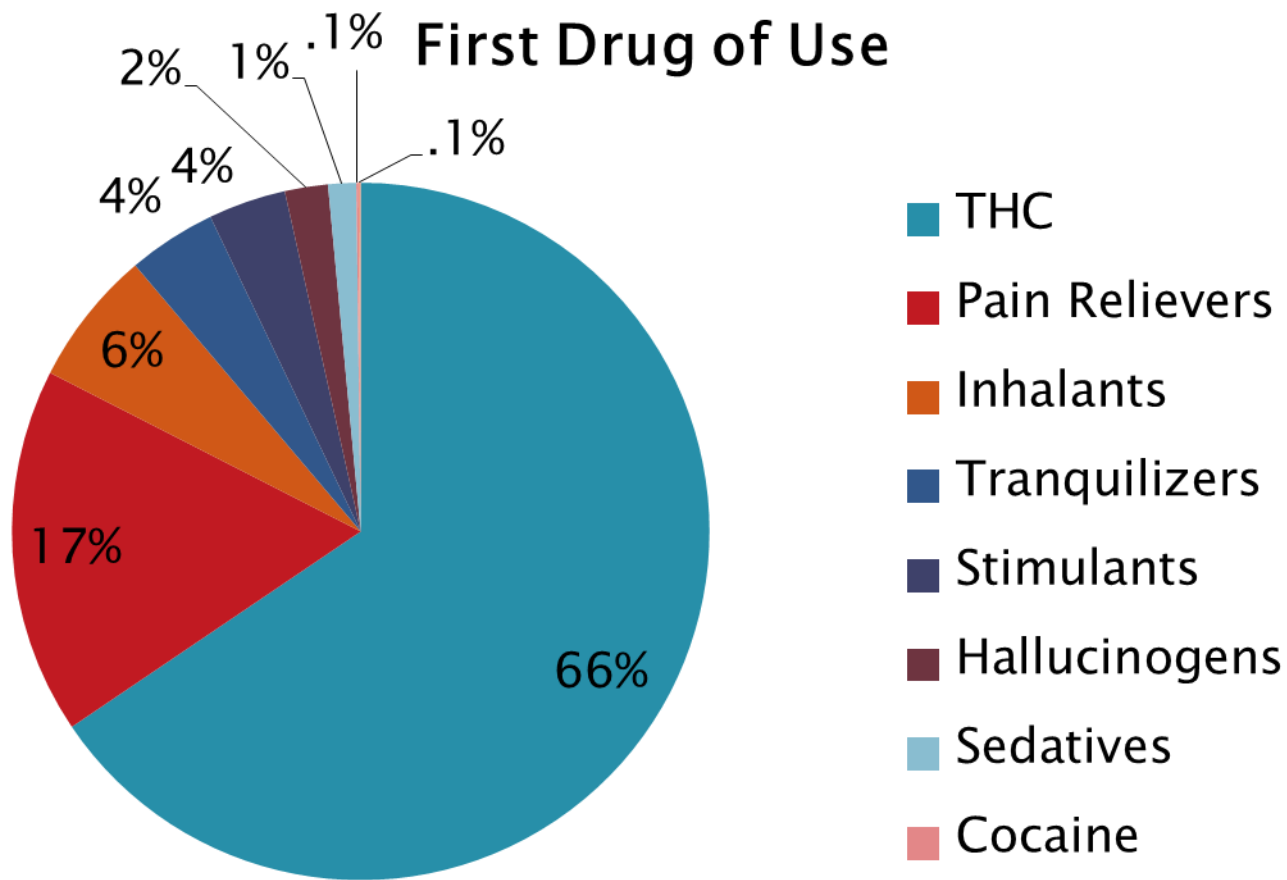


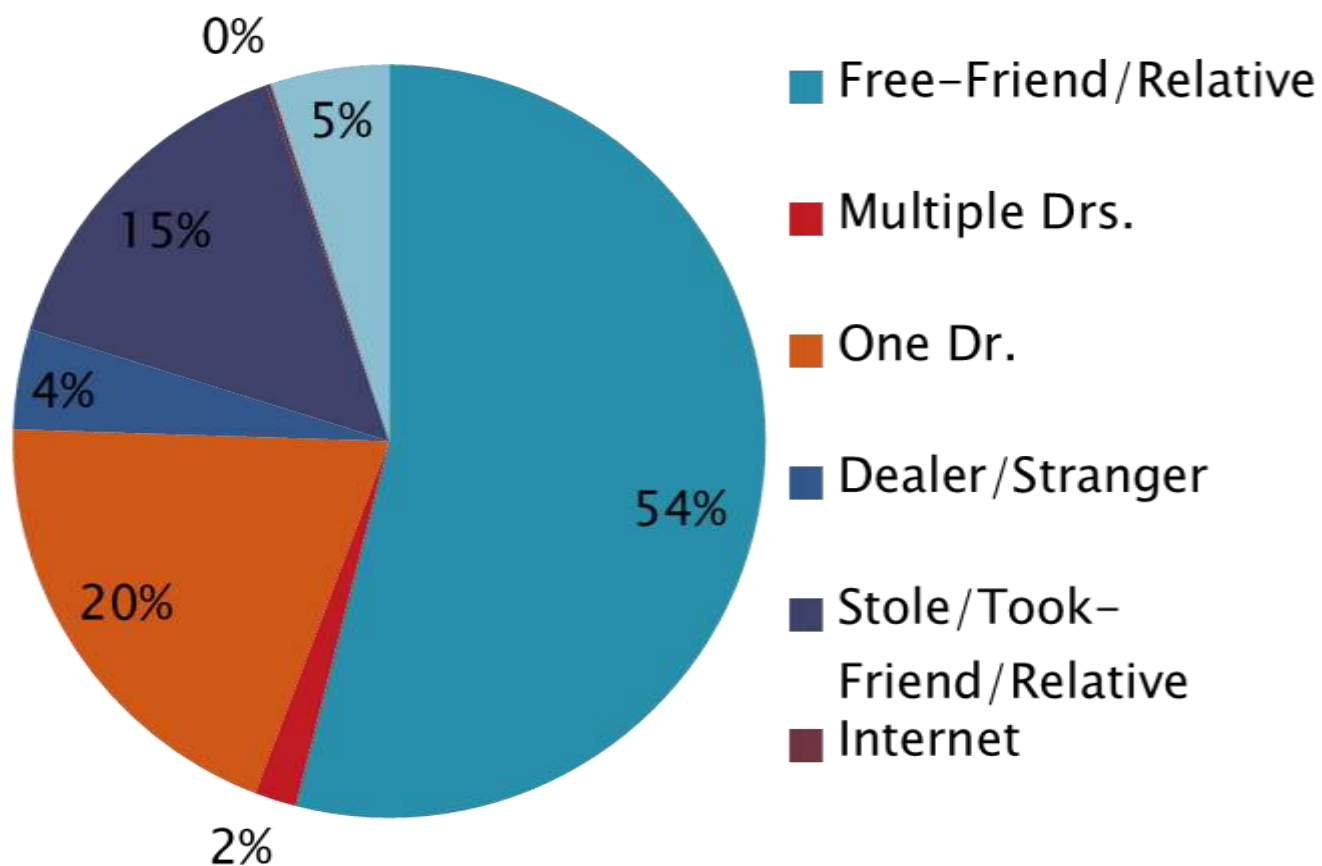
Neonatal Abstinence Syndrome

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University of Kentucky Medical Center



NSDUH, 2012

Source of Illicit Pain Relievers



Public Health Perspective

- ▶ Substance abuse: Public Health Problem and Social Morbidity
- ▶ NSDUH (National Survey on Drug Use and Health) 2011/2012 estimates

Drugs	Annual Rates Women (15–44y)	Rates Pregnancy	Est. Births Affected (2012)
Illicit drugs	10.5%	5.9%	233,217
Tobacco	25.9%	16.4%	632,454
Alcohol	53.8%	8.5%	335,991

Public Health Perspective

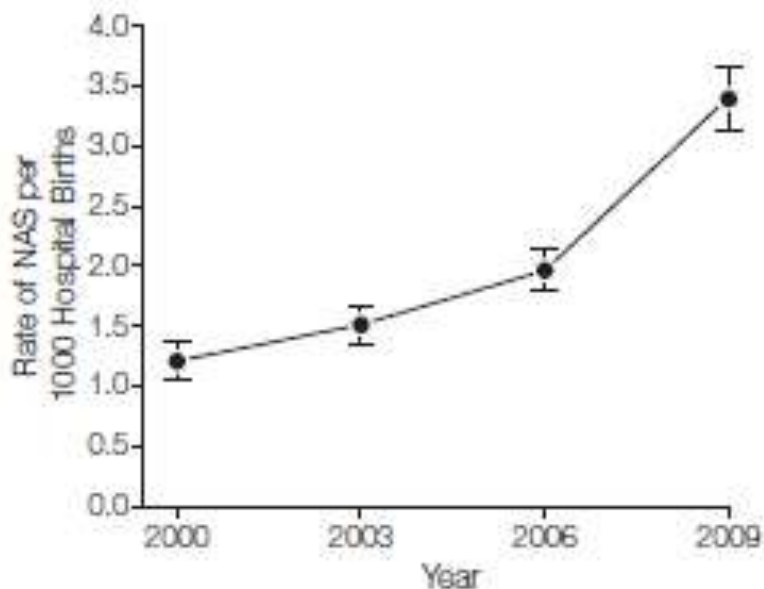
- ▶ Substance abuse: Public Health Problem Social Morbidity
- ▶ NSDUH (National Survey on Drug Use and Health) 2011/2012 estimates

Illegal Drugs	Annual Rates Women (15–44y)	Rates Pregnancy	Est. Births Affected (2012)
Illicit drugs	10.5%	5.9%	233,217
Marijuana	8.2%	5.2%	205,547
Cocaine	0.6%	0.2%	7,905
Pain relievers*	2.4%	0.9%	35,575
	*1.473 million		

Neonatal Abstinence Syndrome– The Epidemic

- ▶ Drug withdrawal syndrome in newborns
- ▶ NOWS–Neonatal Opiate Withdrawal Syndrome
- ▶ Primary cause is maternal opiate use–
prescribed or illicit
- ▶ As opiate abuse, dependency has increased,
NAS has followed
- ▶ NAS frequently compounded by polydrug use
 - Benzodiazepines, barbiturates
 - Neurontin, Lyrica
 - Caffeine and nicotine

Figure 1. Weighted National Estimates of the Rates of NAS per 1000 Hospital Births per Year

