Discerning Drug Mortality Patterns in a Large Database of Toxicology Results

A Southeast Michigan perspective
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Numbers

- 2017: 937
- 2016: 849
- 2015: 711
- 2014: 543
- 2013: 449
- 2012: 419
- 2011: 420

Most Cases Have Multiple Drugs

- 80% of cases have more than one drug in the blood
- An average drug death in Wayne County has 4 to 5 quantified drugs
- About 25% have 6 or more analytes
- 5% have more than 10 analytes
Frequent Combinations

- Alcohol, Heroin
- Alcohol, Cocaine, Fentanyl and / or Heroin
- Alcohol, Carfentanil, Cocaine
- Alprazolam, Codeine, Hydrocodone
- Cocaine, Fentanyl, Heroin
- Multiple combinations thereof

Most Frequently Found Drugs in 2016

<table>
<thead>
<tr>
<th>Drug</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>OXYCODONE</td>
<td>32</td>
</tr>
<tr>
<td>DIAZEPAM</td>
<td>26</td>
</tr>
<tr>
<td>OPIATE (NOS)</td>
<td>24</td>
</tr>
<tr>
<td>FURANYL FENTANYL</td>
<td>23</td>
</tr>
<tr>
<td>U-47700</td>
<td>22</td>
</tr>
<tr>
<td>CLONAZEPAM</td>
<td>12</td>
</tr>
<tr>
<td>TRAMADOL</td>
<td>11</td>
</tr>
<tr>
<td>BENZODIAZEPINE</td>
<td>10</td>
</tr>
<tr>
<td>OXYMORPHONE</td>
<td>8</td>
</tr>
<tr>
<td>BUPRENORPHINE</td>
<td>7</td>
</tr>
</tbody>
</table>

How to decide, in the presence of significant toxicology findings, what the primary vs. contributing causes of death are?
Are there hidden patterns and drug combinations that are not evident with descriptive statistics?

Postmortem Forensic Toxicology

- Things are not always clear cut
  - Postmortem redistribution
  - Several drugs are present with equivocal concentrations
  - You know there may be drug interactions but are not sure, and never will be
  - There may be pathologic findings that may be related to the drug you think caused death
  - .....
  - or maybe not

There Are Tools to Better Understand Drug Use Patterns

- We Have Used CHAID to look at drug use patterns
  - Chi² Automatic Interaction Detection
- A decision tree technique based on adjusted significance testing
- Originally used in marketing research
- Can be used for trend prediction, classification and interaction between variables
- Has been used in medicine to predict risk of heart failure, onset of delirium in ICUs and outcomes in methadone clinics
Results

• Morphine was best predictor of drug abuse as a cause of death
  – In our community this is almost always derived from heroin
  – Chloroquine is commonly found with heroin
  – If positive for morphine, next best predictor of drug abuse was codeine
• Cases positive for morphine were also more likely to be associated with citalopram or alprazolam

Results

• In cases negative for morphine, acetaminophen was next best predictor of drug abuse
  – This was mostly co-occurrent with hydrocodone
  – Acetaminophen, in aggregate data, is a good predictor of drug deaths
• Acetaminophen/hydrocodone was more likely in the absence of methadone use
• In the absence of morphine, you were likely to find acetaminophen/hydrocodone or methadone

Patterns

• Morphine is the best predictor of drug use as a cause of death
• Fentanyl is main predictor in the absence of morphine
• In cases positive for morphine, there is also an association with codeine and alprazolam
• In case negative for fentanyl, acetaminophen is still associated with drug deaths
• Cases positive for fentanyl and associated with midazolam tend to be non-drug deaths
Other Patterns

• Patterns change from year to year
• The increase in fentanyl and analogues has produced a different decision tree
  – Fentanyl is often found in morphine negative deaths
  – When fentanyl first appeared, it was almost always associated with morphine
  – Fentanyl + midazolam is probably hospital related
• Methadone + citalopram is uniformly lethal

Other Patterns

• Cocaine positive deaths divided fairly evenly between morphine(+) and morphine(-) deaths
  – If levamisole(+) not associated with drug deaths
    • In homicides and some suicides
  – Why levamisole (+) cocaine is associated with violent deaths is unknown

Statistical Tools Have Limited Usefulness

• You cannot understand what you don’t see
  – A drug may not be part of the drug screen
  – You only find what you screen for
  – Many communities don’t know what their drug use patterns are
  – Financial considerations
• You need to comprehensively screen all deaths to derive a statistically meaningful decision tree
  – This means you need to collect a minimum set of data in every case
• There is no substitute for thinking about toxicology results in the context of other clinical and pathologic findings.