



# FATAL POISONINGS BY MEDICINAL OPIOIDS IN FINLAND

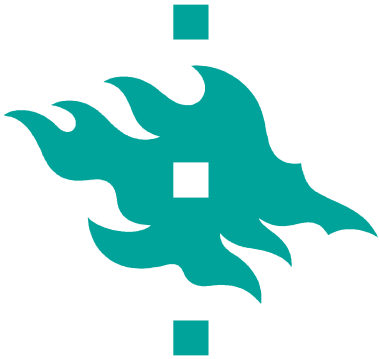
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12.-13.11.2012

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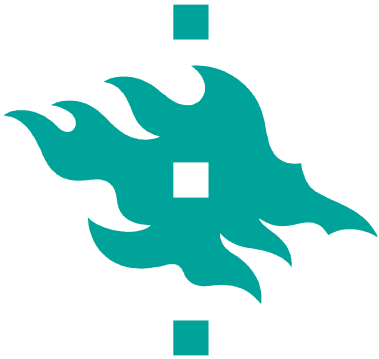
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## **FINLAND IS AN IDEAL COUNTRY FOR POST-MORTEM TOXICOLOGICAL INVESTIGATIONS**

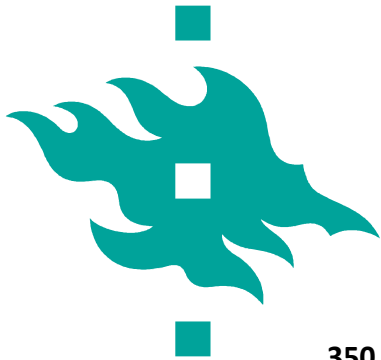
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- ✓ **High autopsy rate.**
- ✓ **Extensive use of post-mortem toxicological services.**
- ✓ **All post-mortem toxicology is centralized to one laboratory by law.**
- ✓ **The screening methods are comprehensive and have been accredited since 1997.**
- ✓ **The laboratory gets as feedback a copy of the death certificate from all cases investigated.**
- ✓ **The laboratory has an information management system with demographic data including a short story of what has happened.**
- ✓ **The National Agency for Medicines publishes statistics annually on the consumption of medicines.**

