

Role of pregabalin and gabapentin in drug related deaths

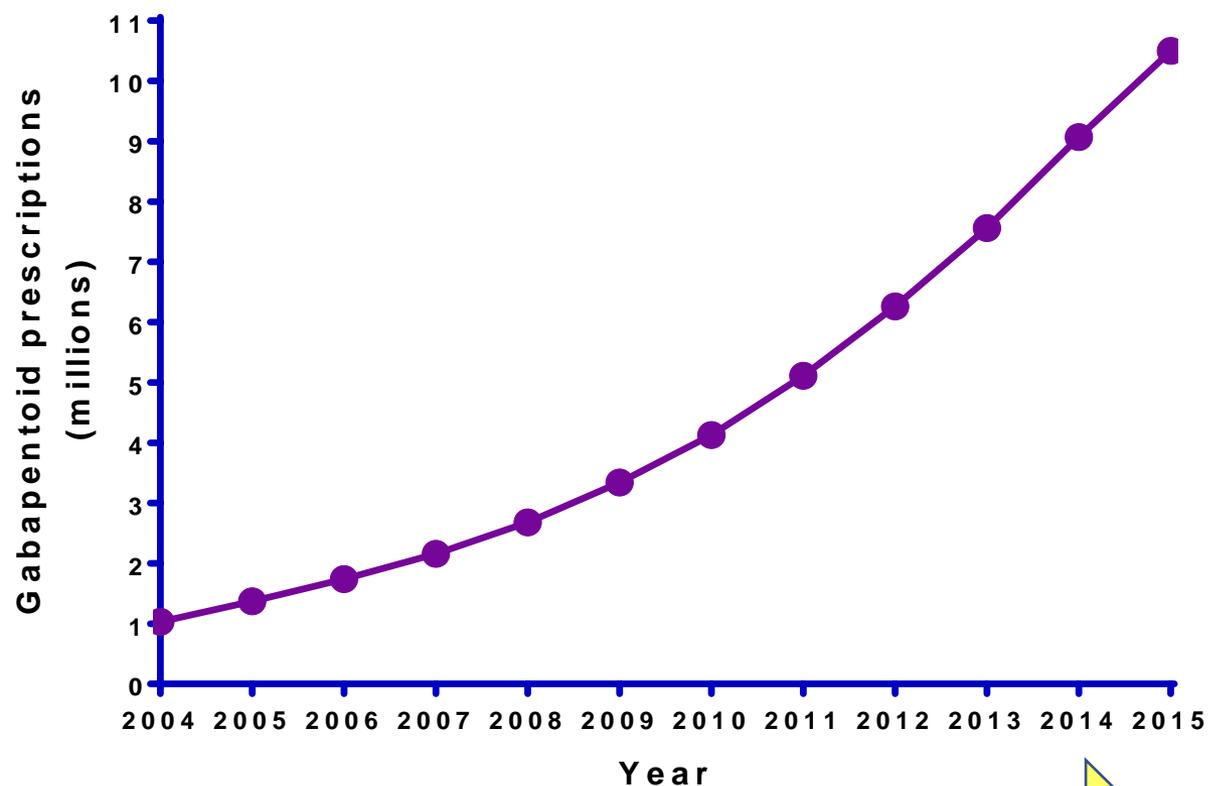
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Pregabalin and gabapentin community prescriptions (England)



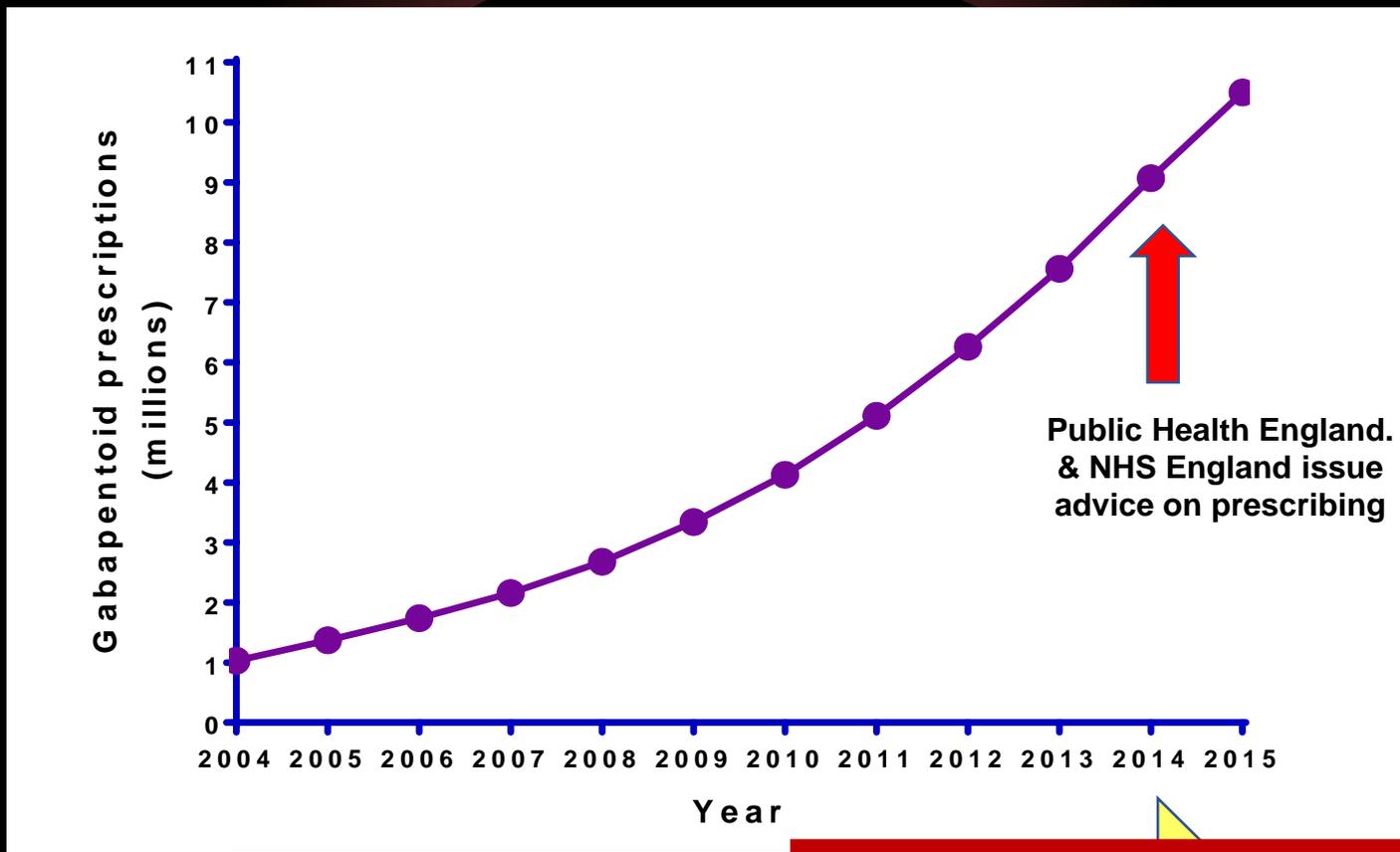
Epilepsy

Pain

Anxiety (pregabalin)

insomnia, migraine, mania,
bipolar disorder and
alcohol withdrawal
(gabapentin)

