dispensed in 2007. Oxycodone products, immediate and extended-release combined, are second among opioids, with approximately 15 million patients filling 42 million prescriptions in 2007. Approximately 1.3 million patients filled 5.5 million prescriptions for the generic Oxycodone ER in 2007, and 400,000 patients filled two million OxyContin prescriptions in 2007.

The highest extended-release Oxycodone prescription volume was found in Florida, California, Pennsylvania, Ohio, New York, and New Jersey. The Teva brand led the extended-release Oxycodone market share with 37 percent, Purdue was second with 27 percent, followed by Watson, with 18 percent. General practitioners, internal medicine, and anesthesiologists were the leading prescribers of extended-release Oxycodone products. And, lastly, these products are most commonly dispensed to patients aged 41 to 65 years.

I would like to acknowledge Mara



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McAdams, a fellow with the Office of Surveillance and Epidemiology for her assistance. This concludes my presentation. Thank you.

CHAIR FARRAR: Thank you very much. We started about 15 minutes late, and have been able to stay basically on schedule. I'd like to try and catch up by about five minutes. We will resume here at 11:10.

I'd like to take this time to remind the panel members that there should be no discussion of the topic during the breaks amongst ourselves or with any member of the audience. I'll see you promptly at 11:10.

DR. WATKINS: And if those members who had pre-ordered your lunches, if you could drop your money off at the meeting registration desk just outside the room during the break, that would be great.

(Whereupon, the proceedings in the foregoing matter went off the record at 11:02 a.m. and went back on the record at 11:15



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a.m.)

CHAIR FARRAR: Okay. We would like to continue now with the presentations, if I could ask people to please take their seats.

The next presentation is Joe Gfroerer on the prevalence and pattern of non-medical use.

MR. GFROERER: Okay. Thanks.

Hello. I'm Joe Gfroerer from the Office of Applied Studies in SAMHSA, and I'm going to present some data from the National Survey on Drug Use and Health, the latest data on OxyContin and pain reliever misuse.

It's important to understand the source of the data and how it's collected in terms of interpreting it. The National Survey on Drug Use and Health is a nationally representative survey. It is also represented within each of the 50 states and D.C. And it covers the civilian non-institutional population age 12 and older.



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Data are collected using face-to-face interviews in people's homes. It takes about an hour to complete the interview. And it's done with computer-assisted interviewing to -- and mainly self-administered -- to improve the accuracy of reporting based on experiments that we've done.

And we get about 67,000 respondents each year. It's continuously in the field. And it's also important in terms of tracking trends to recognize the changes in the survey that actually affected the trends and created breaks in the trend, and those were in 1999 and 2002.

So even though we collected data on prescription drug misuse back into the '70s, we can't do a long-term trend. The data I'm presenting will focus on the 2002 to 2006 time period.

And we have the response rates there at the bottom. The response rate is about 91 percent in 2006 for the selected



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households. That's a percent of those selected that participated. And then, within the household, the persons selected, about 74 percent response rate.

These are the kinds of measures that we obtained during the interview focusing on illicit drug use. That's the main issue in the survey. We go through a whole series of questions on different drugs, starting with tobacco and alcohol and then moving into marijuana, cocaine and then finally into prescription drug misuse, which we define as non-medical use of prescription drugs. And I'll talk more about that in a minute.

But we get measures of recency of use and create estimates of how many people have used in their lifetime, within the past year, and in the past month; frequency of use based on the number of days used in different time periods. We ask for the date -- actually, the age and date of first use, so we can construct incidence data of first time use



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of each drug.

And we also have a series of questions on dependence and abuse that are based on the DSM-IV criteria so we can measure substance use disorders, overall and for each individual substance. And then, also, treatment data asking respondents if they received or needed treatment for substance abuse problems.

So this is the definition for non-medical prescription drug use that is given to the respondents before they answer the questions about the prescription drugs. The drug that was not prescribed for you or you took the drug only for the experience or feeling that it caused, and it's only including prescription drugs, not over-the-counter drugs.

And the strategy is based on getting estimates of all those measures I showed you for four specific therapeutic classes -- pain relievers, tranquilizers,



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stimulants, and sedatives. In order to get that, we define the categories, each of these four categories, by naming the specific drugs within those categories and explaining what it means, what it means -- what a pain reliever is, and giving examples.

And so we get lifetime use of all of these individual specific pharmaceuticals but then limited data on the -- no details, really, on the specific drug, just other than lifetime use, with a couple of exceptions -- OxyContin and methamphetamine. We do go into more detail and get recency of use and age at first use and frequency of use.

So each of these therapeutic classes includes a mix of brand name and generic drugs, and this is mainly to define the category, the four categories for the respondents. It's done by using these pill cards. There's four pill cards, one for each of the therapeutic classes.

This is the pain reliever pill



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card. You can see that it shows photographs of the drugs that we expect are the most prevalent and most recognizable to respondents. And the questioning strategy starts with the first three questions, asking about those top three groupings: Darvocet, Darvon, or Tylenol with codeine; and then Percocet, Percodan, Tylox; and Vicodin, Lortab, and Lorcet. So those are specifically asked about as they are worded there.

Then, another question follows up by saying: did you use any of these other drugs shown on the card below the red line? And then there are check boxes for each of those.

And then, finally, the respondents can report any other drugs by typing them in, even if they are not named on the pill card.

So this is what the data looks like. You can see the top three categories there are those first three above the red line that we specifically ask about, and then



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that's followed by the hydrocodone, codeine, and OxyContin. And these estimates are in terms of number of users in millions in lifetime.

So let me talk about the trends and patterns. And, first, in pain reliever use overall, this is non-medical pain reliever use. Since 2002, for these three measures -- lifetime use, past year use, and past month use -- we have seen small but statistically significant increases in all three of these measures over the five-year period.

And two other measures -- substance disorder -- well, pain reliever disorder -- hasn't changed much. It's at about 1.6 million in 2006. And the number of people reporting that they received treatment for pain reliever problem within the past year has gone up significantly, from 360,000 to 547,000. And these are self-report from the survey.

Looking at the trend by age group



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-- well, a couple of things here. You can see the prevalence is highest in the 18 to 25-year age group, and now we're looking at past year misuse, non-medical use. We don't see any increase for the 12 to 17-years at 7.2 percent in 2006, and small increases, but statistically significant, for the 18 to 25, and 26 to 34.

Now, looking at the lifetime drugs, specific drugs reported in the lifetime among the 18- to 25-year old gives you hints about where those increases might occur, what drugs are involved, and you can see the doubling for OxyContin over on the right there from 2.6 percent ever used to 5.1 percent. Hydrocodone went from 5 to 7.8.

So there is some specific drugs that are more likely to have been increased in use during that period. And for the 26 to 34, it is basically the same drug, same pattern, OxyContin going from 1 percent to 2.7 percent in that period.



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With the state-level data that we collect, we actually -- because of the design of the sample we can pick up sub-state-level patterns, and here is the pain reliever in the past year prevalence. And you can see Kentucky, parts of Colorado, and other parts of the west with the highest rates in red. The blue states in the upper Midwest have the lowest rates, but there are variations within specific areas.

And there is quite a variation in these sub-state areas, from 2.4 percent up to 7.7 percent across these regions.

Now, this is some new data that we began collecting in 2005 where we -- if the respondent reported using pain relievers non-medically, then we follow up asking them, where did they get the pain relievers that they misused.

And the pie on the right shows that over half report getting it free from a friend or relative. You can see there's a



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tiny proportion -- less than -- well, about a tenth of a percent report that they bought it on the internet, and only four percent from a drug dealer or a stranger.

And then, the followup question, for those people who report that they got it free from a friend or a relative, asks, where did the friend or relative get the pain relievers that were misused? And they report in that case -- about 80 percent -- that it came from one doctor. Again, very rare reports of drug dealers and internet purchase.

Now, that was for all pain reliever users in the past year. When you look at the more frequent users, the heavy users, the pattern changes a little bit. Fewer of the heavy users report from -- free from a friend or relative, and slightly more report from a drug dealer or stranger, and a little bit of an increase for internet, but still low percentages.

So this is -- the red bar



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represents those who have used on 100 or more days within the past year, the frequent users.

