Data Sets*

The independent variable of interest in the NHAMCS/NAMCS data set was if a hydro-

TABLE 1. Demographic Characteristics of the Databases Used for Analyses

Characteristic	NHAMCS/NAMCS <sup>‡</sup> (n = 576,178) number (%)	Opioid Subgroup <sup>§</sup> (n = 14,255) number (%)	DAWN <sup>  </sup> (n = 8,216,1659) number (%)	NSDUH <sup>#</sup> (n = 332,712) number (%)
<b>Gender</b>				
Male	232,834 (40)	6,344 (45)	4,273,955 (52)	159,870 (48)
Female	343,344 (60)	7,911 (55)	3,852,246 (47)	172,842 (52)
Unknown	0 (0)	0 (0)	90,458 (1)	0 (0)
<b>Race</b>				
White	455,642 (79)	12,055 (85)	4,657,818 (57)	227,950 (68)
Black	97,662 (17)	1805 (13)	1,919,046 (23)	40,332 (12)
Other*	22,874 (4)	395 (3)	917,073 (11)	64,430 (19)
Unknown	0 (0)	0 (0)	722,722 (9)	0 (0)
<b>Ethnicity</b>				
Hispanic	67,470 (12)	934 (7)	844,831 (10)	43,016 (13)
Non-Hispanic	508,708 (88)	13,321 (93)	7,371,828 (90)	289,696 (87)
<b>Age</b>				
Mean (SD)	41 (24)	46 (18)	<sup>¶</sup>	<sup>**</sup>
<b>Insurance Type</b>				
Private Insurance	226,207 (39)	5,901 (41)	NA	231,691 (70)
Medicare/Medicaid	228,916 (40)	5,213 (37)	NA	55,589 (17)
Other <sup>†</sup>	74,500 (13)	1,917 (13)	NA	66,823 (20)
Self-Pay	46,555 (8)	1,224 (9)	NA	NA

NHAMCS = National Hospital Ambulatory Medical Care Survey, NAMCS = National Ambulatory Medical Care Survey, DAWN = Drug Abuse Warning Network, and NSDUH = National Survey on Drug Use and Health (formerly the National Household Survey on Drug Abuse [NHSDA]). SD = Standard Deviation. NA = Not Available.

\*The "Other" race category includes Asian, Native Hawaiian/other, Pacific Islander, and American Indian/Alaska Native.

<sup>†</sup>The "Other" insurance type category includes worker's compensation, no charge/charity, unknown, and other. For the NSDUH dataset, this also includes 11,461 individuals who had Champus insurance coverage.

<sup>‡</sup>The NHAMCS/NAMCS contains the concatenated data files for the years 1995-2004.

<sup>§</sup>The opioid subgroup consists of the 14,255 patient encounters from the concatenated 1995-2004 NHAMCS/NAMCS data set that included a prescription for a hydrocodone, oxycodone, or morphine-containing product.

<sup>||</sup>The DAWN consists of data from 1995-2002, the latest year for which information of interest is publicly available.

<sup>¶</sup>The DAWN age categories and corresponding number of treatment encounters in each age category are as follows: 6-17 years = 773,931; 18-25 years = 1,618,549; 26-34 years = 2,058,668; 35-44 years = 2,442,496; 45-54 years = 1,012,253; ≥ 55 years = 293,772; and unknown = 16,990.

<sup>#</sup>The NSDUH represents data collected from 1995-2004.

<sup>\*\*</sup>The NSDUH age categories and corresponding number of respondents in each age category are as follows: 12-17 years = 109,751; 18-25 years = 107,191; 26-34 years = 38,838; 35-49 years = 45,275; 50-64 years = 18,257; and ≥ 65 years = 13,400.

codone, oxycodone, or morphine-containing product had been prescribed at a patient encounter. Medications are imputed standard five-digit medication codes.<sup>20</sup> As there are many brand, generic, and combination prescription products that include these substances the medication codes were combined to create one variable for each drug of interest. The

NHAMCS and NAMCS data sets were combined for the years 1995 to 2004, the latest year for which public use data files were available at the time of the analyses.