Pregabalin and gabapentin community prescriptions (England)



Epilepsy

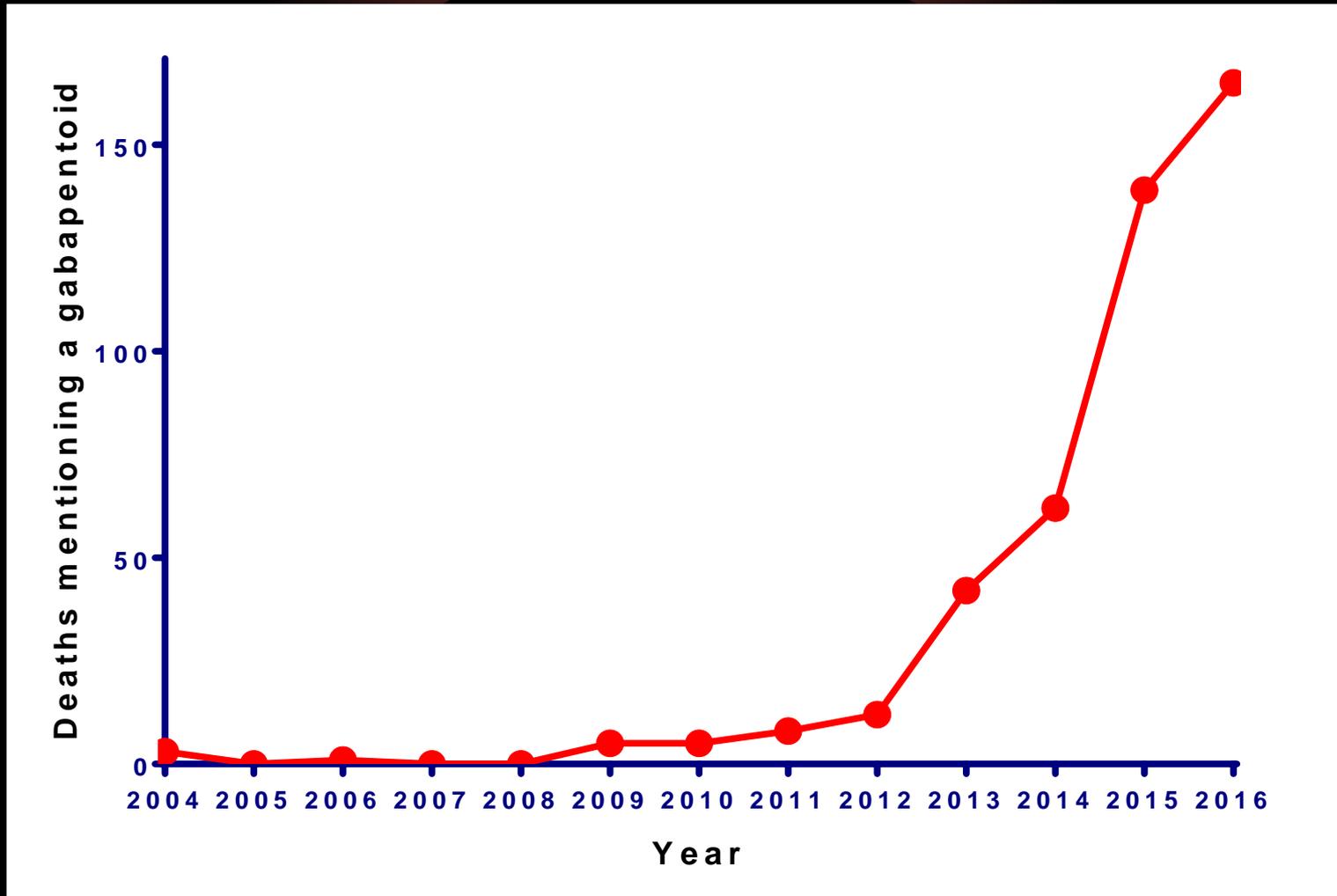
Pain

Abuse

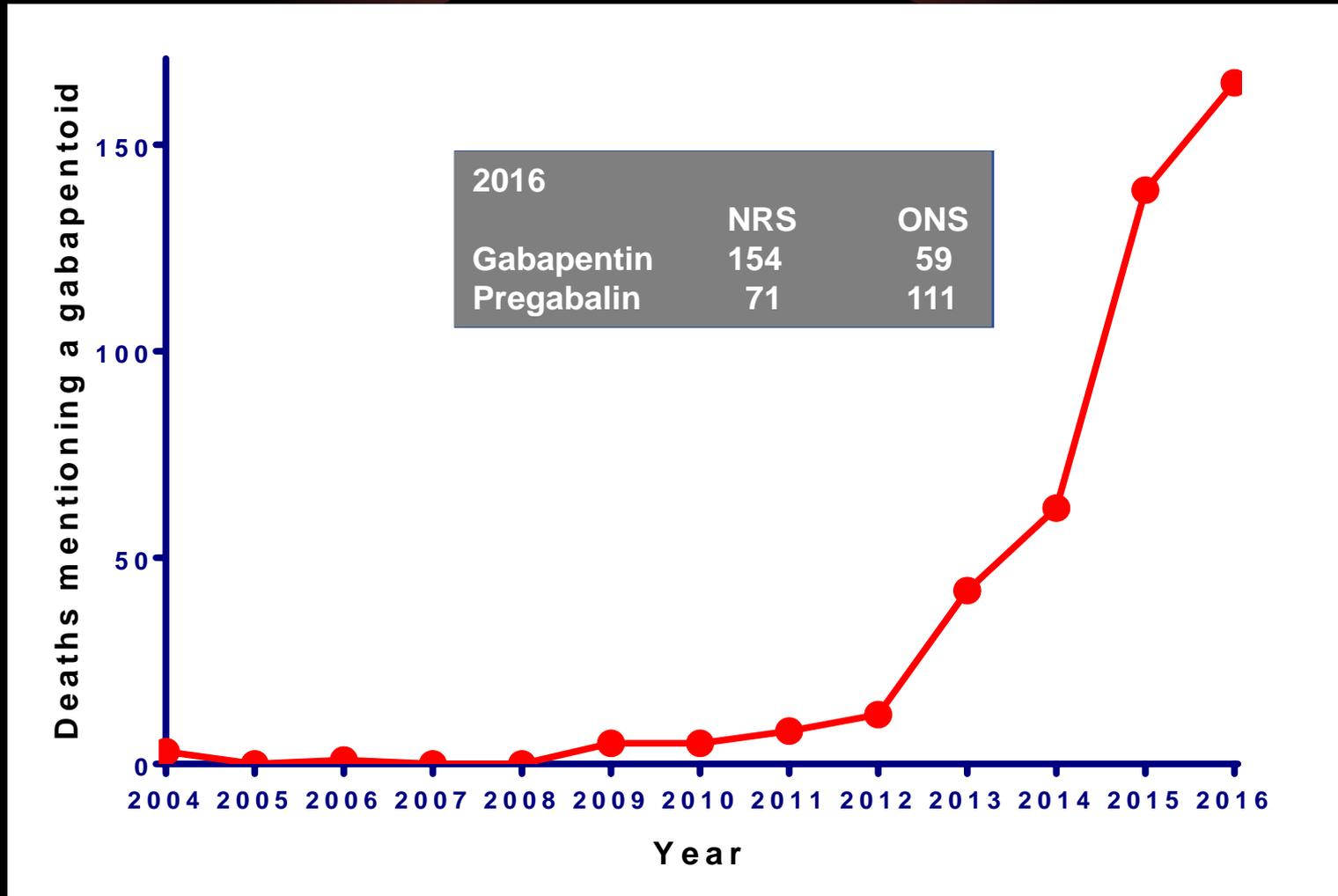
- relaxation
- enhanced sociability
- euphoria
- dissociation
- sedation

