



METHADONE

Methadone Mortality Working Group
November 2008

Dr. Christine Sannerud
Office of Diversion Control
Drug Enforcement Administration



Methadone

- Background
- Pharmacology
- Toxicity
- Diversion, Toxic Exposures, Mortality data
- Methadone Distribution (ARCOS data)
- Methadone Initiative





Methadone - Background

- **In late 1940s** - marketed as pain reliever ("analgesic"), but not extensively used.
- **In the 70s** - shown to be effective as once-daily medication for narcotic (opioid) addiction treatment.
- **In the US** – Established as the standard for treatment of narcotic (opioid) addiction.
- **From late 1990s** – methadone is being increasingly used in pain management

© Talk to FRANK

Methadone – an Opioid



- Methadone belongs to pharmacological class called "Opioids"
- **Opioids** are among the most potent analgesic drugs and are widely used
- **Opioids** are used in the management of acute and cancer-related pain, and chronic non-cancer pain





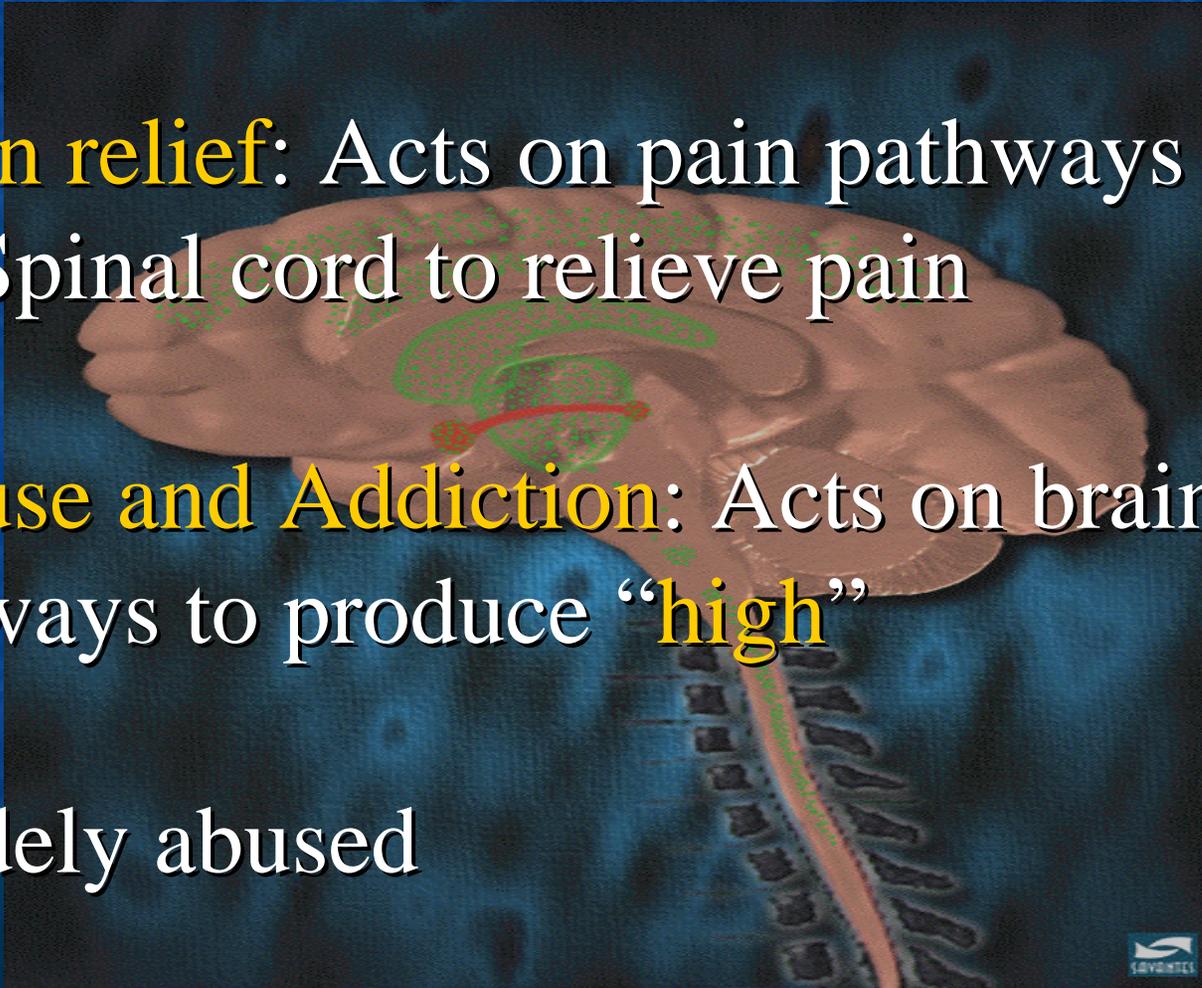
Methadone – An Opioid

- Opioids are of either **natural** origin or **semisynthetic**, or **synthetic**
- **Natural**: e.g., Morphine from opium poppy
- **Semisynthetic**: e.g., hydrocodone (Vicodin), oxycodone (Percocet, OxyContin)
- **Synthetic**: e.g., **Methadone** (Methadose) meperidine (Demerol), fentanyl (Duragesic) etc.