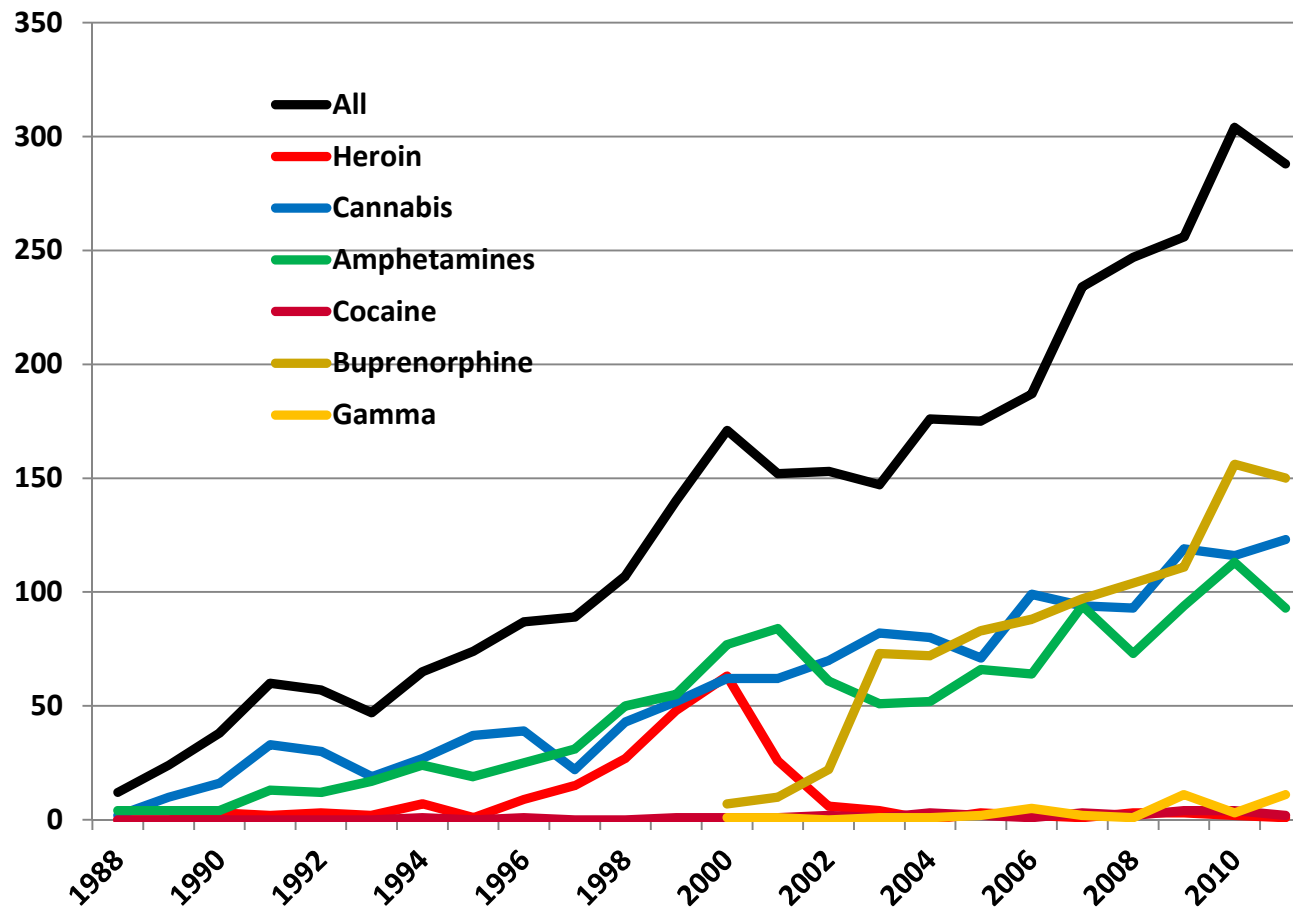


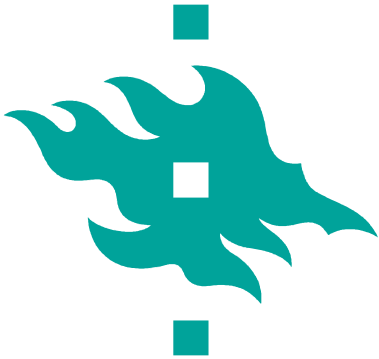
## RISK OF BIAS IN VITAL STATISTICS

- ✓ **All deceased are not investigated, this is true even in traffic accidents.** Mörland J et al. (2011) Drugs related to motor vehicle crashes in Northern European countries. *Accident Analysis and Prevention* 43:1920-1926.
  - ✓ Finland and Sweden: toxicological investigation is performed more than 90 % of cases.
  - ✓ Norway: 71 %
  - ✓ Iceland: 43 %
  - ✓ Denmark: 8 %
  
- ✓ **All positive drug findings do not enter to the death certificate and official statistics.** Lahti R et al. (2009) Blood positive illicit-drug findings: implications for cause-of death certification, classification and coding. *Forensic Sci Int* 187:14-18.
  - ✓ Opioids are inclusively mentioned, 98 %
  - ✓ Amphetamines are well mentioned 81 %
  - ✓ Cannabis is missing in half of the cases 52 %



## NUMBER OF ILLICID DRUG FINDINGS IN FINLAND (1988-2011)

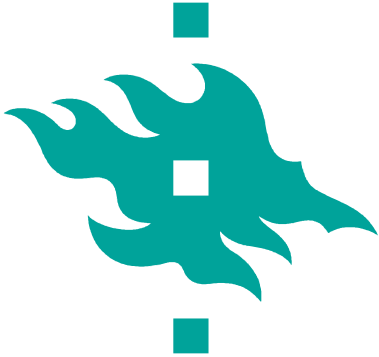




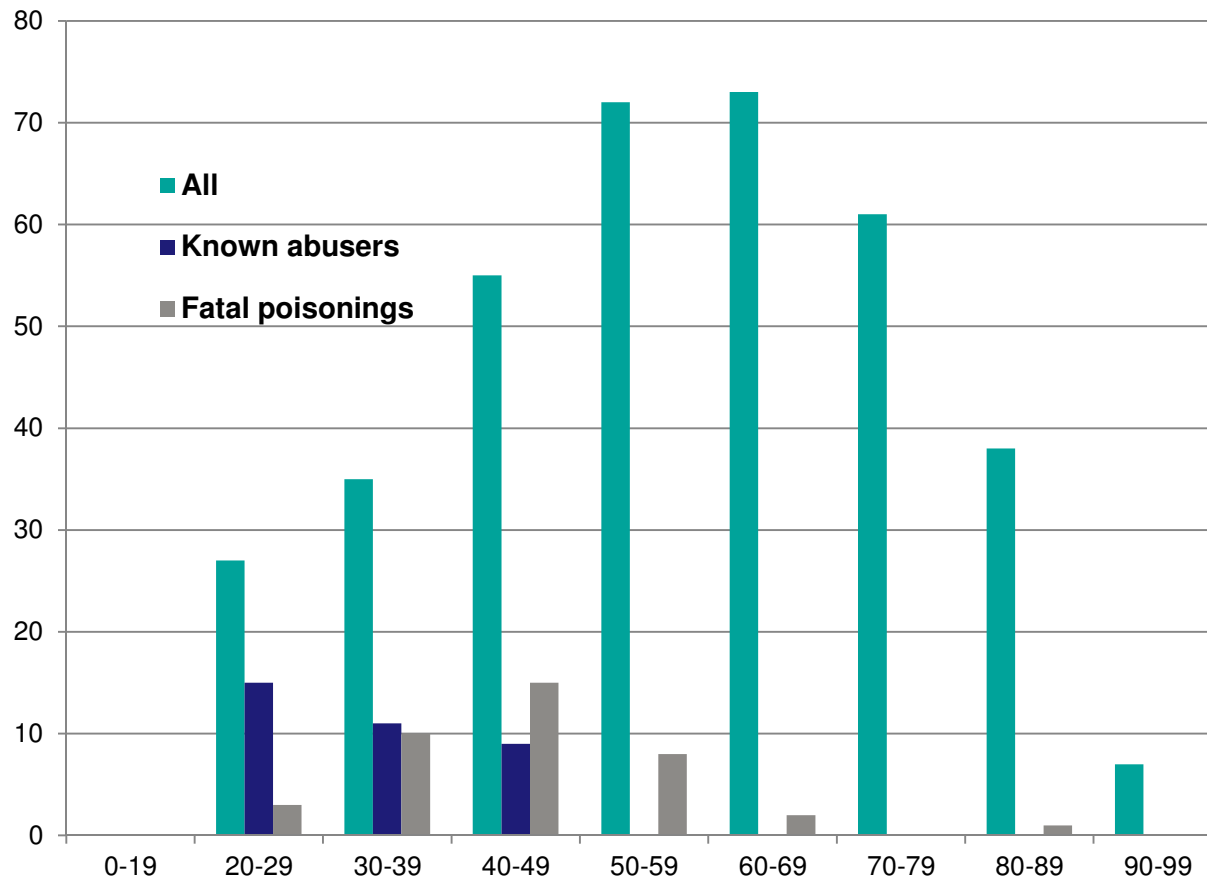
## CODEINE

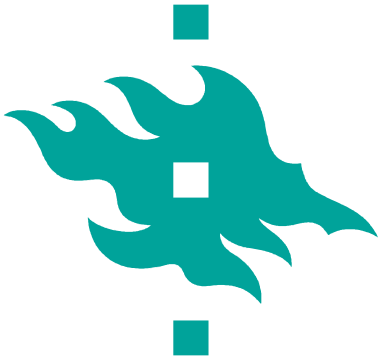
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- ✓ **Is a prodrug and needs an enzymatic activation (CYP2D6)  
7-8 % of population does not get benefit at all!**
- ✓ **Codeine is metabolized to morphine.**
- ✓ **Typically abused orally, a common single dose is 60 mg.  
Codeine is only a weak agonist.**
- ✓ **Available in combination preparations with paracetamol or  
with ibuprofen.**
- ✓ **Obviously is not very euphoric, usually taken for  
withdrawals if a more desired opioid is not available.**
- ✓ **Blood concentration in fatal poisonings is typically  
>0,4 mg/l (therapeutic concentration ad 0,1 mg/l).**
- ✓ **Out of 368 positive finding in 2010 35 were related to abuse  
and 5 out of these were fatal poisonings**



