

The Opioid Epidemic: What labs have to do with it?

Ewa King, Ph.D.

Associate Director of Health

RIDOH State Health Laboratories



Analysis. Answers. Action.

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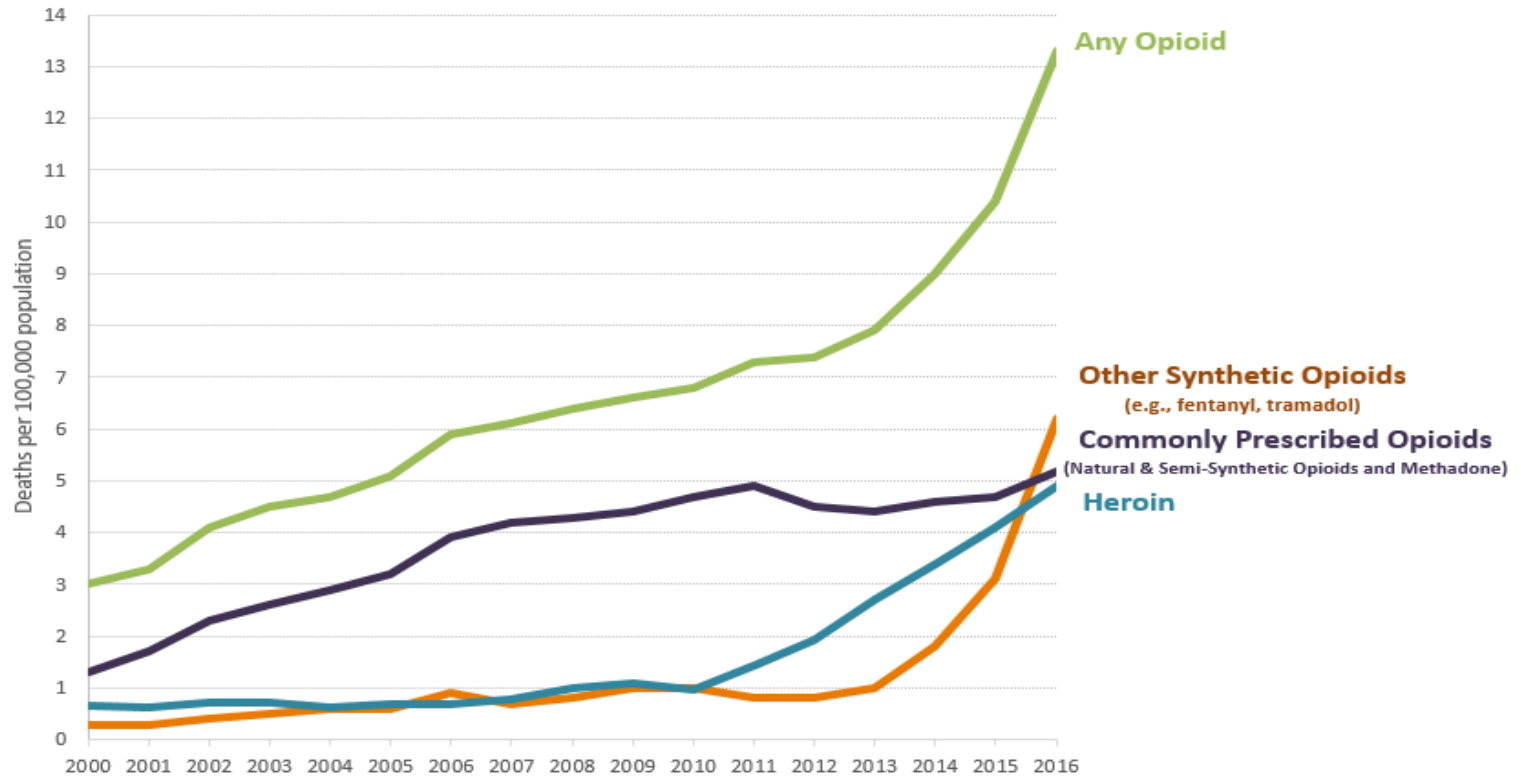
Overview

- Overdose trends
- Opioids and their effects
- Analytical testing approaches
- Toxicology laboratories



