Assessment and treatment of self-poisoning

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Goals of the course

To teach you some pharmacology

To get you thinking about clinical scenarios

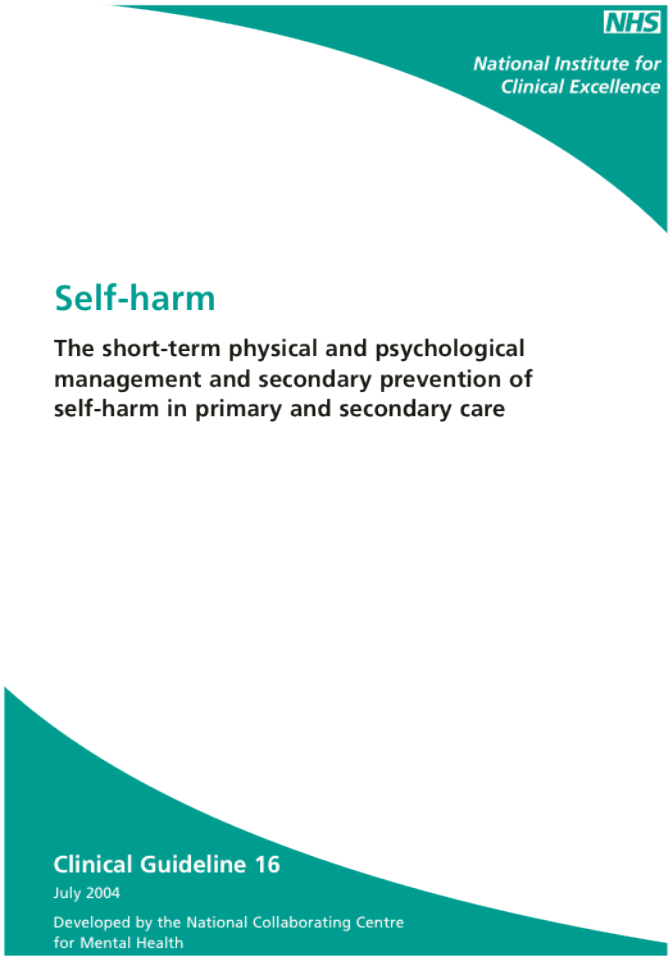
Goals of the lecture:

At the end of the lecture, you should:

- Have an approach to assessment and management of self-poisoning
- Know about TOXBASE and NPIS
- Be aware of antidotes/treatments for common poisons
- Know risk factors which increase acute risk of suicide
- Remember to be respectful and kind to patients in this situation

Initial approach: assessment

- Airway
- Breathing
- Circulation
- Disability



History

<u>For immediate management:</u>

- What taken
- Amount taken
- When taken
- Alcohol?
- Medical comorbidity
- Alcohol dependence
- Nutritional status

Medications frequently used in self-poisoning include paracetamol, antidepressants, benzodiazepines and opiates

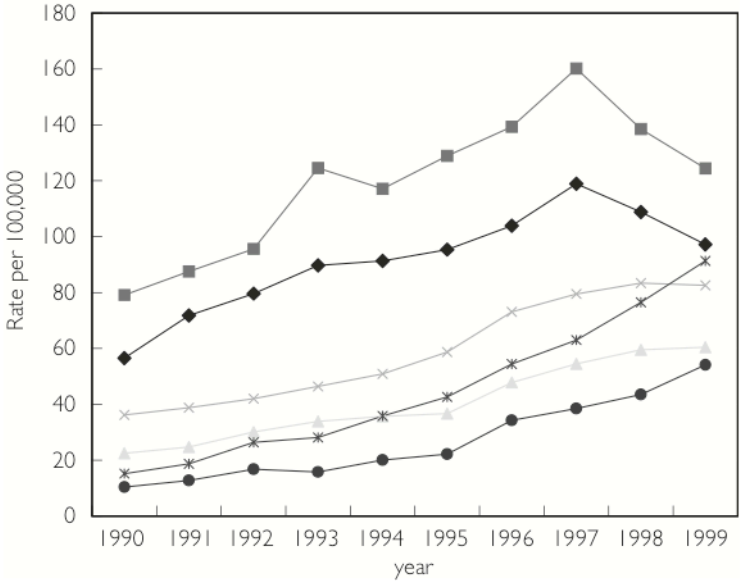


Figure 1 Trends in overdose discharges for paracetamol, antidepressants and opioid overdose and misuse in Scotland by gender (figure reproduced from [40] with permission from the authors and the editorial board of the *Quarterly Journal of Medicine*). Paracetamol m (◆); paracetamol f (■); antidepressants m (▲); antipepressants f (×); opioid misuse and poisoning m (✳); and opioid misuse and poisoning f (●).

Table 2 The 10 most common enquiries to Toxbase during 2000, with frequencies expressed as ratios to that of paracetamol (source: Scottish Poisons Information Bureau).

1	Paracetamol	1.000
2	Diazepam	0.299
3	Aspirin	0.278
4	Ibuprofen	0.262
5	Zopiclone	0.250
6	Ecstasy	0.232
7	Amitriptyline	0.201
8	Dothiepin	0.199
9	Temazepam	0.176
10	Coproxamol	0.171

Camidge, Wood and Bateman (2003) Br J Clin Pharmacol 56: 613-619

Immediate management: general principles

Mainstay of treatment of most overdoses is supportive

Treatment of complications – loss of consciousness, seizures, arrhythmias

Consult TOXBASE .org , phone the National Poisons Information Service

Risk assess re mental health early and have a plan if the patient leaves the department

Bare half-life in mind

Specific situations

Clinical scenario

Mr X, 45, is brought to A&E at 9 pm. A friend became concerned when he texted 'goodbye' to them. They went round to his house, found him and convinced him to come to A&E.

He looks fine and his observations are stable.

He tells you that he has spent the last 16 hours forcing down four boxes' worth of paracetamol.

Mr X is recently divorced and lost his job a week ago because he turned up to work drunk.

Paracetamol overdose

The presentation is unremarkable – the patient is usually feeling nauseous but may appear completely normal.

Toxicity is delayed.