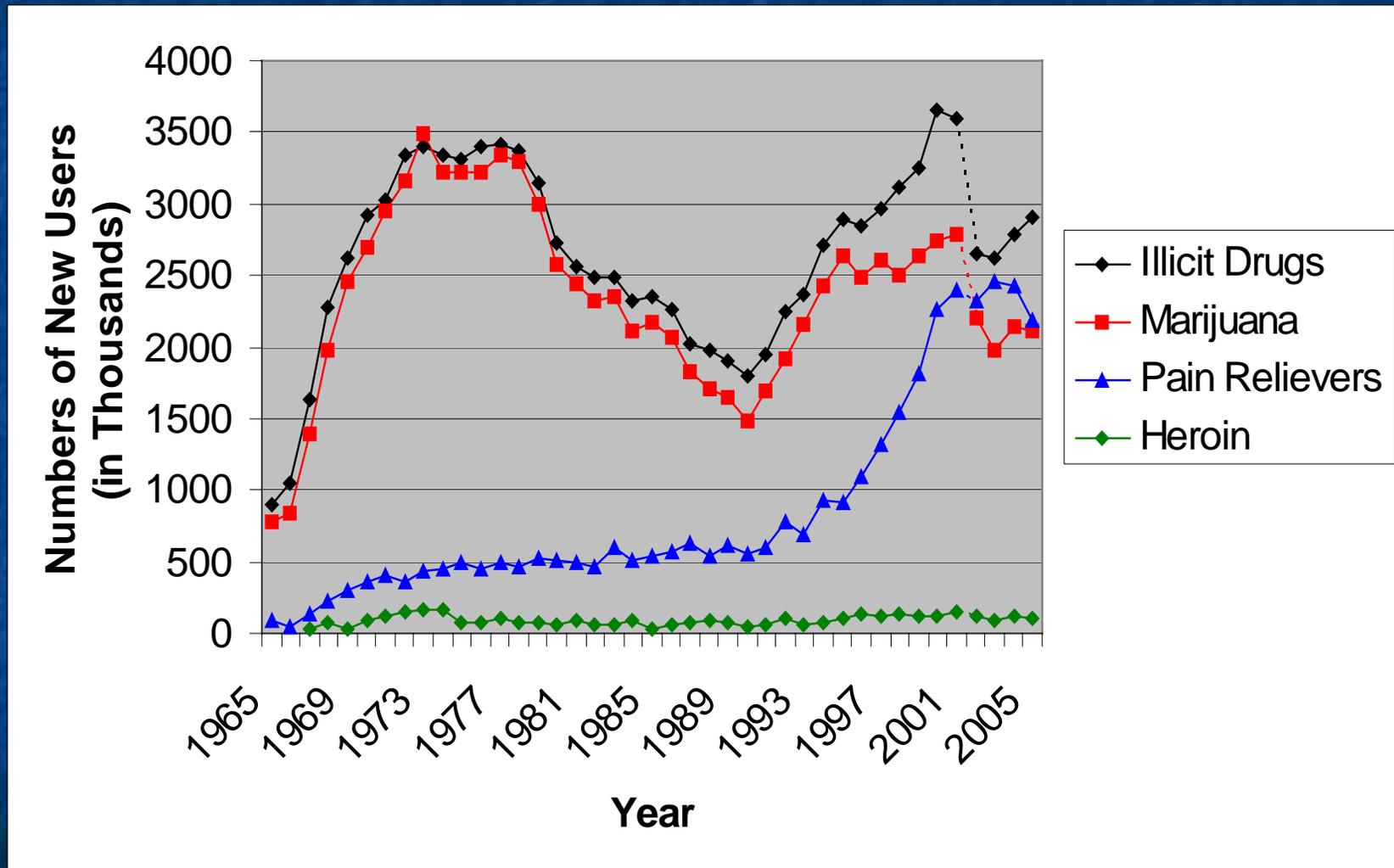
Opioid Actions on Brain and Spinal Cord



- **Pain relief:** Acts on pain pathways in brain and Spinal cord to relieve pain
- **Abuse and Addiction:** Acts on brain reward pathways to produce “high”