(gabapentin)

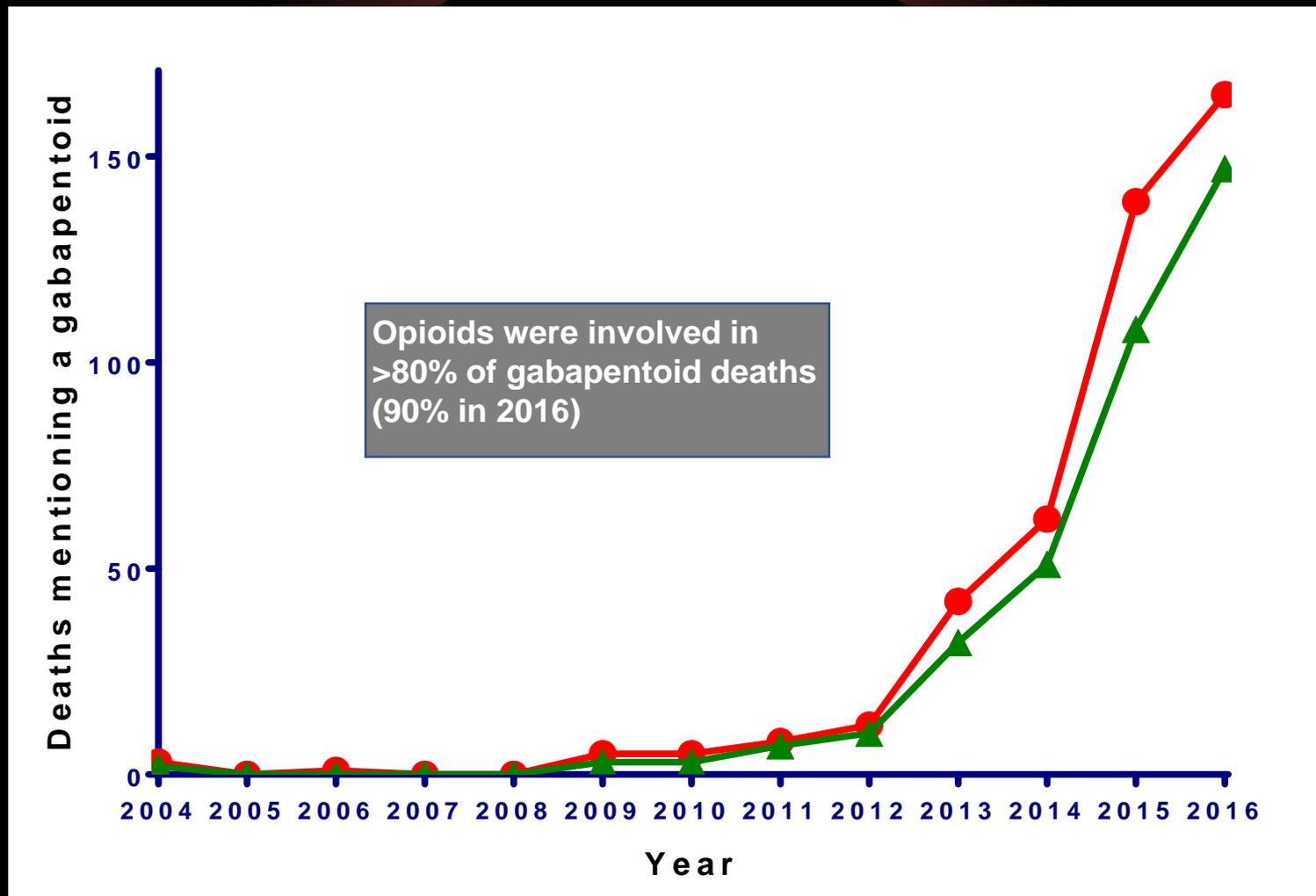
Acute deaths involving gabapentin and pregabalin (England & Wales)