Avoidable deaths from paracetamol poisoning still occur because treatment is not given

Paracetamol causes toxicity via a metabolite that accumulates in overdose

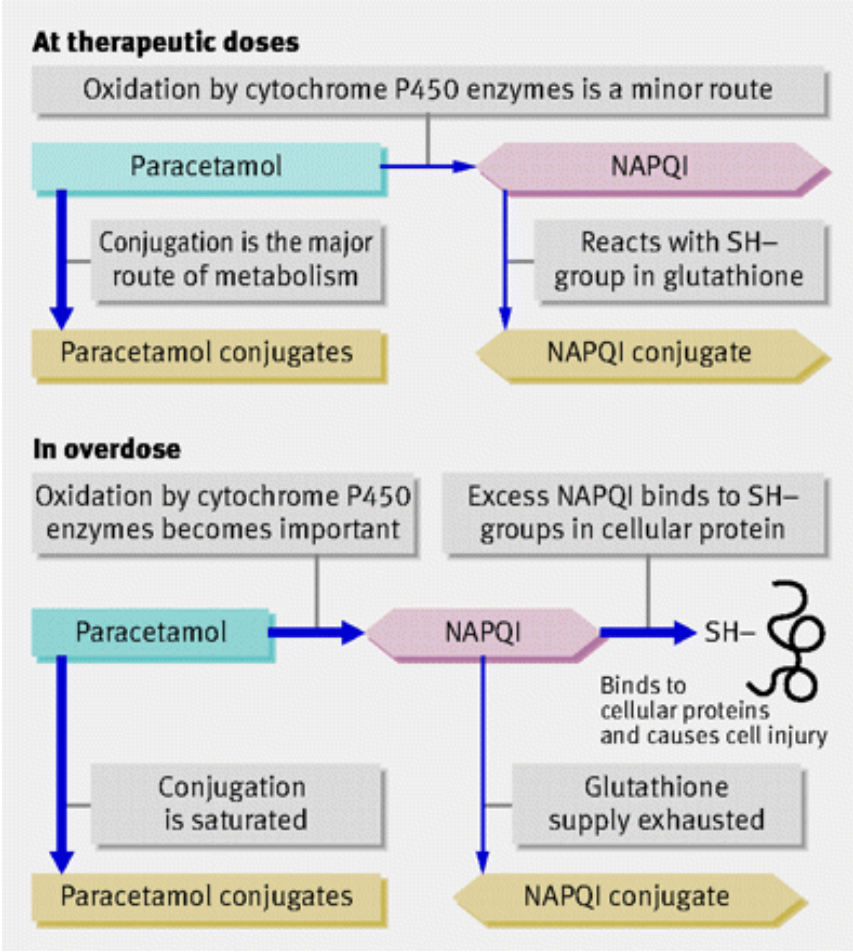
Paracetamol's usual route of metabolism is exhausted

Oxidation to NAPQI occurs

Conjugation of NAPQI does not occur rapidly enough

Glutathione stores exhausted – especially if patient alcohol dependent or malnourished

NAPQI binds to cellular macromolecules and causes cell death in the liver



Investigation

Paracetamol levels – between 4 and 15 hours post overdose are ‘useful’

Liver function, clotting and renal function tests

Venous blood gas

Treatment – N-acetyl cysteine

If paracetamol level is above the treatment line, give N-acetyle cysteine x 4 infusions

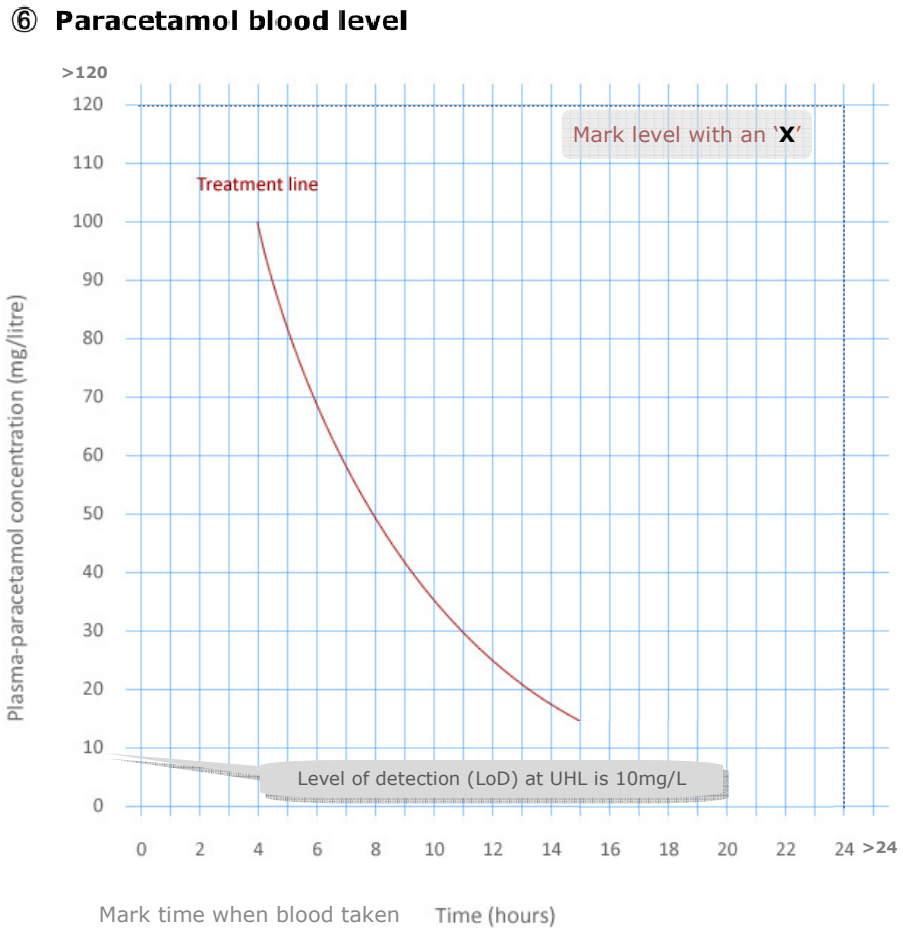
Used to be 2 treatment lines, now 1 – corresponds to old 'high risk' line