- Widely abused



New Drug User Patterns



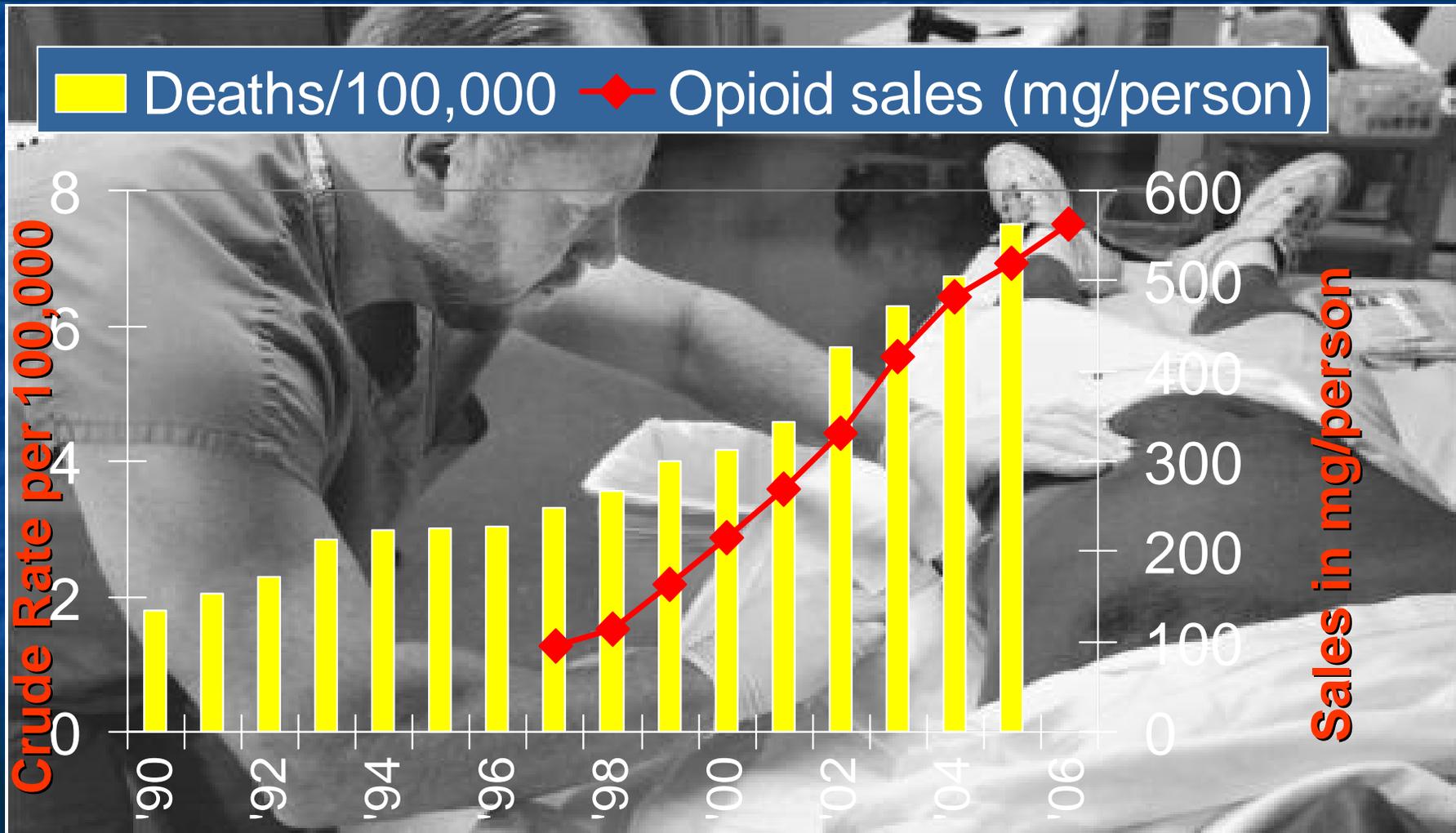
Source: Prescribing Opioids for Chronic Pain, SAMHSA-CSAT: Clinical Challenges in Prescribing Controlled Drugs