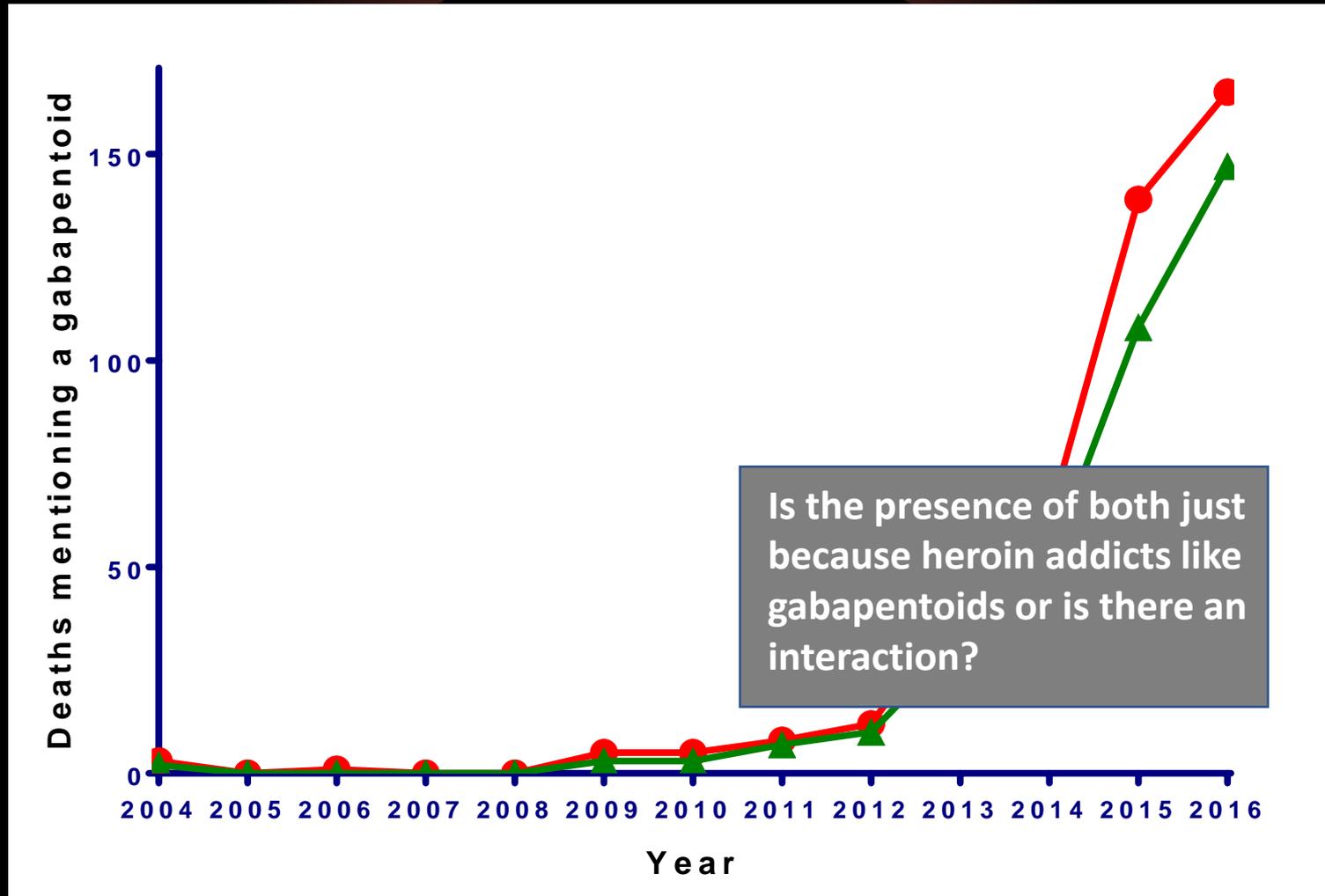
Acute deaths involving gabapentin and pregabalin (England & Wales)



Deaths also involving opioids (England & Wales)



Deaths also involving opioids (England & Wales)



Qualitative Research (October 2014 – February 2015)

Interviews with active heroin users in Bristol

- attending Bristol Drugs Project Needle Exchange
- screened for known opioid users
- £10 fee on completion of interview

Areas discussed

Perceived protection

- from on top heroin use on methadone or Subutex OST

Benefits and hazards of also using non-opioid drugs

- alcohol
- cocaine
- benzodiazepines
- gabapentin and pregabalin

Interviewed 30 users

- 19 males and 11 females
- different lengths of opioid use
 - 20 long term (>10 years)
 - 4 medium term (5 – 10 years)
 - 6 short term (<5 years)
- different styles of use (smoking and injecting)
- different opioid substitution treatments

Use of gabapentoids

- 21 of 30 had used gabapentoids
- most (19 of 21) used pregabalin
 - 3 were daily users
 - 3 used it weekly
 - 5 used it intermittently
 - for 10 it was just a one-off occasion

Street purchase mainly

- 2 obtained it from friends who were prescribed it
- 3 were prescribed pregabalin for chronic pain