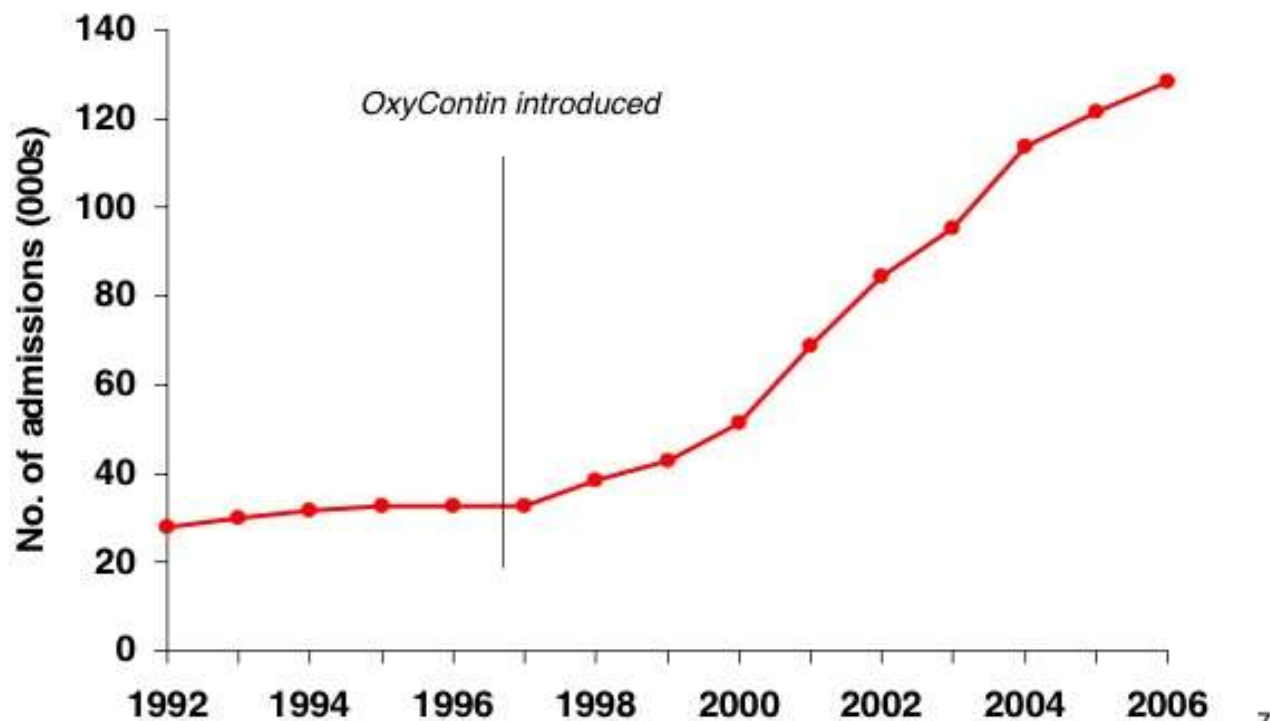


NAS indicates neonatal abstinence syndrome. Error bars indicate 95% CI. *P* for trend < .001 over the study period. The unweighted sample sizes for rates of NAS and for all other US hospital births are 2920 and 784 191 in 2000; 3761 and 890 582 in 2003; 5200 and 1 000 203 in 2006; and 9674 and 1 113 123 in 2009; respectively.

Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009. JAMA 2012;307(18)



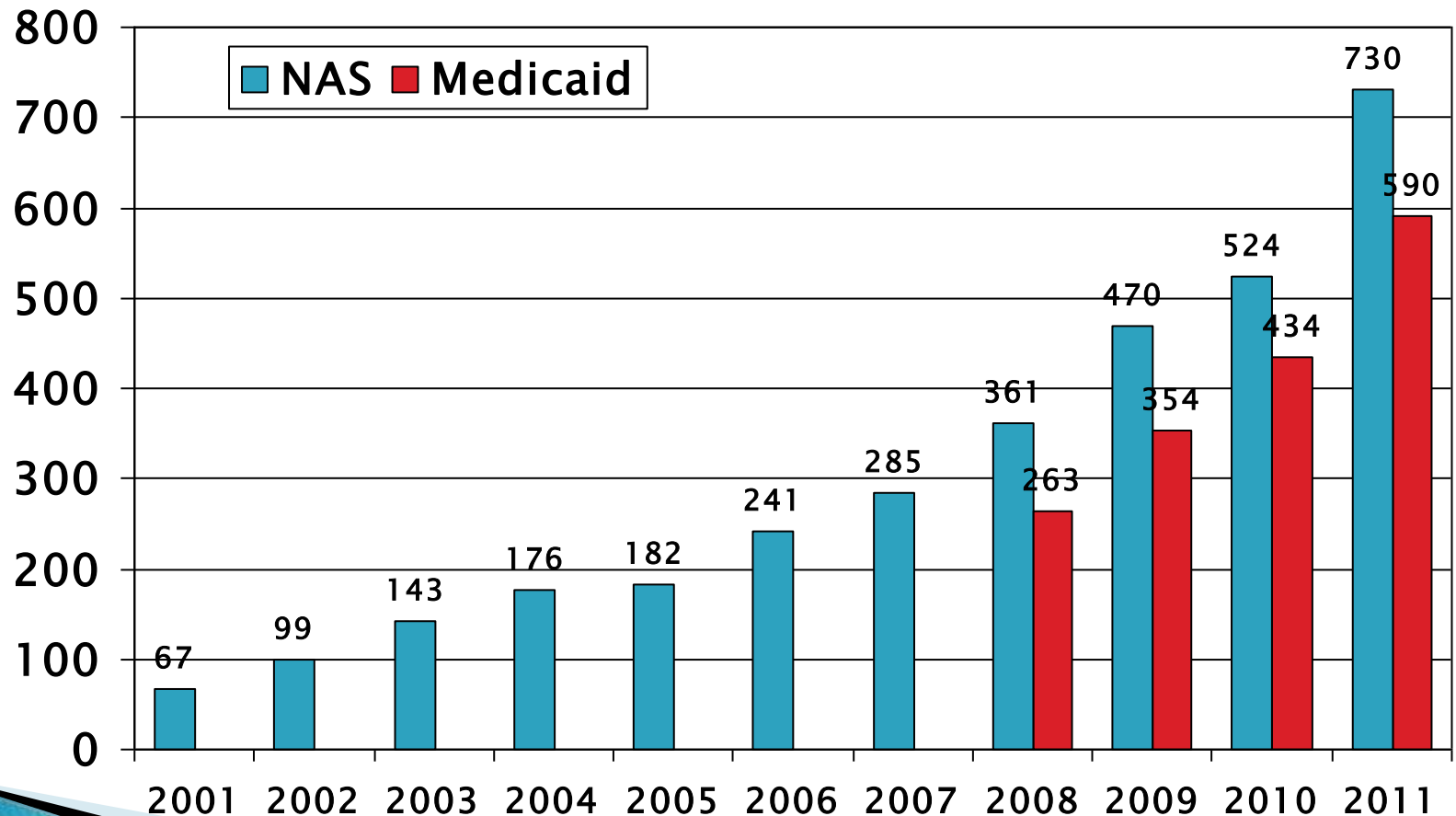
TEDS -- Treatment Admissions Involving Opioid Analgesics¹; 1992-2006