Weight dependent dose

If it is a staggered overdose or more than 15 hours, treat

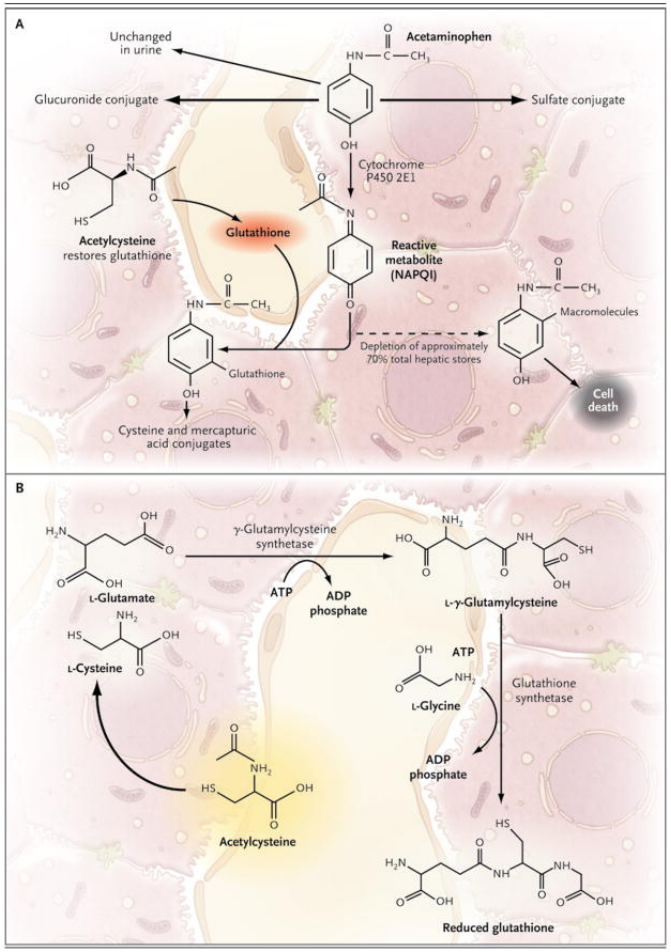
If in doubt, treat

If patient has a history of anaphylaxis, still treat



From www.collemergencymed.ac.uk

N-acetyl cysteine works by restoring glutathione in the liver



NAC provides a precursor for the production of more glutathione allowing conjugation of NAPQI

Side effects:
Vomiting ++

Anaphylaxis - is more likely if:
Female
Relatively small dose of paracetamol
First infusion

Treatment:
Salbutamol nebs, chlorpheniramine
Adrenaline, steroids etc as per ALS if full anaphylaxis

When to think about getting the liver team involved

Table 1

When to contact a specialist liver centre in patients with acetaminophen-induced hepatotoxicity

Progressive coagulopathy: PT in seconds greater than the number of hours since ingestion (or if the INR is >2 at 24 h, >4 at 48 h, and >6 at 72 h)
Renal impairment (creatinine >200 mol/l)
Hypoglycaemia
Metabolic acidosis (pH <7.35)
Hypotension despite fluid resuscitation
Encephalopathy

INR = International Normalized Ratio; PT = prothrombin time. Data from Bernal*et al.* [14].

Bernalet, Lancet 2002

Clinical scenario

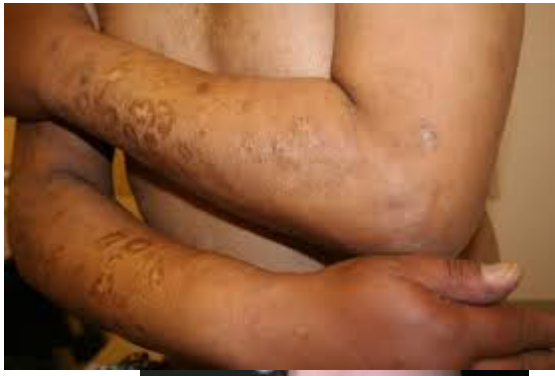
You are call to resus.

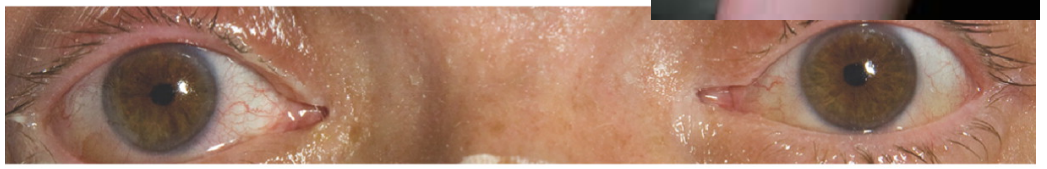
Mr Y is lying in Resus 2, being bagged by a paramedic. He was found in a park, unconscious.

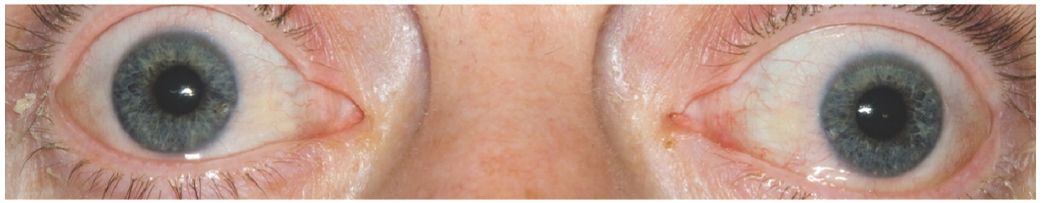
Opiate overdose

Presentation:

- Blue
- Respiratory rate <12
- Unconscious or drowsy
- Pinpoint pupils
- Track marks
- Skin popping







Mechanism of opiate overdose

Opiates suppress respiration via action on regions in the medulla and pons involved in the control of respiratory rhythm