Okay. Now, focusing more on the initiates -- and these would be people who used drugs for the first time within the past 12 months, based on questions in the survey, and these estimates are in thousands, so you can see the number one drug for initiation in 2006 was pain relievers with 2.15 million new users. Marijuana is at about the same, 2.1 million. You can see OxyContin there on the right at 500,000.

Now, it is important to keep in mind, though, that that's not necessarily -- the two million pain reliever users were not using illicit drugs for the first time. Most of them had used other drugs. You can see here from the age at first use that inhalants and marijuana are typically used at -- in the mid-teens for the first time, whereas the pain relievers and other prescription-type drugs, when they're misused for the first time it



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typically occurs in the twenties.

So there is a lag time, which -- and what that means is most of the initiation occurring for pain relievers is -- and OxyContin is occurring among people who have used other drugs. And that's shown here with the lifetime use of other drugs. Among those 2.1 million pain reliever initiates, two-thirds of them had used marijuana, 20 percent had used cocaine, and a third had used other types of prescription drugs non-medically -- tranquilizers, sedatives, or stimulants.

In the OxyContin initiates it's even more pronounced. Ninety-five percent of the OxyContin initiates had used marijuana, and two-thirds had used cocaine. And not only that, but the OxyContin initiates also had, for the most part, already used other pain relievers non-medically. So OxyContin is rarely the first pain reliever that is misused by drug abusers.

Okay. Some of the trends and



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patterns for these -- some of these measures. Basically, there hasn't been much trend. We only have the OxyContin detailed data back to 2004. I can't look at the longer-term trend. But since 2004, there hasn't been any significant changes. We've still got about 500,000 initiates in the past year, 1.3 million past year users, and 330,000 past month users.

Looking at the patterns, the age patterns, again, very pronounced. It's the 18 to 25 group with the highest prevalence; past year use, 1.74 percent of the 18- to 25-year olds. And over on the right what we're showing there is pain reliever dependence among OxyContin users. We don't have OxyContin dependence or abuse. This is the closest we can get, so it's, among the OxyContin users, how many are pain reliever dependent or abusing.

And it shows pretty much the same pattern, the highest rate in the 18 to 25



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group. Very low rates in the 50 and older group. By gender, there is a slightly higher rate of use among males. Dependence or abuse is about the same, males and females.

Very large discrepancy in terms of race-ethnicity, and these are in terms of rates again. These are not numbers of people. So it's not because there's more whites in the population. These are the actual rates. It's really dominated by whites, low rates for blacks and Asians, Hispanics a little higher than blacks and Asians.

Now, this is a pattern that's a little different from what we usually see for many kinds of drug misuse, drug abuse, where the metropolitan areas, large metropolitan areas, have lower rates than small metro and non-metro areas.

And the map that we constructed here, we put together five years of data to look at lifetime OxyContin use, and it does show the similar pattern to what we saw for



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the -- that sub-state map for pain reliever, with some of the red states being in the New England area and in the Appalachian area, also up in Montana and Washington and Alaska.

And here we are looking at past year use of OxyContin and other pain relievers. Among the -- well, we're looking at illicit drug use among the OxyContin users, the other pain reliever users, and then persons who haven't used any pain relievers. Big difference is where the OxyContin users in the past year are more likely to be also using marijuana, cocaine, hallucinogens, and even heroin.

And then, finally, what we've done here is looked at kind of a crude measure of abuse/dependence potential, where we're looking at the past year users of each drug and computing the percent of those users that were dependent or abusing that substance. So, for example, for alcohol, 12 percent of the users of alcohol in the past year are



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dependent or abusing. Five percent of that is dependence, seven percent abuse.

And it shows that the OxyContin abuse is 28 percent, highest of these substances, similar to the cocaine prevalence. Twenty-three percent of users have pain reliever dependence.

And that's all I have for today. Thank you very much.

CHAIR FARRAR: Thank you. We'll move right into the presentation by Judy Ball, also from SAMHSA.

DR. BALL: Good morning. I'm the Director of the Division of Facility Surveys in the Office of Applied Studies, and Facility Surveys includes the Drug Abuse Warning Network.

Today I'm going to be giving you, first, a brief overview of DAWN and then talking about some of the key findings from DAWN from 2006, with comparisons for 2004 and 2005, focusing mostly on non-medical use of



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opiates and opioids.

These estimates I'm going to be showing you today for all three years have not yet been published, so this is the first public presentation of them.

And we are able, with the DAWN data, to divide the oxycodone reports into extended versus immediate release products. So we'll see estimates individually for those.

DAWN relies on a stratified probability sample of hospitals -- short-term, general, non-federal hospitals, with 24-hour emergency departments across the country. The sample is structured so that we have oversampled hospitals in selected metropolitan areas. We call those "oversample areas." And then, we have a sample of hospitals from the remainder of the country, the remainder area. And those two components put together comprise the entire United States.

The national estimates that I'm going to be showing you account for the sample



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design. They also account for unit non-response, that is non-response of whole hospitals, and also for partial non-response in the non-responding hospitals.

I should emphasize here that the sole purpose of the remainder area is to complete the national estimate. So what I'm showing you here are estimates for the entire country, which are derived from the oversample areas plus the remainder area.

This summarizes the data from 2004 to 2006 from DAWN. The sample of hospitals numbered over 500 hospitals in each of the three years. The sample is updated annually. Responding hospitals, we had more than 200 in each year, and those 200 hospitals reported between 169- and 269,000 emergency department visits, drug related.

DAWN data are collected from a retrospective review of ED medical records. Patients aren't interviewed, doctors aren't interviewed, and in 2006 nearly 10 million



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charts had to be reviewed in order to find about 347,000 DAWN cases. That's a capture rate of about three percent. In 2006, only about 15 percent of charts were not reviewed in responding hospitals.

Now, the analysis domain -- we start with all of the drug-related emergency department visits that are submitted to DAWN, and then we can divide those out into medical use and non-medical use. Medical use is when somebody has an adverse event, goes to the emergency room, they took the drug according to how it was prescribed or directed.

So on the medical use side, we only have pharmaceuticals. On the non-medical use side, we have pharmaceuticals, also the illicit drugs and alcohol. And I'll be focusing on the pharmaceuticals, obviously, today.

Now, in DAWN, because the data are collected from a retrospective review of medical records, defining non-medical use is

a little different than it is in the NSDUH. Based on retrospective chart review, we have patients who exceeded or prescribed a recommended dose, patients who used a drug that had been prescribed for someone else. We have cases of malicious poisoning, although they are relatively small in number. And then, we have cases of documented substance abuse. All of this based on the documentation in the medical record.

This category of non-medical use excludes the drug-related suicide attempts, but it includes the suicide ideation, plans, and gestures. So only the attempts, the outright attempts, are taken out of the non-medical use category.

This slide -- I'm going to show you some bar charts that give you an overview of the estimates from 2004 to 2006. And the bars are going to be gray when there is no significant change, like this, and when there's a significant change then they are

going to be in color.

So for the first set of estimates here -- this one -- that's all the drug-related emergency department visits that were reported to DAWN. And I normalized these in terms of hundred thousand population.

So we saw an increase from 2004 to 2006 in all types of drug-related emergency department visits.

For the non-medical use over on the right, over here, we saw an increase overall between 2004 and 2006. And for the medical use, which is -- I have too many buttons here -- the medical use, which is this group, we saw an increase in all three years. We suspect that part of that increase from 2004 and 2005, for example, is due to better case reporting methods.

Now let me turn my attention to the national estimates of non-medical use for the prescription opioids. When we produce estimates, it's important to recognize that



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they're not exact numbers. They're estimates, and they're based on sample data. And so they -- all of the estimates that we have, all of the estimates we produce, have this so-called margin of error associated with them.

And to emphasize this, most of the estimates I'm going to be showing you are going to be in terms of 95 percent confidence intervals. And that is going to look like this. So the green bar represents the confidence interval, and the estimate is the little red box in the center that falls between the upper and lower bound.

So for the non-medical use of all different types of opiates -- I have selected some here -- we see that DAWN estimates about 65,000 non-medical use visits for the oxycodone products. This is all types of oxycodone products. And the 95 percent confidence interval ranges from about 50,000 to about 80,000 visits in 2006, so that's this bar here.