**Methadone
goes well
with
OJ**



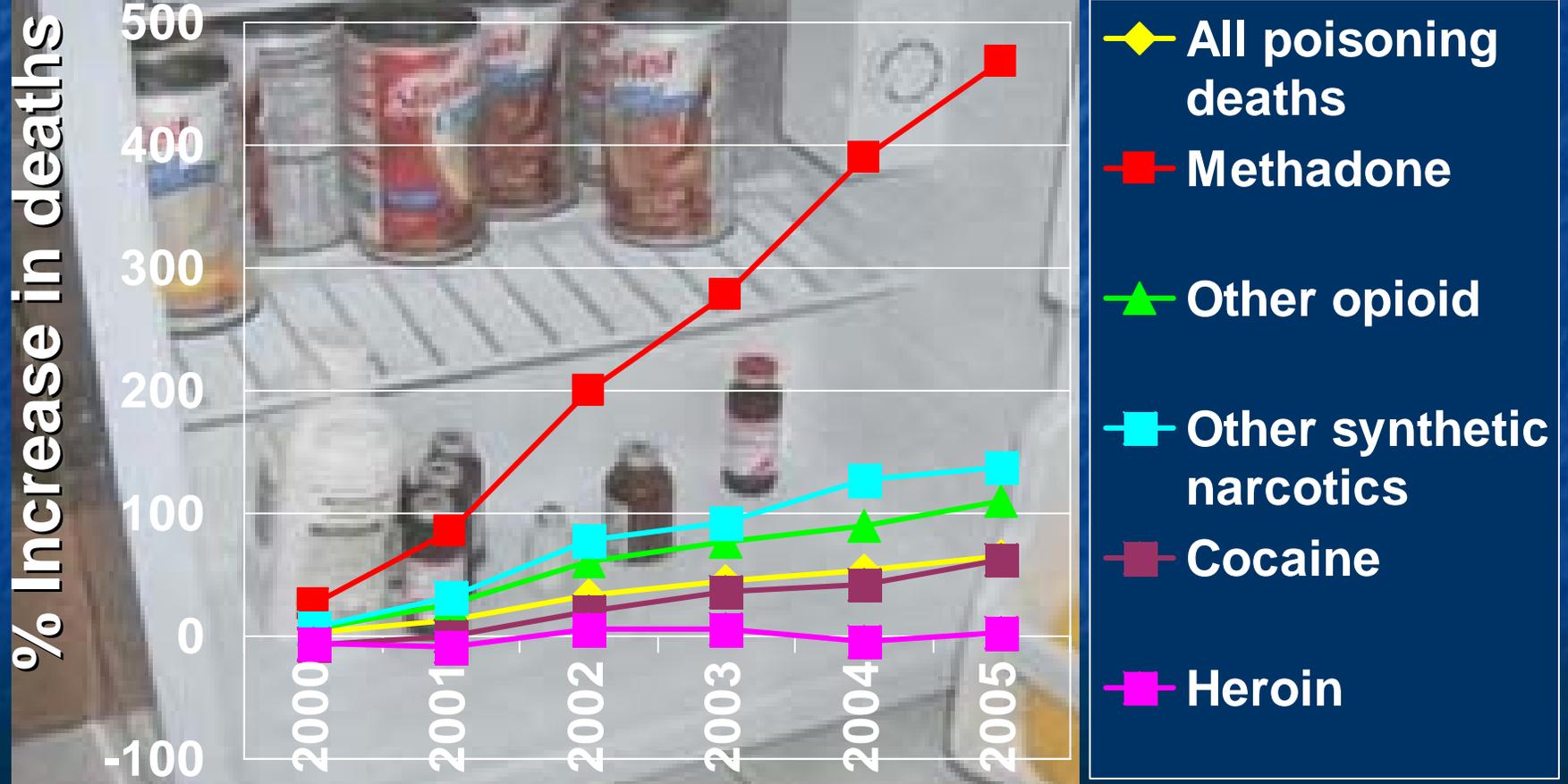
Deaths per 100,000 related to unintentional overdose and annual sales of prescription opioid pain relievers by year, 1990-2006