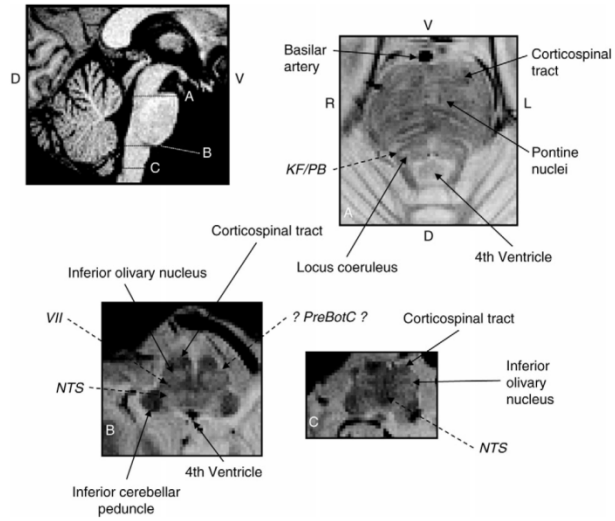
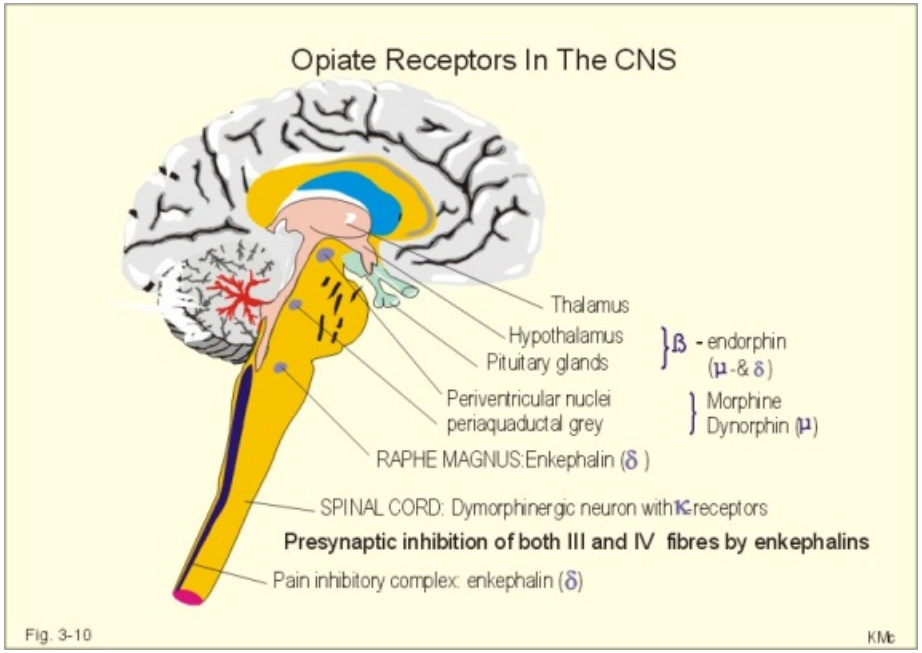


Fig 1 MRI scan of human brainstem showing approximate locations of nuclei that mediate the control of respiration. The top left (saggital) scan shows the position of the slices A (superior pons), B (superior medulla), and C (inferior medulla). The nuclei in italics cannot be identified from the scans, and localization was performed by referring to a histological atlas.[33] All nuclei illustrated are bilateral, but only labelled on one side for clarity. *KF/PB*, Kölliker-Fuse and parabrachial nuclei; *VII*, facial nucleus; *NTS*, nucleus tractus solitarius; *PreBotC*, pre-Bötzinger complex (not identified yet in humans). Orientation: A, B, and C have the same orientation, although only labelled on A: D, dorsal; V, ventral; R, right; L, left.



Opiates also affect responsiveness to increasing concentrations of CO2

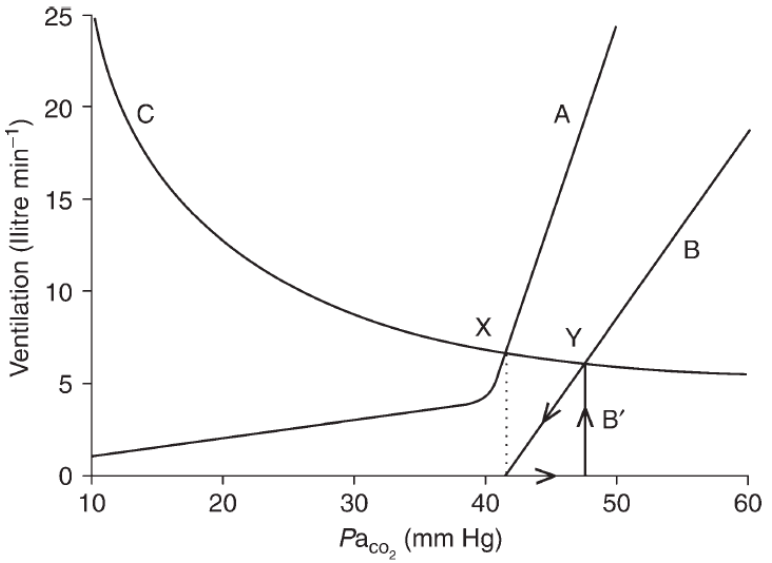


Fig 3 This diagram demonstrates how opiates can induce apnoea at the same Pa_{CO_2} as before opioid administration (dotted line) and also demonstrates that significant reductions in the HCVR only cause small changes in steady-state Pa_{CO_2}. Curve A represents the normal ventilatory response to CO_2 in an awake individual, demonstrating that ventilation is maintained at very low Pa_{CO_2} levels and that apnoea does not occur. Line B represents a 50% depression of the HCVR caused by opioid administration. A notable difference between curve A and line B is that in B apnoea can occur. Note also that in this case Pa_{CO_2} must rise to steady-state values (i.e. along the *x*-axis) for breathing to recommence (line B'). Curve C represents the CO_2 excretion hyperbola and demonstrates how changes in ventilation affect Pa_{CO_2}. Point X represents the awake state and point Y represents opioid-depressed breathing. Despite a 50% depression of the HCVR, the CO_2 changes only relatively modestly, illustrating the limited utility of single measurements of CO_2 in assessing respiratory depression. Figure reproduced with permission from Gross.[52]

Ordinarily, RR increases sharply when a pCO2 of around 40mmHg reached

Opiates suppress this response until much higher concentrations are reached

Investigations and treatment: opiate overdose

Differential diagnosis

- Overdose of another sedating drug – antipsychotics, benzodiazepines
- Pontine haemorrhage