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The estimate for oxycodone products is not significantly differently than the estimate for hydrocodone, which is this bar here. The two confidence intervals overlap. They are not significantly different.

But we have also already heard from the FDA that the hydrocodone prescriptions far outnumber the oxycodone prescriptions.

And also on this slide I show fentanyl and morphine, which are down here. Here's the fentanyl estimate; here's the morphine estimate. Those are significantly lower in terms of ED visits than for hydrocodone or oxycodone.

Now, one of the issues I want to bring to your attention is that because DAWN collects data from medical records, we sometimes don't have as much detail as we would like. So we have an estimate here for the opiates and opioids that were unnamed.



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These are unspecified reports.

And the estimate for these is not significantly different than the estimate that I showed you for oxycodone and hydrocodone. It's an important thing to keep in mind. So we don't know exactly what opiates or opioids are contained in this estimate.

Another problem sometime arises when you have patients who are receiving buprenorphine or methadone for opiate addiction treatment. When a patient presents to the emergency department, that may be an important factor that is recorded in their medical record, but sometimes we can't tell if the methadone or the buprenorphine was actually related to this visit. It may be an incidental finding.

But it's important to keep in mind in the background, and here we see the numbers for methadone over here. And this estimate is also not significantly different than hydrocodone and oxycodone. But we can almost



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be sure that it means something different. And the buprenorphine numbers are quite low.

Okay. Moving on to the oxycodone estimates broken down by release type. Oxycodone, as well as other products -- pharmaceuticals -- can be reported to DAWN by the brand name, by the trade name. They can be reported by a generic name, or they can be reported by ingredient.

And to look at the extended versus immediate release oxycodone products, what we did was we took all of the terms in the DAWN drug vocabulary and classified them according to extended release, immediate release. And here is the list or a partial list of the ones that we've included in extended and immediate release categories.

So on the extended release side over here, OxyContin obviously is categorized there, and it compromises most of the extended release reports that we have received. We added alternate terms to the DAWN drug



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vocabulary in order to pick up the generics when they came on the market. We haven't gotten much for our efforts to include all of these terms.

On the immediate release side, most of the immediate release formulations reported to DAWN are Percocet -- the acetaminophen-oxycodone combination. But we do also receive some reports of the aspirin and ibuprofen combination products, as well as oxycodone immediate release itself.

We also have -- we also receive reports that we can't classify according to release type. And in most cases, it's when the drug is reported to DAWN simply as oxycodone. There are some other alternate terms, but 97 percent of the unknown release types were reported to DAWN simply as oxycodone, based on the documentation in the medical record.

Okay. So here are the confidence intervals for 2004 for the oxycodone products



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broken down by extended, immediate release, and unknown release type. So you see here that the extended release bar goes from about 15,000 visits up to 30,000, with an estimate of 22,000; immediate release, 12- to 25,000, with an estimate of 18,000. These are not significantly different. The unknown release type over here is, however, significantly lower at about 5,000 visits.

For 2005, we see the same pattern. In 2006, we see a similar pattern. Now, this slide puts together all three -- all three years together, and it shows that for the extended release oxycodone we saw no increase, actually no change in statistical terms, from 2004, 2005, and 2006.

Immediate release, we saw an increase, a significant increase, from 2004 to 2006, but not 2005 to 2006. And for the unknown release type, we saw an increase in all three years.

Now, we've already heard that the



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generics went on the market in -- I guess started in 2004. We can't tell the extent to which this increase in the unknown release type is due to the generics or some other type of non-specific reporting.

Now, if we compare this to the ED visits that are associated with medical use of these same drugs, we see a slightly different pattern. The extended release oxycodone rose significantly from 2004 to 2006. Immediate release, also an increase from 2004 to 2006. And the unknown release type also increased in all three years.

Drilling down to the non-medical use, extended release oxycodone we see no significant difference across the three years. Immediate release, increase from 2004 to 2006. And the unknown release type, again, increase across all three years.

This chart puts side by side the non-medical use and medical use types of ED visits, and then breaks them down in the



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release type, so that we see that the immediate release oxycodone on the medical use side is higher than the extended release, probably reflecting the prescription pool.

We had more extended release on the non-medical use side than the medical use side. And in both cases, the non-medical and medical use, the number of the unknown types is rising as a proportion of the total.

This puts the oxycodone numbers for all three years and compares them to the hydrocodone estimates, which are -- the hydrocodone is the green bar in the background. And we can see here, as I mentioned earlier, that the extended release oxycodone isn't increasing much across the years. It's not a significant increase.

Immediate release is increasing, and the unknown type is increasing. But these estimates for oxycodone combined are not significantly different than for hydrocodone.

Now, this chart breaks down the



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emergency department visits per hundred thousand population by age group and by gender. And these are presented as rates per hundred thousand population because they correct for the different population sizes in each of these categories.

So in this chart and in the ones that will be coming in the next series, the gender bars are on the left, male blue, female pink. The set of bars, then, to the right are the age groups, and in the age groups the two red bars are the youngest ages, below age 21; the two gray bars on the other side are above age 55 and over; and the blue bars are adults in the center.

So this non-medical use for all of the opiates and opioids combined, we see a similar rate for the males and females. The ED visit rates for the age groups from 18 up through 54 are not significantly different. The little yellow star here on the 12 to 17 bar highlights that it is a -- has a



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significantly lower rate than the other age groups.

We see a similar pattern for hydrocodone. The visit rates are similar for males and females and for all of the age groups from age 12 up through 65.

The pattern for all of the oxycodone is a little different. Males are still not different than females. We see a significantly lower rate among the 12- to 17-year olds compared to the older age groups, and then we see this peak in the 21- to 24-year olds, which is a significant increase and is greater than the -- for example, the 30 to 34 group where it sort of drops off.

Looking again by release type, the extended release oxycodone, we, of course, see lower rates overall. I kept these charts on the same scale so as not to mislead you by just changing the size of the chart. Males and females, again, the same rates.

The ages 12 to 17 and 18 to 20 are



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significantly lower than the 21- to 24-year olds, and then we see this dip is sort of exaggerated for the 30- to 34-year olds, which is less than the 21 to 24. And then, we see a drop off also in the 55 to 64, and the 65 and over age group.

The pattern for immediate release oxycodone is similar. We see the lower level for the 12 to 17, but then it's different when you look at the other age groups. Eighteen to 20 and up through the adult ages are not significantly different. Then we see another drop off at age 55.

And the unknown release type, smaller still. The estimates for the 12 to 17 groups, and 18 to 20, there is not enough data there to produce a good estimate. And the 21- to 24-year old age group is significantly higher than its adjacent category.

Now, considering that we are looking at emergency department visits involving non-medical use of pharmaceuticals,



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it is worthwhile to take a look at what happens to the patients after they are released from the ED. Sometimes this is a pretty good measure of the severity of the problem they came in with. If they are admitted to a hospital, they are probably better off than if they were sent home.

I've broken the dispositions here into ones that there is no evidence of followup care and those that had some evidence of followup care. "Some followup care" means they were referred to detox or substance abuse treatment, they were admitted as in-patients, or they were transferred to another health care facility.

And this is for the oxycodone reports, broken down by release type. And you can see that the -- for the most part patients who come to the emergency department for non-medical use type problems, the majority of them receive -- or there is no evidence of followup care in the medical record. It



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doesn't mean that they don't receive any, but it wasn't documented in the medical record.

Then, in terms of number of drugs, Joe presented information on the number of drugs involved, and we can do that with DAWN as well. The take-home message from this is that the typical non-medical use emergency department visits involves multiple drugs, and those multiple drugs may be alcohol, illicit drugs, other prescription drugs, even other opiates or opioids, maybe combined with the oxycodone.

And we don't see much difference here across the different types of oxycodone, whether it's extended, immediate release.

So, in conclusion, concerning the non-medical use emergency department visits involving the opiates and opioids, overall these visits are nearing a quarter of a million in a year, and about a quarter of those are oxycodone involved, and about a quarter are hydrocodone.



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We have seen an increase in both the immediate and the unknown release types. With the increase in the unknown release, we don't know exactly why that's happening. And poly-drug use is typical across all of this.

We see the highest visit rates in patients who are age 21 to 54, and the majority of patients who are treated in hospitals -- hospital emergency rooms are treated and released.