## CODEINE POSITIVE CASES (URINE/BLOOD) IN 2010 (N=368)





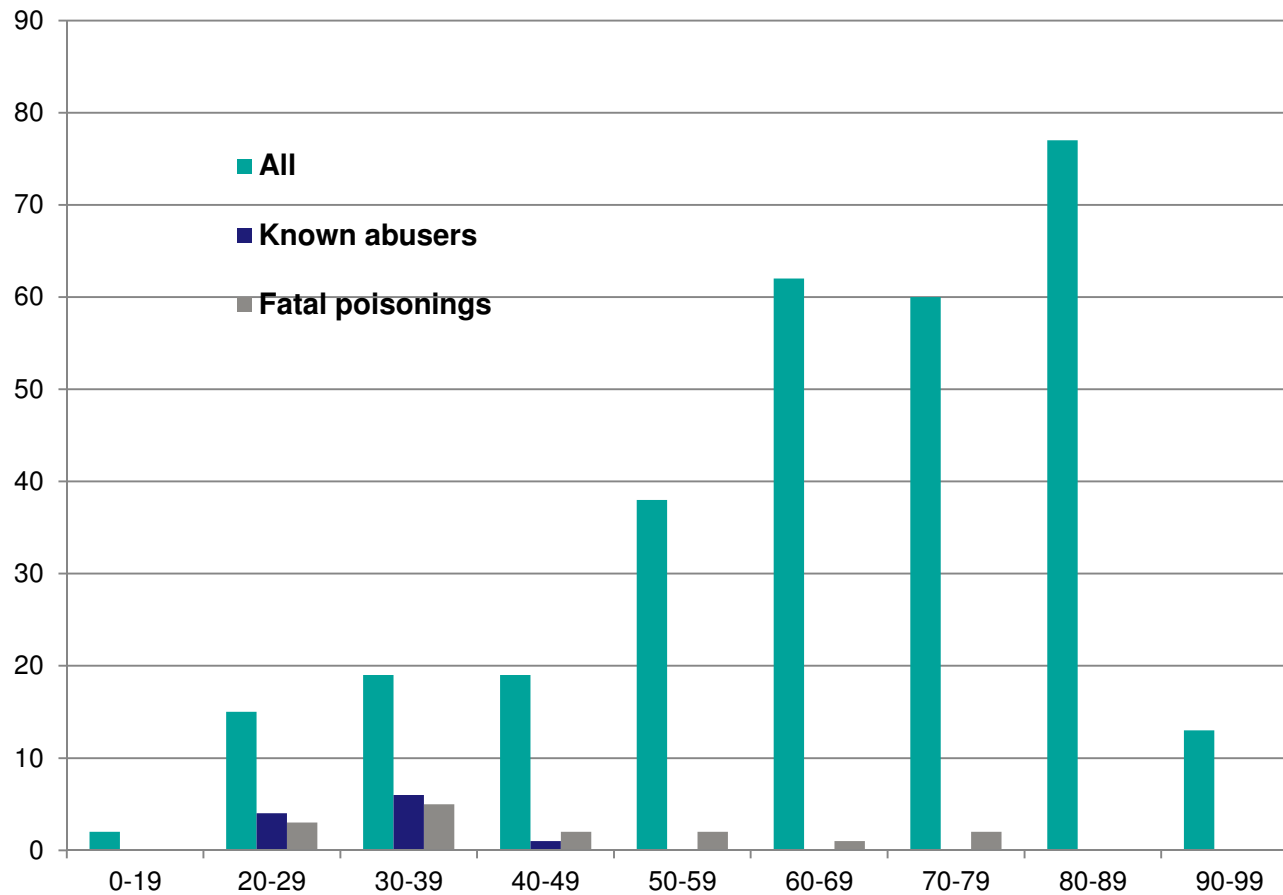
## OXYCODONE

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- ✓ **Effective also when taken orally.**
- ✓ **Has increased its popularity in treatment of pain.**
- ✓ **Is known to be abused**
- ✓ **A usual abused dose is 10 - 15 mg orally.**
- ✓ **Has a short half-life, 2- 8 h.**
- ✓ **Blood concentration in fatal poisoning is typically >0,2 mg/l (therapeutic concentration ad 0,1 mg/l).**
- ✓ **Out of 305 positive finding in 2010 11 were related to abuse and 5 out of these were fatal poisonings.**



## OXYCODONE POSITIVE CASES (URINE/BLOOD) IN 2010 (N=305)



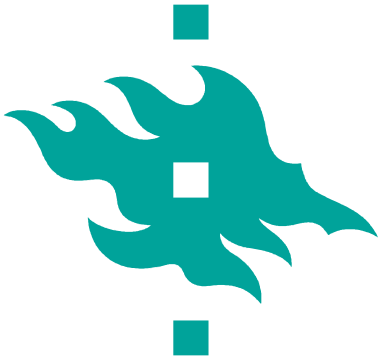




# TRAMADOL

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- ✓ Is a prodrug and needs an enzymatic activation (CYP2D6)  
7-8 % of population does not get benefit at all!
- ✓ Typical oral daily dose is 400 mg .
- ✓ Is a weak agonist, and has a low abuse potential.
- ✓ Metabolite (O-desmethyltramadol) is more active than the parent drug. Those who are ultra rapid metabolisers are in danger with high doses.
- ✓ **O-desmethyltramadol is available also as a designer drug!**
- ✓ Is a serotonin active drug, in high doses or together with other similarly acting drugs danger of serotonin syndrome.
- ✓ Has only a weak effect on breath control.
- ✓ High doses inflict convulsions.
- ✓ Typical concentration in fatal poisonings >2 mg/l  
(therapeutic concentration ad 0,6 mg/l).