Source: Paulozzi, CDC, Congressional Testimony, 2007

Poisoning Deaths in the U.S

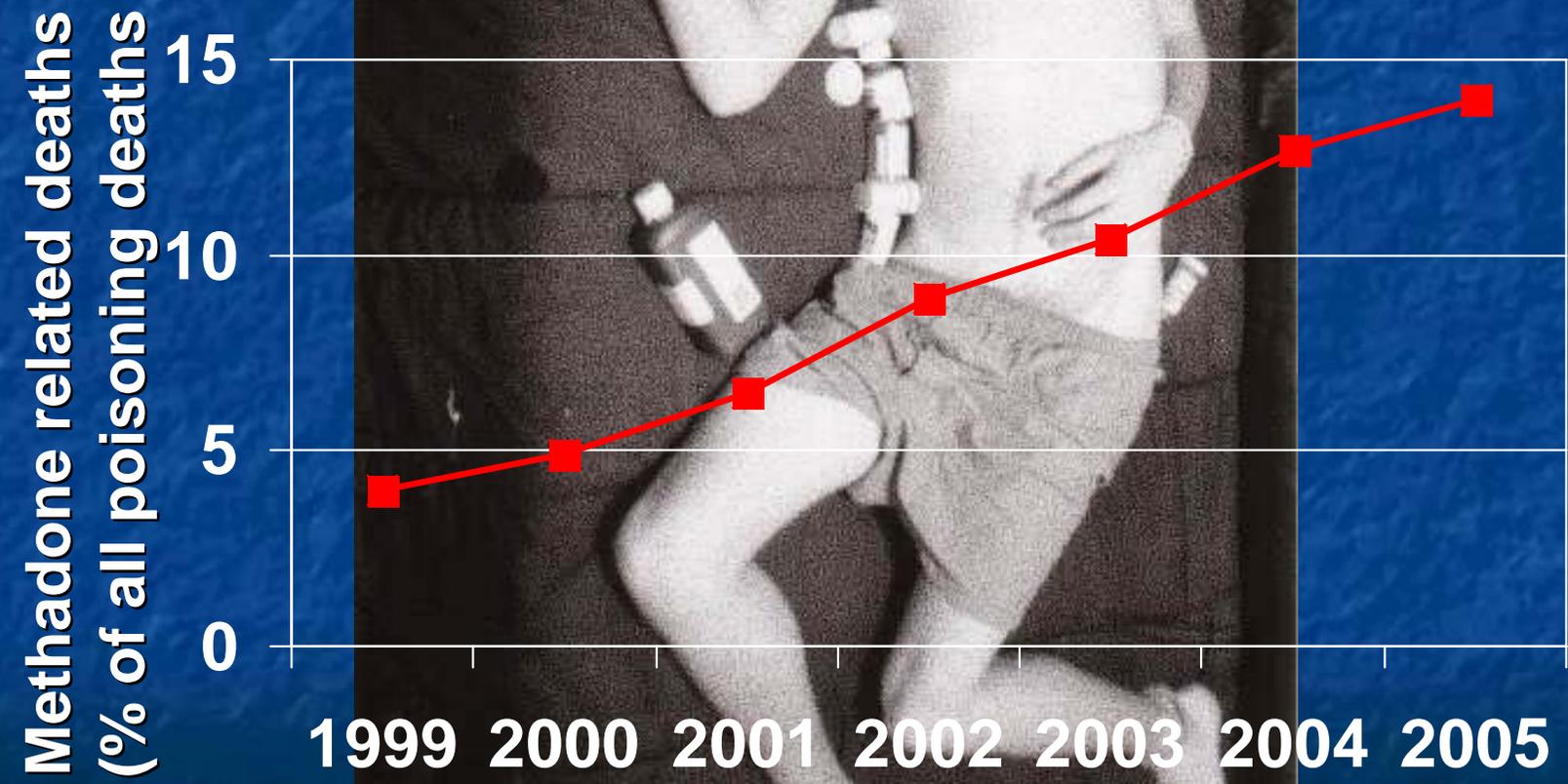
% Increase



Source: CDC 10



Methadone Related Deaths (% of all Poisoning Deaths)