Now, a couple of important considerations. DAWN does depend on emergency department medical records, and so the link between the emergency department visit and the use of the drug has to be documented somewhere. It doesn't have to be a causal link. The drug can simply be implicated in the visit. But there has to be something in the medical record that links the drug and the visit.

Emergency department records don't give us dose levels, and they don't give us



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the source of the drug. We used to try to collect source, and the data just aren't there.

Non-specific drug reports are a problem. When opiates or opioids are simply reported as opiates, we can't do much with that information except to bring it to your attention. And the unknown release type is also problematic, as we see it increasing.

And, finally, let me mention that unique names are really essential for good surveillance, that we have a problem with the generics because they don't have a name that we can put in the DAWN drug vocabulary and pick them up. And, frankly, the new proposed OxyContin formulation may also be a problem. If it's called OxyContin, we won't be able to differentiate it from old-style OxyContin or the 80 milligram tablet.

Thank you.

CHAIR FARRAR: The last speaker from SAMHSA is Deborah Trunzo.



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Just a comment to the panel. We'll have a few minutes for questions to this group right after this last presentation. So please write down your questions. We won't be able to take too many right now, but we should be able to take a few.

MS. TRUNZO: Okay. Good morning. I'm Deborah Trunzo. I'm also from the Office of Applied Studies at SAMHSA, and my presentation today will cover admissions to substance abuse treatment for opioid analgesics, based on data from SAMHSA's treatment episode data set.

The treatment episode data set, or TEDS, is an administrative database of client-level information on admissions to substance abuse treatment. States collect the data from their publicly-funded treatment providers and transmit a standard set of variables to SAMHSA.

We estimate that TEDS covers roughly about 80 percent of all treatment



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admissions to specialty substance abuse treatment facilities, accounting for more than 1.8 million admission records each year.

The standard TEDS data elements include client demographics, drug use history, and treatment-related variables. Today I will focus on the first two categories, especially drug use history. This includes the top three substances of abuse at time of admission, and for each of these route of administration and age at first use.

One limitation of TEDS for today's purposes is that the drugs of abuse are reported in generic categories, not specific formulations or brand names, since these distinctions are not really critical to the development of a treatment plan.

The basic TEDS data elements divide opioid drugs into two broad categories -- heroin and opiates other than heroin. The category opiates other than heroin is basically comprised of opioid analgesics and



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is reported by all states.

Sixteen states, however, report drugs of abuse in more detail, including eight types of opioid analgesics, and I'll be talking about these in a minute.

In 2006, four percent of TEDS admissions reported that their primary drug of abuse was an opioid analgesic. In addition to these 70,000 admissions, another 58,000 reported that pain relievers were their secondary or tertiary drug. So all together 128,000, or seven percent, of all TEDS treatment admissions reported pain relievers as one of their top three substances of abuse.

While pain relievers accounted for a relatively small number of admissions in 2006, the number of such admissions has increased dramatically in the last 10 years. Between 1992, the first year for which we have data, and 1997, the number of admissions involving pain relievers remained flat at about 30,000 per year. But in 1998, two years



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after the introduction of OxyContin, admissions for abuse of opioid analgesics began a sharp upward trend.

As shown in this graph, the increase in admissions for abuse of opioid analgesics cannot be attributed to an increase in admissions overall. Since 1997, total admissions have gone up by 12 percent and primary heroin admissions by only 4 percent. In contrast, primary opioid analgesic admissions increased by almost 400 percent, and admissions with any involvement of opioid analgesics increased by nearly 300 percent.

As I mentioned earlier, 16 states were able to report opioid analgesics in more detailed categories, as shown in this table. For those admissions in which a specific opioid analgesic was recorded, oxycodone was clearly the dominant substance, accounting for 82 percent of the cases.

The next most frequently reported drugs, codeine and hydrocodone, accounted for



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only six percent and five percent of the cases, respectively. Unfortunately, many ended up in the "other" category. This is most likely due to failure on the part of treatment providers to record the specific drug, because we have no reason to believe that there is another opioid drug not listed here that accounts for a large number of these other admissions.

The states in blue on this map are the 16 that reported the specific pain relievers that I showed you in the previous slide. Almost all of the 15,300 oxycodone admissions were reported by Maryland, Maine, New Jersey, Ohio, and Kentucky.

This graph shows the percent change in admissions for specific pain relievers between 2000 and 2006, based on data from those same 16 states. The change for most drugs was slight, but for oxycodone the increase was more than 1,500 percent.

Okay. Now I'm going to return to



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talking about admissions for all opioid analgesics combined. This map shows how rates per 100,000 population varied by state in 2006. The state with the highest rate is shown in dark blue, and that state is Maine. States with admission rates above the 90th percentile but less than Maine's are shown in medium blue and include Massachusetts, Rhode Island, Maryland, and Delaware.

The gray-blue states are those with admission rates between the 75th and 90th percentiles, and the yellow states have rates between the 50th and 70th percentiles, and the white states are below the 50th percentile.

But in terms of absolute numbers, the states with the largest populations, of course, reported the largest numbers of pain reliever admissions with one exception, and that, again, was Maine.

This chart shows admission rates for pain relievers by level of urbanization for the year 2000, which is shown in blue, and



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2006, which is shown in green. Well, the rates increased at all levels of urbanization during the time period. A pattern across urban and rural areas remained pretty much the same.

Level of urbanization is measured in terms of metropolitan statistical areas or MSAs. These range from central city areas in large MSAs to non-metropolitan areas with no cities. The data demonstrate that admission rates for pain relievers in small metropolitan areas and non-metropolitan areas were substantially higher than admission rates in the large metropolitan areas.

Okay. The next few slides are going to focus on drug use history and demographic characteristics of admissions for opioid analgesics. More than half of all TEDS admissions, regardless of drug, report abuse of more than one substance. In 2006, 56 percent of all TEDS admissions reported a secondary or tertiary substance in addition to



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their primary drug of abuse.

An even larger proportion of primary opioid analgesic admissions did so. Sixty-three percent reported abuse of multiple substances at the time of admission to treatment. The green bars on this chart show the percent of primary opioid analgesic admissions reporting abuse of more than one substance and the particular substances involved.

The most frequently reported secondary substance was alcohol, reported by 22 percent of primary pain reliever admissions, followed by marijuana at 20 percent and cocaine at 17 percent. Ten percent of primary pain reliever admissions reported tranquilizers as the secondary substance, and only seven percent said that they have used heroin in addition to pain relievers.

The yellow bars show the primary drugs of abuse for admissions who reported



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pain relievers as their secondary drug. For these admissions, heroin and alcohol were equally likely to be the primary drug at 29 percent each, followed again by cocaine and marijuana.

This graph demonstrates how route of administration for opioid analgesic admissions varies by age. In 2006, oral was by far the most common route for all ages, accounting for 74 percent of pain reliever admissions. Inhalation accounted for 13 percent, and injection for 10 percent.

But note that admissions involving inhalation and injection were concentrated in the younger age groups. Very few admissions over the age of 35 inhaled or injected opioid analgesics.

Here we see the corresponding information for oxycodone admissions in the subset of 16 states. The pattern is quite different here. Among the youngest oxycodone admissions, the number injecting the drug was



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almost the same as the number taking the drug orally.

And also, in contrast to all pain reliever admissions, oxycodone admissions were more likely to inject the drug than inhale it. But similar to all pain reliever admissions, injection and inhalation fell off sharply as age increased.

This table compares the characteristics of opioid analgesic admissions in 1997 to those in 2006. The proportion of males remained virtually unchanged over the 10-year period at about 56 percent, while the proportion of whites increased slightly from 83 to 88 percent.

Pain reliever admissions in 2006 were younger than those in 1997, with the proportion under the age of 20 having doubled and the proportion over 30 having dropped by a third. In 2006, there were relatively more new users admitted to treatment, new users being those who used the drug for less than



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three years before treatment admission.

And, lastly, the percent of admissions taking pain relievers orally by -- orally or by injection decreased, while the percent inhaling the drugs increased.

This final chart shows age at first use among primary opioid analgesic admissions between 1997 and 2006. And there are a couple of noteworthy findings here. The first is that age at first use for opioid analgesic admissions decreased during the time period, mainly driven by the increase in those initiating use between the ages of 18 and 24. And that is shown in the green band.

