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

FENTANYL	430	OXYCODONE	32
HEROIN	334	DIAZEPAM	26
COCAINE	322	OPIATE (NOS)	24
ALCOHOL	84	FURANYL FENTANYL	23
ALPRAZOLAM	71	U-47700	19
HYDROCODONE	60	CLONAZEPAM	12
CARFENTANIL	55	TRAMADOL	11
MORPHINE	47	BENZODIAZEPINE	10
ACETYL FENTANIL	39	OXYMORPHONE	8
METHADONE	39	BUPRENORPHINE	7

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?

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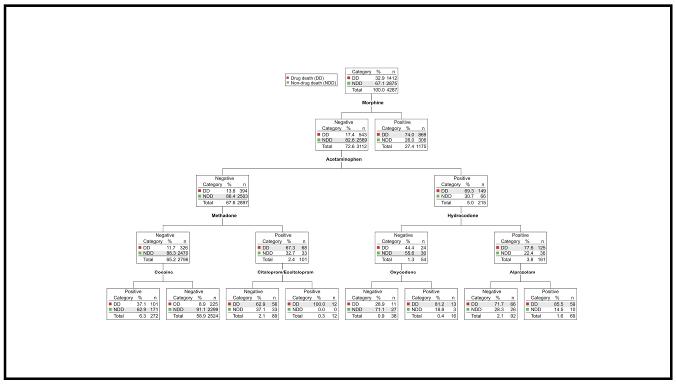
Postmortem Forensic Toxicology

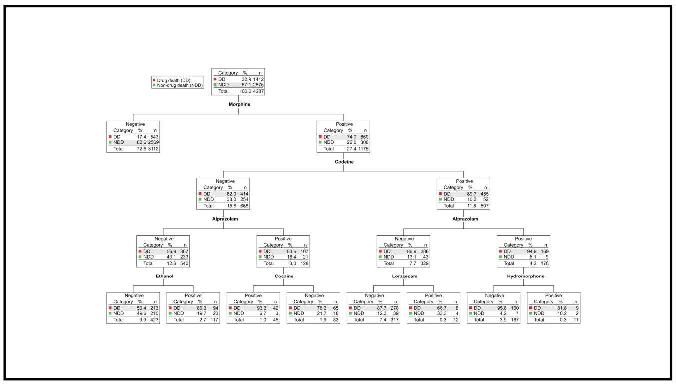
- Things are not always clear cut
  - Postmortem redistribution
  - Several drugs are present with equivocal concentrations
  - You know there may be drug interactions but are not sure, and never will be
  - There may pathologic findings that may be related to the drug you think caused death
  - …..or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

There Are Tools to Better Understand Drug Use Patterns

- We Have Used CHAID to look at drug use patterns
  - Chi^2 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



Drug death (DD)
Non-drug death (NDD)
Category % n
DD 32.9 1412
NDD 67.1 2875
Total 100.0 4287
Morphine
Negative
Category % n
DD 17.4 543
NDD 82.6 2569
Total 72.6 3112
Positive
Category % n
DD 74.0 869
NDD 26.0 306
Total 27.4 1175
Acetaminophen
Negative
Category % n
DD 13.6 394
NDD 86.4 2503
Total 67.6 2897
Positive
Category % n
DD 69.3 149
NDD 30.7 66
Total 5.0 215
Methadone
Hydrocodone
Negative
Category % n
DD 11.7 326
NDD 88.3 2470
Total 65.2 2796
Positive
Category % n
DD 67.3 68
NDD 32.7 33
Total 2.4 101
Negative
Category % n
DD 44.4 24
NDD 55.6 30
Total 1.3 54
Positive
Category % n
DD 77.6 125
NDD 22.4 36
Total 3.8 161
Cocaine
Citalopram/Escitalopram
Oxycodone
Alprazolam
Positive
Category % n
DD 37.1 101
NDD 62.9 171
Total 6.3 272
Negative
Category % n
DD 8.9 225
NDD 91.1 2299
Total 58.9 2524
Negative
Category % n
DD 62.9 56
NDD 37.1 33
Total 2.1 89
Positive
Category % n
DD 100.0 12
NDD 0.0 0
Total 0.3 12
Negative
Category % n
DD 28.9 11
NDD 71.1 27
Total 0.9 38
Positive
Category % n
DD 81.2 13
NDD 18.8 3
Total 0.4 16
Negative
Category % n
DD 71.7 66
NDD 28.3 26
Total 2.1 92
Positive
Category % n
DD 85.5 59
NDD 14.5 10
Total 1.6 69