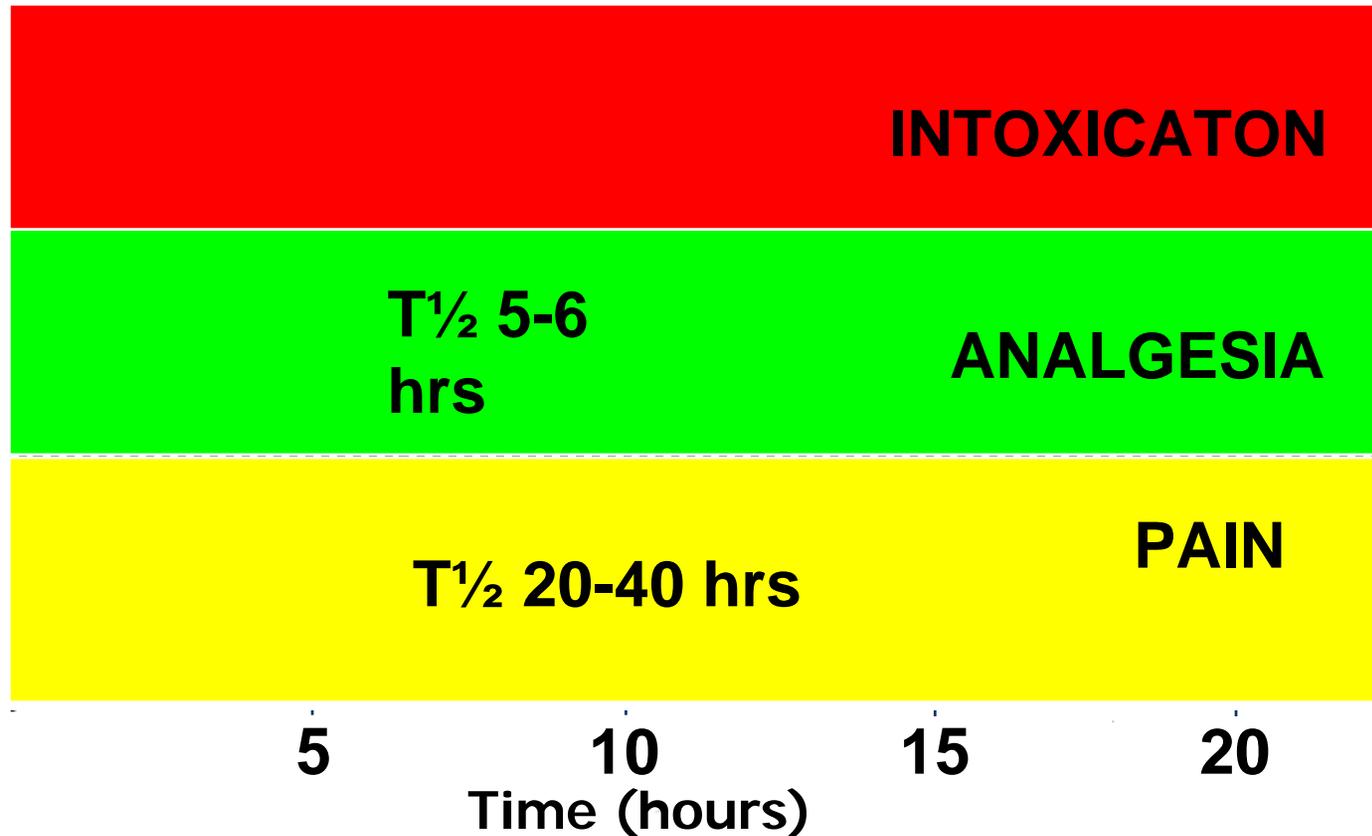
Source: CDC



Methadone - Pharmacokinetics

- Well absorbed (>80%) taken orally.
- Body eliminates methadone (**half-time up to 59 hrs**) slowly, while methadone's pain relieving action lasts much shorter (**4-8 hrs**).
- Patient may feel the need to repeat dose at **intervals shorter** than body can handle
- Repeated dosing may lead to **accumulation** in the body and result in serious toxicity.

