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Overview

• MNDOSA Planning & Scope
• Laboratory Component
• Lessons Learned (to date)
MNDOSA Objectives

• Determine the burden of substance use/overdoses seen in select emergency departments and hospitals in Minnesota.

• Identify clusters of drug overdoses.

• Identify substances causing clusters, unusual or atypical clinical presentation, and severe illnesses in order to inform approaches to treatment and prevention.

• Describe the populations most affected to help focus and guide prevention efforts.
Funding

• LRN-C
  • Staff time
  • Instrumentation
  • Vendor contract (SOPs, calibrators, controls)

• CSTE
  • Grant (via SAMHSA)
  • Medical Records Abstractor
  • Small amount for analysis

• CDC
  • Enhanced State Opioid Surveillance (ESOOS) Grant
  • Bulk of sample analyses

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Snapshot of Minnesota

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Review: **Who** will be reported with MNDOSA?

- **All patients** who are **hospitalized** or **present to the ED** (regardless of discharge status) where the principal diagnosis is attributed to the **recreational use** of one or more of the following (including withdrawal symptoms):
  - **Prescription drugs**, including:
    - cold medicines
    - barbiturates
    - benzodiazepines
    - other anticonvulsants (Lyrica, gabapentin, etc.)
    - sleep medications
    - stimulants (Adderall, Ritalin, etc.)
    - antidepressants
    - antidiarrheal medications (loperamide, etc.)
    - muscle relaxants
  - **Natural substances used for recreational purposes**, including:
    - marijuana
    - mushrooms
    - psychoactive drugs
    - hallucinogens
    - other herbal substances with intoxicating effects
  - **Other substances**, including:
    - inhalants
    - other???
  - **Synthetic**, non-prescription drugs, including:
    - synthetic **cannabinoids** (K2, spice, etc.)
    - synthetic **cathinones** (i.e. bath salts)
    - other synthetic hallucinogens (2-C compounds, NBOMBe or “super LSD”, etc.)
  - **Drug combinations**, including:
    - Speedball (cocaine and heroin)
    - Methamphetamine and fentanyl
  - **Opioids** (including heroin)
  - **Traditional illicit drugs**, including:
    - amphetamines
    - cocaine
    - PCP
    - LSD
  - **Natural substances used for recreational purposes**, including:
    - marijuana
    - mushrooms
    - psychoactive drugs
    - hallucinogens
    - other herbal substances with intoxicating effects
  - **Other substances**, including:
    - inhalants
    - other???
Clinician identifies patients in ED meeting MNDOSA reporting criteria:

• **Signs/symptoms attributed to drug or substance use/abuse (excluding alcohol only cases)**

• **Drug or substance use/abuse was recreational, NOT:**
  
  • **Accidental, unintentional overmedication** (i.e. tried to make up a missed dose, forgot they already took a dose, accidentally doubled the dose, etc.)

  • **Adverse reaction** to medication that was taken as recommended

  • **Accidental ingestion** (i.e. accidental child poisoning, took wrong medication unintentionally, etc.)

• **Drug or substance use/abuse was NOT:**

  • Intentional overdose (i.e. suicide attempt)

  • Assault (i.e. “date rape”, malicious poisoning, etc.)
Current participating sites

St. Luke’s Hospital – November 2017

Essentia Health - St. Mary’s Medical Center – November 2017

Hennepin County Medical Center – February 2018

(reports only)

(Four additional Essentia Health in NE MN being added.)
## MNDOSA reports, November 1, 2017 – May 28, 2018

<table>
<thead>
<tr>
<th>Number of ED visits reported</th>
<th>854</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients reported</td>
<td>736</td>
</tr>
</tbody>
</table>

### "Patients of Special Interest"

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Deceased</td>
<td>4 (&lt; 1%)</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>180 (21% of all visits)</td>
</tr>
<tr>
<td>Atypical clinical presentation</td>
<td>49 (6% of all visits)</td>
</tr>
</tbody>
</table>

### Number of Visits, n (%)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Single visit</td>
<td>658 (89%)</td>
</tr>
<tr>
<td>Two visits</td>
<td>58 (8%)</td>
</tr>
<tr>
<td>Three visits</td>
<td>14 (2%)</td>
</tr>
<tr>
<td>Four or more visits</td>
<td>6 (1%)</td>
</tr>
</tbody>
</table>
Suspected drug/substance, non-exclusive drug category
(as reported to MNDOSA)
How will reports be made to MNDOSA?

Report **ALL** eligible cases to MNDOSA

Is the case a “Patient of Special Interest”?

If yes:Were lab specimens collected?

If yes:Send lab specimens to MDH Public Health Laboratory
How will reports be made to MNDOSA?

Report **ALL** eligible cases to MNDOSA

Is the case a “**Patient of Special Interest**”?

- If yes: Were lab specimens collected?
  - If yes: Send lab specimens to MDH Public Health Laboratory

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How will reports be made to MNDOSA?

Report **ALL** eligible cases to MNDOSA

Is the case a “**Patient of Special Interest**”?

- **die**
- **hospitalized**
- **unusual clinical presentation**
- **part of a cluster**

Were lab specimens collected?

If yes:

Send lab specimens to MDH Public Health Laboratory

Protecting, maintaining and improving the health of all Minnesotans
Report **ALL** eligible cases to MNDOSA

Is the case a “**Patient of Special Interest**”?  
- die  
- hospitalized  
- unusual clinical presentation  
- part of a cluster

If yes:

Were lab specimens collected?

