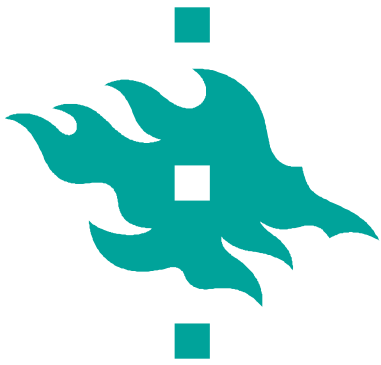




# Pregabalin and gabapentin in opioid overdose deaths

**Ilkka Ojanperä and Margareeta Häkkinen**  
**Hjelt Institute, Department of Forensic Medicine,**  
**University of Helsinki, Finland**



# Introduction

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- Pregabalin (PRG) and gabapentin (GBP) are GABA (gamma-aminobutyric acid) analogues which bind to alpha-2-delta subunit of the voltage-dependent calcium channel in the central nervous system
- They have no activity through binding to GABA<sub>A</sub> receptors, but they increase GABA synthesis in the brain
- GABA is the most important inhibitory neurotransmitter in the brain, and increase in GABA decreases release of excitative neurotransmitters
- PRG and GBP are medications for treating neuropathic pain and partial seizures
- PRG also for generalized anxiety disorder
- Abuse liability of these drugs has become an increasing concern



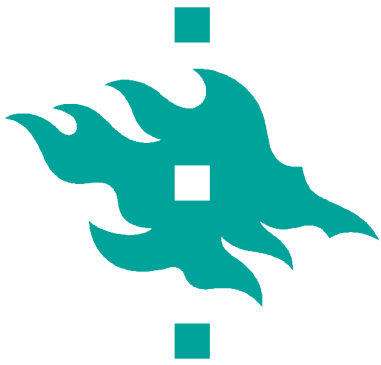
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- PRG may have higher potential for addiction because it has rapid absorption and faster onset of action
  - Unlike that of PRG, absorption of GBP is saturable
  - PRG has been in Finland on the market since 2004
  - Signs of PRG abuse emerged in 2007, based on postmortem data
  - PRG abusers typically use concomitant benzodiazepines, opioids, and alcohol
  - Administration route in abuse cases is usually oral, but also intravenous abuse have been detected



# Consumption of PRG (DDD 0.3 g) and GBP (DDD 1.8 g) in Finland

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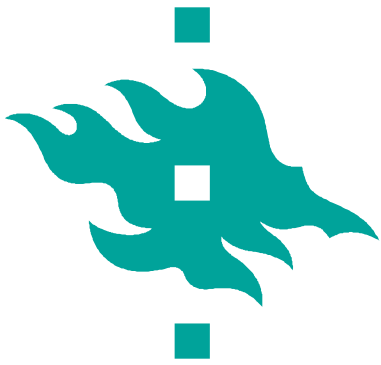
Year	Consumption (DDD/1 000 inh/day)	
	PRG	GBP
2004	0.07	1.14
2005	0.96	1.00
2006	1.73	0.93
2007	2.56	0.91
2008	3.39	0.96
2009	3.99	0.96
2010	4.45	0.98
2011	4.74	1.04
2012	5.04	1.17



# Methods

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- Our study comprised all deaths with postmortem PRG or GBP findings in Finland
- During 2010-2011, deceased totaled 101,472, medicolegal autopsy 22,421, and postmortem toxicology 13,766 (13.6% of all deaths)
- Lack of a valid PRG or GBP prescription and either known drug abuse history, drug injecting, or laboratory findings of illicit drugs defined an abuse case
- In PRG or GBP poisonings, forensic pathologist had determined the underlying cause of death as drug poisoning with PRG or GBP as the main finding

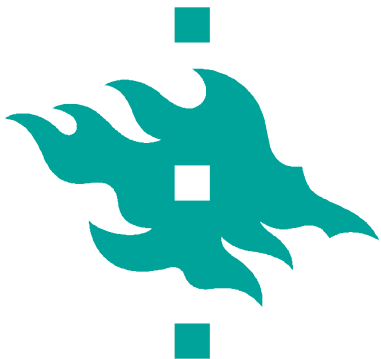


# Results

Häkkinen M et al. Profiles of pregabalin and gabapentin abuse by postmortem toxicology. *Forensic Sci Int.* 2014;241:1-6.