The second finding is that over the entire 10-year span age at first use occurred before the age of 25 for at least half of all pain reliever admissions. Initiates over the age of 45 accounted for only five percent of all admissions.

This suggests that the reason for initiation was other than legitimate medical

use in a large proportion of cases. If reason for initiation was medically prescribed treatment of pain, we would expect age at first use to be much less heavily concentrated in the younger age groups.

Okay. In summary, the number of treatment admissions for abuse of opioid analgesics has risen sharply in the past decade. In states identifying specific pain relievers, the increase in pain reliever admissions can be attributed almost entirely to oxycodone.

Admissions for abuse of opioid analgesics are likely to have other substance abuse problems as well. The youngest opioid analgesics admissions are those most likely to inject or inhale the drug. And first use of opioid analgesics by persons admitted into treatment for abuse of these drugs is more likely to occur before the age of 25 than after the age of 25.

Thank you.

CHAIR FARRAR: Okay. I want to thank the SAMHSA people for helping us to catch up in terms of time. We have until 12:15 to ask questions.

One short note, only four of the microphones can be on at any one time. What I'd ask the Committee to do is to signal with your microphone or your hand if you have a question. We'll take your name down and call you in order, but then turn your microphone off. Apparently, if we get more than four, there is a very loud noise, which we'll all object to.

So I open the floor for questions about the SAMHSA presentation specifically.

DR. WOLFE: I just wonder if any of you, or all of you, could just speculate on these pretty striking differences you see in terms of the immediate release versus the extended release, the big increase over time in the immediate release, and sort of a flat curve or flat line for the extended release.



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Anyone.

CHAIR FARRAR: Would one of the SAMHSA folks --

DR. BALL: I'm the one charged with speculation.

(Laughter.)

With the emergency department data, one of the things that we have to keep in mind is that the reason people go to emergency departments may be affected by a whole lot of things other than drug use. They may seek care in an emergency department because of a problem -- because it's very severe, but they may also seek care in an emergency room because they don't have insurance.

So equating the emergency department data with the prevalence data with the treatment data, there are difficulties just making those comparisons, because we are not looking at the same populations.

Why the DAWN data show that the



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number of visits associated with the immediate release products is increasing over time, I don't know the answer to that. It may be a reflection of the amount of drug that's out there. I think we saw from the presentation this morning that the number of immediate release prescriptions was continuing to rise.

It may be that the unknown category that I talked about is taking more out of one group than another. If we had known what that was, maybe it would have shown a different difference. I don't know. But that's the extent to which I am willing to speculate.

CHAIR FARRAR: Dr. Gardner?

DR. GARDNER: I'm not getting a good feeling for where we are learning about the prevalence of the problem in children, in people under the age of 18. And as I look across the databases, I wonder if someone could tell me where you think that's likely to be. It seems that the national survey,



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although it says it begins with age 12, it doesn't tell us how many of your respondents were between 12, and, say, 18.

It seems that with DAWN they need to get to an emergency department in order to be included. And with TEDS they have to be in treatment at that age. And as I look at the proposed risk map that the sponsor has offered us, using RADARS it seems to be people who are 18 and over.

So I'm a little confused about how we're learning about -- for example, I asked my colleague if someone -- if paramedics are called to a party where there has been an overdose and a young person died, will that person be taken to the ER, or where would we get data about those. So could you help me understand where we will learn going forward about the extent of the problem in young people.

DR. BALL: On the emergency department side, if a patient -- if paramedics



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are called and a patient has died and doesn't go to the emergency room for treatment, then they wouldn't show up in the DAWN data. The same is true for patients who might die after their emergency department visit. DAWN is only able to observe what happens in the emergency department. So a patient is admitted to an in-patient unit and then dies later; DAWN wouldn't pick that up.

The DAWN numbers that I showed, starting at age 12, it's not because DAWN doesn't go below age 12. It's because the numbers under age 12 are so small that the estimates are too imprecise to report.

And, Joe, I can let you talk about the NSDUH.

MR. GFROERER: I didn't present a lot on the 12 to 17, but I did show that the overall prevalence between '02 and '06 declined, wasn't statistically significant, basically 7.6 down to 7.2 percent for the past year use. So we don't see -- and in other



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analyses we have done we haven't seen any indications of increasing use of prescription -- increasing misuse of prescription drugs in the 12 to 17.

And the 12 to 17 data is -- represents the entire 12 to 17 population. We have -- we can break it down by single year of age, and what it shows is the -- within increasing age the rates get higher, but overall 12 to 17 rates are not increasing.

CHAIR FARRAR: Dr. Maxwell?

DR. MAXWELL: Dr. Gfroerer, don't go away. I've got a question for Dr. Ball, too.

Monitoring the Future, which is the school survey sponsored by NIDA, does show increases, does it not, in abuse of prescription drugs? That might not be a fair question without the data here, but that is --

MR. GFROERER: Yes, I can't answer that.

DR. MAXWELL: -- a source that we

did talk about today.

MR. GFROERER: Yes, I don't know.

DR. MAXWELL: Okay. And, Dr. Ball, I wanted to ask you, because the risk maps keep talking about DAWN, would you clarify for us? The data you presented were the national estimates. How many metro areas are actually sampled in DAWN for which estimates are available?

DR. BALL: The years that I showed -- 2004, '05, and '06 -- we had 13 oversample areas that were represented -- representing themselves in the national estimate, and in 2006 we had 12. That was following the demise of New Orleans in the DAWN sample. So 13 metro areas in 2004 and 2005, 12 in 2006.

DR. MAXWELL: Thank you.

CHAIR FARRAR: I'm next, and I'd like -- actually, you could stay there for a minute. I have a question.

(Laughter.)

Specifically, you started the



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presentation by saying that there has been an increase in opioid abuse and misuse in general over the past 10 years and that at least some of that is better recording. And the one slide that you showed, number 21, that had actually a comparison between the two seemed to show the same increase in hydrocodone use as in oxycodone use, and I'm just trying to understand how you can help us -- so you can help us to understand the monitoring of any particular drug within that mix, with two specific questions.

One is, it seems to me that the strength of the data is in comparison between a particular drug and other drugs that are also reported. The second problem -- the problem with that, though, is that whenever a drug becomes popular, and we see this with the AERS reporting to the FDA, that all of a sudden you get a rash of reports, because people pay attention to that drug and are sure to write it down.



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And I wonder if you could comment on how that affects the data, in particular with regards to possibly being able to assess a change in the use of oxycodone products over the years, which is really what we're being faced with here.

DR. BALL: There are a lot of questions in there. I cannot talk with DAWN data about changes over the past decade. DAWN was redesigned in the early 2000s. The full impact of the redesign occurred in 2004, and so we cannot make any comparisons from 2004 forward to anything from 2004 backward.

In the last Advisory Committee meeting that I presented data, I think I showed data from '94 to 2002. Those numbers are not comparable to the numbers from DAWN now, because the redesign changed everything so dramatically.

The use of comparator drugs is quite common. And one of -- many of the charts I showed here looked at comparisons.



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We can look at hydrocodone and oxycodone and see that they are not significantly different in terms of the number of emergency department visits we are seeing.

We can look at these individually over time. In the interest of time, I didn't show a lot of other drugs. But that certainly is a legitimate way to look at these things.

It is possible for some drugs to be more geographically isolated than others, so you may pick them up in different hospitals. I don't know the extent to which this is happening with these particular drugs.

The increase that I noted that may be a coding phenomenon had to do with the medical use visits, not the non-medical use visits. Before the redesign, DAWN did not capture medical use of pharmaceuticals. Before the redesign, DAWN captured only things that were labeled "drug abuse."

And one of the reasons we changed that during the redesign was we learned that



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if we went looking in medical records for drug abuse to be written out so explicitly, oftentimes we wouldn't find it. There are lots of good reasons for not writing it down. Sometimes it means the insurance company won't pay for it, among other reasons.

So with the redesign, we change the case criteria so we start with a very broad screen. We look at all types of drug-related emergency department visits. Again, the drug has to be implicated. It doesn't have to be a causal link.

And then, after we get all of the drug-related events, then we parse them out into these categories of medical use, non-medical use. And the non-medical use we break down in many different ways.