Opioid overdose crisis

Overdose Deaths Involving Opioids, United States, 2000-2016

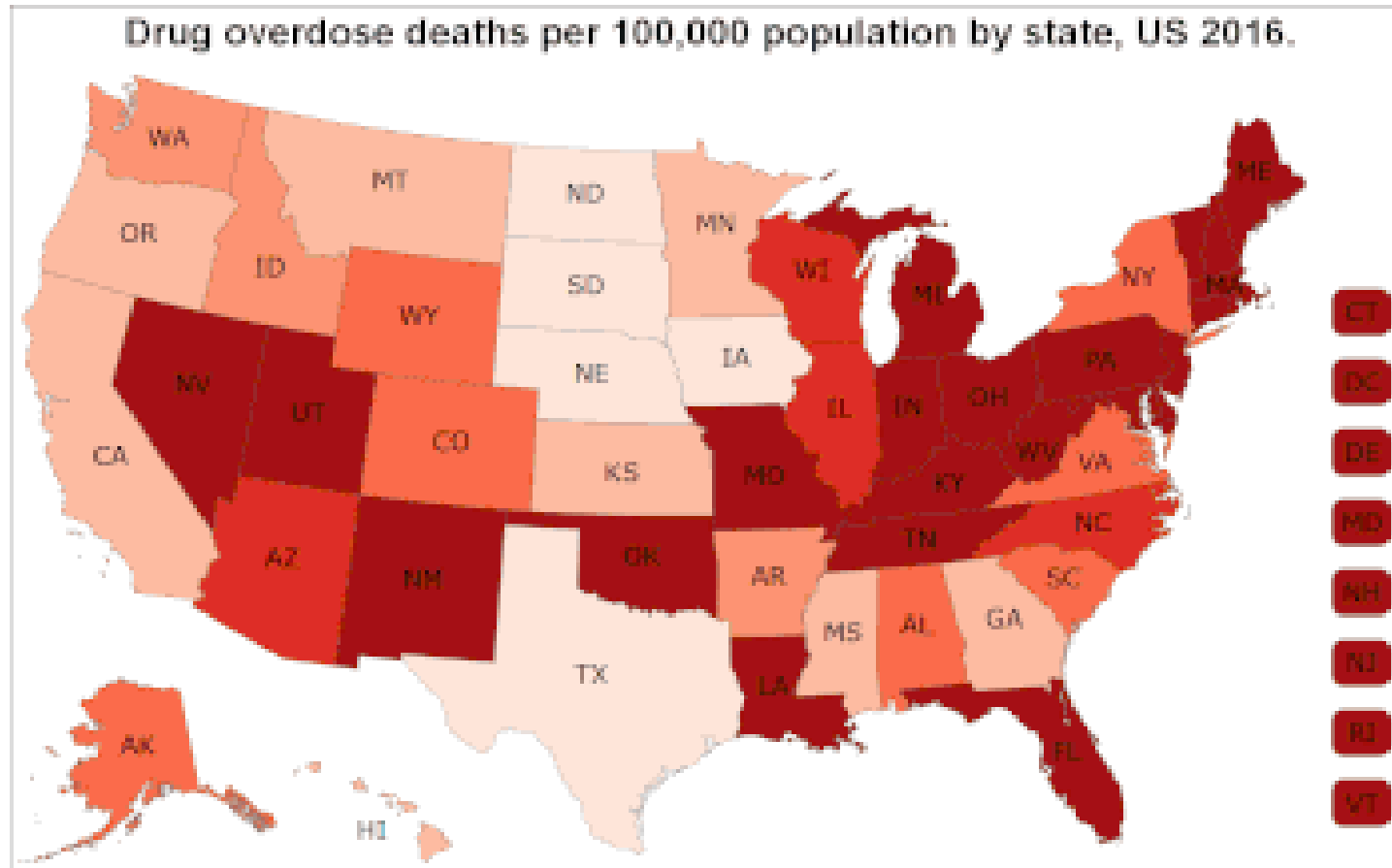


SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. <https://wonder.cdc.gov/>.

www.cdc.gov
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Opioid overdose crisis