¹ Includes admissions where primary, secondary, or tertiary substance was reported as *Other opiates/synthetics*. Excludes admissions for non-prescription use of methadone.

NAS Hospitalizations (Kentucky Newborns)

Number



Year



- Inappropriate Marketing
- Off-label and Inappropriate Use
- Financially Lucrative
 - Suboxone and Subutex Programs
- FDA Not Helping



ASSOCIATED PRESS

Ex-doctor Pleads Guilty In Overdose Deaths

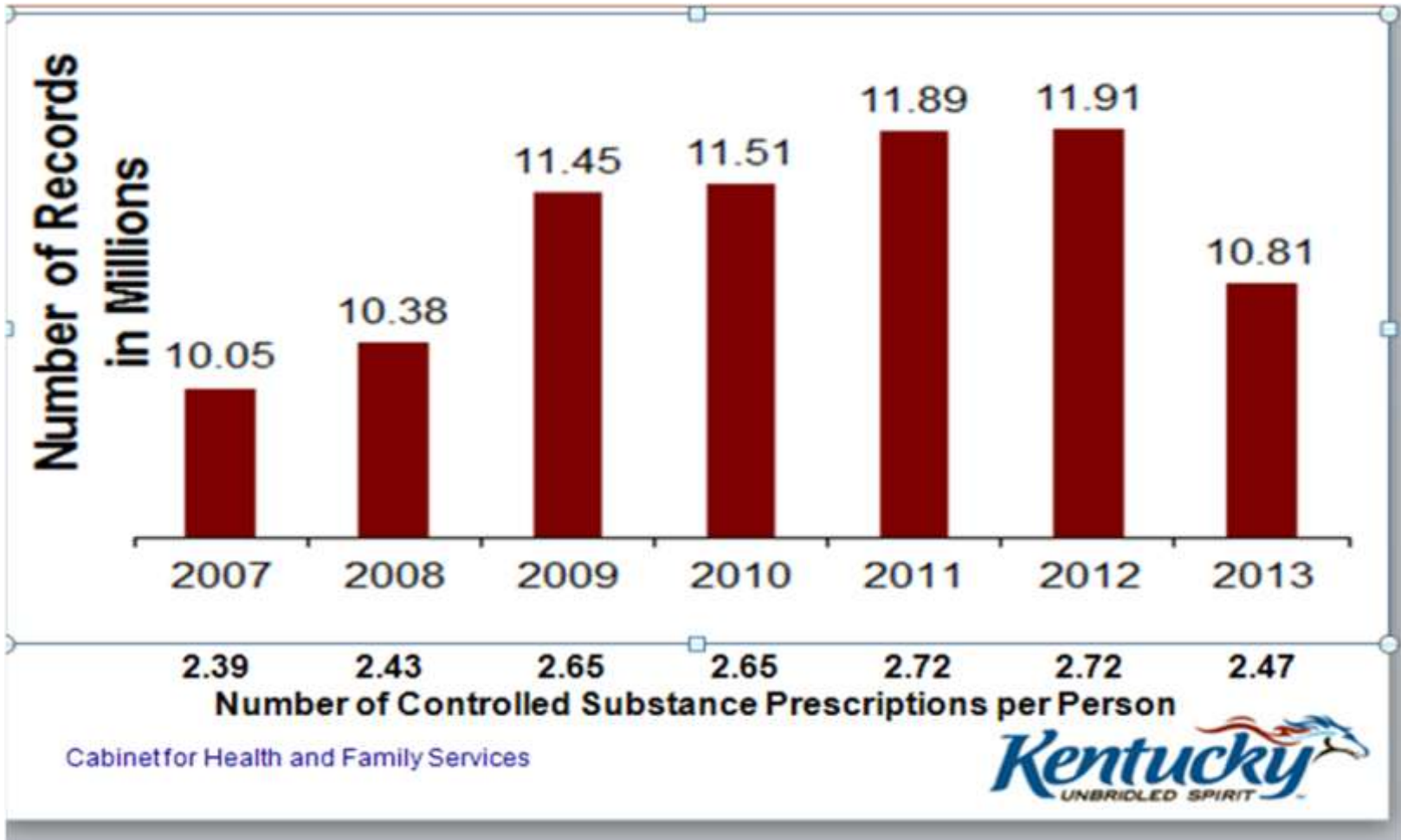
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Department of Justice

