FORENSIC TOXICOLOGICAL ANALYSIS OF DEATHS DUE TO DRUG OVERDOSE - A DESCRIPTIVE RETROSPECTIVE STUDY OF 1100 AUTOPSIES DONE AT THE OFFICE OF THE MEDICAL EXAMINER, COUNTY OF COOK FROM JANUARY 2017 TO DECEMBER 2017

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INTRODUCTION

According to the United States Centers for Disease Control and Prevention (CDC):

In 2016 there were 63,632 drug overdose deaths in the United States.

19,493 deaths involved synthetic opioids which include fentanyl.[1]

INTRODUCTION
Definitions

- Opiates: Alkaloid compounds naturally found in the opium poppy plant Papaver somniferum. E.g. morphine, codeine[2]
- Opioids: Any compound which produces morphine-like effect by binding to mu- opioid receptor e.g. fentanyl, methadone, hydrocodone[2]
- Fentanyl: A synthetic narcotic 80-100 times more powerful than morphine

- Fentanyl analogue – Designers of fentanyl e.g. acetylfentanyl, butyrylfentanyl, 3 methylfentanyl, carfentanyl
- Structurally unique synthetic opioids- Non fentanyl derived synthetic opioids[3] e.g. U 47 700, U 49 900, AH 7921 MT45

OBJECTIVES

- 1. Drug trends in fatalities
- Prevalence of fatalities due to illicit drugs
- Prevalence of fatalities due to prescribed drugs
- Prevalence of adulterants
- Combined drug pattern and drugs combined with ethanol

OBJECTIVES

- 2. Demographics of fatalities
- 3. Drug concentrations in different body compartments
- 4. Comparison of mean lethal drug concentrations against standard minimum lethal drug concentrations
- 5. Correlation of time since death to peripheral blood drug concentrations

METHODOLOGY

A retrospective descriptive case control study was carried out on all accidental deaths due to drug overdose at the Office of the Medical Examiner, County of Cook, USA from 1st January 2017 to 31st December 2017.

1100 medico-legal autopsies were critically analyzed with toxicology results.

ANALYTICAL METHODS

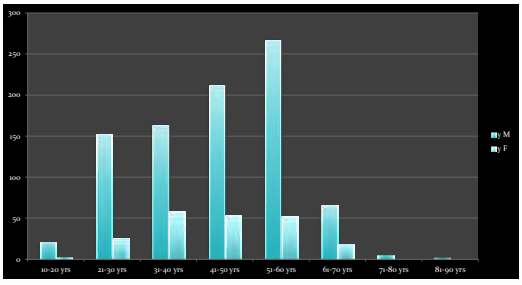
More than 90% of drugs were quantitatively analyzed by LCMS/MS. Ethanol was quantitatively analyzed by GC Headspace. Cocaine, cocaethylene and benzoylecgonine were analyzed by GCMS.

RESULTS
AGE ADJUSTED SEX DISTRIBUTION

Sex: 79% (n = 869) of fatalities were male. 21% (n=231) were female.

Age: 65% (n = 717) of fatalities were below 50 year age group. Out of that 60.4% represented below 40 year age group (n = 437).

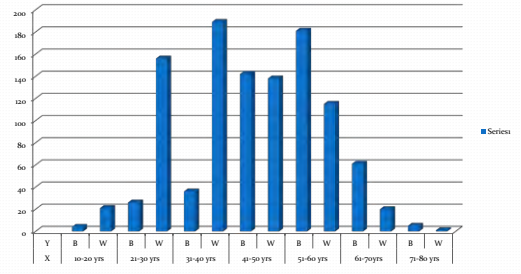
AGE ADJUSTED SEX DISTRIBUTION



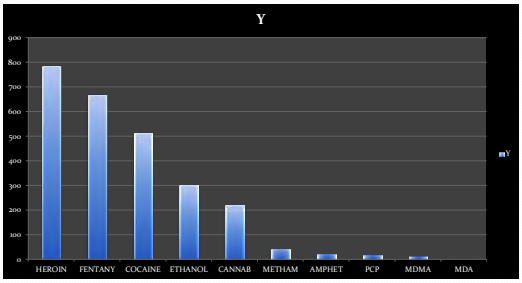
RESULTS
AGE ADJUSTED ETHNICITY DISTRIBUTION

Race: 57.6% (n= 634) of fatalities were White.
41.4% (n=456) were African American.