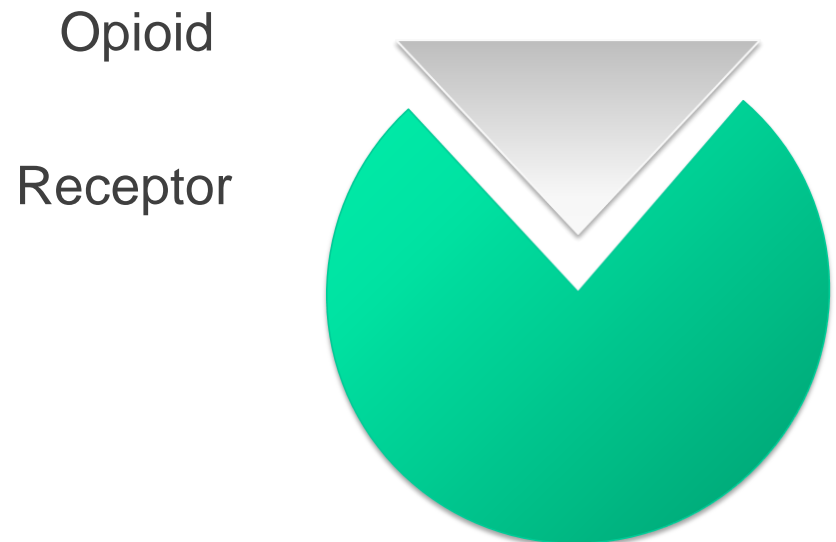
Source: Annual Surveillance Report of Drug-Related Risks and Outcomes | United States CDC National Center for Injury Prevention and Control | 2017

Opiates and Opioids

- Opiates vs. Opioids
- Opiates:
 - Naturally occurring, derived from the poppy plant
- Opioids:
 - “Opiate-like” drugs in effects, not chemical structure
 - Includes opiates
- Narcotic analgesics
- CNS depressants
- DEA Schedule I or II controlled substances
- Additive effect with other CNS depressant drugs

Efficacy of Opioids

- How do opioids work?
- Bind with opioid receptors
- Brain, spinal cord, GI tract, and throughout the body
- Pain, emotion, breathing, movement, and digestion



Effects of Opioids

Physiological

- Pain relief
- Cough suppression
- GI motility
- Respiratory depression
- Pupillary constriction
- Itching
- Constipation
- Dependence

Psychological

- Drowsiness/ sedation
- Mental confusion
- Loss of memory
- Lethargy/ apathy
- Euphoria/ tranquility
- Mood swings
- Depression
- Withdrawal
- Dependence

Opiates

Opiates

- Naturally occurring alkaloids

Opium

- Latex from the opium poppy plant

Codeine:

- Mild to moderate pain
- Antitussive

Morphine:

- Severe pain
- Metabolite of codeine and heroin



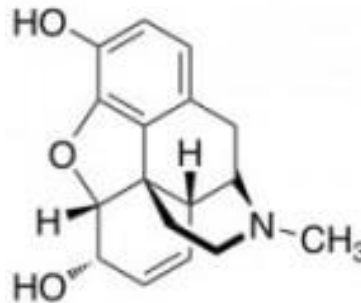
Opiates

Semi-synthetic Opiates:

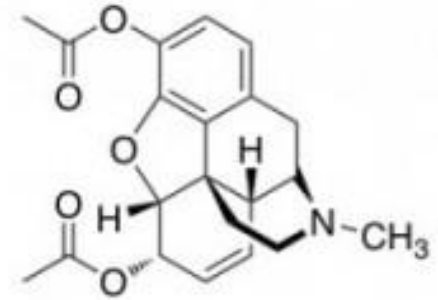
- Synthesized from a natural opiate

Heroin:

- Schedule I narcotic



morphine



heroin

Hydrocodone (Vicodin):

- Mild to moderate pain
- Metabolizes to hydromorphone (Dilaudid)

Oxycodone (Oxycontin/Percocet):

- Moderate to severe pain
- Metabolizes to oxymorphone (Opana)