Concatenation of the NHAMCS and NAMCS created a database containing a total of 576,178 patient encounters. The overall sample was predominantly female (60%), White (79%), and had

private (39%) or public (Medicare/Medicaid) (40%) insurance coverage. African-Americans and individuals of Hispanic ethnicity comprised 17% and 12% of the sample, respectively. This is approximately equivalent to the representation in the general population for these racial and ethnic groups. The mean age of the concatenated data set was 41 (SD  $\pm$  24) years.

#### *The DAWN Data Set*

The number of ED drug episodes per year for which a mention of a hydrocodone, oxycodone, or morphine-containing product appeared on the data collection instrument was abstracted. The sampling methodology for the DAWN changed in 2003 and information obtained prior to 2003 cannot be directly compared with data obtained afterwards.<sup>21,22</sup> As a result, data of interest were available from 1995-2002. The majority of the DAWN sample was male (52%), White (57%), and of non-Hispanic ethnicity (90%). African-Americans constituted a larger percent in the DAWN sample (23%) than they do in the general US population.

#### *The NSDUH Data Set*

Annual percentages of the sample population who indicated ever non-medical use of hydrocodone, oxycodone, or morphine were obtained. Information related to non-medical use of morphine was available for the 10-year time period of 1995-2004. A question regarding non-medical use of hydrocodone and oxycodone was first asked as part of the NSDUH in 1999. With a mean age of 21, the NSDUH sample was primarily composed of females (52%), Whites (69%), and individuals of non-Hispanic ethnicity (87%). As NSDUH oversamples the 12-17 and 18-24-year-old age groups, it was expected that the mean age would be younger than that of the other databases.

#### *Statistical Analysis*

In order to account for the sampling structure of the NHAMCS and NAMCS, SURVEY procedure programs for the statistical package (SAS Institute, Inc., Cary, NC) provided on the Centers for Disease Control and Prevention

(CDC) website were used.<sup>23</sup> The clustering and stratification variables were either already present or created in the datasets, depending on the year, and followed noted documentation.

Kendall's tau was used to measure the strength of the association between prescribing and drug-induced and drug-related ED visits and the association between prescribing and self-reported non-medical use. The NHAMCS/NAMCS and the DAWN datasets are compared for the years 1995 to 2002, and the NHAMCS/NAMCS and the NSDUH datasets are compared for the years 1999 to 2004 for hydrocodone and oxycodone and from 1995 to 2004 for morphine.

The range of values for Kendall's tau is between  $-1$  and  $+1$ . Negative values indicate that the two variables move in opposite directions (inverse association) while positive values designate both variables move in the same direction (direct association). A value of zero would indicate that there was no association between the two variables. This test was selected because it outperforms Spearman's rank correlation test<sup>24,25</sup> and can be utilized with data that is not normally distributed.<sup>26</sup>

