Drug-related deaths – the Swedish case

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Disposition

- Background
- Analyses of changes in methodology (recording practices) with focus on forensic tox analyses
- Results of new corrected (adjusted) time series of drug deaths (DD=presences of drugs in deaths) and DRD
- Why so confusing, lessons to learn, implications, future

Background

- The reported increase: used to in order to support and to criticise the current Swedish drug policy ('everyone' is fuelled by an increase!)
- But DRD increase or not?
- Why CAN involvement in this?
- CAN commissioned to follow drug trends by different indicators; DRD is one important indicator
- CAN not a Governent body but and umbrella organisation of different NGOs; and
- A centre of competence within the ANDT-field; epid., prevention, communication...

Background

Flow chart, from a death to a statistic in the GMR (Cause-of-death register)



- (NBHW):
- •Coding of all deaths (underlying and contributory), and
- Updating the General Mortality Register (GMR)
- •From the GMR: Drug-related deaths in Swedish-GMR and EMCDDA-GMR (Selection B)

Background Different indicators (time series) of drugrelated used in Sw during past 15-20 yrs

- <u>Drug-related deaths underlying or contributory cause of deaths (from</u> GMR): T40.0-T40.9, except DXP, F11-F16. More or less the Selection B but incl. contributory causes and few non-poisoning codes, e.g. O35.5 (maternal care for suspected damage to fetus by drugs), T40, F11-F16, from the GMR) **Swedish-GMR**

- <u>Selection B, only underlying cause of deaths (reported to the</u> EMCDDA): F11, F12, F14-F16, F19) or poisonings: X and Y-codes: (X41, X42, X61, X62, Y11, Y12) in combinations with T-codes (T40.0-T40.9, except DXP, and T43.6). **EMCDDA-GMR**

- <u>Deaths with a selection of substances found in national forensic</u> <u>toxicological database</u> : <=60 yrs of age for opioid medicines and in hierarchical order and not incl. oxycodone, tramadol, DXP). Presence of some substances among forensically investigated deaths (called

Background Trends in number of drug-related deaths according to the three indicators



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Background Trends in number of drug-related deaths according to the three indicators, per 100 000 inh 15 +



Thus:

According to all three: dramatic increases

Increase (more than +100% since 2006), especially in opioids: methadone, buprenorfin, fentanyl, oxycodone (thus, opioid pharmaceuticals)

Recent years, no decrease in heroin

A (new) report from the National Board of Health and Welfare (NBHW)

- Commissioned by the Government to develop the drugrelated statistics further
- Seen in the light of the increase and an uncertainty of how to interpret this increase, what does it stand for?: real increase and/or due to recording practices

The report:

Background, definitions, analyses of the 2014 drug-related data (cause of death register (GMR), changes in recording practices (methodological changes) affecting the statistics, discussion and conclusions The NBHW-report

Changes in recording practices (methodological changes)

Two parts

- Coding practices for all causes of deaths certificates (done at the National Board of Health and Welfare)
- Changes in practices in toxicological tests (done by the National Board of Forensic Medicine)

(The CAN-report focus on the latter)

The NBHW-report

1. <u>Coding practices</u> for all causes of deaths certificates (done at the National Board of Health and Welfare)

- **T50.9:** (others, non specified drugs/medicines) *not included* in the DRD-series, but from 2006/07 more information on the causes of death certificates – deaths previously would be under the T50.9 will now have codes *included* in the DRD-series
- **Tramadol**: Until 2012 coded as T39.3, after that T40.8. T39.3 *not included*, T40.8 *included*
- NPS: Number increased, previously under T50.9 (*not included*) from 2014 under T43.6 (*included*)
- Dextropropoxifen (DXP): not included and removed from the market in March 2011. Other substances 'replacing' DXP included

Altogether: all these changes – drive the DRD-time series upward

2. Changes in the toxicological testing (done at the National Board of Forensic Medicine) (also mentioned in the NBHW-report)

- Previously most tests done after request from forensic doctor, but now...
- More routine screening and
- More substances routinely screened
- Lower cut-off (quantification /concentration) (e.g. halving of the methadone quantities)
- September 2011: new analysis apparatus (mass spectrograph (Time of Flight)

Altogether: all these changes – drive the DRD-time series upward – the more you search, the more you find.

2. Changes in the toxicological testing (done at the National Board of Forensic Medicine)

The NBHW-report: not do any 'deeper' analyses of toxdata (needed more detailed data). But stated that changes in coding and toxicological tests: explain *all increase* from approx. 2006-2011, and *some/most* (?) of the increase 2012-2014

- More detailed analyses are needed before any "final answer".
- CAN-study: focus on analyses of toxdata, with data on individual level, in-depth analyses, contribute to an increased understanding

Analyses of toxdata

Toxicological 'raw' data, number of opioid deaths with and without DXP (most likely some substitution) (Source: National forensic toxicological database)



Analyses of toxdata Methodological effects: lowered threshold value for methadone (weak effect) (Source: National forensic toxicological database)



Analyses of toxdata Methodological effects: lowered threshold value for oxicodone (clear effect) (Source: National forensic toxicological database)



− Oxicodone deaths lower cut (≥0.005 µg/g)

----- Oxicodone deaths, the higher cut-off whole period ($\geq 0.05 \ \mu g/g$)

However, except for oxycodone...