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- During 2010-2011, PRG findings numbered 316, and GBP 43
- Drug abuse was associated with 48.1% of the PRG and 18.6% of the GBP findings
- PRG poisoning accounted for 10.1% of all PRG cases and GBP poisoning for 4.7% of all GBP cases
- In the drug abuser cases, PRG poisoning represented 19.1%, and GBP poisoning 12.5%
- Poisonings in other cases than abuse cases were rare
- All abuse cases included additional psycholeptics and/or alcohol
- Opioids were involved in 90% of the abuse cases
- Drug abuse was most common in age groups 20 – 49 y



# PRG findings in fatal opioid poisonings

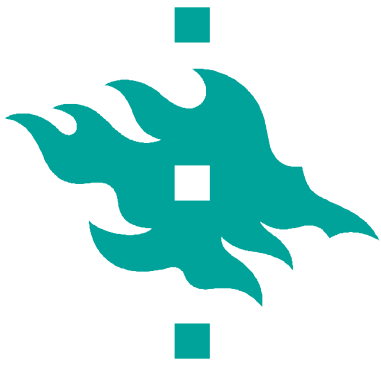
	All cases			Known abuse		
	N <sub>all</sub>	N <sub>PRG</sub>	% <sub>PRG</sub>	N <sub>all</sub>	N <sub>PRG</sub>	% <sub>PRG</sub>
Buprenorphine	117	29	24.8	114	27	23.7
Codeine	87	16	18.4	33	11	33.3
Fentanyl	28	3	10.7	25	3	12.0
Methadone	34	11	32.4	34	11	32.4
Oxycodone	33	6	18.2	16	2	12.5
Tramadol	86	30	34.9	56	25	44.6
<b>Total</b>	<b>387</b>	<b>95</b>	<b>24.5</b>	<b>278</b>	<b>79</b>	<b>28.4</b>