AGE ADJUSTED ETHNICITY DISTRIBUTION



FATALITY PATTERN DUE TO ILLICIT DRUGS



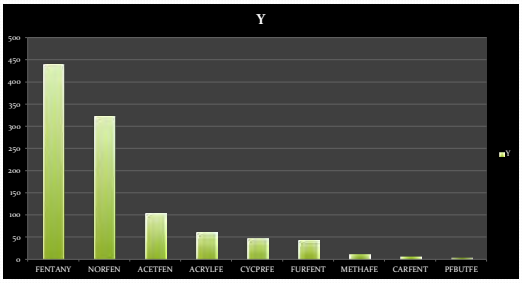
RESULTS
Illicit Drug Frequencies

Heroin was the most common illicit drug of abuse, causing or contributing to 71% of fatalities (n=782). It was followed by: Fentanyl and designer opioids (n=666), Cocaine (n= 512), Methadone (n=40), Methamphetamine (n=40), Amphetamine (n=20), PCP (n=18), MDMA (n=11), and MDA (n=3)

RESULTS
Ethanol and Combined Drug Deaths

53.1% (n= 585) of fatalities were due to combined drug toxicity. Combinations of 2 to 11 drugs were present . Heroin + Cocaine (n=66) was the most common combination. Heroin + Cocaine + Fentanyl (n=64) was second most common. 27% (n=298) of fatalities were due to combined drugs with ethanol. Only 16.8% (n= 185) fatalities were due to single drug toxicity.

DEATHS DUE TO FENTANYL AND ITS NOVEL OPIOIDS

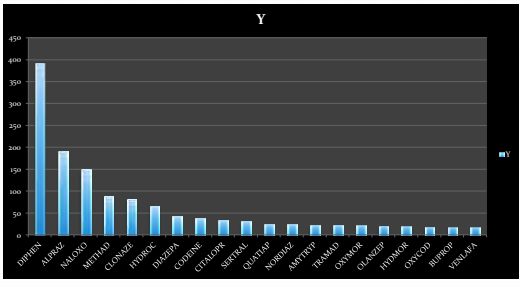


RESULTS

Frequencies of Fentanyl and its Analogs

39.9% (n=439) of fatalities were positive for fentanyl. 29.3% (n=322) were positive for norfentanyl. 9.55% (n=104) were positive for acetyl fentanyl followed by Acrylfentanyl (n= 59), cyclopropylfentanyl (n= 44), furanylfentanyl (n= 44), Methoxyacetylfentanyl (n= 11), PFBF (n= 8), carfentanyl (n=3).

FATALITY PATTERN DUE TO PRESCRIBED DRUGS



RESULTS
Prescription Drugs

Prescription drugs may not contribute to death depending on circumstances. Some represent cutting agents, metabolites or emergency medical treatments.

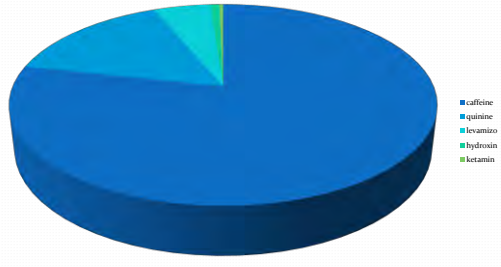
The 10 most common in descending order were Diphenhydramine, Alprazolam, Naloxone, Methadone, Clonazepam, Hydrocodone, Diazepam, Codeine, Citalopram, and Sertraline.