Taken orally some time prior to heroin injection

Doses varied – 250mg tablet to 1500mg taken orally as tablets

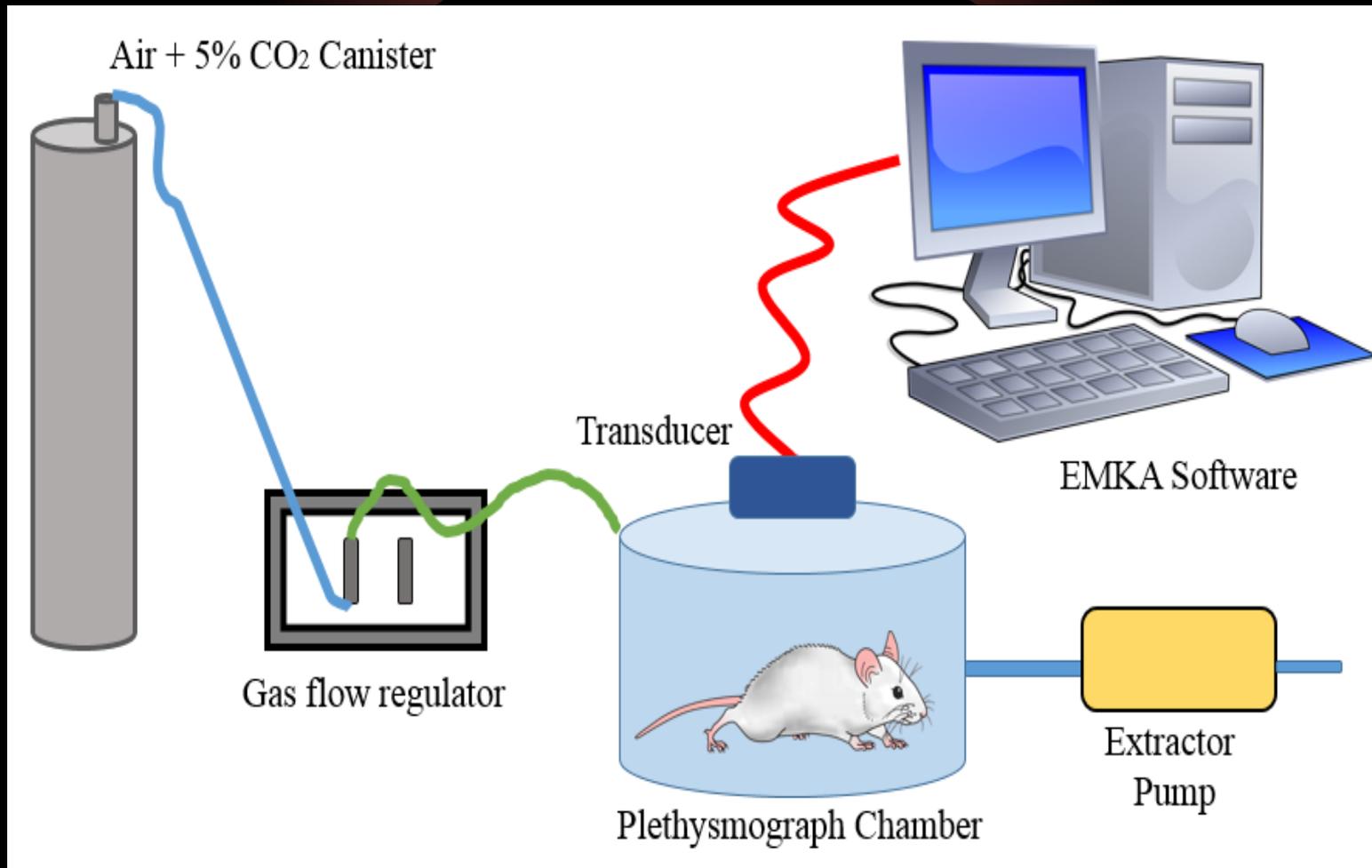
Perceived effects of gabapentoids

- give a buzz on their own (feeling of being drunk)
- enhance the effect of the heroin
- caused blackouts and loss of control (zombies)
- increased the risk of overdose
- helps to cope with withdrawal between heroin doses
- reduced craving for heroin

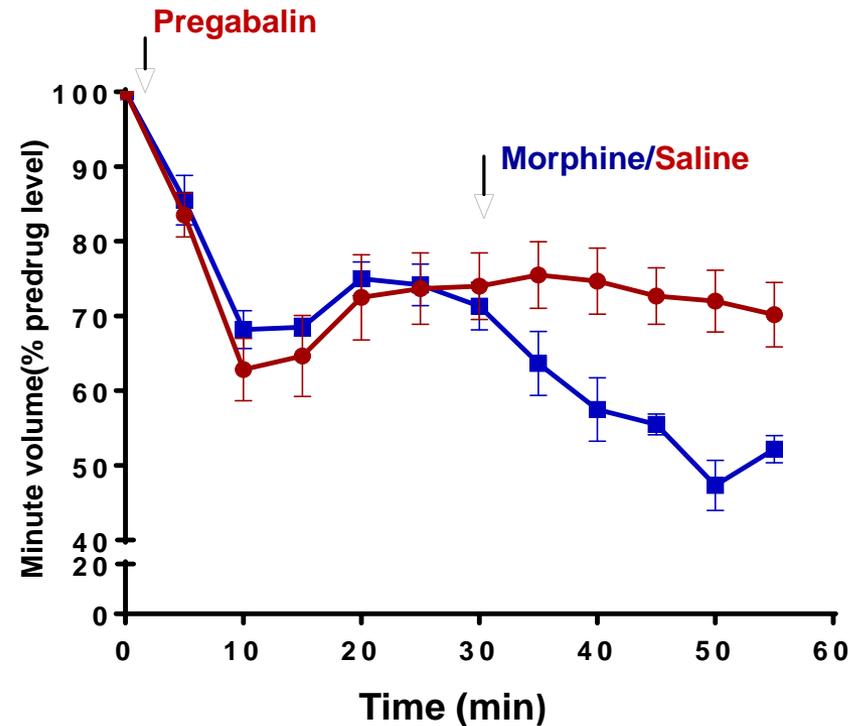
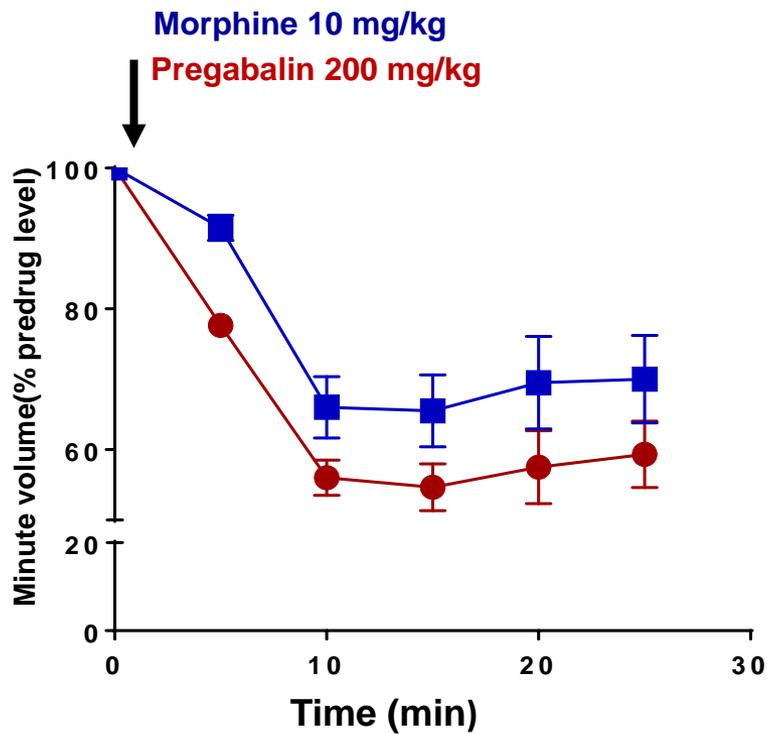
Preclinical studies of pregabalin

- Does pregabalin depress respiration?
- If so is it additive with opioids?
- Does pregabalin alter opioid tolerance?