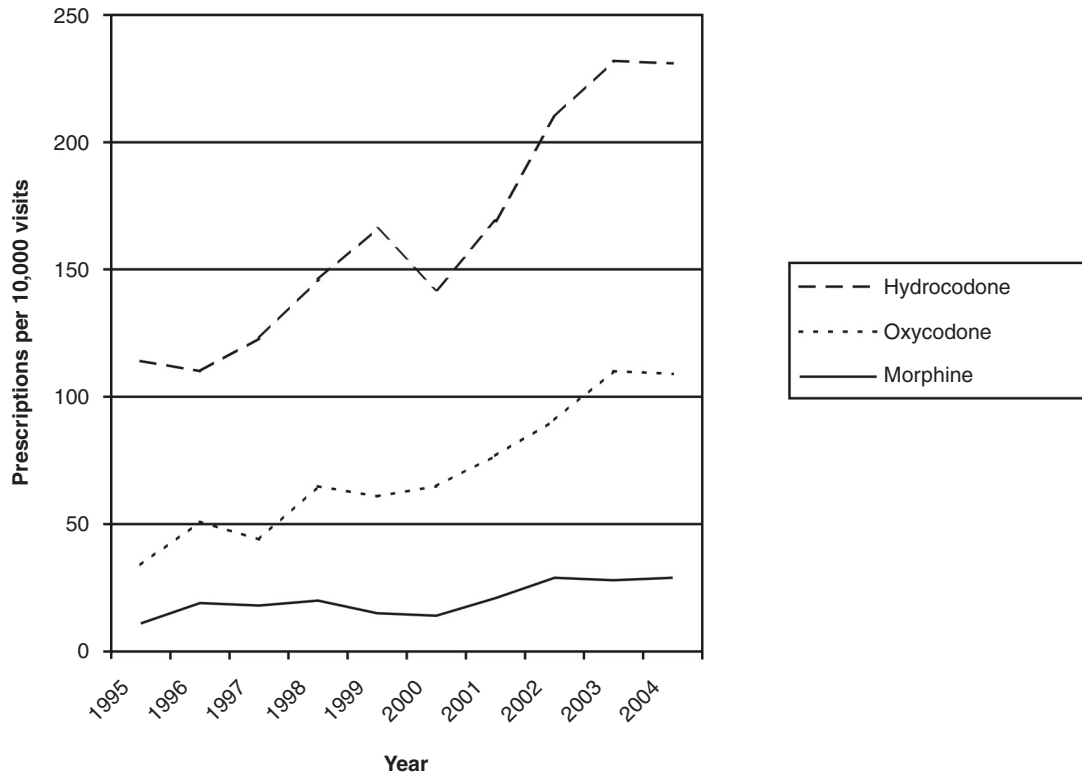
Data were analyzed using SAS, version 9.1 (SAS Institute, Inc., Cary, NC). A  $p$ -value  $< 0.05$  was considered to be statistically significant. Given the large sample size, an *a priori* power calculation was not performed.

## **RESULTS**

The prescription rate (number of prescriptions per 10,000 patient encounters) in the concatenated NHAMCS/NAMCS data file for hydrocodone, morphine, and oxycodone-containing products increased 2.03, 2.64, and 3.21 fold, respectively, over the time period 1995-2004 (Figure 1).

Using DAWN data, drug-induced and drug-related ED visits for hydrocodone, oxycodone, and morphine-containing products increased in absolute numbers from 1995 to 2002 (Figure 2). During this 8-year time period, the rate of increase (ED drug mentions) for oxycodone was 5.60 fold, as compared to 1.16 and 1.60 fold increases for morphine and hydrocodone, respectively.

FIGURE 1. Prescribing trends for hydrocodone, oxycodone, and morphine, 1995-2004



Note: Based upon data obtained from the concatenated 1995-2004 National Hospital Ambulatory Medical Care Survey (NHAMCS) and National Ambulatory Medical Care Survey (NAMCS) data set.

The percent of the NSDUH sample indicating non-medical use of hydrocodone, oxycodone, and morphine is illustrated in Figure 3. The rate (percent of the sample population per year) of non-medical use of hydrocodone and oxycodone has consistently increased since 1999, when these drugs were first included in the survey, with reported ever use of hydrocodone increasing 1.04 fold and oxycodone use increasing 6.41 fold. After experiencing an initial increase, reported non-medical use of morphine has declined since 2000, although there has been an overall 86% increase of ever use since 1995.