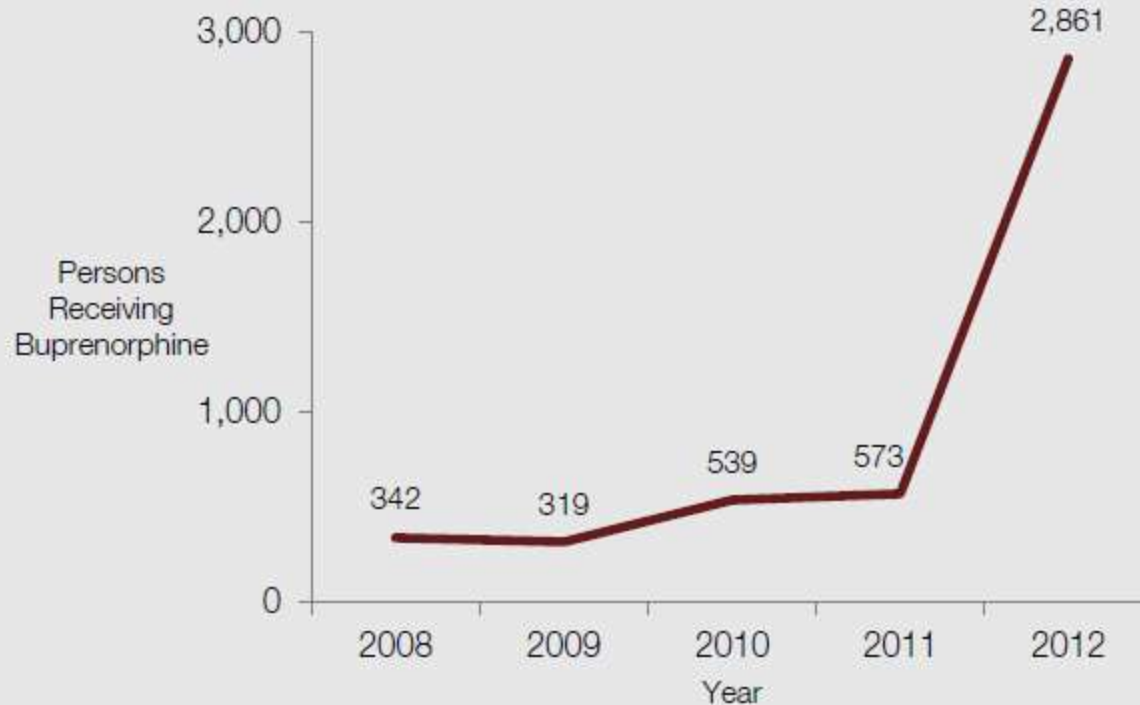
Office of Public Affairs

DR IMMEDIATE RELEASE Monday, February 10, 2014

Government Settles False Claims Act Allegations Against Kentucky Addiction Clinic, Clinical Lab and Two Doctors for \$15.75 Million



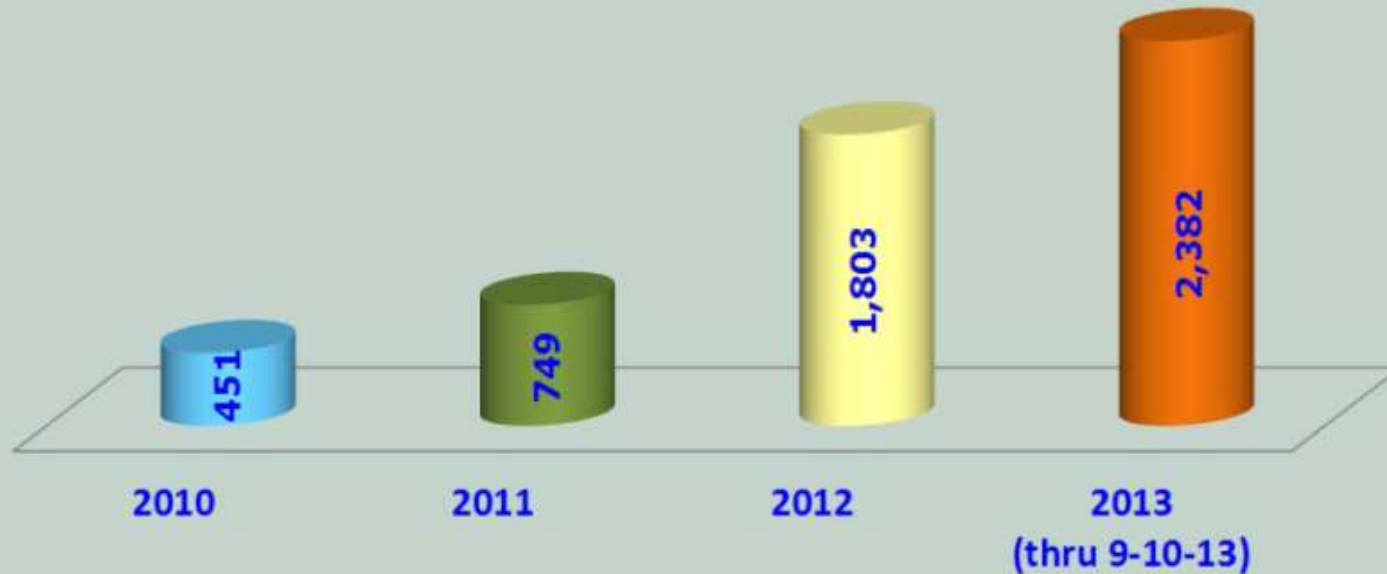
Persons Enrolled in Substance Use Treatment in Kentucky Receiving Buprenorphine: Single-Day Counts (2008-2012)⁷