...more or less the same concentration of opioids in blood over time (table 4), despite increased screening

'New' cases have not lower quantities of opioids

Effects of increased screening: number of screening tests, number of positive cases 2008-

	Fentanyl		Metha	adone E		Bupren	Buprenorphine		Morphine		Codeine		Oxycodone		Tram	ramadol	
Year	Num- ber of screen -ings tests	Num- ber posi- tive cases	Num- ber of screen -ings tests	Num- ber posi- tive cases		Num- ber of screen -ings tests ²	Num- ber posi- tive cases		Num- ber of screen -ings tests	Num- ber posi- tive cases	Num- ber of screen -ings tests	Num- ber posi- tive cases	Num- ber of screen -ings tests	Num- ber posi- tive cases	Num- ber of screen -ings tests	Num -ber posi- tive cases	
2008	72 ¹	22	5,111	87		460	65		2,369	114	2,369	97	5,111	33	5,111	191	
2009	59	20	5,248	96		601	53		2,262	118	2,262	100	5,248	50	5,248	227	
2010	52	26	5,223	103		1,169	72		1,988	112	1,988	106	5,223	50	5,223	197	
2011	1,670	49	5,015	98		1,656	84		2,926	146	2,926	116	5,015	56	5,015	180	
2012	4,992	84	4,992	135		1,783	106		4,992	189	4,992	124	4,992	102	4,992	192	
2013	5,143	81	5,143	135		2,023	113		5,143	186	5,143	130	5,143	135	5,143	202	
2014	5,363	113	5,363	139		2,294	160		5,363	219	5,363	147	5,363	170	5,363	176	

¹ The numbers for 2008-2010, do not refer to screening tests but verification tests done by the request of responsible pathologist. Source: national forensic toxicology database

Number of positive fentanyl cases before and after implementation of routine screening (from 0% to 100% screening)



Number of positive buprenorphine cases before and after implementation of routine screening (from 0% to 100% screening)



Buprenorphine, positive cases

 Predicted number of buprenorphine positive cases, net of increased screening and changes in testing procedure

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Number of forensically examined deaths with positive finding of opioids before and after corrections for increased screening and lowering of threshold values (methadone, oxycodone, DXP) (blue line = corrected time series) Source: national forensic toxicology database.



Corrections for both lowered threshold values and increased screening

Number of drug deaths (opioids, illicit drugs) in forensically examined deaths, with all corrections and Toxreg, both anchored on 2008. Source: national forensic toxicology database.



Selection B, with and without estimated corrections, both anchored on 2008.



Still and increase...

- 1. Substantially lower than what has previously been reported
- 2. Increase is due to an increase in opioids (methadone, fentanyl, buprenorphine, oxycodone)
- 3. 70-75% of all drug deaths (and DRD) due to pharmaceutical opioids
- 4. An increase in most age groups, men and women
- 5. Strong correlations between drug deaths (presence of drugs) and drug-related deaths

What about polydrug use?:

Polydrug use

Studying alcohol and/or benzodiazepine involvement in opioid deaths

- Decrease in relative terms (%) for alcohol
- Stable or increase for benzodiazepines
- Alcohol cannot explain the increase in opioid deaths
- Benzodiazepines could be an important contributory factor

Polydrug use: different combinations of alc and /or benz findings in all forensically investigated opioid deaths (increase only in blue: opiods and benz, no alc)



Why this confusing situation, and how to improve

- Sweden has all the necessary data, but no one has the whole picture
 - Linking toxdata with cause-of-death data on individual level would be an improvement
- Poor coordination between the relevant Nat. Boards (auth)
- The drug issue, and the statistics has not been prioritised, time series (indicators) produced mechanically
 - More in-depth control of syntax, data etc are needed every year
- Toxreg only a time series, not a register has been disseminated broadly (even to EMCDDA). Often incorrectly presented as DRD (instead of DD) and a selection criteria with no consensus among experts

Future

National Board of health and Welfare: Develop(ed) a new series of DRD-death indicator

- Still including both underlying and contributory cause of death,
- Only including poisoning, not F-codes
- And include more substances: *Poisoning – pharmaceuticals and other synthetic narcotic substances*: T36-T39, T40.2-T40.4, T40.6, T41-T43.5, T43.8-T50.8 *Illegal drugs*: T40.0-T40.1, T40.5. T40.7-T40.9, T43.6
 - Other and non specified drugs, pharmaceuticals and biological substances: T50.9

Future plans, RMV and CAN, using forensic data

1. Select the number of detected substances classified as narcotics according to the Swedish Medical Products Agency in forensically examined deaths. Both total number of deaths and number of deaths per substance or group of substances, e.g., opioids, benzodiazepines and amphetamines. Monitored over time and give a good picture of drug involvement in groups at high risk of premature death.

2. Select the number of <u>poisoning deaths</u> in step 1, regardless of substance, in all forensically examined deaths. Here too, the total number of deaths and number of deaths per substance or group of substances can be monitored over time.

3. Select the number of poisoning deaths where <u>opioids</u> are considered to be the immediate cause of death. Here, all opioid deaths will have to be assessed at RMV. Will give us a good sense of the development of opioid-related deaths.

Comparability, conclusions

- 1. The Swedish trend data (without corrections) is not really comparable over time
- 2. The Swedish level of DRD, but also trends, are not fully comparable with other EU-countries
- 3. It is not plausible that the Swedish rate of 93 deaths per million compared do the EU-average of 19 per million mirrors true differences
- 4. Most likely, also other countries have done methodological changes, along already existing differences