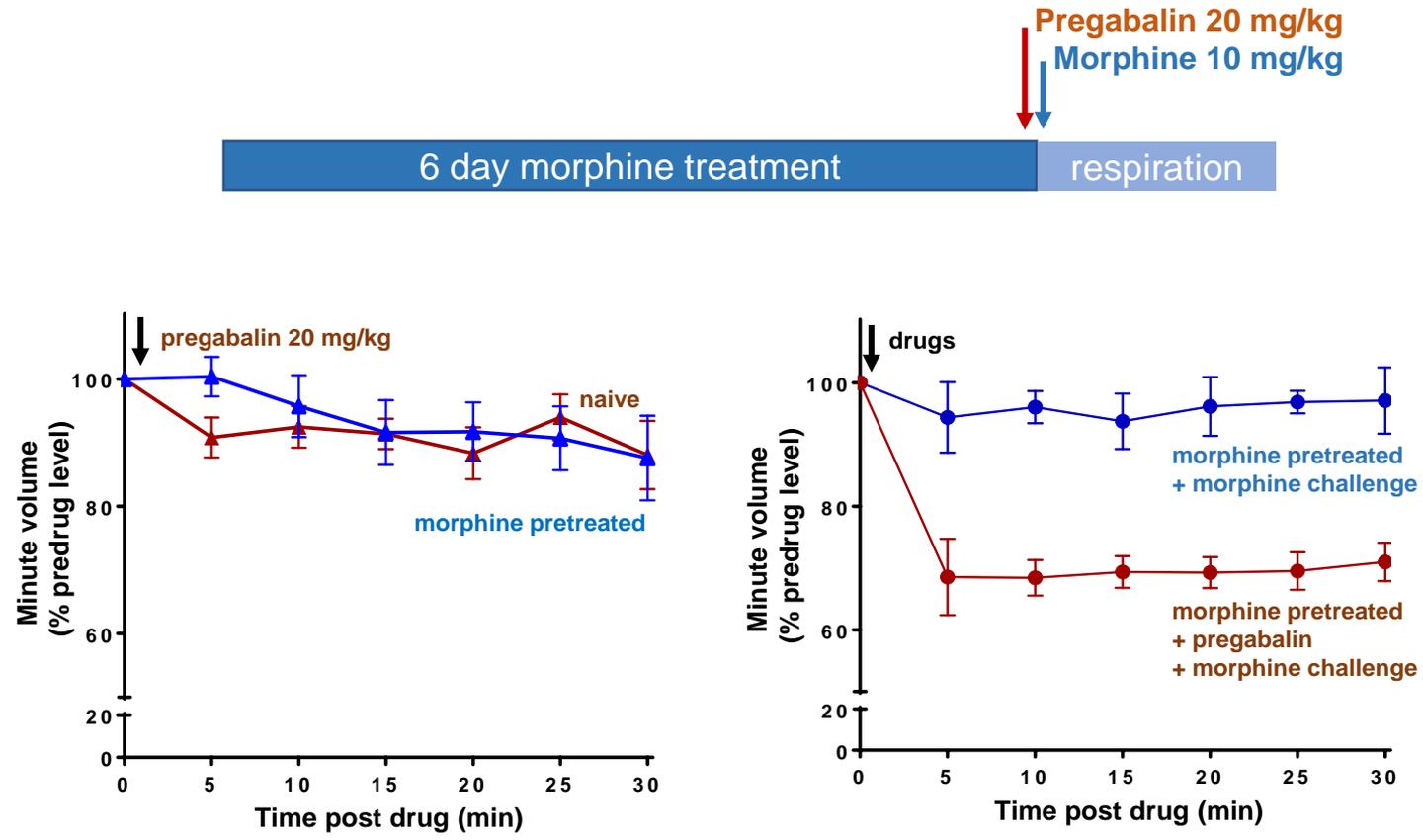
Monitoring mouse respiration



Pregabalin and morphine additively depress respiration



Low dose pregabalin reverses morphine tolerance



Pregabalin – opioid interaction

Acute

- pregabalin (*high dose*) additive with
morphine
methadone
fentanyl
oxycodone

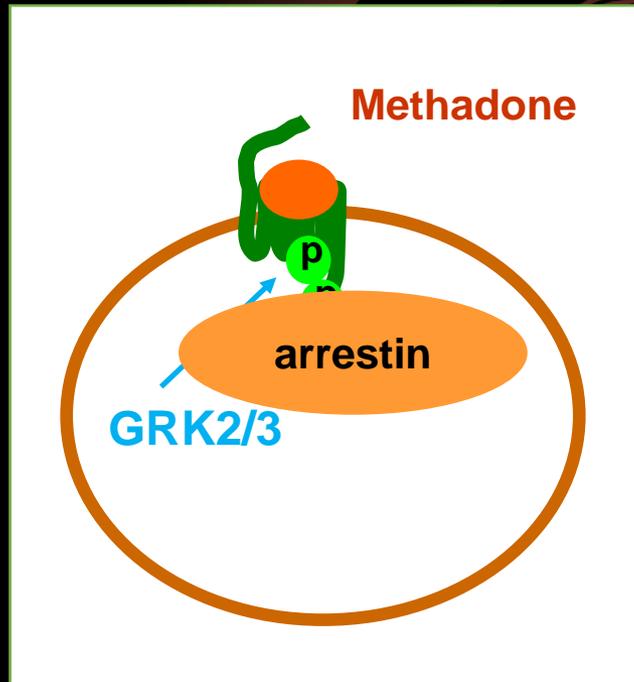
Tolerance

- pregabalin (*low dose*) reverses
morphine tolerance
oxycodone tolerance

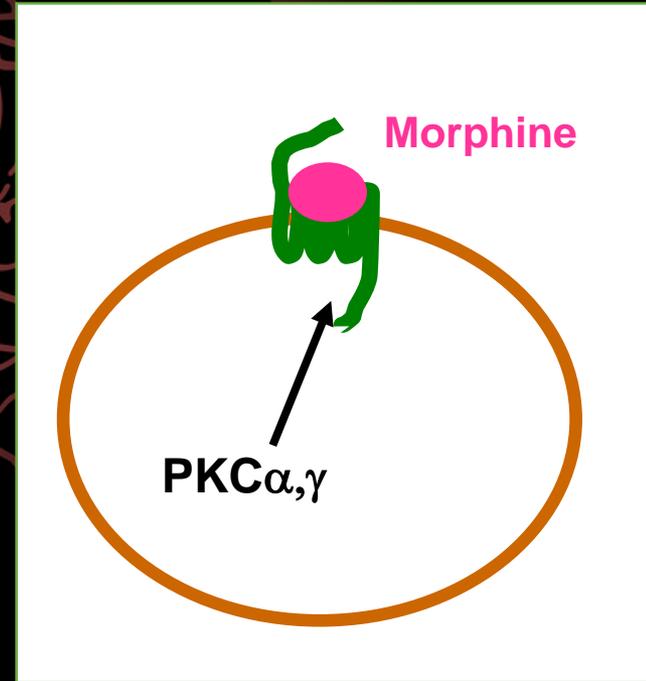
BUT NOT