The number of persons in Kentucky who received buprenorphine as part of their substance use treatment increased from 2008 to 2012.

In a single-day count in 2012, 1,837 persons in Kentucky were receiving methadone as part of their substance use treatment, and 2,861 were receiving buprenorphine.

Kentucky State Police Total Heroin Submissions



Overdose Deaths

Bell County	93.2 per 100,000
Clinton County	49.3 per 100,000
Breathitt County	44.3 per 100,000
Floyd County	43.9 per 100,000
Perry County	42.8 per 100,000
Harlan	42.1 per 100,000

NAS of the 2000's

- ▶ Triggered by rampant prescription pain drug use
- ▶ Suburban and rural vs an inner city urban problem
- ▶ Restrictions on prescriptions leading us back to heroin
- ▶ ? Methadone alternatives escalating the rates of addiction?
- ▶ Increasing numbers of newborns are the collateral damage

Addressing NAS

- ▶ Identify those at risk
- ▶ Universal screening of women and babies is controversial
- ▶ Identification and control of pregnant woman can help decrease number of infants who withdraw
- ▶ Get women through detox and onto replacement before delivery

Detecting NAS Risk

- ▶ Laboratory Screening
 - Urine, meconium, cord, hair
 - Need expanded panels to detect all of the opiates, including buprenorphine, methadone
 - May be negative even with exposure
 - Confounding drugs may not be detected
 - May not indicate abuse or dependency—self fulfilling prophecy
- ▶ History
 - Unreliable
 - Look for risk factors: High G's, Late care, DCBS involvement, ER visits, extensive pain history, risky lifestyle, tracks, erratic behavior

Onset of Symptoms

- ▶ Opiates block glutamate (excitatory neurotransmitter), inhibits release of noradrenaline
- ▶ With removal of source (mom) sudden upsurge in transmitters
- ▶ Variable depending on opiate used, other drugs confounding opiate use
- ▶ Most babies will exhibit signs by 96 hours with methadone or subutex, other prescription opiates
- ▶ Preterm infants have fewer symptoms, may exhibit later, last shorter period of time
- ▶ Controversy over association with maternal dose

Signs and Symptoms of Opiate Withdrawal/NAS

- ▶ Typically involve 4 areas:
 - CNS
 - Excessive cry, disordered sleep, hyperactive reflexes, tremors, hypertonia, myoclonic jerks, seizures
 - Respiratory
 - Tachypnea
 - GI
 - Hyperphagia, disordered feeding, vomiting, diarrhea
 - Autonomic
 - Sweating, fever, mottling, yawning, nasal stuffiness, sneezing
- ▶ Baby unable to feed, grow, sleep, interact with caregivers in normal manner

Determining Treatment Needs

- ▶ Various Scoring Systems
- ▶ Most frequently used is Modified Finnegan
- ▶ Assigns points to severity of symptoms in all four areas
- ▶ Less frequently used scoring systems:
 - Lipsitz modification of Finnegan
 - Brazelton's Neurobehavioral Assessment Scales (NBAS)
 - NICU Network Neurobehavioral Scale (NNNS)

Finnegan Scoring

System: CNS Disturbances	Score
Cry (excessive, continuous)	2 - 3
Sleep (<1, 2, 3 hrs after feed)	3 - 2 - 1
Reflexes (overactive /very overactive Moro reflex)	2 - 3
Tremors (mild, disturbed / Moderate, disturbed / mild, undisturbed / mod –severe, disturbed)	1 – 2 – 3- 4
Increased Muscle tone	2
Myoclonic jerks	3
Convulsions	5
Excoriations	1