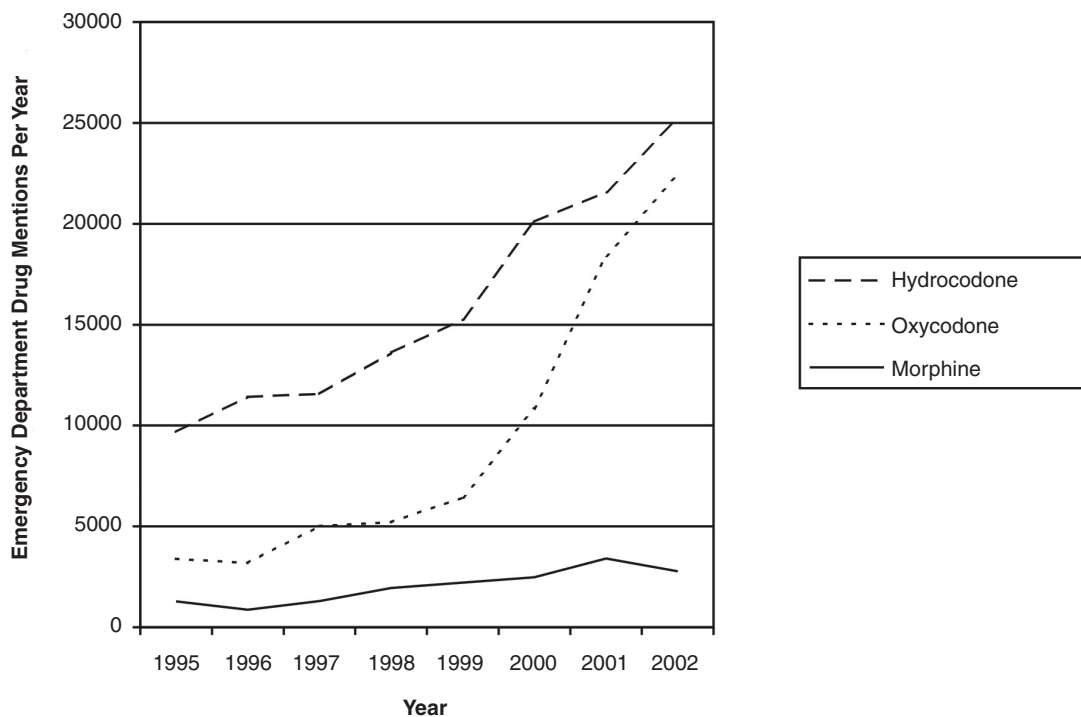
In examining the graphed trend lines there appeared to be an association between the slopes of the lines, for both hydrocodone and oxycodone, across all 3 data sets. Not only was increased prescribing of oxycodone and hydrocodone (based upon data obtained from NHAMCS/NAMCS) associated with increased

non-medical use (using self-report from the NSDUH survey) but it was also associated with a greater number of ED visits (using data gathered as part of the DAWN). A relationship between prescribing and drug-induced and drug-related ED visits seemed to be present for morphine as well, but the association between prescribing and non-medical use was less clear.

In Table 2 Kendall's tau measure of correlation quantifies the association between the trends observed between Figures 1, 2, and 3 for hydrocodone, oxycodone and morphine. Results from the DAWN and NSDUH data sets are separately compared to the concatenated NHAMCS/NAMCS data set. For both hydrocodone and oxycodone, the NHAMCS/NAMCS comparisons for the DAWN and NSDUH are all statistically significant with strongly correlated results (range 0.73 to 0.87). In contrast, for morphine, neither of the comparisons resulted in a statistically significant p-value and the cor-



FIGURE 2. Trends in drug-induced and drug-related emergency department visits for hydrocodone, oxycodone, and morphine, 1995-2002



Note. Information consolidated from the Drug Abuse Warning Network (DAWN) database, Tables 2.4.0 and 2.8.0. Based upon annual emergency department (ED) mentions from 1995-2002 for hydrocodone, oxycodone, and morphine.

relations were weak or negative for the DAWN and NSDUH, respectively.