Because of the new focus, the brand-new focus on the medical use cases, the adverse events associated with somebody taking a prescription or over-the-counter pharmaceutical as prescribed or directed,



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because that was brand new we know that there was a learning phenomenon going on.

And so we have to be particularly careful about interpreting those early changes from 2004 to 2005 in the non-medical use visits as though those visits were actually going up. We think that we were just getting better at capturing them.

Did I get all your questions?

CHAIR FARRAR: Thank you.

Steve Passik?

DR. PASSIK: One of the things I always have trouble understanding in looking at the household survey data is the lumping together of two categories, one of which sort of didn't really exist before.

I mean, you know, when -- before the shift away from things like marijuana to prescription drugs, there wasn't this huge group of young people who were sort of self-treating. There aren't that many 17-year olds with glaucoma who are, you know, using



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marijuana for an actual symptom, whereas that's sort of a phenomenon that has been evolving with college-age women, self -- you know, using medicines that aren't prescribed, not to get high but to treat pain and sleep disturbances and things of that sort.

Do we know anything about the differences in the downstream implications of how people answer that very first question? I mean, did you take it to get high? And then, what happens downstream? For example, you presented data on dependence and that sort of thing, versus if they used for -- because they were in that growing class of -- growing group of self-treaters that are out there.

MR. GFROERER: Well, unfortunately, we don't -- we can't get that level of detail on the motivations and the followups. It's a cross-sectional survey, and we have limited time to ask not only about the broad categories but particularly about specific drugs. And that's why we construct



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the questionnaire the way it is, basically to save time.

Most of the interview focuses on marijuana, cocaine, alcohol, tobacco, and other drugs, so there is a limited time for the prescription drug.

We are looking at a redesign, where we might alter some of the definitions that we use and the drugs covered and some of the additional information about motivation and things like that.

CHAIR FARRAR: We're going to have time for two more. And I'd like to try and ask the Committee to keep the questions focused on the question for today, which is how we'll use these systems to monitor.

Dr. Bickel?

DR. BICKEL: I'm interested in the TEDS data set, because that's the one that is probably going to map most closely to the sponsor's plan of their epidemiological study analysis plan looking at the proportion of



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study participants at outpatient treatment programs.

And I just was wondering -- one of the big changes that have happened in those programs in the last several years is the advent of physician-based buprenorphine treatment. I was wondering how that influences your assessment of people seeking treatment for opioid dependence and those measures that you reported.

MS. TRUNZO: Yes. Well, people seeking treatment from -- you know, in office-based treatment will not be included in TEDS. So, yes, that is one of the limitations of TEDS.

Another in this instance is that most of the facilities included in TEDS receive funding through the single state authority, the state substance abuse authorities, and some states end up reporting OTP data to TEDS and others don't. And a lot of OTPs are private for profit and may not be



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included in TEDS. But the office-based treatment is completely out of scope.

CHAIR FARRAR: Dr. Nelson?

DR. NELSON: There is one other set of data I wonder if any of you can comment on, which is the set of patients who actually died related to any of these medications, medical examiner data or the vital statistic data, if you have anything to report about that.

DR. BALL: DAWN does collect data from medical examiners and coroners in selected metropolitan areas and states around the country. One of the reasons for not presenting any of the mortality data here today is because the mortality data are even more difficult to analyze and use for this purpose than the emergency department data.

It is relatively infrequent that a medical examiner reports to us a drug by its brand or trade name. Typically, it's reported by its generic or chemical, its ingredient,



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and so trying to do the kind of analysis that I did here, breaking extended release, immediate release, unknown release type out, simply is impractical with the medical examiner data.

I know that there have been other attempts to collect more specific data from medical examiners around the country, but it's not something that is being done at SAMHSA. And I think as far as vital statistics data is concerned, one of your colleagues on the Committee may be better to address that than I -- Dr. Paulozzi.

DR. PAULOZZI: That would be me. Yes, we've done some studies looking at medical examiner data and looking at vital statistics data at the CDC. And pictures are similar in terms of age distribution with the data you've seen from emergency departments.

And in terms of non-medical routes of exposure, one study in West Virginia showed about 15 percent people using a non-medical



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route of exposure for prescription opioid drugs.

CHAIR FARRAR: Dr. Zuppa?

DR. ZUPPA: For the TEDS data set, I found it very alarming that for people age 12 to 20 use the drug IV as often as they did oral, and I was wondering if there was any examination of how that changed over time.

MS. TRUNZO: We could look at it over time, but that's restricted to that limited number of states, the 16 states that reported the detailed drug. I didn't look at the change over time in terms of route of administration of oxycodone, but I could do that for those few states.

DR. PAULOZZI: With respect to TEDS, how did you handle the people with multiple routes of exposure?

MS. TRUNZO: With multiple routes of administration?

DR. PAULOZZI: Right. Administration.

MS. TRUNZO: Well, TEDS only records one route of administration per primary, secondary, or tertiary drug. So --

DR. PAULOZZI: Well, if a person reports multiple routes, is there a hierarchy for --

MS. TRUNZO: Well, since we lumped all opioid analgesics together, there was only one route of administration associated with them, if it was reported as a primary drug or a secondary drug. So I guess I'm not quite understanding.

DR. PAULOZZI: Well, the person comes in and says, "I used the drug both orally and by injection."

MS. TRUNZO: Oh, I see what you're saying. Well, at the provider level, the information is gathered when a person comes in for assessment. And I don't know how individual providers handle that, what they end up recording, whether they -- you know, the most frequent route of administration



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maybe, I'm assuming. But, you know, there's probably 10,000 different providers whose data ends up coming into TEDS. So I'm sure that there is probably variation going on there.

DR. BURLINGTON: Hi. Bruce Burlington. In trying to look at the SAMHSA presentations and understand how they relate to Purdue's proposed epidemiological study, I'm struggling to understand the impact of secular trends.

I mean, I believe Purdue has said they are going to collect baseline data, and roughly two years from now they will be looking at another point in time and trying to figure out whether the frequency of patients admitted to treatment programs who were using oxycodone to get high has gone down or up or stayed the same.

Does SAMHSA have any insight at all into whether there is, you know, any possibility of teasing out secular trends of oxycodone in the ER?



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CHAIR FARRAR: Actually, that was exactly the question I was going to ask, which is, to all three speakers, if you could give a very short answer to the question of whether you think it's going to be possible within the data sets that you have presented to tease out whether a specific product that is produced called OxyContin, we'll be able to dissect out that from other oxycodone use within the data sets that you've got, understanding that physicians very often will simply write OxyContin as a brand in the same -- as a generic, in the same way that Xerox became a generic and Kleenex.

I wonder if you could comment as to whether you think the data sets you've got will be able to differentiate between the use of the new product and the old product, or the generics.

MR. GFROERER: Well, as I said before, the survey has the pill card which shows OxyContin, and there are specific



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questions asking about OxyContin. There is no further differentiation. I mean, that's basically it. So we will be able to track trends in the reporting of that item on the questionnaire.

CHAIR FARRAR: And that card will have the -- a diagram for the different products that are currently oxycodone-based?

MR. GFROERER: We typically update the pictures on a regular basis. So we'll be looking at that. And possibly the pill card would be updated to show the new pictures.

I did want to add one thing related to the tracking of the treatment, and maybe Deb could say something about this. I would think -- and maybe you have some data on the lag time between first use and entry to treatment. That could be an issue in terms of using the treatment admissions, to see the impact, you know, at a particular point in time of a new drug.

MS. TRUNZO: To answer the first

question directly, no, there is no plan in TEDS to get more specific than we already are. TEDS is driven by what states require of their providers, and unless, you know, a substantial number of states require that differentiation from their treatment providers we wouldn't receive that data in TEDS.

And, yes, TEDS is capable of showing duration of use before treatment entry, to follow up on Joe's point.

DR. ANAND: I was struck --

DR. BALL: As I mentioned earlier, this will be problematic in DAWN for capturing the new formulation of OxyContin if it's approved versus the old formulation, if they are both called OxyContin. We can produce estimates, we can break them out as finely as the information is submitted to us based on what was recorded in the medical record.