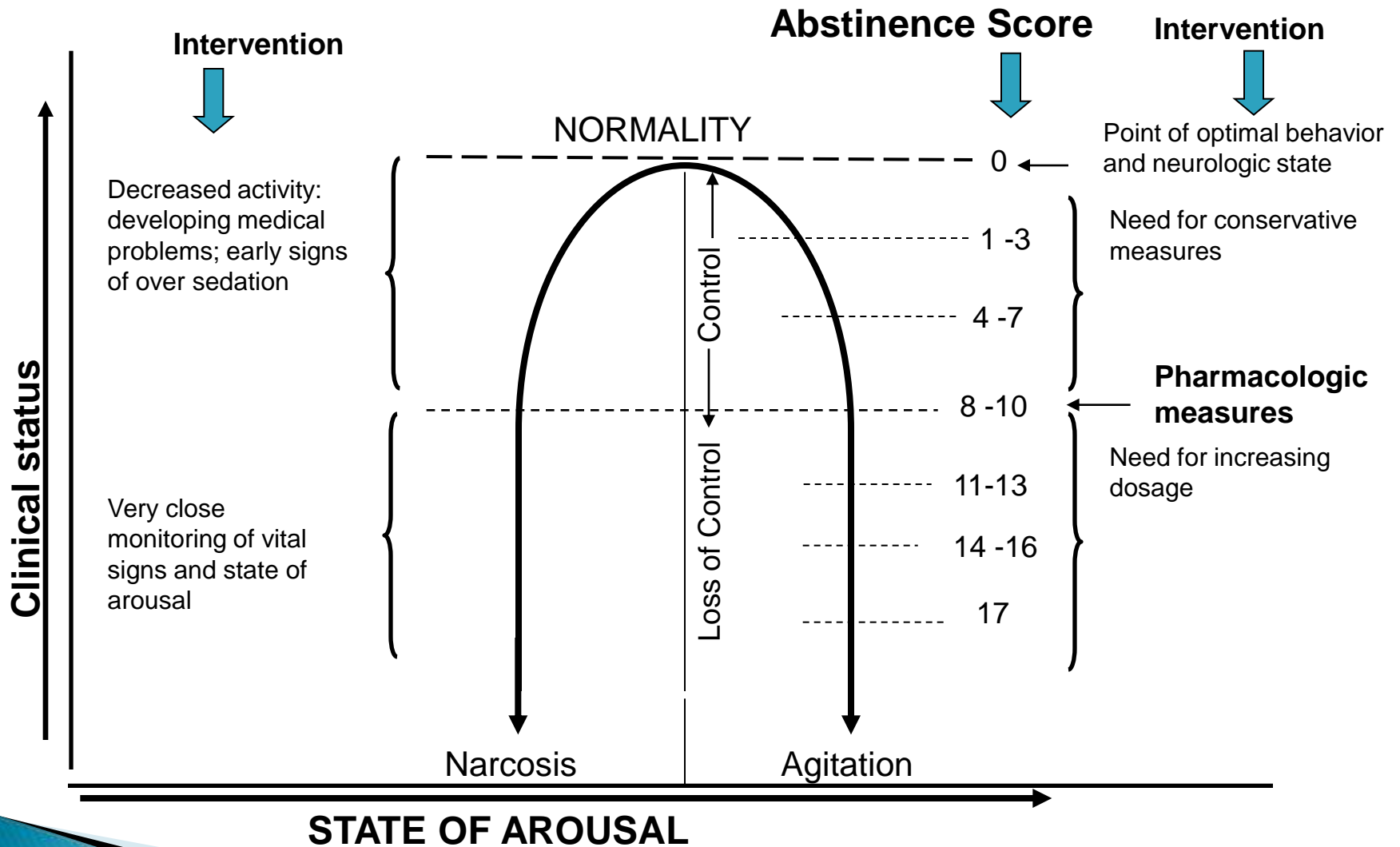
Finnegan Scoring

Gastrointestinal Disturbances	Score
Excessive Sucking	1
Poor Feeding	2
Regurgitation / projectile vomiting	2 - 3
Loose stools / watery stools	2 - 3
Respiratory System manifestations	2
Nasal Flaring	2
Respiratory rate >60/min / RR >60/min and retractions	1 - 2

Finnegan Scoring

Other Disturbances (Autonomic)	Score
Sweating	1
Fever 37.3 – 38.3° C / =>38.4° C	1 - 2
Frequent yawning (>3-4 in 4 hr)	1
Mottling	1
Nasal stuffiness	2
Sneezing (>3-4 in 4 hr)	1

Considerations When Initiating Pharmacologic Treatment



Modified from Finnegan, 1985 in *Current Therapy in Neonatal-Perinatal Medicine*

Pharmacologic Treatment of NAS

- ▶ Use a similar drug
 - Methadone or Subutex = morphine
 - Barbiturates = phenobarbital
- ▶ Clonidine showing promise as alternative to morphine in opiate withdrawal
- ▶ Advance until symptoms are captured, baby can sleep, interact with caregivers, feed adequately
- ▶ Wean slowly with goal of minimal symptoms

Additional Risks of NAS

- ▶ Separation from mother
- ▶ Judgmental attitudes create block to family involvement
- ▶ Interruption of breastfeeding
- ▶ Care in hospital environment increases length of stay
- ▶ Excessive costs of hospital model

Table 1. Characteristics of Newborns Diagnosed With Neonatal Abstinence Syndrome vs All Other US Hospital Births in 2009^a

Characteristics	Neonatal Abstinence Syndrome		All Other US Hospital Births	
	Unweighted, No. (n = 9674)	Weighted % (SE)	Unweighted, No. (n = 1 113 123)	Weighted % (SE)
Male sex	5309	55.0 (0.5)	585 755	51.1 (0.8)
Clinical conditions				
Respiratory diagnoses	2993	30.9 (0.7)	255 623	8.9 (0.1)
Low birthweight, <2500 g	1733	19.1 (0.5)	174 038	7.0 (0.2)
Feeding difficulty	1749	18.1 (0.7)	67 582	2.8 (0.1)
Seizure	207	2.3 (0.2)	3385	0.1 (<0.1)
Insurance				
Medicaid	7510	78.1 (0.8)	500 384	45.5 (0.7)
Private payers	1541	15.5 (0.7)	529 351	47.5 (0.7)
Self-pay	453	4.7 (0.3)	44 725	4.3 (0.2)
Other	162	1.7 (0.2)	29 509	2.7 (0.1)
Zip code income quartile				
1 (lowest)	3309	36.3 (1.3)	295 761	28.0 (0.6)
2	2547	26.9 (0.8)	274 445	26.2 (0.4)
3	2228	23.1 (0.9)	269 044	24.8 (0.4)
4 (highest)	1344	13.7 (0.7)	243 501	21.1 (0.7)
Hospital characteristics				
Urban	8257	88.6 (1.1)	963 206	87.7 (0.4)
Teaching	5036	54.3 (2.1)	510 141	44.0 (1.0)
Children's	1720	19.8 (2.1)	142 853	11.8 (1.2)