Methadone Single Dose Effects

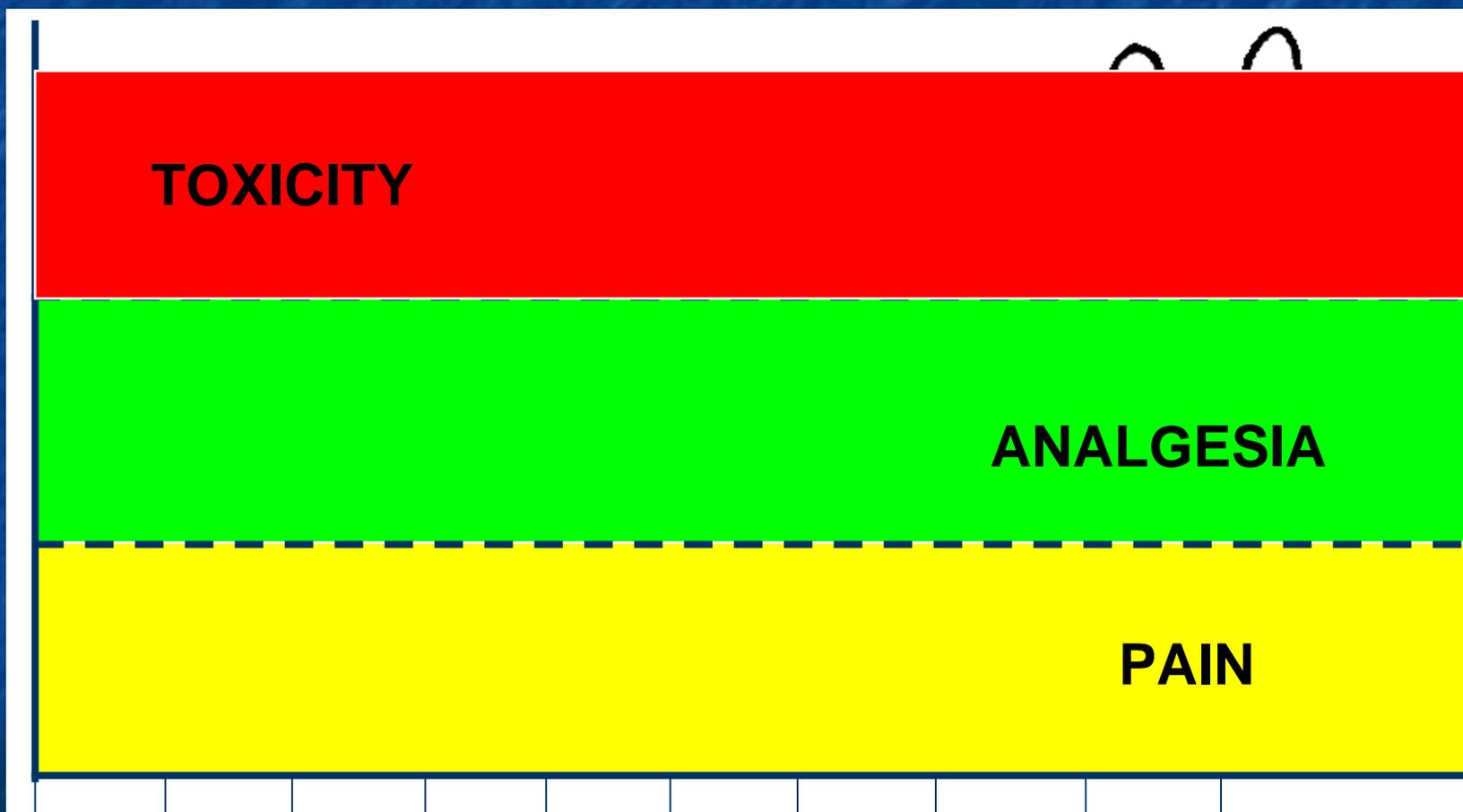


Ref: Nilsson MI, et al. Acta anaesth. scand 1982, Suppl 74, 66-69

Source: Resource Manual for CME course entitled "Prescribing Opioids for Chronic Pain" – Offered by the New England Chapters of the American Society of Addiction Medicine with support from CSAT, SAMHSA