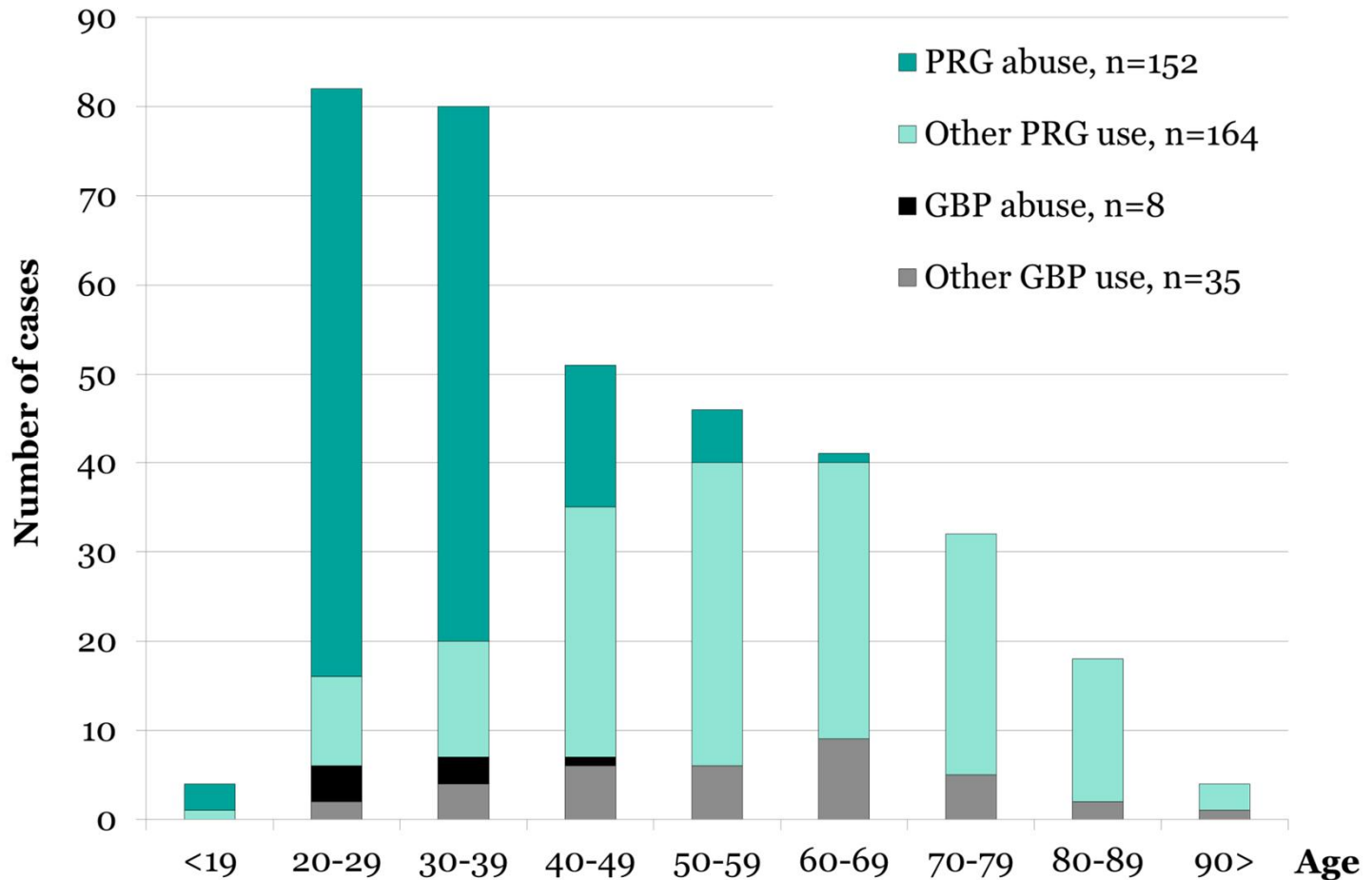
# Comparison of PRG and GBP findings between drug abuser and other cases

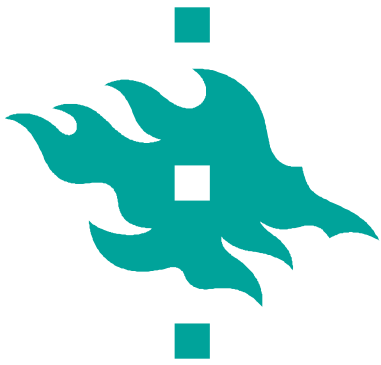
		Cases, %	Poisonings, %	Alcohol, %	Opioids, %	Concentration, median (range), mg/L
<b>Abuse</b>	PRG	48.1	19.1	16.4	91.4	15 (0.43-110)
	GBP	18.6	12.5	37.5	87.5	12 (0.62-45)
<b>Other use</b>	PRG	51.9	1.8	22.0	56.7	5.8 (0.28-110)
	GBP	81.4	2.9	17.1	62.9	8.3 (2.7-93)