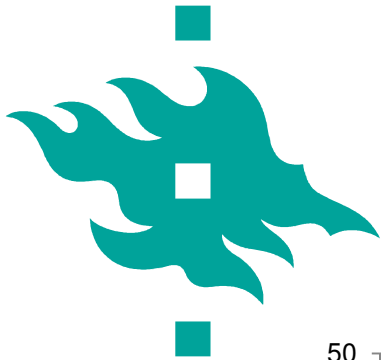


## TRAMADOL (2)

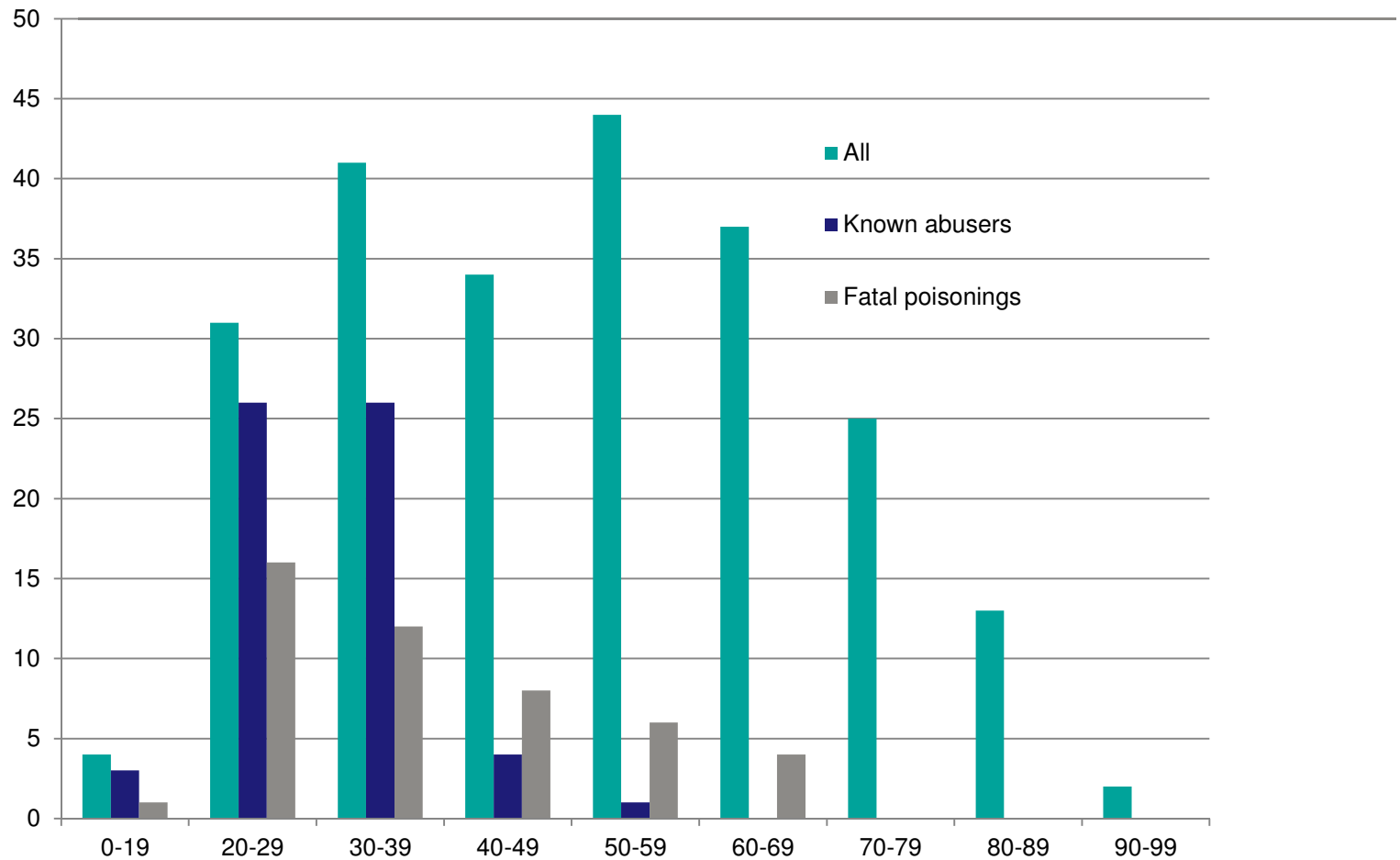
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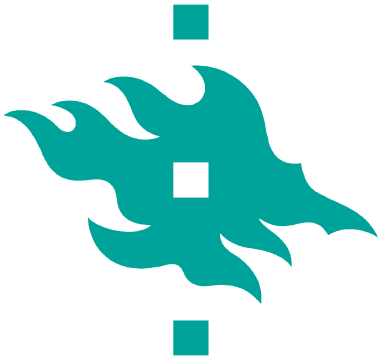
- ✓ Out of 231 positive finding in 2010 60 were related to abuse and 27 out of these were fatal poisonings
- ✓ Most abusers were male (22, 81 %), age: range 18-35 y , median 27 y.
- ✓ There were 5 women (19 %), age: range 22-56 y, median 32 y.
- ✓ Typically abused orally.
- ✓ Found concentrations: range 1,3-40 mg/l, median 7,0 mg/l
- ✓ Special case: Two men were found death in an apartment.