^aData were obtained from the Kids' Inpatient Database. Subcategories of the unweighted numbers may not sum to total because of missing values.

Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009. JAMA 2012;307(18)

Mean Charges/NAS Hospitalization

2000 \$39,400.00

2009 \$53,400.00

77.6% of charges to state
Medicaid programs

Medical Risks and NAS

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Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009. JAMA 2012;307(18)

Non-Pharmacologic Treatment

- ▶ Complete treatment is an art form and requires multi-disciplinary team
- ▶ Goal is to prevent disruption of normal care, family bond and prevent pharmacologic treatment
- ▶ Begin with behavioral management
- ▶ Encourage maintenance of maternal/child bond
- ▶ Rooming-in with mother
- ▶ Skin to Skin Care/Kangaroo Care
- ▶ Frequent small ad lib feeds
- ▶ Light weight swaddle to avoid overheating
- ▶ Breastfeeding if in supervised program

Management Models

- ▶ **Mother–Infant pairing**
 - Most effective model, least used
 - Least need for pharmacologic intervention
 - Most breastfeeding
 - Shortest length of stay
- ▶ **NICU Care**
 - Least effective, most used
 - Long LOS, costly
 - High pharmacologic intervention
 - Disruptive to breastfeeding
 - Disruptive to family unit
 - Sets parents up to fail

Optimizing Care in a Bad Environment: Prenatal Management

- ▶ If identified before delivery, counsel before
- ▶ Team with OB and/or replacement clinic staff
- ▶ Risk of withdrawal
 - Methadone 75–90%
 - Subutex 50–75%
 - Polydrug Variable
- ▶ Discuss breastfeeding possibility
 - Test milk if questionable
- ▶ Stress management
- ▶ Begin teaching skills for behavioral care, how to minimize withdrawal

Optimizing Care in a Bad Environment

- ▶ Find advocates and drivers for change, develop NAS champion team
 - Studies show mothers feel judged, belittled
- ▶ Protocol for pharmacologic treatment
 - Protocol-driven management of withdrawal moves faster than non-protocol
- ▶ Standard behavioral and developmental care
 - Encourage parent presence and kangaroo care
 - Quiet environment
 - Non-nutritive sucking
 - Music/OT/Massage
 - Additional tools that can be given to parents to help them manage their infants

Optimizing Care in a Bad Environment

- ▶ Standard baby care
 - Light weight swaddles that allow self-soothing
- ▶ Simethicone
- ▶ Butt protocol
 - Critic aid AF
 - Anti Monkey Butt
- ▶ If not breastfeeding, use consistent formula
 - Good Start Soothe
 - Low lactose
 - Probiotic
 - May need elemental formula for severe diarrhea

NAS and Breastfeeding

- ▶ Many still discourage
- ▶ AAP—not if using illicit drugs
- ▶ Should be in supervised program and stable in that program
- ▶ Methadone has fairly vast body of evidence for safety with breastfeeding
- ▶ Not much with subutex
- ▶ Most drugs cross into breastmilk, but very limited

Methadone and Breastfeeding

Study	N	PP Days Collected	Dose, mg/d	BM/ Plasma	Conc BM, $\mu\text{g/ml}$	mg/d
Kreek 1974	1	4-8	50	0.13	0.05	0.06
Blinick	10	3-10	10-80	0.83	0.27	
Kreek 1979	2	5-8	25,50	.05-1.2	.01-.12	.06-.1
Pond	2	7,21		.32,0.61	.01-.7	.01-.03
Geraghty	2	11, 14	73 (s60)	0.66, 1.22	.13, .17	.07, 09
Wojnar-Horton	12	3-26	20-80	0.44	0.12	17.4 $\mu\text{g}/\text{kg/d}$
McCarthy	8	2-202	25-180		0.095	0.05

NAS and Breastfeeding

- ▶ Encourage if in supervised treatment program
- ▶ Recognize that baby may have frequent stools due to breast feeding, not due to withdrawal
- ▶ Don't stress about "night withdrawal"
- ▶ Spike in scores lack of mom, not MBM

Preparation for Home

- ▶ If unable to room-in through out stay
 - 24–48 hours of care by parent
 - Supportive period of learning for behavioral care, developmental management, feeding
 - Learn home medication taper
 - Clonidine taper
 - Social Services follow-up for family
 - Medical and developmental follow-up for baby

NAS Outcome

- ▶ Environment key in outcome
- ▶ Risk for ADHD?
- ▶ Risk for later addiction?
- ▶ Severity of withdrawal not associated with severity of long-term outcome
- ▶ Close developmental follow-up and early initiation of services if delay
- ▶ Consider MRI in babies who do not respond to treatment in typical manner