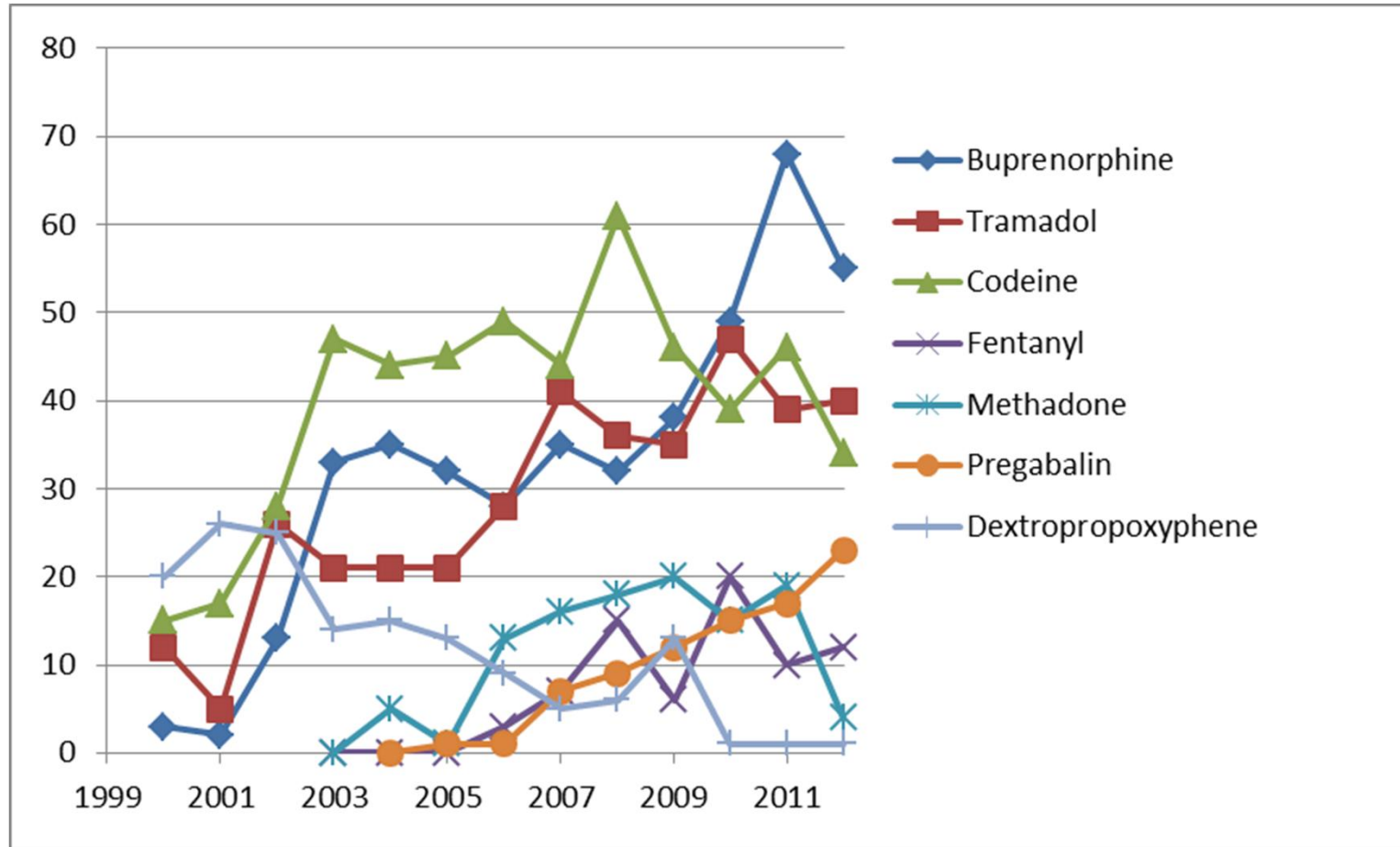


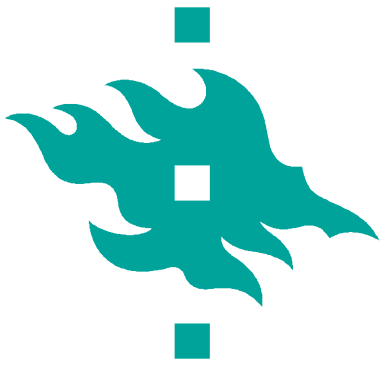
# Age profiles of PRG and GBP related cases





# Fatal poisonings by an opioid or pregabalin as main finding 2000-2012





# Conclusions

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- This study revealed considerable PRG abuse
- Approximately a half of the PRG findings and a fifth of the GBP findings were related to abuse
- PRG and GBP deaths were polydrug cases
- Abuse of these medicines can be fatal, especially when combined with opioids
- Compared with PRG, the abuse potential of GBP seems to be lower