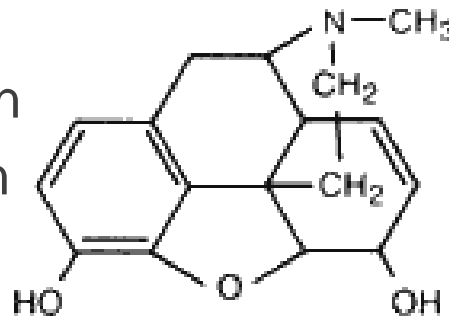
Opioids

All drugs with “Opiate-like” effects

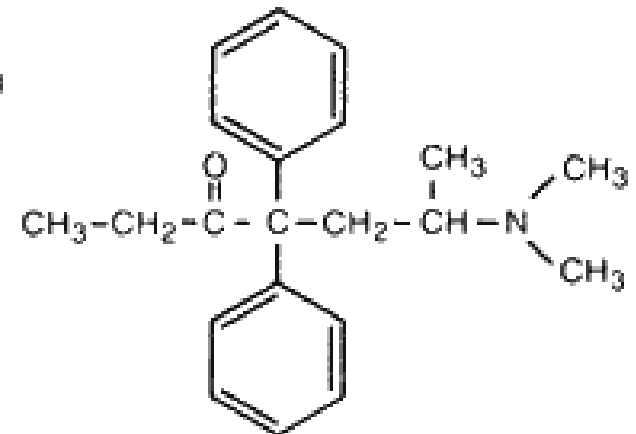
- Psychological and physical
- Includes natural opiates
- Synthetic: different chemical structures

Methadone:

- moderate to severe pain
- treats narcotic addiction
- Syrup or pills



MORPHINE



METHADONE

Meperidine (Demerol)

Tramadol (Ultram):

- Moderate to severe pain

Synthetic opioids

- **Fentanyl** (Duragesic, Sublimaze):
 - Powerful, fast acting narcotic analgesic
 - 80-100 times more potent than morphine
 - 50 times more potent than heroin
- **Rx:**
 - to treat severe pain or as a surgical anesthetic
 - IV, pills, patches, lozenges, lollipops
- **Illicit:**
 - powder shipped from China or Mexico
 - counterfeit pills
 - frequently sold as heroin
- snorted, smoked, or injected

Novel or “designer” opioids

- Synthetic drugs of abuse
- Minor change to the original chemical structure (more than 1400 compounds described in literature)
- Analog of a pharmaceutical or research drug
- Mimic effects of the original drug
- Circumvent existing legal restrictions/ DEA scheduling
- Illicitly produced/ Not clinically tested or FDA approved
- “Not for human consumption”
- “Research chemical”
- Pills, powders, counterfeit tablets

Designer Opioids

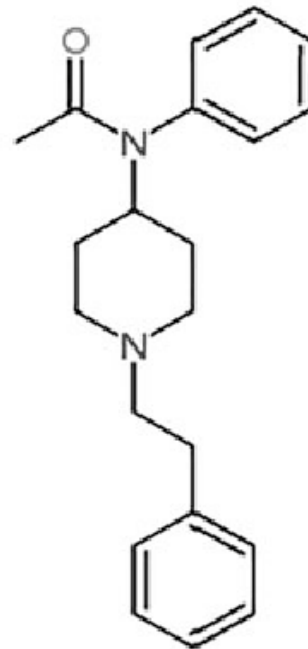
- **Fentanyl analogs:**

- Acetyl-
- Acryl-
- Butyryl-
- Furanyl-
- Carfentanil
- 4-ANPP

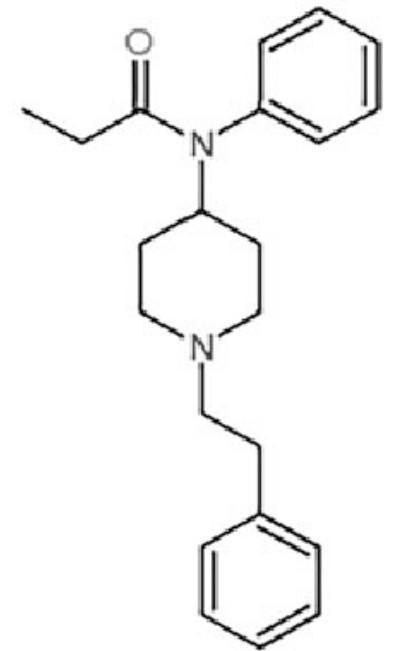
- **Designer Opioids:**

- AH-7921
- MT-45
- U-47700 (Pink/Pinky)