But when we tried to pick up generic OxyContin and put a bunch of terms in our drug vocabulary to do that, either there



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wasn't a lot of it coming in or it wasn't getting recorded that way in the medical record. So we don't know if that increase that I showed in the unknown release type is actually related to the generic form that was just being reported as oxycodone.

If the new -- the new formulation goes on the market, and it's on the market at the same time as the old formulation, the 80 milligram, we won't be able to tell the difference if they are both called OxyContin. Just a fact of how the data are recorded.

There is another -- there is another component to our surveillance, though, that is worth mentioning, and that is that the national estimates are produced annually, and we're in the process right now of producing 2007 estimates. We're sort of midway through 2008.

DAWN does have another component where the data, as they are being submitted, can be queried on a real-time basis. And the



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detail of the drugs, right down to the actual term that the drug was reported, is available on that system. Purdue has access to that system for their products. The FDA has access. We maintain that system at SAMHSA to provide that access.

And there are some techniques within DAWN Live!, which the system is called, to make sure that you are looking -- over time looking at the same hospitals, at the same reporting level. And while you can't officially do trends, it can give you indicators for what is going on across time periods in that way.

CHAIR FARRAR: Just before you go, I guess my question is that in the data that you collect, it's only as good, obviously, as the data that you have. But understanding that the person recording the data might write "oxycodone ER" when they really used OxyContin, the brand, or they might write "OxyContin" when they were using one of the



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generics.

If both of those are available on the market, it will be hard for you to know which one is which, unless they are specifically indicated in the medical record.

DR. BALL: Yes. Our reporters are trained to report the drug as specifically as it is entered on the chart. So if OxyContin is documented in the chart, they should record that, not oxycodone.

If they -- if reporters input a non-specific opiate, if they just put in opiates in the system, they get a prompt back that says, "That a class of drugs. Can't you be more specific? Look in the chart for a name." So there is training and such to try to help that, but ultimately we are depending on the medical record.

CHAIR FARRAR: Thank you.

Dr. Anand, the last question.

DR. ANAND: I was struck both in the national survey and in the TEDS database



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by the percentage of caucasians who have shown sort of increases in the use. And from the 1,500 percent increase in the TEDS database, can you sort of break that down? Is that because of the demographics of the state from which the data is collected, or are there other reasons for that?

MS. TRUNZO: I could look at it by demographics for those states, but -- and then compare that to, well, opioid analgesics as a whole, the demographics for those from all states combined and, you know, see how it differed or was the same.

CHAIR FARRAR: I'd like to thank the people from SAMHSA for coming and sharing their data with us.

The next presentation is by Cathy Dormitzer, Division of Epidemiology.

DR. DORMITZER: Hi. My name is Cathy Dormitzer, and I'll be presenting a brief summary of drug abuse rates in the United States.



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I'm going to be presenting a brief background on why I'm presenting these estimates, the methods used to calculate these rates, the rates themselves, and some conclusions that were drawn from these estimates.

You listened to three presentations. Dr. Ball presented data from the Drug Abuse Warning Network, which was DAWN, and she presented emergency room visits on past year, non-medical use. Dr. Gfroerer presented data from the National Survey on Drug Use and Health, or NSDUH, which presented non-medical use of pain relievers. And Dr. Worthy presented information on drug utilization, which are the estimates of the number of retail prescriptions for the different opioid analgesics.

I'm going to be presenting these estimates per 10,000 retail prescriptions. And this presentation is going to be providing some information on the non-medical



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use of opioid analgesics in the context of drug utilization. In other words, are we seeing high numbers because there is high drug utilization? Are the low numbers the result of low drug utilization? Or are some analgesics more likely to be misused than others?

As you can see, I have been using rates in quotes, and that is because the estimates really are not rates. The data sets each have different sampling methodologies. They are using different populations, and the methods that we use to calculate the point estimates and the respective confidence intervals are somewhat different.

Furthermore, these data are in no way linked. So a more appropriate name really would be estimates adjusted for use. But everyone is going to be calling them rates.

And as you can recall, Dr. Ball presented estimates on emergency room visits related to hydrocodone, oxycodone, and



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fentanyl. And hydrocodone and oxycodone looked very much the same, and fentanyl looked significantly lower.

But we also saw a presentation where we saw that hydrocodone had roughly three times more prescriptions than oxycodone, and oxycodone had probably seven times more prescriptions than fentanyl.

So now I'm presenting estimates using non-medical use emergency room visits over the estimates of the number of retail prescription. And each bar includes all formulations, so the hydrocodone right over -- okay. Well, I can't do it. The middle, you can see that hydrocodone is significantly lower than for oxycodone and fentanyl, and that's because the number of hydrocodone prescriptions is so much larger than for oxycodone.

And oxycodone includes immediate release and extended release oxycodone. And as you can see, that is somewhat lower than



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for fentanyl.

Now, what we can see is that the estimates of the number of emergency room visits for extended release and immediate release were very similar. But drug utilization shows that immediate release has much higher retail prescriptions than extended release.

And now when we look at the number of ED visits per 10,000 prescriptions, what we're seeing is immediate release is much lower than for extended release. Extended release is roughly 37 versus somewhere around nine for immediate release per 10,000 prescriptions.

Now I'm turning to NSDUH. Dr. Gfroerer presented data on the number of past-year initiates. In other words, they used for the first time in the past year, the past year users, and the past year users with dependence. So now I'm putting numbers of people over 10,000 prescriptions.



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And as you can see, the number of people that began to use OxyContin in the past year was roughly 500. And past year with dependence is, you know, between 350 and almost 400.

Past year users includes the past year initiates, it includes the past year with -- past year users with dependence, and it also includes past year users who are the casual users. In other words, they have used it but they are not exhibiting problems, and that is roughly about 1,200 per 10,000 prescriptions.

Oops. I made a mistake. This is the -- so as you can see, it is actually 1,900 per 10,000 prescriptions, so roughly 20 percent users per 10,000 prescriptions. And it's roughly, you know, under 800 past year initiates per 10,000 prescriptions, and it's lower for past year users with dependence. So these -- ignore what I have just said. This is -- these are the real numbers.



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So, in summary, what we are seeing is that DAWN and NSDUH does provide information on the public health burden of non-medical use of opioids. And prescription data can be used as a proxy for drug availability. In other words, how much drug is out there in the community.

And then, the rates of non-medical use of oxycodone ER is much higher than for immediate release.

And we can conclude that OxyContin and their generics do have a higher rate or ratio of non-medical use than comparator drugs. And the numbers -- for the most part, the rates are staying stable. And as we see increasing use, you know, we see parallel lines, that as utilization goes up so do the numbers of emergency room visits or non-medical use.

And so that concludes my presentation. And we'll be taking questions after lunch, right? Okay. Thank you.

CHAIR FARRAR: Next is Lieutenant Commander Kristina Arnwine.

DR. ARNWINE: Good afternoon. My name is Lieutenant Commander Kristina Arnwine, and I am a team leader in the Division of Medication Error Prevention in the Office of Surveillance and Epidemiology.

This afternoon I am going to provide you an overview of how the currently marketed OxyContin tablets are reportedly being manipulated. I will first describe how we identified our reports, followed by a discussion of how the reports were further classified and evaluated for methods of manipulation. Finally, I will end with a summary of our findings.

Before going into the AERS review, I would like to provide a brief background to spontaneous adverse event reporting. It is a voluntary system for consumers and health care professionals to report adverse events. Under the Code of Federal Regulations, sponsors of



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an approved NDA product are required to report adverse events. These reports are sent to the agency through the FDA MedWatch program and stored in the AERS database.

Spontaneous adverse event reporting is useful, since it includes all U.S.-marketed products. It is best if you take events not seen in clinical trials, and is a good tool for events with a rare background rate and short latency.

However, there are some limitations, such as extensive underreporting, the quality of reports may be variable, there may be reporting biases based on notoriety, media attention a particular product is receiving, or if it's a new drug.

The actual numerator and denominator are not known, and so the quantification of risk assessment is subject to limitations. And the causality of a drug event association is often in question.

With regard to OxyContin, we



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searched the FDA adverse event reporting system database to identify reports involving the improper manipulation of OxyContin tablets. The AERS database was searched using medication error MEDRA terminology, and our search was limited only to the brand name OxyContin.

