

The prevalence of mortality due to rebound toxicity after “treat and release” practices in prehospital opiate overdose care: A systematic review

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DISCLOSURES

- No financial conflicts to declare
- Just some friends doing a review for fun



BACKGROUND

- Death from fentanyl overdose was declared a public health crisis in Canada in September 2015
- There has been a 79.2% increase in illicit drug related death in BC between 2015 and 2016

STUDY QUESTION

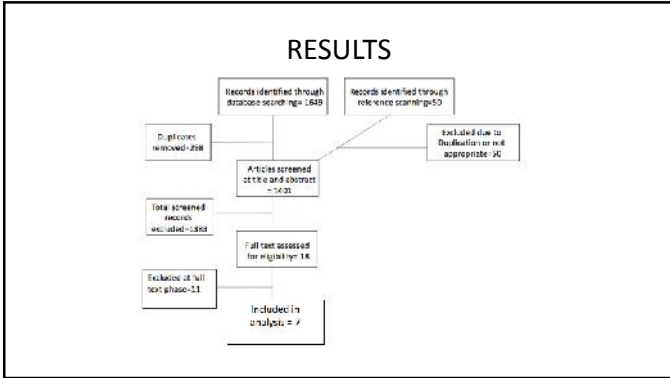
- **P:** In patients presenting to EMS with suspected opiate overdose,
- **I:** does complete reversal with naloxone and subsequent release
- **O:** result in mortality or adverse event within 48 hours.

METHODS

- Cochrane methodology was followed
- PubMed, Cochrane Central, Embase and CINAHL
- No search limits applied
- Reference hand searching

DATA SELECTION

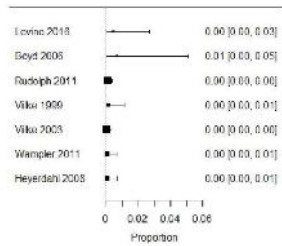
- Primary studies or systematic reviews
 - EMS
 - Reversed from suspected opiate OD with naloxone
 - Refused or discharged on scene
 - Outcome of mortality or adverse event from suspected rebound toxicity.



- ### RESULTS
- 4912 pooled patients
 - Mean age 36.0 years (SD=5.48)
 - Three studies were conducted in Scandinavia , 4 in the US
 - Two studies were set in a fire-based system. (ALS or ALS/BLS)
 - Two studies had a paramedic/doctor crew configuration, (Oslo & Copenhagen)
 - 0.4 mg – 2.0 mg (with additional doses when required)
 - IV, IM, IN

- ### RESULTS
- 4 of 4912 = 0.00081% of patients had mortality from possible rebound toxicity with in 48 hours
 - No reports of altered level of consciousness suspect to rebound toxicity.

RESULTS



LIMITATIONS

- Included study's design
- Catchment area limitations
- Missing data
- Little data of adverse events
- No gray literature search

CONCLUSIONS

- Prevalence of mortality in the included studies was very low.
- We still know little about adverse events associated with rebound toxicity.

Acknowledgments

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THANK YOU!



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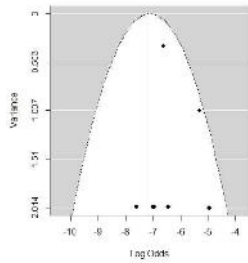
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Supplementary material

Agreement, Heterogeneity, ROB and Bias

- Kappa = 1
- Heterogeneity:
 - I² statistic; 0.00%
 - Wald's Test statistic; p-value=0.9740
- Modified QUIPS tool: no high risk of bias studies
- No evidence of publication bias



Study	Setting	Mean age-EMS patients (years)	n EMS treatment group	% female EMS patients	intervention	Primary outcome	Secondary outcome
Levine 2016	US EMS/LAFD ¹	41	205	13	Naloxone with release	Death within 24 hours	Death with in 30 days
Boyd 2006	Helsinki EMS	26	71	17.2	Naloxone with release	Death within 12 hours	Rebound toxicity
Rudolph 2011	Copenhagen MECLU ²	-	2241	-	Naloxone with release	Death within 48 hours	Death likely to rebound toxicity
Vilke 1999	US EMS/SDFD ¹	39.8	317	16.3	Naloxone with release	Death within 12 hours	N/A
Vilke 2003	US EMS/SDFD ¹	37.7	998	16.7	Naloxone with release	Death within 12 hours	N/A
Wampler 2011	US EMS/SAFD ⁴	38	592	28	Naloxone with release	Death within 48 hours	Death with in 30 days
Heyerdahl 2008	Oslo EMS, outpatient clinic and ED	34	528	31	Naloxone with release	Death due to rebound in 1 week	N/A

Author (year)	Goal: To judge the risk of selection bias	Goal: To judge the risk of attrition bias	Goal: To judge the risk of measurement bias related to how PF was measured	Goal: To judge the risk of bias related to the measurement of outcome	Goal: To judge the risk of bias due to confounding	Goal: To judge the risk of bias related to the statistical analysis and presentation of results.
Levine 2016	Low	N/A	Low	Low	Low	Low
Boyd 2006	Low	N/A	Low	Low	Low	Low
Rudolph 2011	Low	N/A	Low	Low	Moderate	Low
Vilke 1999	Low	N/A	Low	Low	Low	Low
Vilke 2003	Low	N/A	Low	Low	Moderate	Low
Wampler 2011	Low	N/A	Low	Low	Moderate	Low
Heyerdahl 2008	Low	Low	Low	Moderate	High	Low