Acetylfentanyl



Fentanyl



Fentanyl Analogs

- **Acetyl Fentanyl:**

- tablets or powder
- ~10 times more potent than morphine
- less potent than fentanyl
- Rhode Island: 2013
- 15 deaths

- **Furanyl Fentanyl:**

- pills or powder
- More potent than morphine
- Less potent than fentanyl



- Both cross-react with fentanyl ELISA assay
- Both DEA Schedule I

Fentanyl Analogs

- **Carfentanil:**
- tranquilizing agent for large mammals
- DEA Schedule II drug
- small amount is fatal
- absorbed through skin
- 10,000 times the potency of morphine
- 100 times more potent than fentanyl
- white powder or pills
- mixed in heroin
- No cross-reactivity with fentanyl ELISA screening assay



Opioids Potency



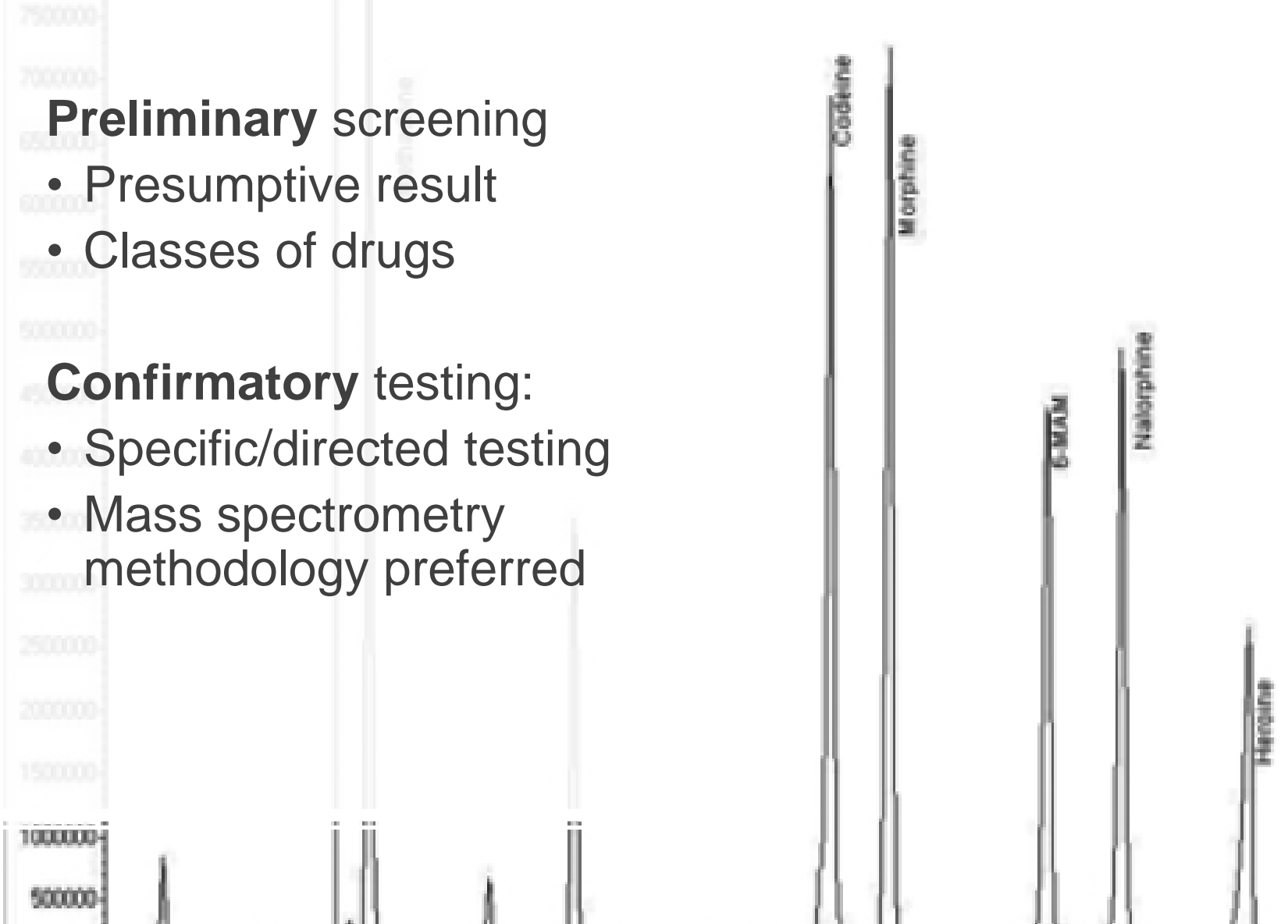
Drug toxicology testing

Preliminary screening

- Presumptive result
- Classes of drugs

Confirmatory testing:

- Specific/directed testing
- Mass spectrometry methodology preferred



Preliminary Tests

Immunoassay

- Presumptive Screens
- Qualitative assays
- Designed to narrow down the classes of drugs

Disadvantages

- Limited scope of testing
- False negatives and positives are possible
- Not forensically defensible without confirmation