	30 y (2010/2841)	27 y (2010/2842)
Tramadol	16 mg/l	11 mg/l
Alprazolam	0,10 mg/l	0,09 mg/l
Pregabalin	15 mg/l	14 mg/l



## TRAMADOL POSITIVE CASES (URINE/BLOOD) IN 2010 (N=231)

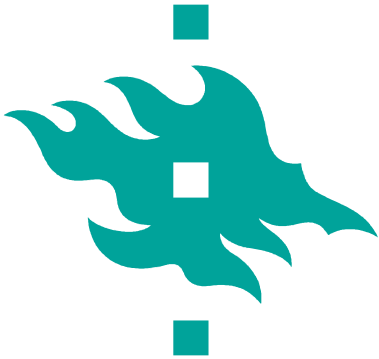




## FENTANYL

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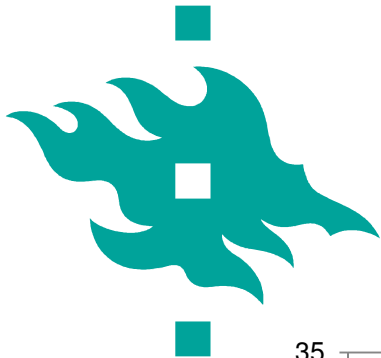
- ✓ Is a synthetic "low dose" opioid and is in the treatment of pain 50 – 100 times more potent than morphine
- ✓ When injected half –life is 1 – 6 h, but in dermal use 13 – 22 h.
- ✓ Dermal patches are intended to be used in chronic pain only.
- ✓ Typical i.v. dose is 25 – 200 µg!, dermal doses 12 – 100 µg/h.
- ✓ One patch may contain 16,8 mg fentanyl , **which is equivalent to 84 single doses or 8 – 16 lethal doses!**
- ✓ Fentanyl can cause severe respiratory depression.
- ✓ In fatal cases the blood concentrations can be low, > 0,2 µg /l (therapeutic concentration 1 – 10 µg /l).
- ✓ Background information which indicates abuse: cut patches found in oral cavity, fentanyl was extracted from patches and injected.