Investigations

Definitely – naloxone challenge, ECG

Maybe – CXR, abdominal X-ray, urine drug screen

Treatment

Ventilation until they start fighting it

Be aware of half-life – heroin 4 hours, methadone 30 hours

Clinical scenario

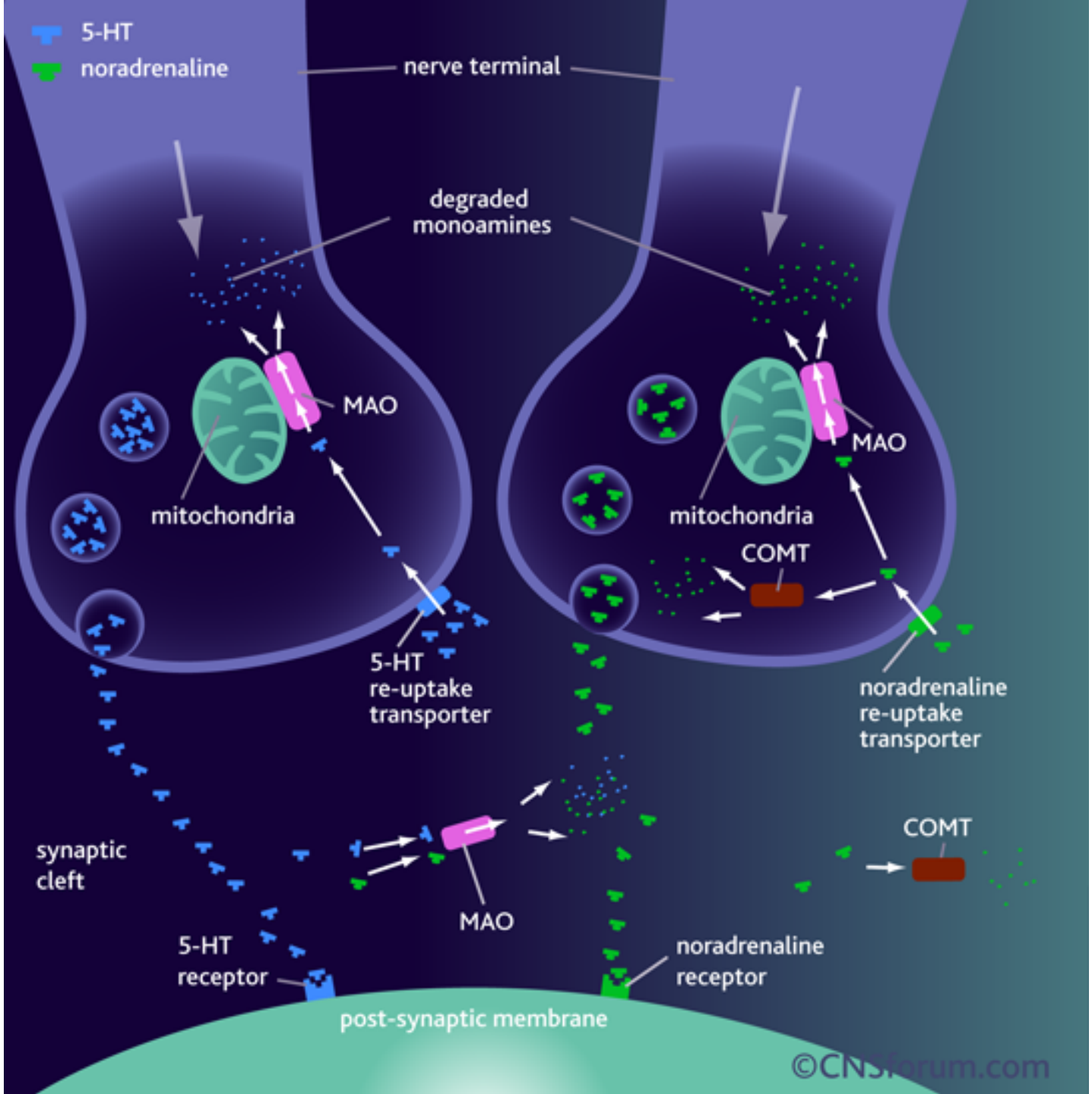
Mr Z is mute, perched on his trolley and bright red in the face. He does not answer any of your questions. You call the psychiatrist on call saying that this man 'is textbook crazy' and needs psych admission.

She comes to find you a while later, saying that it looks more like a delirium than anything else. She also contacted his wife, who was very concerned as he had been missing for several hours and she had found two empty bottles of his antidepressant in the bathroom.

The psychiatrist is worried that Mr Z is delirious from an overdose and that he needs investigation and treatment.

Tricyclic antidepressant overdose

- Tricyclic antidepressants are no longer first line for depression because of their toxicity in OD
- Ecological studies suggest a decreased rate of of suicide since SSRIs introduced
- However, amitryptiline particularly is still very commonly prescribed by GPs for treatment of insomnia and chronic pain


5-HT
noradrenaline
nerve terminal
degraded monoamines
MAO
mitochondria
5-HT re-uptake transporter
MAO
mitochondria
COMT
noradrenaline re-uptake transporter
synaptic cleft
MAO
COMT
5-HT receptor
noradrenaline receptor
post-synaptic membrane
©CNSforum.com

TCA overdose is complicated, because the pharmacology of TCAs is complicated

TCAs are ‘dirty drugs’/’rich pharmacology’

- Inhibit reuptake of NA and 5HT
- Alpha-adrenergic inhibition
- Muscarinic receptor antagonism
- Inhibit Na+/K+ ATPase pump in myocardial membrane