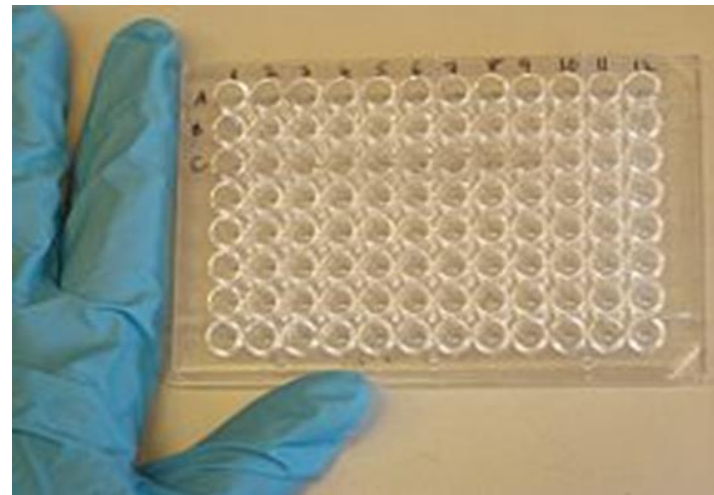
Newer technologies increasingly in use: e.g. HR MS (TOF)

ELISA Tecan System



ELISA screening at RISHL

- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabinoids
- Carisoprodol
- Cocaines
- Methamphetamines
- Tricyclic Antidepressants
- Zolpidem
- Opioids:
 - Fentanyl
 - Methadone
- Opiates:
 - Oxycodone
 - Buprenorphine



Confirmatory Testing

- Second phase of forensic (but not necessarily clinical) drug testing
- Positive screening tests can be confirmed utilizing a more specific and sensitive chemical principle.
- Qualitative or quantitative analysis
- Gas or liquid chromatography
- Mass spectrophotometer detector
- GC/MS, LC/MS, LC/MS/MS

Confirmatory Testing

Advantage:

- Detect and identify specific drugs present
- Broad scope of analytes, including metabolites
- Detect minute amounts
- Forensically defensible
- Widely accepted methodology
- Extensive scientific literature and information

Disadvantage:

- Requires separation of the drug from the sample matrix
- Labor intensive
- Expensive instrumentation

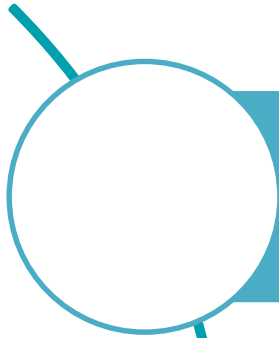
GC/MA and LC/MS/MS



Analysis. Answers. Action.