RESULTS
Prevalence of Adulterants

Adulterants are pharmacologically active substances that may modify or potentiate the effects of the drug that they are mixed with. Quinine and caffeine are common heroin adulterants.

61.2% of our fatalities were positive for caffeine followed by quinine, levamisole, hydroxyzine and ketamine. But the contribution of recent coffee and soft drinks to caffeine concentrations cannot be differentiated from adulterants.

PREVALENCE OF ADULTERANTS IN FATALITIES



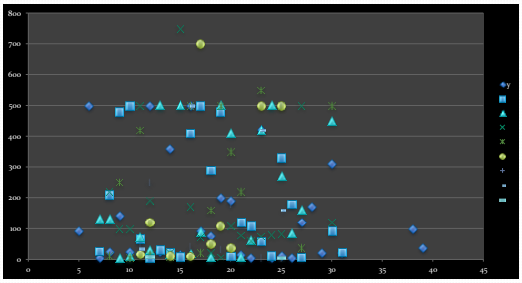
RESULTS

Drug Concentrations in Different Body Compartments

Peripheral blood samples were tested for expanded toxicology in 93.7% of fatalities followed by central blood, urine, bile, liver tissue and cavity blood.

Urine was the best sample for 6-mam concentrations.

CORRELATION OF TIME SINCE DEATH TO URINARY 6 MAM CONCENTRATION

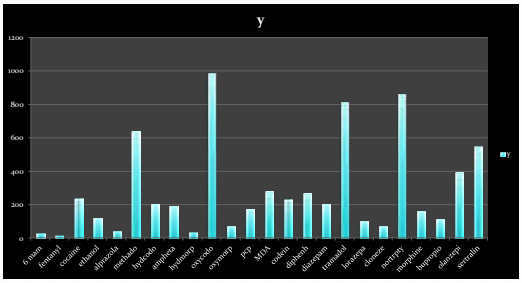


RESULTS

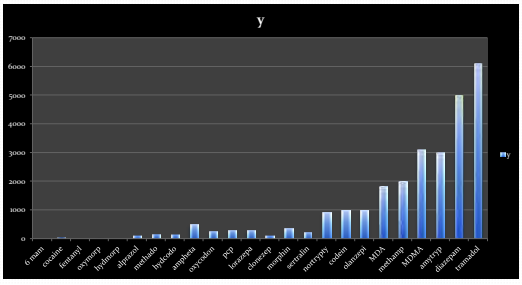
Correlation of Mean Lethal Drug Concentration with SMLDC

Our mean lethal drug concentrations were well below the standard minimum lethal drug concentrations in these combined drug fatalities.

MEAN LETHAL DRUG CONCENTRATIONS IN FATALITIES



STANDARD MINIMUM LETHAL DRUG CONCENTRATIONS

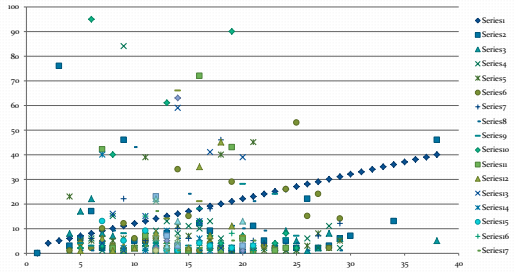


RESULTS

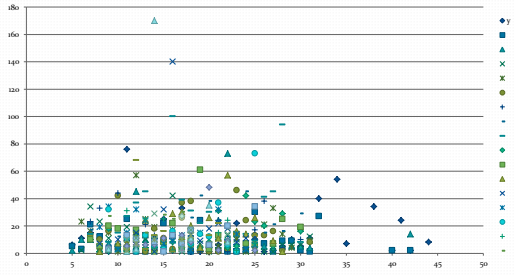
Correlation of Time Since Death to Peripheral Blood Drug Concentrations

Peripheral blood samples were successfully positive for heroin , fentanyl, cocaine and ethanol in between 5 to 30 hours of time since death.