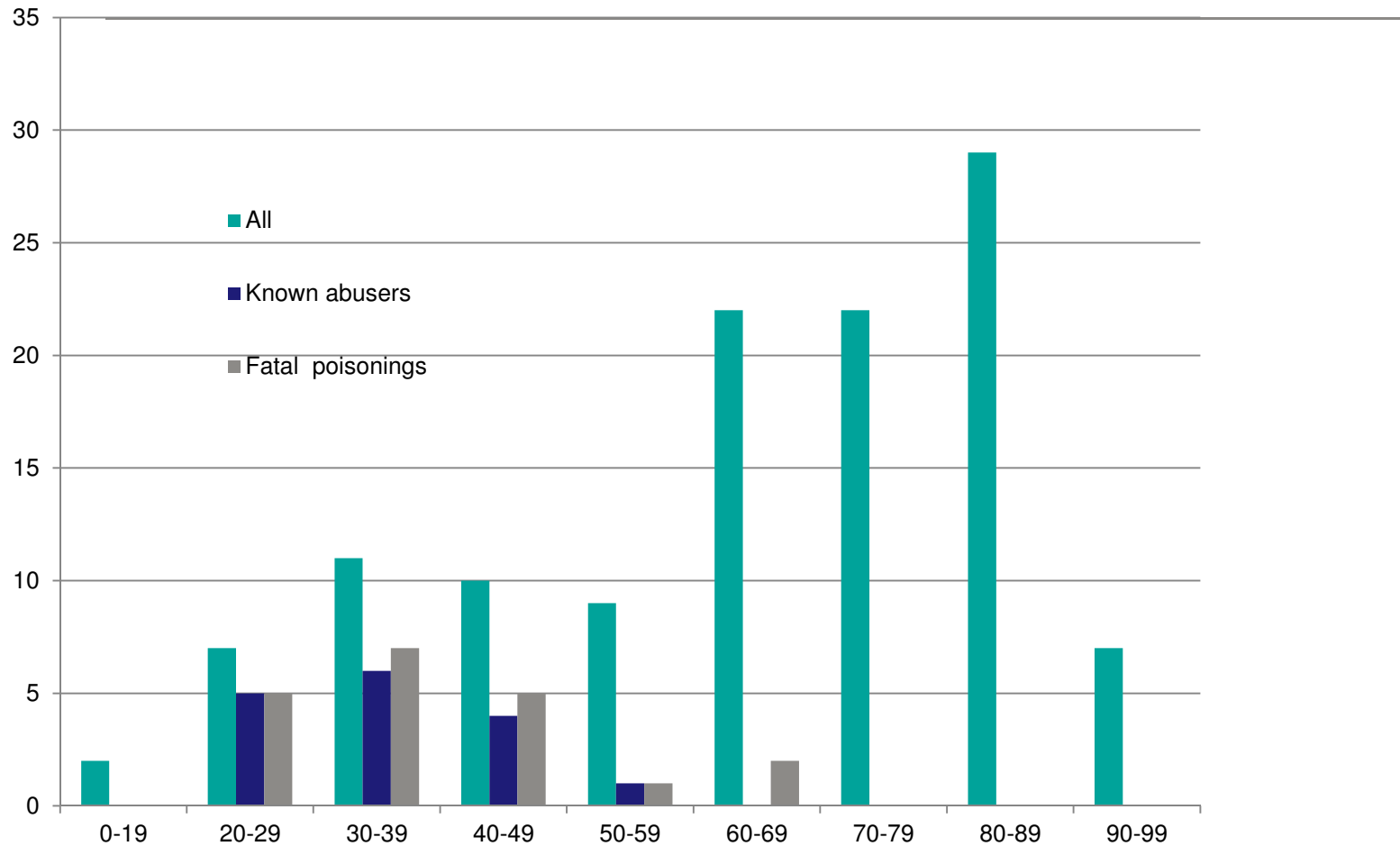
## **FENTANYL (2)**

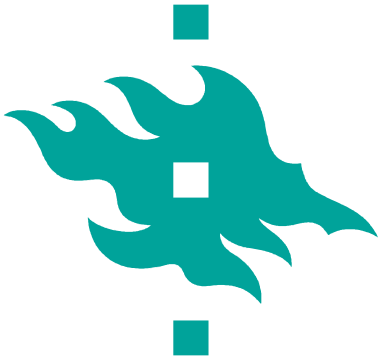
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- ✓ **In 2010 out of 119 positive findings 16 were related to abuse and all were fatal poisonings by fentanyl.**
- ✓ **Most abusers were male (14, 88 %), age: range 22-53 y, median 36 y.**
- ✓ **There were 2 females (12 %), age: range 24 – 28 y.**
- ✓ **Dermal patches were mentioned in background information in 6 cases.**
  - ✓ **In 2 cases a piece of a patch was found in oral cavity.**
- ✓ **Fentanyl was certainly abused i.v. in 5 cases.**
- ✓ **Range of found blood concentrations was 0,5 – 38 µg/l, median 8,1 µg/l.**