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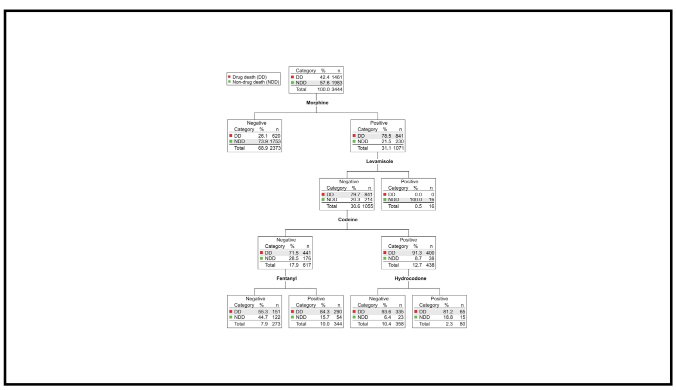
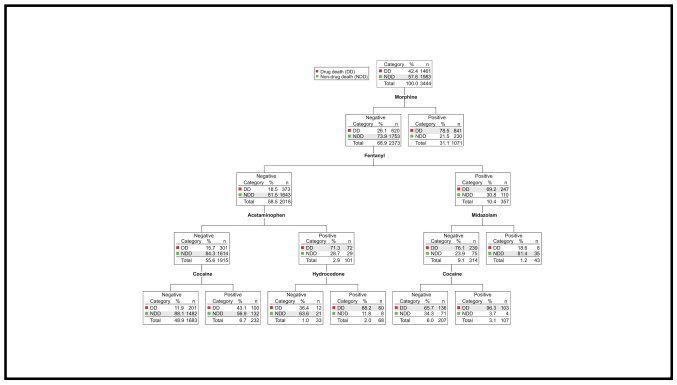
Total 72.6 3112
Positive
Category % n
DD 74.0 869
NDD 26.0 306
Total 27.4 1175
Codeine
Negative
Category % n
DD 62.0 414
NDD 38.0 254
Total 15.6 668
Positive
Category % n
DD 89.7 455
NDD 10.3 52
Total 11.8 507
Alprazolam
Alprazolam
Negative
Category % n
DD 56.9 307
NDD 43.1 233
Total 12.6 540
Positive
Category % n
DD 83.6 107
NDD 16.4 21
Total 3.0 128
Negative
Category % n
DD 86.9 286
NDD 13.1 43
Total 7.7 329
Positive
Category % n
DD 94.9 169
NDD 5.1 9
Total 4.2 178
Ethanol
Cocaine
Lorazepam
Hydromorphone
Negative
Category % n
DD 50.4 213
NDD 49.6 210
Total 9.9 423
Positive
Category % n
DD 80.3 94
NDD 19.7 23
Total 2.7 117
Positive
Category % n
DD 93.3 42
NDD 6.7 3
Total 1.0 45
Negative
Category % n
DD 78.3 65
NDD 21.7 18
Total 1.9 83
Negative
Category % n
DD 87.7 278
NDD 12.3 39
Total 7.4 317
Positive
Category % n
DD 66.7 8
NDD 33.3 4
Total 0.3 12
Negative
Category % n
DD 95.8 160
NDD 4.2 7
Total 3.9 167
Positive
Category % n
DD 81.8 9
NDD 18.2 2
Total 0.3 11