Our initial error search retrieved a total of 7,300 reports. However, to narrow this number, the narratives were searched electronically using the terms crush, chew, inhale, dissolve, inject, and snort.

As a result of the narrative search, 380 reports were evaluated; 171 of these reports were excluded from further analysis because they did not involve the manipulation of OxyContin. They either described manipulation of a concomitant medication or the search term described the route of administration of a concomitant medication.

Thus, 209 reports were further

evaluated to determine the method of improper manipulation of OxyContin tablets.

We wanted to determine if a particular strength of OxyContin was more vulnerable to manipulation. More than one-half of the total reports did not indicate a product strength. However, the 10 milligram, 20 milligram, and 40 milligram strengths were reported in 51 reports, 25 reports involve 80 milligram tablets, and five reports involved either the 60 milligram or 160 milligram tablets. And we know that the 60 milligram and 160 milligram strengths are no longer marketed.

Prescription dispensing data indicates that the lower strengths are dispensed more frequently compared to the 80 milligram strength, and the sponsor's reformulated product will cover these lower strengths.

When evaluating these reports from a context of use perspective, we noted that 22



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of the 209 reports involve medication errors in which health care professionals manipulated the OxyContin tablets for ease of administration; for example, crushing for administration through a gastric tube.

This occurred despite warnings throughout the professional insert, including a box warning and warnings on the container label stating that OxyContin tablets are to be swallowed whole and not chewed or crushed.

The remaining 187 reports involved the manipulation of OxyContin tablets for the purpose of abuse.

When we reviewed the narratives, we wanted to -- when we reviewed the narratives, we identified other methods of manipulation terms associated with the use of OxyContin in addition to the queried terms. These terms are highlighted in yellow on the screen.

However, we did not go back and conduct a second search of the AERS database



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using these terms. The methods presented here describe both medication errors and abuse. Not all reports indicated the method of product manipulation, nor did they indicate how the product was administered. However, when classifying these reports, preference was given to methods of preparation.

In reports where the method of preparation could not be identified, those reports were classified by method of administration. We noted the most prevalent method of preparation reported was crushing, followed by chewing. And the most prevalent manner of administration was injection, followed by snorting.

In summary, it is apparent that the manipulation of OxyContin tablets is most commonly associated with abuse. However, we note that manipulation is not completely representative of all abuse of OxyContin. Based on the reports evaluated, there does not seem to be a discernible trend with regard to



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what strengths of OxyContin are most closely associated with manipulation.

The new formulation of OxyContin is designed to deter abuse. However, it does not prevent the most common methods of manipulation reported to date.

This new formulation may make tablets more difficult to manipulate, which may lead to new and more creative methods of product manipulation. We recommend consideration be given to the consequences of administration of manipulated tablets of the new formulation, such as potential adverse events resulting from dissolution of the reformulated tablets in a solvent that has not been tested by the sponsor, or, if there is a potential for adverse events related to injection of the reformulated tablets.

We also recommend the new formulation be closely monitored for effectiveness of the abuse deterrents through post-marketing surveillance.



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This concludes my presentation. Thank you.

CHAIR FARRAR: Thank you very much.

We will now break for lunch and will reconvene in 45 minutes, here in this room at 1:30 promptly for the open session. Please take any personal belongings that you may want at this time. The ballroom may be closed for a few minutes to entry. It will be secured by the FDA staff during the lunch break.

Panel members, please remember that there is to be no discussion of the topic during lunch, amongst ourselves or with any member of the audience.

See you at 1:30.

DR. WATKINS: And for those Committee members, your lunch will be served in Room 817. And anyone who has not yet paid, please drop your payment off at the meeting registration desk.

(Whereupon, at 12:46 p.m., the proceedings in the foregoing matter recessed for lunch.)



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(1:35 p.m.)

CHAIR FARRAR:  If we can get started, please.

Both the Food and Drug Administration and the public believe in a transparent process for information-gathering and decision-making.  To ensure that transparency at the open public hearing sessions of the Advisory Committee meeting, the FDA believes that it is important to understand the context of an individual's presentation.

For this reason, the FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the Committee of any financial relationships that you may have with the sponsor, its products, and if known, its direct competitors.

For example, any financial information may include the sponsor's payment



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of your travel, lodging, or other expenses in connection with your attendance at this meeting.

Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and its Committee place great importance on the open public hearing process. The insights and comments provided can help the agency and its Committee in their consideration of the issues before them. That said, in many instances, and for many topics, there will be a variety of opinions.

One of our goals today is for this open public hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore,



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please speak only when recognized by the Chair, and we thank you for your cooperation.

I'd like to comment that we had some very late requests for additional time to speak here today. And, unfortunately, given the number of speakers we are not going to be able to accommodate them today.

So let's move ahead.

DR. WATKINS: Our first speaker is Micke Brown.

MS. BROWN: I never thought I was that short.

Esteemed Committee members and audience, my name is Micke Brown, and I am the Director of Advocacy for the American Pain Foundation and a pain management nurse. I have no financial disclosures.

I am speaking on behalf of the American Pain Foundation as well as the multitude of persons who live with pain each day. The American Pain Foundation represents people just like us. They are parents,



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children, siblings, co-workers, friends, and loved ones. The difference is is that they carry a burden every day, and that burden is pain.

Pain does not discriminate. It affects anyone, no matter the gender, the age, the ethnic group, or the socioeconomical status. It behooves me to call attention that there is an epidemic of chronic pain in our nation. Though pain affects more than 76 million Americans -- 76 million Americans, please listen to that number -- it continues to be untreated, undertreated, or inappropriately treated in our nation.

This occurs in spite of the knowledge base that without timely, appropriate, tailored care, pain weakens the immune system and allows for a slower recovery for those who have disease or injury. Persistent pain leads to needless suffering and lost productivity. Chronic pain is not only emotionally and physically debilitative



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for patients; it places a tremendous burden on families and caregivers.

The undertreatment of pain contributes to excessive health care costs and lost work productivity of approximately $100 billion every year. The pain crisis will become even more salient, given the rise in life expectancy as well as the aging babyboomer population.

The utility of opioid therapy as a safe and effective strategy to relieve pain and to improve functioning in appropriately selected and monitored patients has been demonstrated over the decades by pain experts.

This is highlighted in a landmark document released by the American Pain Foundation on this very day. An esteemed roundtable of pain experts sounded a collective and urgent call for a more balanced perspective of benefits and risks of opioid analgesics that include adopting methods to reduce the likelihood that strong pain



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medications will fall into unsafe hands.

In keeping with the concept of balance, it must be acknowledged that there are societal pressures that have polarized the concerns about public safety against access to medical care.

The dramatic rise of non-medical uses of prescription drugs, which has paralleled the increase in use of opioids for legitimate medical use, have fueled fears and for some blurred the lines between the law and the practice of medicine, yet people with severe, long-term pain need access to strong medications, which will include the use of opioids to help restore their physical functioning and a quality of life.

At the present time, there are no other chronic diseases where patients are subjected to the level of scrutiny and prejudice that pain patients must endure in order to obtain their medications that they require.



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We must reduce the stigma around these medications and ensure that patients with a legitimate medical need have access to opioid therapy as indicated by their health care provider. As with any medication, there are risks, but these risks can be managed.

The development and approval of extended release opioid medications, which are intended to be less easily adulterated than the older formulations, is a welcome advance. This technology has been called for and forward by health care professionals, patients, advocates, families, law enforcement, and regulators, including the FDA.

There are thousands, perhaps millions, of people with moderate to severe pain who could benefit from extend release opioid medications. Many patients do not have access to these medicines because far too many health care providers fear that these medicines might get into the wrong hands.



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There is concern that those who will abuse them by crushing them, or using other forms of alteration, therefore, the providers are hesitant to do what is needed.

There is also worry that has been reported by patients over and over again that they themselves are at risk for theft. Formulations that deter or defeat adulteration may help to reduce the fear of prescribing these therapeutically valuable analgesic medications.

New formulas should help improve access for those of greatest need, while lessening the likelihood that they will continue to be targets by those who would choose to misuse or abuse.

As an organization dedicated to improving the quality of life of people affected by pain, we at the American Pain Foundation believe that advances towards abuse-resistant and tolerance-resistant formulations of opioid medications would be a



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