## FENTANYL POSITIVE CASES (URINE/BLOOD) IN 2010 (N=119)

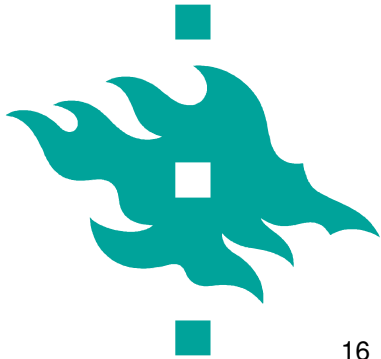




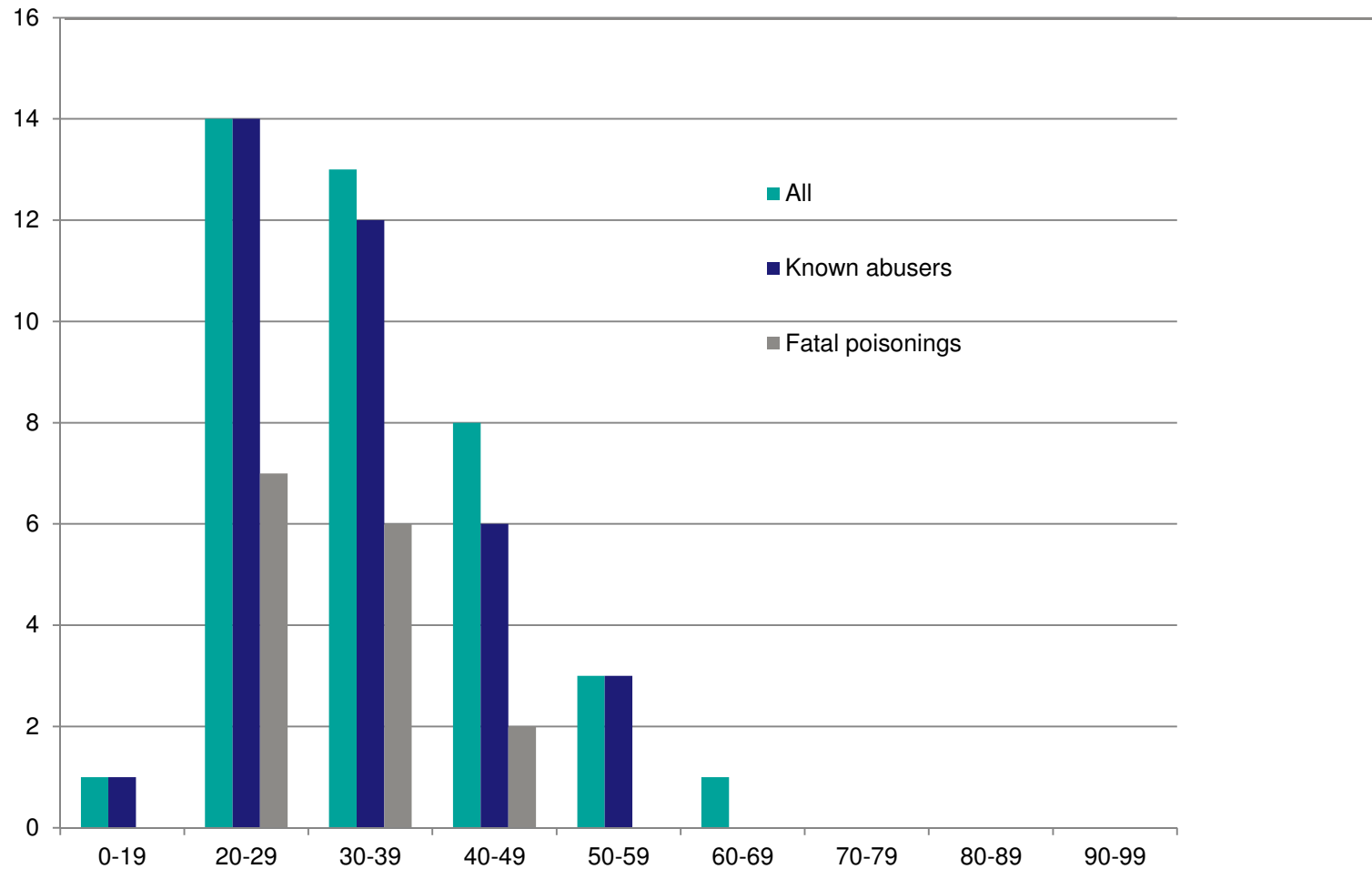
## METHADONE

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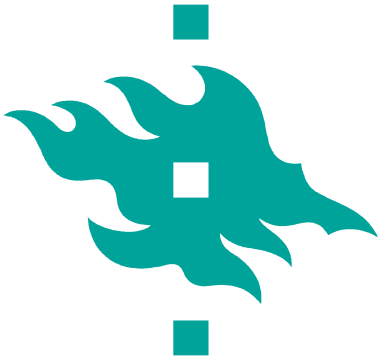
- ✓ Nowadays more common in maintenance treatment, typical daily oral dose is more than 80 mg.
- ✓ Is long acting and hence special attention must be paid to dosing, especially in the beginning of treatment.
- ✓ Out of 40 positive findings in 2010 36 were related to abuse and 15 out of these were fatal poisonings
- ✓ Most abusers were male (13, 87 %), age: range 20 – 44 y, median 30 y.
- ✓ There were 2 females (13 %), age: range 20 – 33 y.
- ✓ In 4 times the drug derived from a friend's treatment.
- ✓ Methadone was used i.v. 4 times.
- ✓ Found blood concentrations: range 0,1 – 1,9 mg/l, median 0,4 mg/l (therapeutic concentration 0,05 – 1 mg/l).



## METAHDONE POSITIVE CASES (URINE/BLOOD) IN 2010 (N=40)



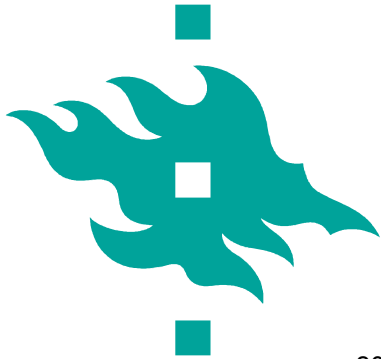




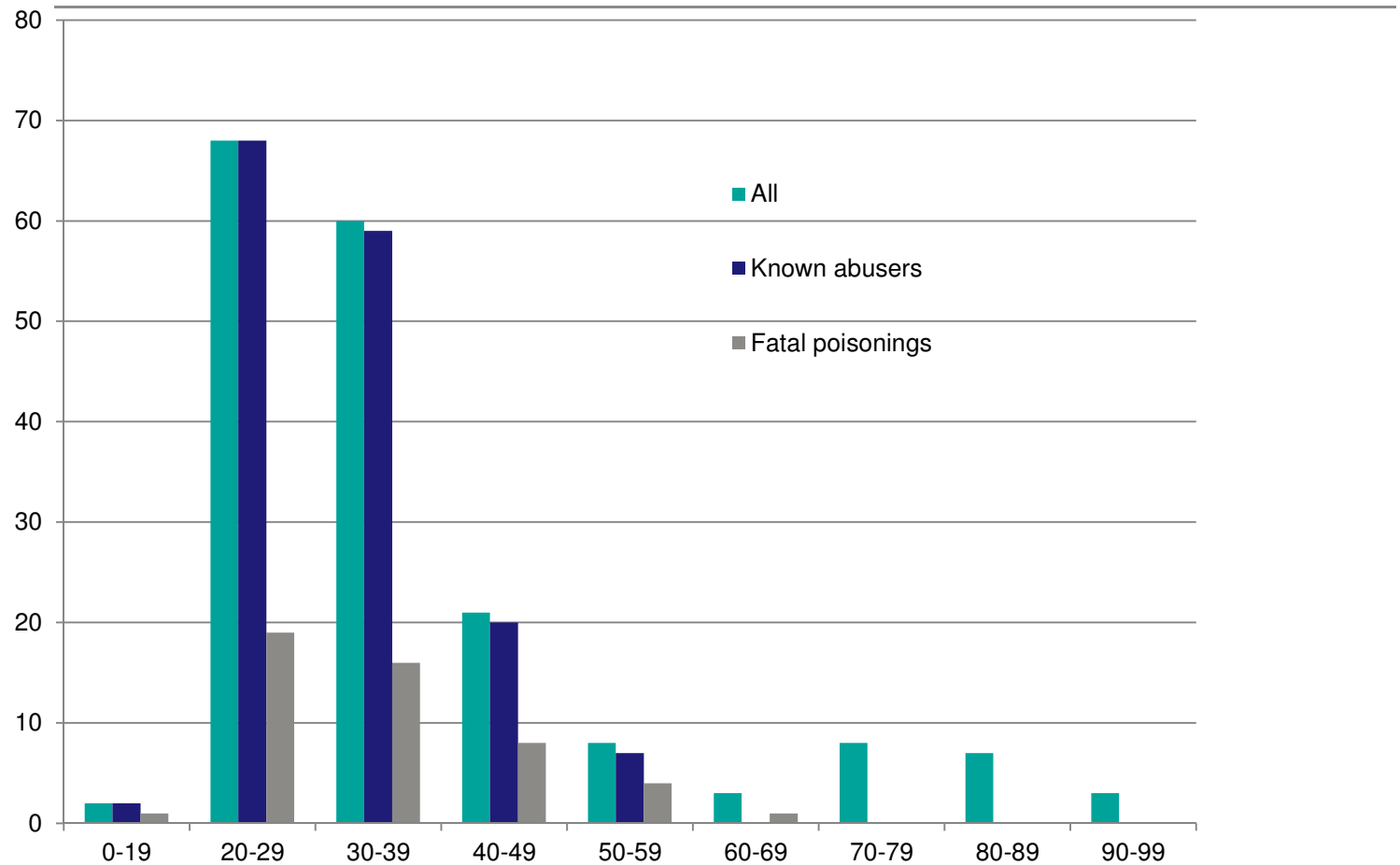
## BUPRENORPHINE

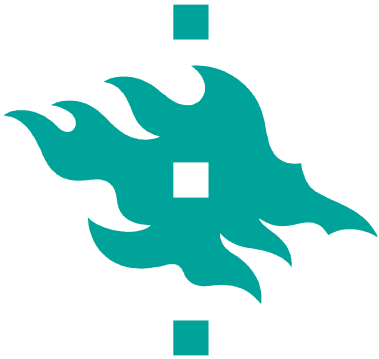
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- ✓ **At present most common opioid in the treatment of addiction in Finland .**
- ✓ **In treatment we use Suboxone (buprenorphine+naloxon) but in streets Subutex (buprenorphine) is available.**
- ✓ **Out of 180 positive finding in 2010 156 were related to abuse and 46 out of these were fatal poisonings by buprenorphine.**
- ✓ **Most abusers were male (39, 85 %), age: range 18 – 56 y, median 31 y.**
- ✓ **There were 7 females (15 %), age: range 22 – 44y, median 28 y.**
- ✓ **Found blood concentrations range: 0,23 – 33 µg/l, median 1,3 µg/l (therapeutic concentration 0,5 – 10 µg/l).**
- ✓ **Found typically together with alcohol and benzodiazepines.**