Toxic Effects of Multiple Methadone Doses



Source: Resource Manual for CME course entitled *"Prescribing Opioids for Chronic Pain"* – Offered by the New England Chapters of the American Society of Addiction Medicine with support from CSAT, SAMHSA

Examples of Substances – May Enhance Methadone Effects

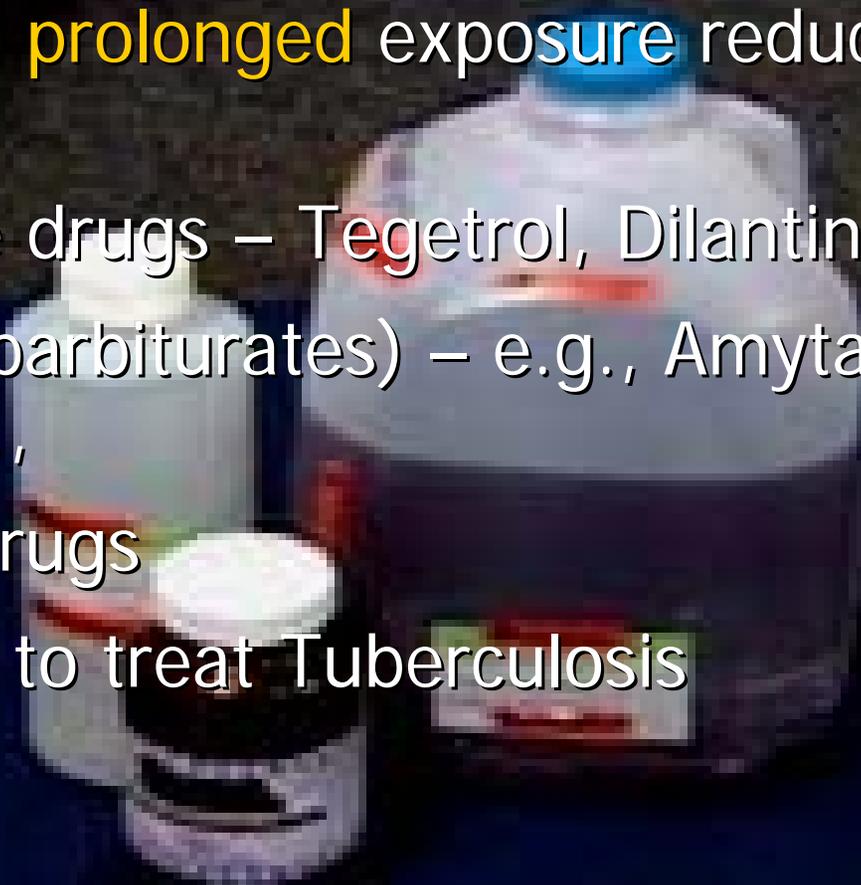


- These reduce elimination of methadone by body
- Some antidepressant drugs – e.g., Prozac, Paxil, Zoloft etc.
- Depressants (e.g., alcohol, anesthetics, benzos, some sedatives, other opioids)
- Some drugs used for fungal infections
- Some antibiotics – e.g., Erythrocin
- Grapefruit juice

Examples of Substances – May Reduce Methadone Effects



- These upon **prolonged** exposure reduce methadone effects
- Anti-seizure drugs – Tegetrol, Dilantin
- Sedatives (barbiturates) – e.g., Amytal, fioricet, fiorinal, etc.,
- HIV/AIDS drugs
- Drugs used to treat Tuberculosis
- Cocaine
- Smoking





Methadone Deaths– Two Major Mechanisms

- 7 years Methadone use,
some prior Heroin
- **Respiratory depression**
Normal Brain
 - Major hazard (Similar to other opioid analgesics)
 - Respiratory depression typically occurs later and persist longer than its peak analgesic effects
 - **Toxicity on heart**
 - Not shared by other opioids
 - Shared by **LAAM**, a previously marketed addiction treatment drug.

(SPECT Brain scan from Brainplace.com, Dr. Daniel Amen)