methadone tolerance

Drug specific mechanisms of opioid tolerance

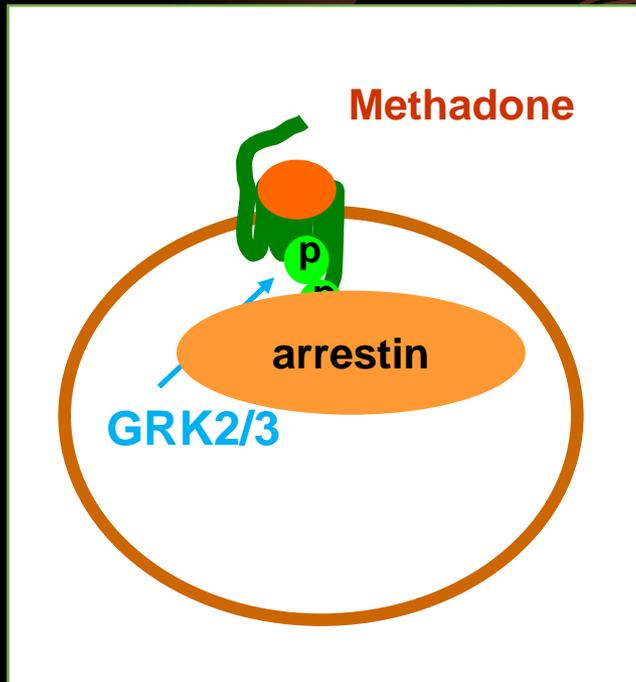


Methadone
Fentanyl

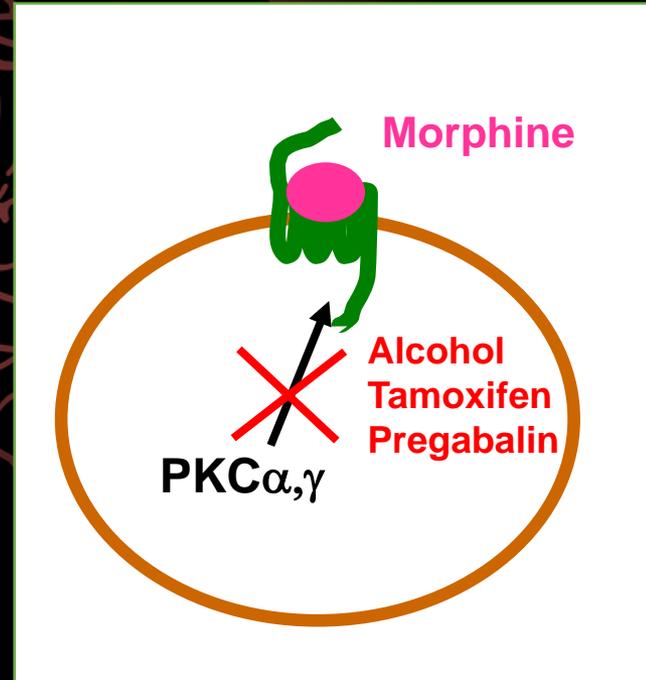


Morphine
Heroin
6-MAM
Oxycodone

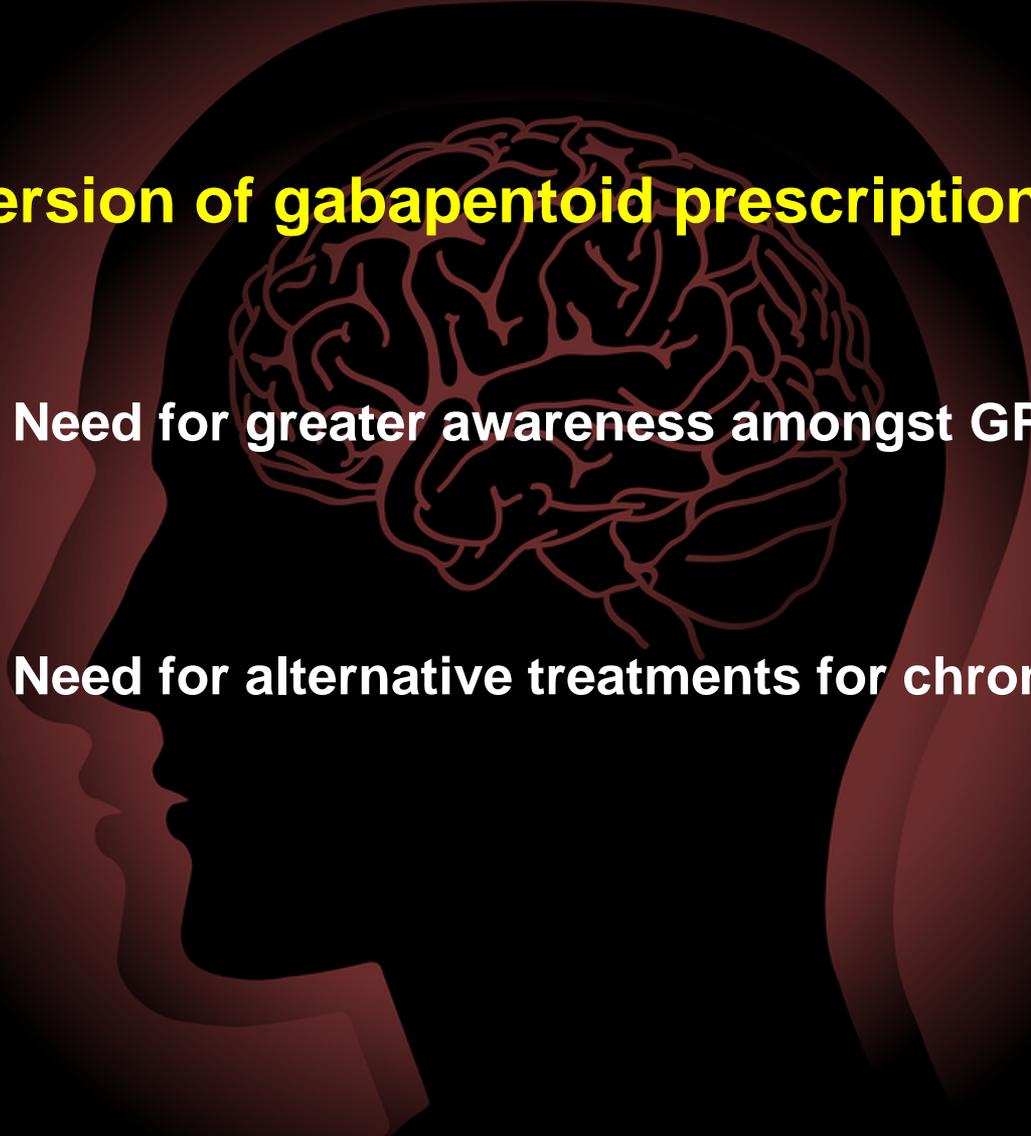
Agonist specific mechanisms of opioid tolerance



Methadone
Fentanyl



Morphine
Heroin
6-MAM
Oxycodone



Diversion of gabapentoid prescription

- **Need for greater awareness amongst GPs**
- **Need for alternative treatments for chronic pain**