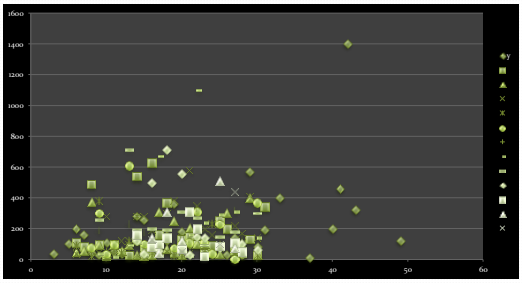
CORRELATION OF TSD TO PERIPHERAL BLOOD 6-MAM CONCENTRATION



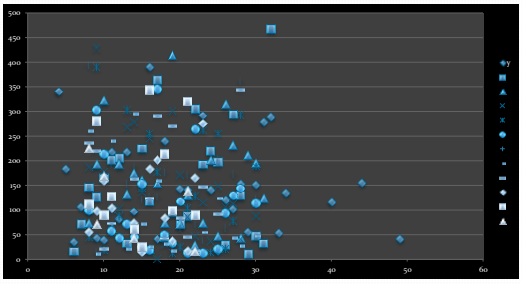
CORRELATION OF TIME SINCE DEATH TO FENTANYL CONCENTRATION



CORRELATION OF TSD TO COCAINE CONCENTRATION



CORRELATION OF TIME SINCE DEATH TO ETHANOL CONCENTRATION



DISCUSSION

- Demographics highlighted the highest fatality rate in the below 50 year age group. The 15-54 age group had the highest rate of drug overdose deaths in 2016 (35 per 100,000) which is similar to our study.[1]
- Fatalities among the male population was four-fold higher than females in our study giving a male: female ratio of 4: 1.

DISCUSSION

- A high proportion of these fatalities resulted from combined drug toxicity at levels lower than the standard lethal concentration highlighting the cumulative deleterious effects of drug combinations. [2]

DISCUSSION

There had been a five-fold increase in drug overdose deaths involving synthetic opioid from 3,105 in 2013 to approximately 20,000 in 2016.

Illicitly manufactured fentanyl analogues are 50-100 times more potent than morphine is primarily responsible for these rapid increase in fatalities.[4]

DISCUSSION

In our study 8 novel fentanyl analogues were detected.

17 designer fentanyl derivatives have been detected worldwide. [5]

DISCUSSION

There were 15 fatalities due to U47700 and 3 fatalities due to U 49900 in our study.

U 47700 was the structural isomer of AH-7921 which were developed as structurally unique synthetic opioid analgesics not structurally related to fentanyl.[2]

DISCUSSION

- In our designer fentanyl deaths most of the drug concentrations were below standard lethal levels. This can be explained by cumulative drug toxic effects in multiple drug combinations[2].

DISCUSSION

Toxicology samples collected within 30 hours of tsd were successfully positive for expanded toxicology panels. Samples collected up to 165 hours of time since death were positive for expanded toxicology panels which signifies that well controlled mortuary cooling system and maintenance of cold chain in toxicology samples preserve drug concentrations . [2]

CONCLUSION

High fatality rate in youth is attributed to loss of productivity of the country. Urgent strategies must be implemented to address drug trafficking and smuggling to prevent drug overdose deaths in the youth in the world.

We suggest establishing a national guideline to standardize the immediate cause of death of drug fatalities which would give more accurate statistics of drug overdose patterns.

REFERRENCES

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4. Julie K. O' Donnel phD, John Halpin, MD; Cristine L Mattson, phD ; R Mathev Gladdon, phD. Deaths involving Fentanyl, Fentanyl Analogs and U 47700- 10 states, July- December 2016. Morbidity and mortality weekly report, vol-66. Centre for Disease Control. October 27 2017.

5. Jones CM, Einstein EB, Compton WM. Changes in synthetic opioid involvement in drug overdose deaths in the United States 2010-2016. JAMA. 2018;319(17):1819-21. doi:10-1001/jama.2018.2844.