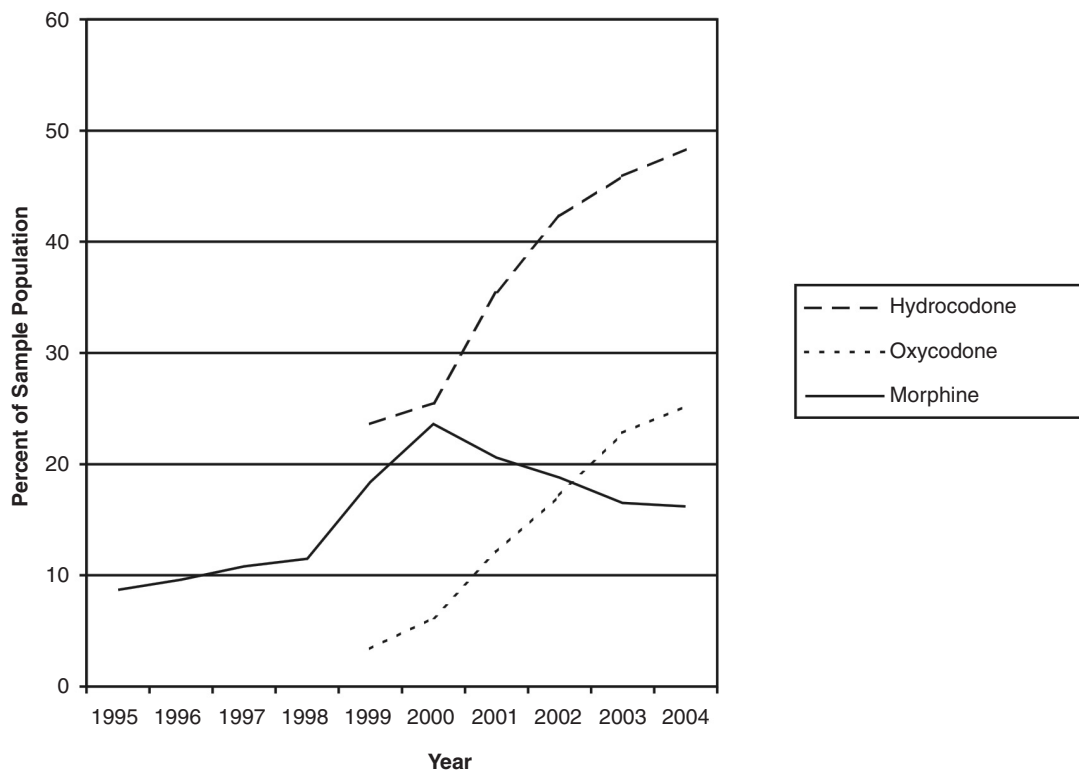
For the combined NHAMCS/NAMCS dataset, logistic regression was used to determine predictors of receiving a hydrocodone or oxycodone-containing prescription. Variables associated with receiving a prescription for hydrocodone and oxycodone were analyzed separately. The probability of receiving a hydrocodone-containing prescription was associated with male gender (OR = 1.13, 95% CI 1.08, 1.18,  $p < 0.0001$ ), White race (OR = 1.40, 95% CI 1.21, 1.62,  $p < 0.0001$ ), age  $\geq 35$  (OR = 1.83, 95% CI 1.71, 1.95,  $p < 0.0001$ ), and being "self-pay" (OR = 1.22, 95% CI 1.06, 1.40,  $p = 0.0049$ ). The likelihood of receiving an oxycodone-containing prescription was associated with male gender (OR 1.24, 95% CI 1.17, 1.32,  $p < 0.0001$ ), White (OR = 1.73, 95% CI 1.37, 2.19,  $p < 0.0001$ ) or African-American race (OR = 1.61, 95% CI 1.21, 2.14,  $p < 0.0001$ ), and age  $\geq 35$  (OR = 2.83, 95% CI 2.55, 3.15,  $p <$

0.0001). The major difference in outcome between the two analyses was that in the hydrocodone analysis, African-American race did not have an effect on the likelihood of receiving a prescription, while in the oxycodone analysis both White and African-American race significantly increased the likelihood of receiving a prescription for an oxycodone-containing product.

## DISCUSSION

The increased rate of prescribing of hydrocodone and oxycodone-containing products has been associated with a strong positive and statistically significant increase in self-reported non-medical use as well as in drug-induced and drug-related ED visits. For oxycodone-containing products, there has been a disproportionate increase in non-medical use and ED visits relative to the increase in prescribing.