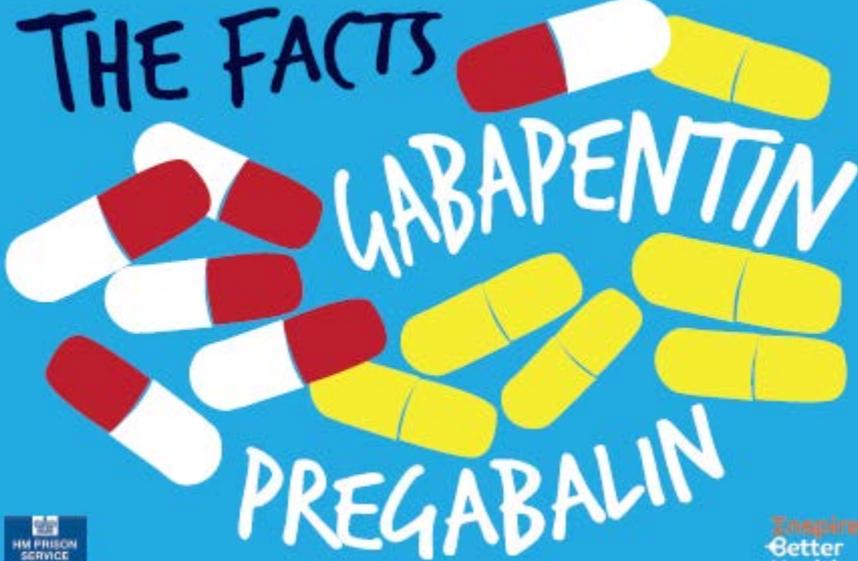
HM Prison Service (South West of England)

Dr Catherine Glover, Medical Director

THE FACTS

GABAPENTIN

PREGABALIN



HM PRISON SERVICE
Inspire Better Health

PREGABALIN AND GABAPENTIN - THE FACTS

WHAT ARE PREGABALIN AND GABAPENTIN?

They were originally used to treat epilepsy. They are also licenced to treat nerve pain and some types of anxiety.

WHY DO WE WORRY ABOUT IT?

- Use of these drugs can lead to dependence.
- Pregabalin and Gabapentin can cause, drowsiness, sedation, slow down breathing, and in extreme cases death.
- There are particular issues in secure settings where deaths have been found to involve illicit and/or diverted medication.

WHAT TO BE AWARE OF...

- Deaths involving Pregabalin or Gabapentin have increased drastically in the last 5 years, 78% of these are associated with opiate use.
- Opiates & Pregabalin together slow down breathing further.
Naloxone does not reverse respiratory depression caused by Pregabalin/Gabapentin.

WHAT USERS ARE SAYING:

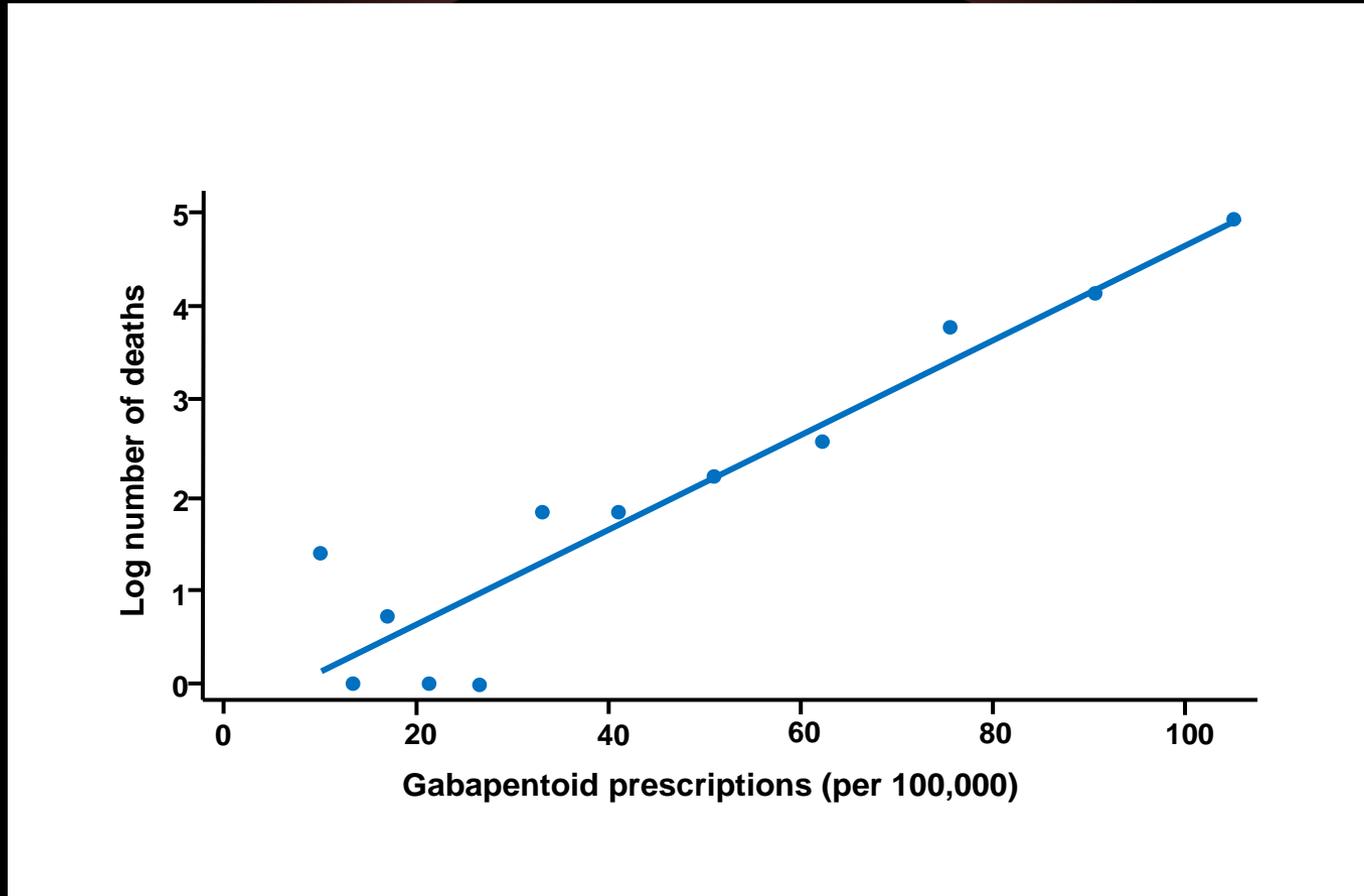
"There is more chance for overdose if you take heroin and Pregabalin together because Pregabalin takes, like, two/three hours to kick in. So, like, and then we think 'argh it hasn't kicked in, oh I'll have a dig', so we have a dig and then that kicks in, and then there's more chance of you going over."

"They're like zombies; they don't know what they're doing... Pregabalin does make people feel like a zombie."

"Don't like 'em... I woke up just feeling like jelly, didn't know what happened."

"That's one of my last overdoses. I knew the heroin was strong and I didn't know, I was naive."

Correlation between number of prescriptions and number of deaths in a year



- **5% increase in overdose deaths per 100 000 increase in prescriptions**