Drug death (DD)
Non-drug death (NDD)
Category % n
DD 42.4 1461
NDD 57.6 1983
Total 100.0 3444
Morphine
Negative
Category % n
DD 26.1 620
NDD 73.9 1753
Total 68.9 2373
Positive
Category % n
DD 78.5 841
NDD 21.5 230
Total 31.1 1071
Levamisole
Negative
Category % n
DD 79.7 841
NDD 20.3 214
Total 30.6 1055
Positive
Category % n
DD 0.0 0
NDD 100.0 16
Total 0.5 16
Codeine
Negative
Category % n
DD 71.5 441
NDD 28.5 176
Total 17.9 617
Positive
Category % n
DD 91.3 400
NDD 8.7 38
Total 12.7 438
Fentanyl
Hydrocodone
Negative
Category % n
DD 55.3 151
NDD 44.7 122
Total 7.9 273
Positive
Category % n
DD 84.3 290
NDD 15.7 54
Total 10.0 344
Negative
Category % n
DD 93.6 335
NDD 6.4 23
Total 10.4 358
Positive
Category % n
DD 81.2 65
NDD 18.8 15
Total 2.3 80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Category % n
DD 42.4 1461
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Morphine
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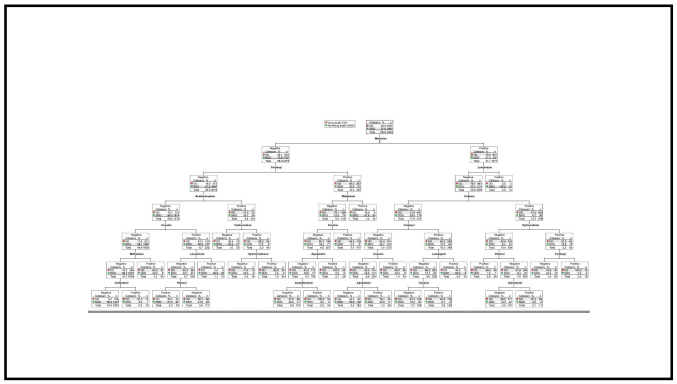
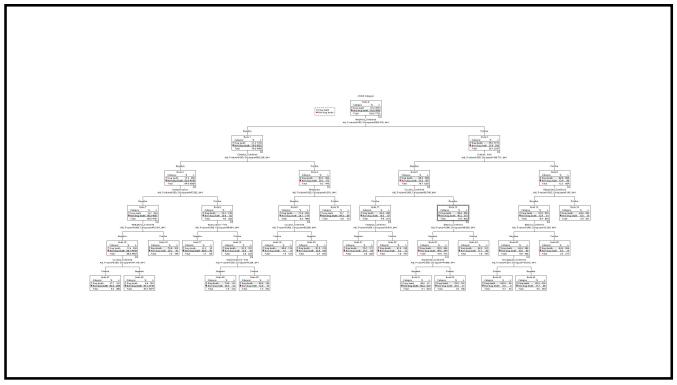
Category % n
DD 26.1 620
NDD 73.9 1753
Total 68.9 2373
Positive
Category % n
DD 78.9 841
NDD 21.1 230
Total 31.1 1071
Fentanyl
Negative
Category % n
DD 18.5 373
NDD 81.5 1643
Total 58.5 2016
Positive
Category % n
DD 69.2 247
NDD 30.8 110
Total 10.4 357
Acetaminophen
Midazolam
Negative
Category % n
DD 19.7 301
NDD 80.3 1614
Total 55.6 1915
Positive
Category % n
DD 71.3 72
NDD 28.7 29
Total 2.9 101
Negative
Category % n
DD 76.5 209
NDD 23.5 64
Total 8.1 314
Positive
Category % n
DD 18.6 6
NDD 81.4 26
Total 1.2 43
Cocaine
Hydrocodone
Cocaine
Negative
Category % n
DD 11.9 201
NDD 88.1 1482
Total 48.9 1683
Positive
Category % n
DD 43.1 100
NDD 56.9 132
Total 6.7 232
Negative
Category % n
DD 36.4 12
NDD 63.6 21
Total 1.0 33
Positive
Category % n
DD 88.2 60
NDD 11.8 8
Total 2.0 68
Negative
Category % n
DD 65.7 136
NDD 34.3 71
Total 6.0 207
Positive
Category % n
DD 96.3 103
NDD 3.7 4
Total 3.1 107





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 mainly 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 in 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.

Questions?

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