Clinically, antimuscarinic effects prominent

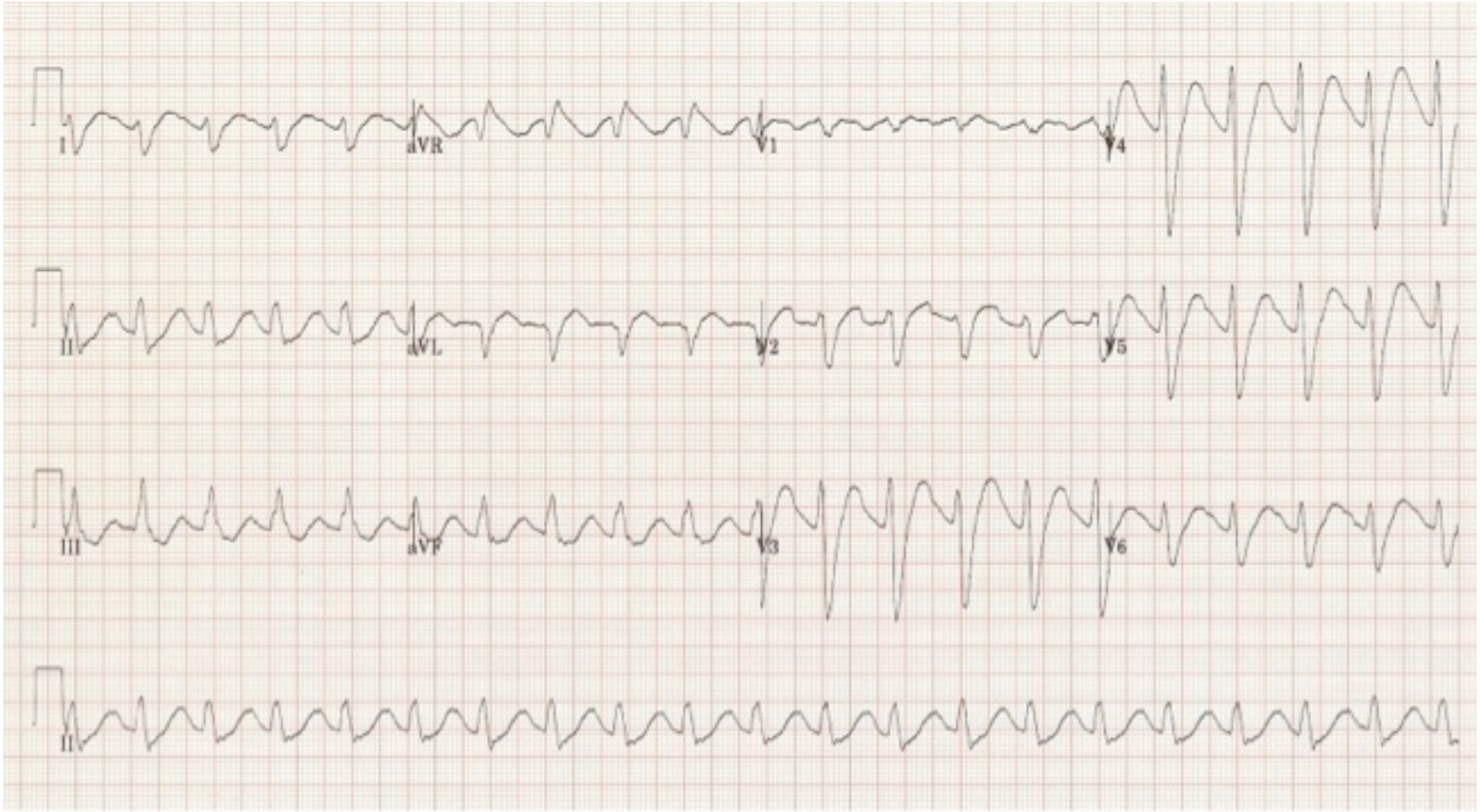
Muscarinic receptors are stimulated by acetyl choline

In the brain, ACh is important in alertness

In the periphery, ACh is important in

- Smooth muscle contraction
- Secretions – sweat, saliva

TCA overdose produces dangerous cardiotoxicity



Investigation and treatment: TCA overdose

- ECG and cardiac monitoring until 12-24 hrs normal ECG
- Arterial blood gas – acidosis
- Narrow differential – anti-arrhythmic OD, anti-cholinergic OD – antipsychotics, Nytol

Treatment

- IV fluids - correct hypotension
- IV sodium bicarbonate – increase sodium gradient across myocardial membrane, increase plasma protein binding by TCA – until pH 7.55
- Benzodiazepines for seizures

Assessment of risk in intentional overdose

Guiding principles:

Do this early

Collateral is very important

Have a plan for if the patient leaves/wants to leave

History

Circumstances of the attempt

- Intent
- Lethality of attempt
- Violence of attempt
- Planning
- Last acts
- Concealment
- How they feel now

History

Precipitants of the event:

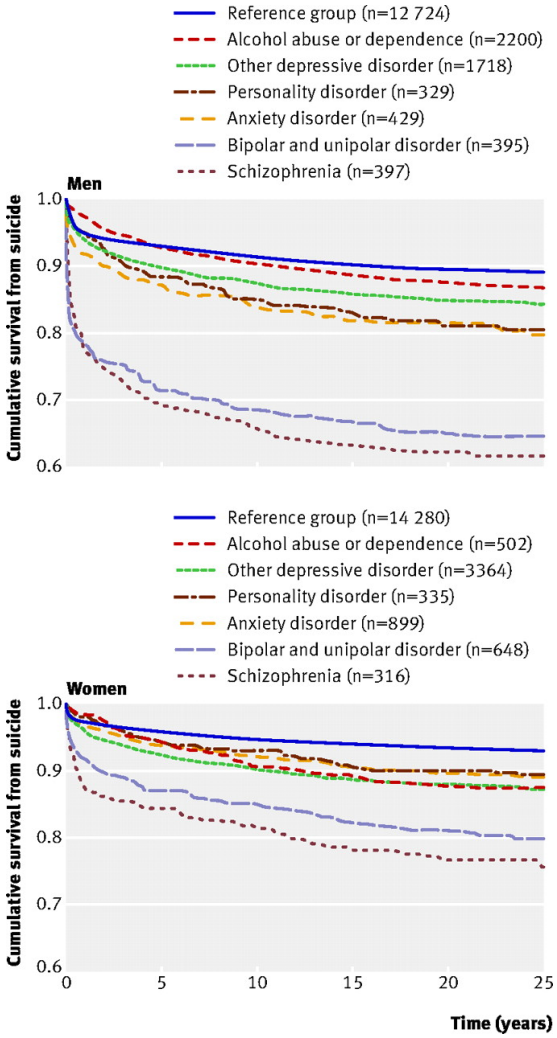
- Why now?
- Concurrent mental disorder
- Concurrent substance misuse/dependence
- Support
- Protective factors