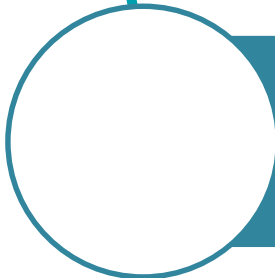
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The universe of toxicology laboratories



Clinical toxicology

(therapeutic drug monitoring, overdoses or poisonings diagnosis, pain management clinics)



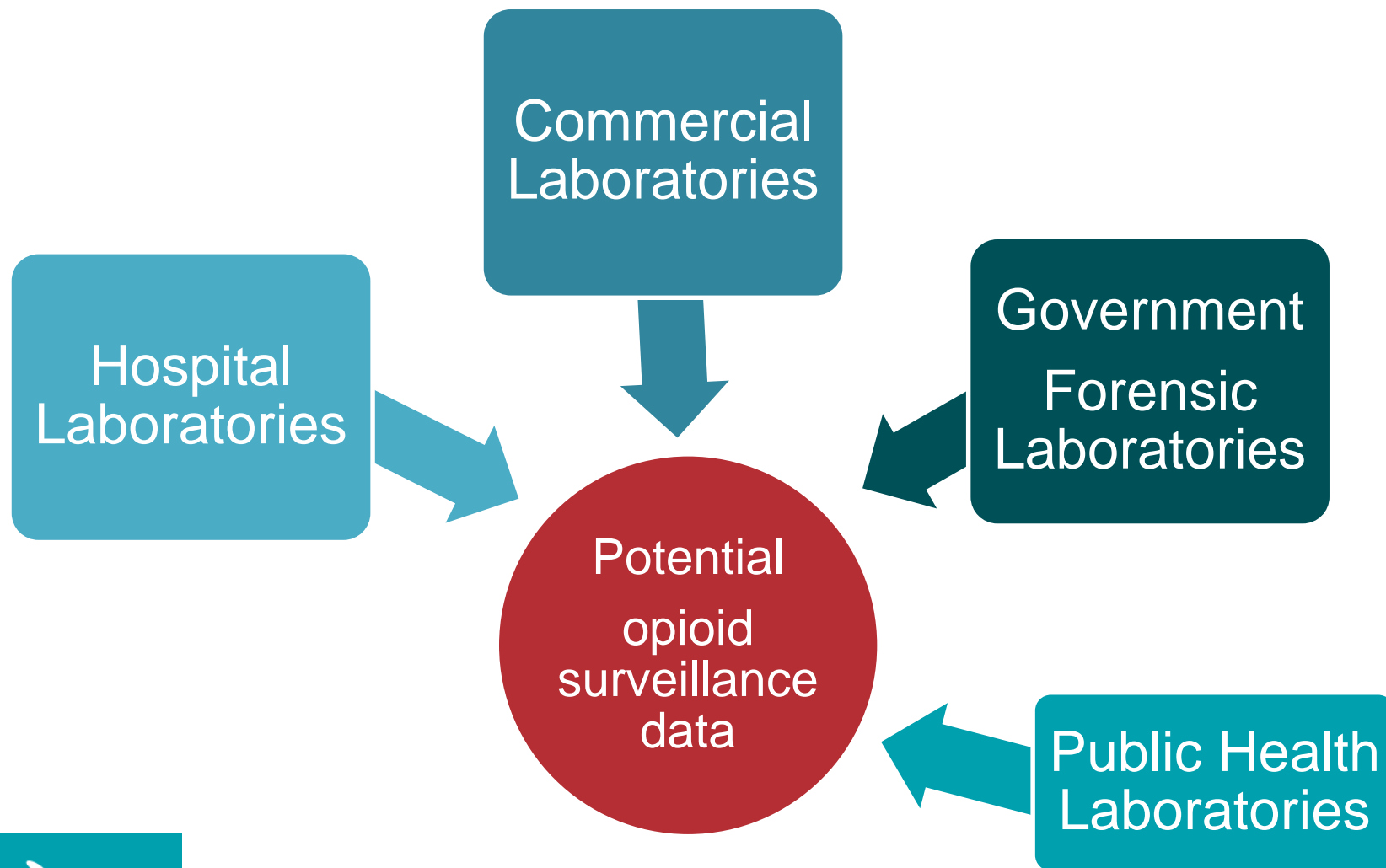
Employment drug testing, addiction treatment centers, athletic performance-enhancing checks (sports doping)