## BUPRENORPHINE POSITIVE CASES (URINE/BLOOD) IN 2010 (N=180)

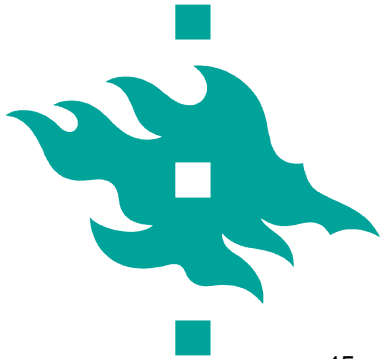




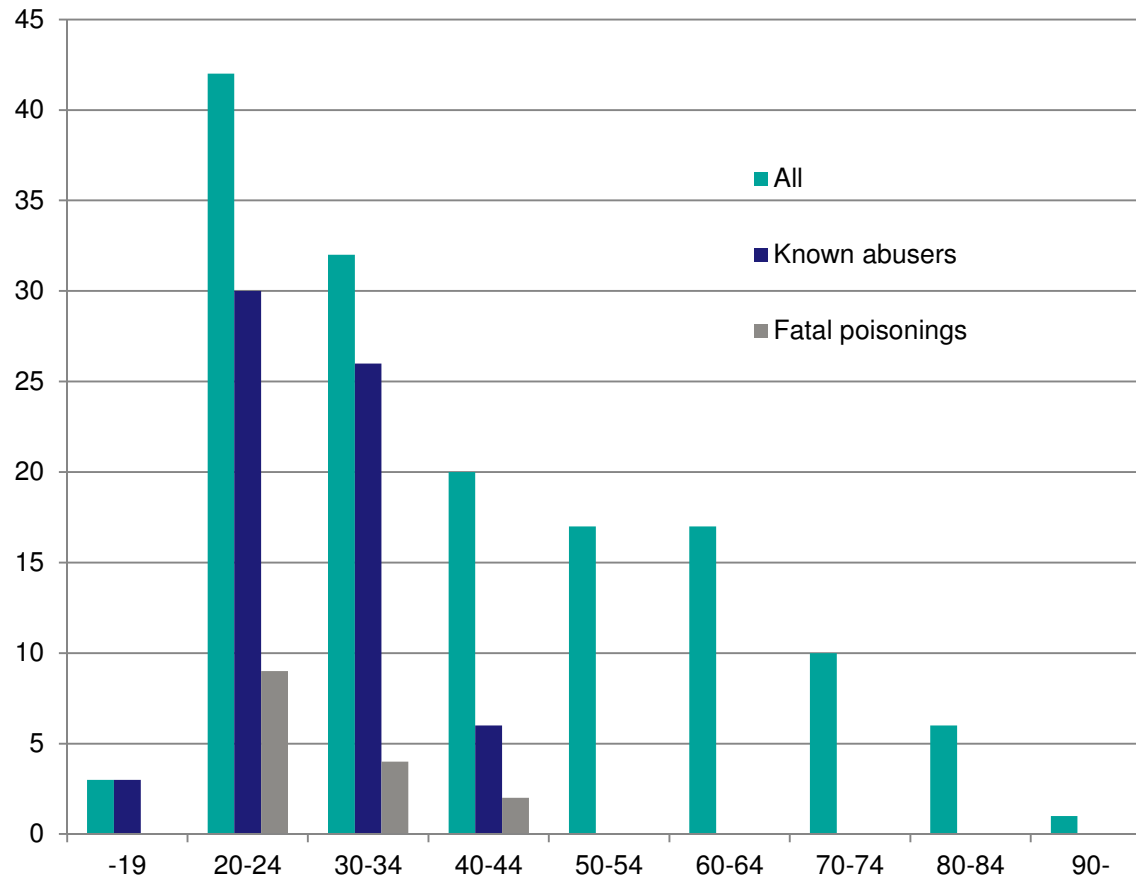
## **PREGABALIN, AN EMERGIN PROBLEM**

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- ✓ **Pregabalin (Lyrica) is found increasingly together with other abused drugs in Finland.**
- ✓ **Is classified as an antiepileptic drug and thus is more freely prescribed.**
- ✓ **Out of 148 positive finding in 2010 65 were related to abuse and 15 out of these were fatal poisonings by pregabalin.**
- ✓ **In 2010 abused pregabalin was typically found together with opioids: 59 times out of 65 cases (91 %) some opioid was present, most often buprenorphine (44 times, 68 %).**
- ✓ **Found blood concentrations in fatal poisonings range 17 – >100 mg/l, median 34 mg/l (therapeutic concentration ad 8,6 mg/l)**



## PREGABALIN POSITIVE CASES (URINE/BLOOD) IN 2010 (N=148)





## OPIOIDS IN FINLAND, PRESENT STATUS IN ABUSE

	Abuse potential	Concentration in fatal poisonings	Present status	Origin
Codeine	small	high	small	prescription
Tramadol	small	high	great	prescription
Oxycodone	great	more than therapeutic	moderate	prescription
Fentanyl	great	therapeutic	great	prescription
Methadone	great	therapeutic	great	treatment
Buprenorphine	great	therapeutic	very great	street
Heroin	great	therapeutic	small	street
Propoxyphene	great	high	small	(street)