History

Predisposing factors:

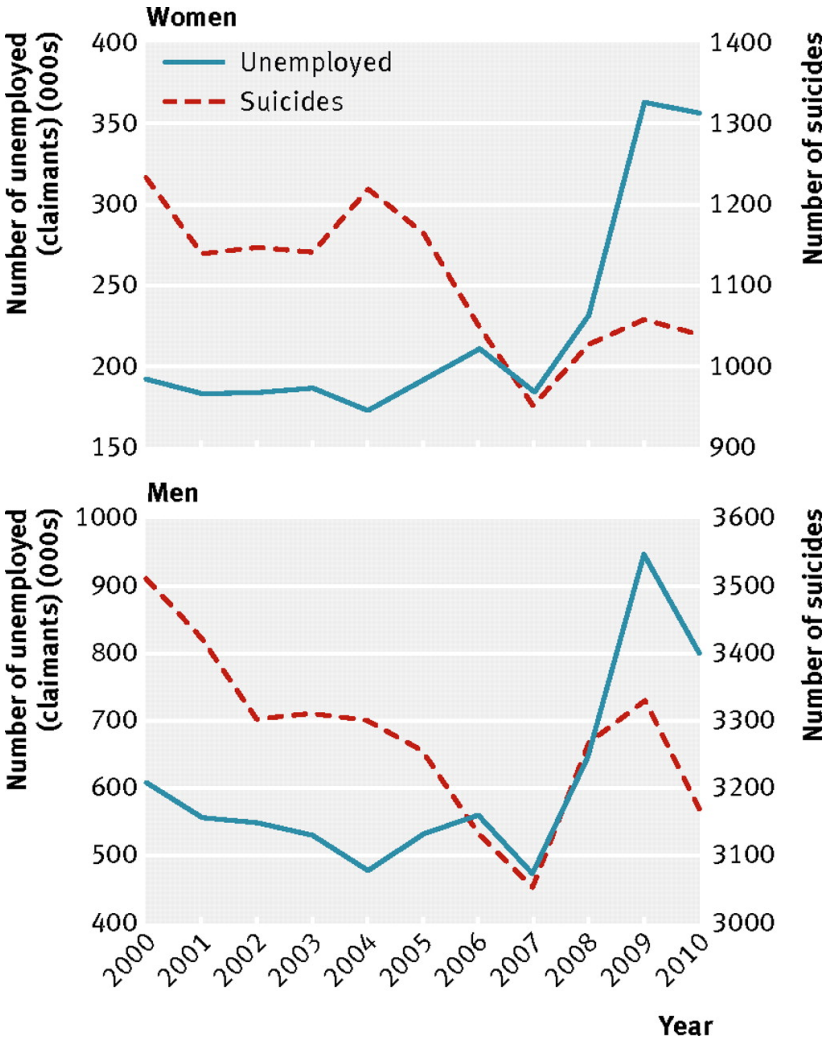
- Previous attempt
- Older age
- Male sex
- Unemployment
- Psychiatric history
- Family history of suicide
- Availability of means

Survival graphs for suicide by psychiatric disorder in people admitted to hospital during 1973-82 for attempted suicide in Sweden and followed to 2003.



Tidemalm D et al. BMJ 2008;337:bmj.a2205

Trends in the numbers of suicides and unemployment claimants in England, 2000-10, by sex.



Barr B et al. BMJ 2012;345:bmj.e5142

Deaths by jumping from Clifton Suspension Bridge halved after placement of barriers

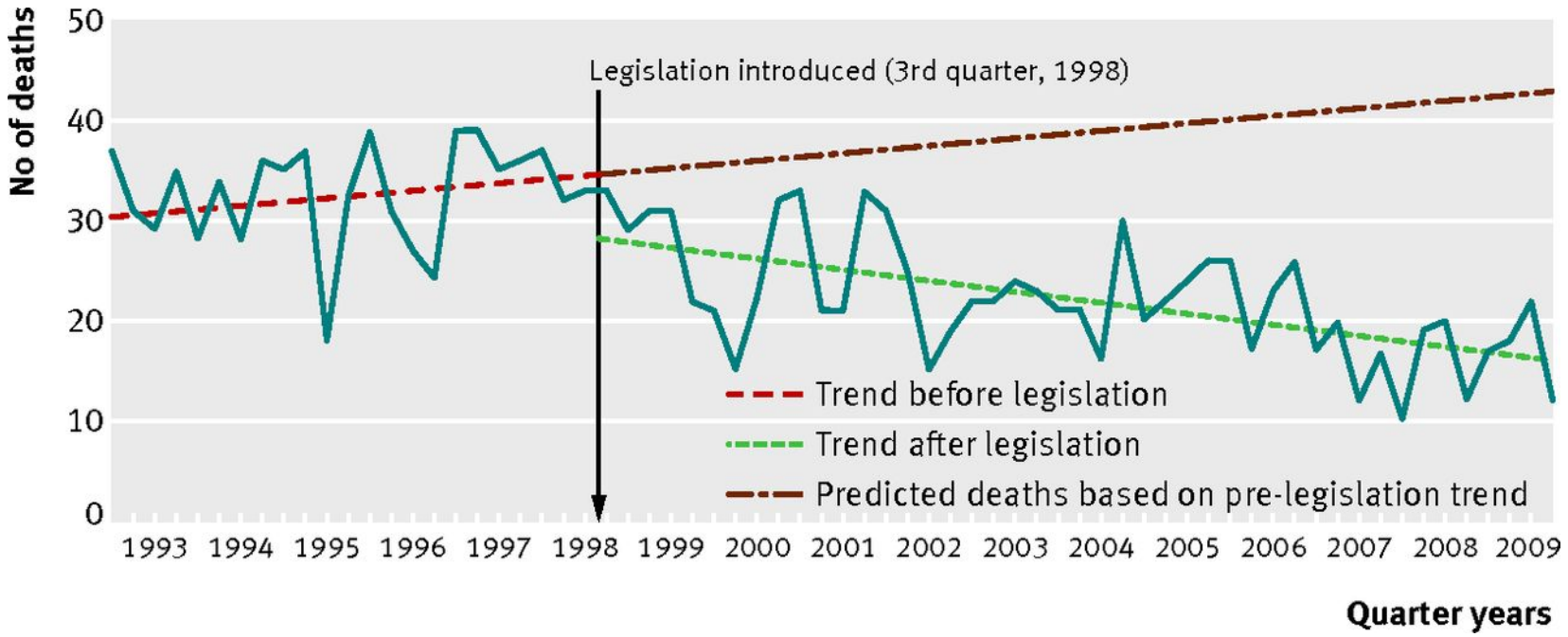
Table 1 Suicides by jumping before (1994–98) and after (1999–2003) the installation of preventive barriers on the Clifton suspension bridge