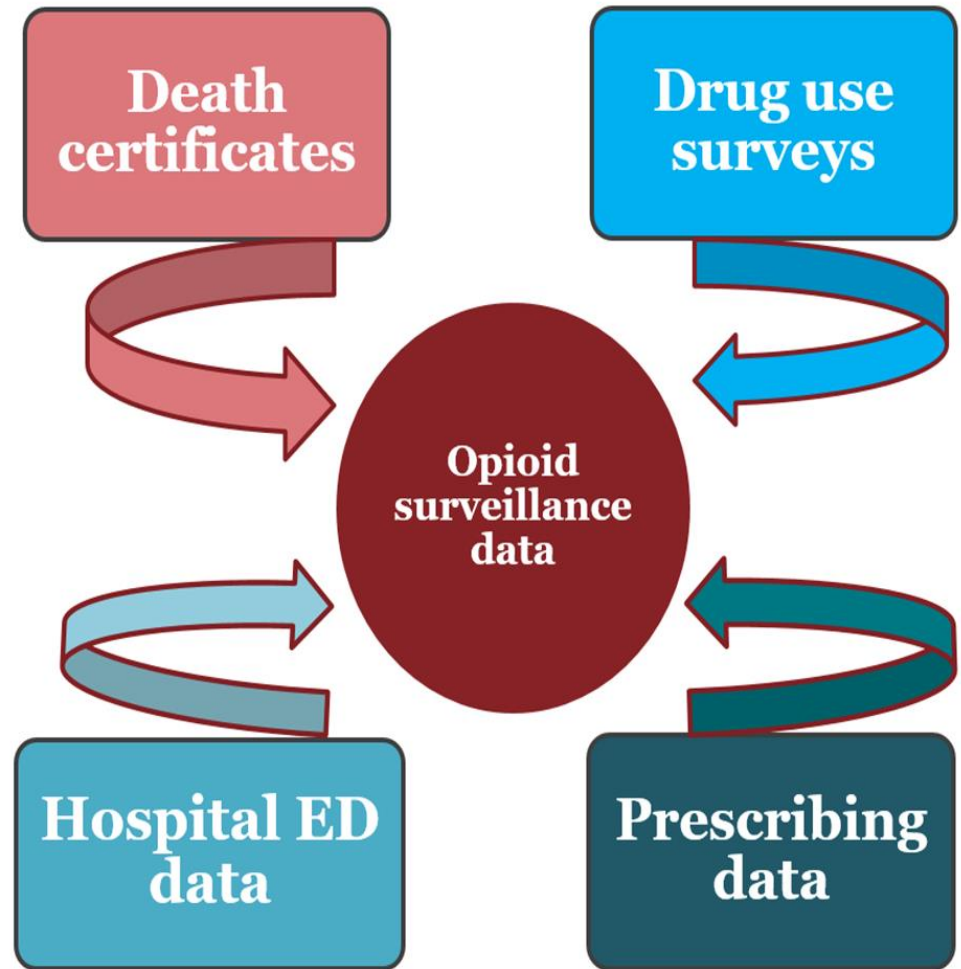
Forensic toxicology

(cause of death investigations, including fatal overdoses)

Laboratories and overdose surveillance



Opioid Surveillance



Current issues in toxicology testing

- Scope of testing (list of analytes) not standardized
- Different methodologies
- No clear reference laboratory system
- Inadequate capacity (specially in the forensic area)
- Inadequate capability to test for novel analogs-”designer opioids”

Barriers to a standardized approach

- Expensive instrumentation
- Expensive calibration/IS/QC standards for isotope dilution LC/MS/MS
- Differing accreditation requirements for clinical vs. forensic laboratories
- Regulatory oversight
- Lack of standardization of methodology or defined list of target analytes

New public health initiatives

- Funding for the states:
 - CDC ESOOS Enhanced State Opioid Overdose Surveillance
 - Opioid Crisis Cooperative Agreement: “SURGE”
- New requirement for “biosurveillance”
for non-fatal overdoses
- New testing programs for public health laboratories

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Thank you!

Ewa King, Ph.D.

ewa.king@health.ri.gov