If yes:

Send lab specimens to MDH Public Health Laboratory

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How will reports be made to MNDOSA?

- Report **ALL** eligible cases to MNDOSA
  - Is the case a “Patient of Special Interest”? 
    - If yes: 
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        - If yes: 
          - Send lab specimens to MDH Public Health Laboratory

Protecting, maintaining and improving the health of all Minnesotans
How will reports be made to MNDOSA?

Report **ALL** eligible cases to MNDOSA

Is the case a “**Patient of Special Interest**”?  
If yes:

Were lab specimens collected?  
If yes:

Send lab specimens to **MDH Public Health Laboratory**

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Submit remaining blood and/or urine specimens for “Patients of Special Interest” who had toxicology samples drawn

- **Urine**
  - 5mL
  - collected in small vials
  - specimen must be *frozen* if not shipped the day it was collected

- **Whole blood**
  - collected in EDTA preserved (purple top) tubes
  - *kept cold*
Lab specimen results

- Lab results will be used for **surveillance purposes only**, and reported to:
  - MDH
  - the site contact

- Lab results **will not be used for diagnostic or clinical purposes**

- Lab results **will not go in the patient’s medical record**

- Each site will receive an aggregated monthly report, summarizing all patients reported to MNDOSSA and aggregate lab results
Laboratory Testing

• Analytical Method Adaptation
• Analytes
• Validation
• CLIA
• Results
• Lessons Learned

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Analytical Method

• Developed on an LC-QQQ (Agilent 6460) for qualitative (presence/absence) reporting, adapted from PinPoint Testing, LLC analytical methods

• Four calibrators and a single QC per compound, isotopically-labelled IS when available
  • Intent to evaluate potential for full quantitative method

• Blood and urine matrix

• Due to the large number of compounds and existing methodologies, used 3 analytical methods
  • Opioids (fentanyl and fentanyl-analogs) – 19 compounds (15 more being brought online)
  • Designer Drugs (e.g., synthetic cannabinoids, cathinones) – 68 compounds (additions here as well)
  • Multi-Drug Panel (e.g., stimulants, benzodiazepines, barbiturates, etc.) – 131 compounds
Analytical Method

• Single sample clean-up procedure (SLE) for all three analytical methods (allows parallel processing), created Zephyr application for automation

• Urine panel – deconjugation step

• Same column (Phenomenex Kinetex Phenyl-Hexyl 50 x 2.1mm, 1.7µm) and mobile phases for the methods

• Dynamic (dMRM) acquisition mode (scheduled MRM)
  • Example - Multi-Drug Method: 246 MRMs/5 minutes, minimum dwell 3.44ms at 2 scans/sec
Validations

• Extraction recovery was consistent and sufficient to detect all compounds
• No false positives or false negatives
• Accuracy and precision was very good for most compounds
• See the extracted MRM screenshot
• See the Multi-Drug Panel QC Accuracy pdf (excludes aripiprazole)
Analytes

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Accuracy and Precision

Protecting, maintaining and improving the health of all Minnesotans
• LRN-C and Biomonitoring
  • SOPs
  • Validations
  • Reports
Results

Number of Panel Analytes Reported per Sample

Analytes Detected

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Results

• Acetyl Fentanyl, Acetyl Norfentanyl, alpha-hydroxyalprazolam, Alprazolam, Amphetamine, Bupropion, Caffeine, Codeine, Cotinine, Diphenhydramine, EDDP, Fentanyl, Lorazepam, MCPP, Methadone, Methamphetamine, Metoprolol, Midazolam, Morphine, Norephedrine, Norfentanyl, Pseudoephedrine, Trazodone

• 6-MAM, Amphetamine, Caffeine, Codeine, Cotinine, Desmethylolanzapine, Dextromethorphan, Dextrorphan, Diphenhydramine, Fentanyl, Lorazepam, Methamphetamine, Morphine, Norbuprenorphine, Norephedrine, Norfentanyl, Pseudoephedrine, THC-COOH
*Includes Fentanyl, Norfentanyl, Acetyl Fentanyl, Acetyl Norfentanyl

**All reports of heroin (n=4) tested positive for fentanyl or a fentanyl analogue, one also tested positive for 6-MAM
Lessons Learned…So Far

- Lack of knowledge and experience using public health condition codes in medical records
- Creating lab order panels in Electronic Medical Record systems in order to submit specimens to health laboratories can be challenging for hospitals
- Efficient and successful transportation of samples from the hospitals to the lab can be expensive
- The Agilent 6460 LC-QQQ performed well, needed upgraded acquisition software and firmware
- Potential for quantitative methods on the LC-QQQ, however the number of compounds per method is limited
Lessons Learned...So Far

- The number of drugs of abuse, metabolites, and adulterants keeps getting larger
- Targeted QQQ methods have hard limits on the number of compounds that can be included
- Epidemiologists always want more data
- Conclusion: A better strategy might be to use a targeted and non-targeted screening method (e.g., high resolution MS/MS or QTrap QQQ scan) for compound identification, and then follow-up with quantitation with a targeted LC-QQQ (or QTOF MRM-HR) method, if desired/necessary. (Are we doing it backwards?)
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MDH State Epidemiologist

• Ruth Lynfield
Questions?

Paul Moyer
Environmental Laboratory Section Manager
(651) 201-5669
paul.moyer@state.mn.us