Site of suicide by jumping	1994–1998	1999–2003	Difference in means (95% CI)[1]	*P*
Clifton suspension bridge				
All suicides				
Deaths/year, mean	8.2	4.0	−4.2 (−5.9 to −1.4)	0.008
Total deaths	41	20		
Male				
Deaths/year, mean	8.0	3.0	−5.0 (−2.6 to −6.3)	0.001
Total deaths	40	15		
Female				
Deaths/year, mean	0.2	1.0	0.8 (−0.08 to 8.4)	0.1
Total deaths	1	5		
Sites in Bristol other than the suspension bridge				
All suicides				
Deaths/year, mean	6.2	8.4	2.2 (−0.9 to 7.2)	0.2
Total deaths	31	42		
Male				
Deaths/year, mean	5.2	5.2	0 (2.2 to −3.8)	1.0
Total deaths	26	26		
Female				
Deaths/year, mean	1.0	3.2	2.2 (0.2 to 7.7)	0.023
Total deaths	5	16		
All sites in England and Wales (rates per 100 000)				
All suicides	0.34	0.36	0.02 (0.01 to 0.06)	0.2
Male	0.54	0.53	−0.01 (−0.07 to 0.06)	0.8
Female	0.15	0.20	0.05 (0.01 to 0.10)	0.005

1. Poisson regression analyses.

Bennewith, BJPsych 2007

Fig 1 Suicide and open verdict deaths involving paracetamol only, in people aged 10 years and over in England and Wales, 1993-2009, and best fit regression lines related to 1998 legislation .



Hawton K et al. BMJ 2013;346:bmj.f403

Lithium treatment decreases suicide in bipolar disorder

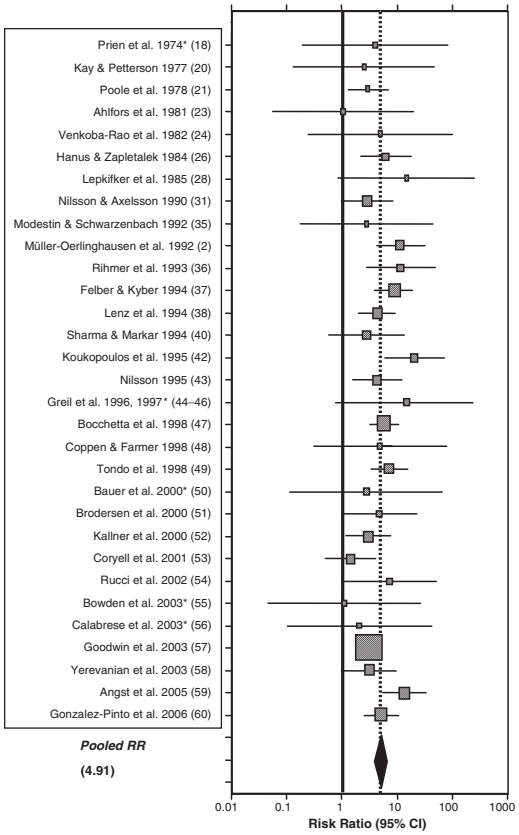


Fig. 1. Forest plot Risk Ratios (RR) as shaded squares proportional to study weight and their 95% confidence intervals (CI) base on random-effects meta-analysis of suicidal risk [rates of suicides and/or attempts per 100 person-years ('%/year')] in 31 studies, wi two arms (with and without lithium treatment) and non-zero suicidal risk in at least one arm (see Table 1) (2, 18, 20, 21, 23, 24, 26, 2 31, 35–38, 40, 42–60). The computed pooled risk ratio (RR) (black diamond) = 4.91 (95% CI 3.82–6.31, $z = 12.5$, $p < 0.0001$). *Randomized, controlled trials.

Public health interventions are of crucial importance in reducing completed suicide

Our day-to-day role as doctors involves identifying and treating mental illness

Lithium decreases risk of suicide by ~5x in bipolar disorder

Alcohol detoxification reduces risk of suicide in alcohol dependence

Baldessarini Bipolar Disorder 2006

Empathy

‘When people are suicidal, their thinking is paralyzed, their options appear spare or non-existent, their mood is despairing and hopeless permeates their entire mental domain. The future cannot be separated from the present, and the present is painful beyond solace. “This is my last experiment” wrote a young chemist in his suicide note. “If there is any eternal torment worse than mine, I’ll have to be shown”.

- Kay Redfield Jamison

Managing your emotions

Suicidal behaviour is difficult to process emotionally

Interacting with patients in general may give rise to uncomfortable emotions

Be aware of unconscious rules you have about how patients should behave towards you – compliance with your advice etc. and how you feel when they don't play by your rules

It is very important not to let these emotions influence your clinical judgement or professionalism

In other words: be kind.

Also talk about your difficult emotions in supervision or ask your friendly liaison psychiatrist for advice about dealing with them

‘I remember sitting in his office a hundred times during those grim months and each time thinking, What on earth can he say that will make me feel better or keep me alive? Well, there never was anything he could say, that’s the funny thing. It was all the stupid, desperately optimistic, condescending things he didn’t say that kept me alive; all the compassion and warmth I felt from him that could not have been said; all the intelligence, competence, and time he put into it; and **his granite belief that mine was a life worth living**’.