FIGURE 3. Trends in self-reported non-medical use of hydrocodone, oxycodone, and morphine, 1995-2004



Note: Based upon data collected as part of the National Survey on Drug Use and Health (NSDUH), formerly the National Household Survey on Drug Abuse (NHSDA). Information for morphine was available for the years 1995-2004. Questions specific to non-medical use of hydrocodone and oxycodone were asked beginning in 1999.

Interestingly, while the rate of increase in prescribing for morphine-containing products is greater than that for hydrocodone- (but less than that for oxycodone-) containing products, there is little relationship with drug-induced and drug-related ED visits and there has actually been a decline in self-reported non-medical use of morphine since 2000.

The increased number of prescriptions for hydrocodone, oxycodone, and morphine-containing products over the ten-year time period 1995-2004 would be expected to result in an increase in the supply of these drugs. This increase in supply could mean that there are more drugs available to be diverted for non-medical use. The increases in self-reported non-medical use and drug-induced and drug-related ED visits for hydrocodone and oxycodone could be a manifestation of this. As it is doubtful that there has been an increase in the incidence of acute

pain syndromes or the prevalence of chronic pain syndromes, it would be unlikely that these increases are solely the result increased numbers of patients seeking treatment. An increase in patient demand for hydrocodone and oxycodone-containing products is plausible.

Based upon the results of this analysis, as well as available literature, it is reasonable to postulate that an increase in drug supply could contribute to more use of the drug as well as the subsequent development of problems including non-medical use. An analysis of the Automation of Reports and Consolidated Orders System (ARCOS) and DAWN data from 1997-2002 examined the relationship between increased legitimate retail level distribution of prescription opioid analgesics and opioid analgesic abuse, and also reached this conclusion.<sup>2</sup> A report based upon information obtained through the Researched Abuse Diversion and



TABLE 2. Correlation Between Opioid Prescribing and Drug-Induced and Drug-Related Emergency Department (ED) Visits and Between Opioid Prescribing and Prevalence of Self-Reported Non-Medical Use

Drug	Datasets Compared	Correlation Coefficient	P-Value†
Hydrocodone	NHAMCS/NAMCS DAWN*	0.79	0.0065
	NHAMCS/NAMCS NSDUH†	0.73	0.0388
Oxycodone	NHAMCS/NAMCS DAWN*	0.76	0.0088
	NHAMCS/NAMCS NSDUH†	0.87	0.0146
Morphine	NHAMCS/NAMCS DAWN*	0.26	0.3223
	NHAMCS/NAMCS NSDUH†	-0.55	0.1260

NHAMCS = National Hospital Ambulatory Medical Care Survey, NAMCS = National Ambulatory Medical Care Survey, DAWN = Drug Abuse Warning Network, and NSDUH = National Survey on Drug Use and Health (formerly the National Household Survey on Drug Abuse [NHSDA]).

\*The concatenated 1995-2002 NHAMCS and NAMCS data sets were used for comparison with DAWN.

†The concatenated 1999-2004 NHAMCS and NAMCS data sets were used for comparison with NSDUH (NHSDA).

‡Kendall's tau was utilized for each comparison.

Addiction-Related Surveillance (RADARS) system described an association between an increase in the number of prescriptions written for methadone, without any significant change in the methadone maintenance population, and higher levels of diversion and abuse.<sup>27</sup> This increase in prescriptions was attributed to use for pain management. Prescriptions from physicians have been identified as part of the supply for between 30 and 70% of patients who were dependent on prescription opioids.<sup>6,28,29</sup> There is some suggestion that in those states where certain prescription narcotics must be written on special prescriptions, the street value of those drugs is greater.<sup>30</sup>

These findings have an important clinical implication. Physicians need to be aware that some of the opioid prescriptions that they write may be diverted for non-medical use and that this non-medical use may lead to the need for

emergency department care. Some recent work supports this. For example, in one study of full-time undergraduate students conducted in 2005, investigators found that lifetime prevalence of non-medical use of prescription opioids was 14.3% and past year use was 7.5%.<sup>31</sup> White students were more likely than African-American or Asian students to report non-medical use of prescription opioids. The leading sources of the prescription opioids were parents and friends. Given what is known, it would seem reasonable to suggest that physicians should caution adults, especially adults with teen-age children, to guard prescription opioids to prevent diversion and non-medical use.

### Strengths and Limitations

To our knowledge this is the first study to report the association between prescribing patterns, drug-induced and drug-related ED visits, and self-reported non-medical use for hydrocodone, oxycodone, and morphine. We are unaware of any previous studies that have shown a statistically significant relationship between hydrocodone and oxycodone prescribing and drug-induced and drug-related ED visits. Analyses such as this one, and others, help to characterize the relationship between prescribing, non-medical use, and drug-induced and drug-related ED visits. Additional strengths of this study include the large sample size and the high quality and consistency of the data sources (NHAMCS, NAMCS, DAWN, and NSDUH).

### Limitations of the Data Sets

This is a cross-sectional study subject to ecological fallacy. The four data sources utilized (NHAMCS, NAMCS, NSDUH, and DAWN) are all federally sponsored cross-sectional studies of nationally representative samples drawn from the U.S. population. As they are population-based studies that do not utilize the same sample, our ability to draw inferences is limited. By its very nature, secondary data analysis and the tests of association utilized are not conducive to establishing cause-and-effect relationships. However, it is reasonable to conclude that increased physician prescribing and the resultant increase in supply could be a con-

tributing factor in the increased non-medical use and drug-induced or drug-related ED visits of the drugs studied, specifically for hydrocodone and oxycodone.

Beginning in 2002, there were several methodological changes to the NSDUH survey including a cash incentive for respondents who completed the questionnaire.<sup>32</sup> The impact of each individual change on survey response is not known but the net effect was an increase in drug use prevalence. Previous field tests with offering an incentive demonstrated an improved response rate and it is likely that this had the largest impact on increasing response rate. The increase in response rate from 2001 to 2002 was slightly less than ten percent, with the largest gains among those aged 12-25-years old.

### *Limitations of the Analyses*

For the purposes of this analysis, a data break was not used between 2001 and 2002 NSDUH data, either graphically or in the analyses. If the changes described above had resulted in an overestimation of non-medical use, we would have expected there to be an increase for all three drugs (hydrocodone, oxycodone, and morphine). The exception to this would be if the majority of the non-medical use was in the 12-25-year-old age group, in which case an increase in prevalence could be anticipated based upon the improved response rate. An increase was only observed for hydrocodone and oxycodone. For morphine there was a decline in reported non-medical use.

### *Conclusions*

We have established that a statistically significant and strongly positive association exists between the increase in prescribing of hydrocodone and oxycodone-containing products, the increased prevalence in self-reported non-medical use, and drug-induced and drug-related ED visits. The logistic regression analyses have yielded a picture of the patient population most likely to receive a prescription for these drugs.

To determine if the associations observed in this study between increased supply as a result of prescribing and increased problems manifested by non-medical use and drug-induced

and drug-related ED visits represent an actual cause and effect relationship, different study methodology is warranted. The question that is most interesting, "What happens to prescription opioids in the patient population most likely to be prescribed them?" is unable to be answered by a secondary data analysis. Extensions of this course of inquiry would also address the following questions: what are the indications for which patients are prescribed opioids, what is the disposition of prescribed opioids (i.e., is non-medical use more or less common), are those who are prescribed an opioid more likely to have an opioid-related or opioid-induced ED visit, and what portion of prescribed opioids are diverted?

The most direct way to answer the above questions would be to perform a prospective cohort study. Utilizing this type of study design would provide the reliable and accurate information that would need to be gathered on opioid prescriptions received and filled, non-medical use or diversion of opioids, and ED visits. Some private health insurance entities (e.g., a large health maintenance organization [HMO]) or public health plans (e.g., Medicaid) would have a sufficient number of enrolled patients to employ this methodology.

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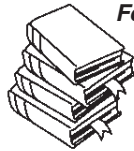
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