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Deprescribing Antidepressants: An evening with Dr Mark Horowitz

This session will start shortly

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Deprescribing Antidepressants: An evening with Dr Mark Horowitz

F2F and Zoom webinar – 17 March 2025 and 6.30 pm

Presenters

Dr Mark Horowitz

Dr Anna Seth

Angus Thompson

Acknowledgement of traditional owners

We acknowledge the Tasmanian Aboriginal people as the traditional owners and ongoing custodians of the land on which we are meeting today. We pay our respects to Elders past and present.

We would also like to acknowledge Aboriginal people who are joining us today.

Learning outcomes

After this session, I will be able to:

- ✓ Outline approaches to antidepressant deprescribing that may be unsuccessful
- ✓ Develop confidence to discuss antidepressant deprescribing strategies with patients
- ✓ Differentiate clinical features of antidepressant withdrawal from other causes of similar symptoms
- ✓ Identify key resources to support antidepressant deprescribing in clinical practice, including evidence-based guidelines, tools, and patient education materials

Deprescribing

MedsAware
Deprescribing Action Week
10–16 March 2025
EMPOWERING **SAFE AND SUSTAINABLE** USE OF MEDICINES

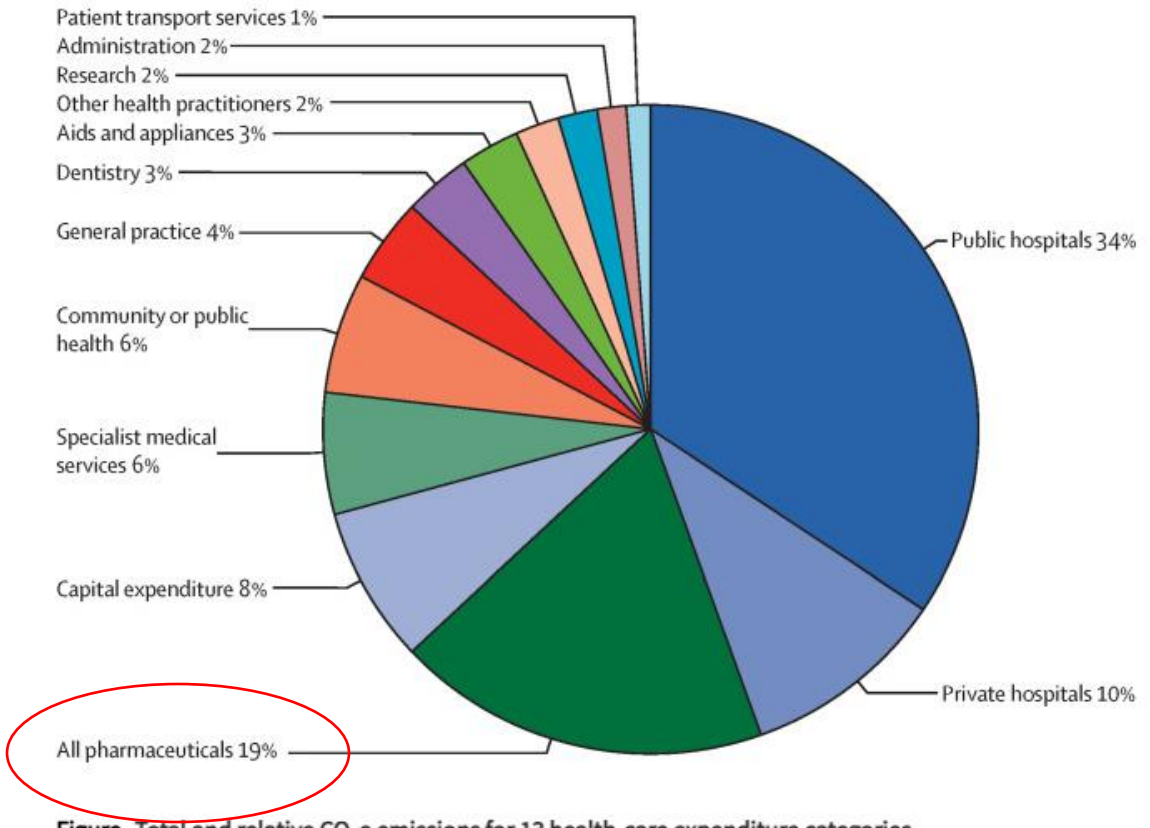
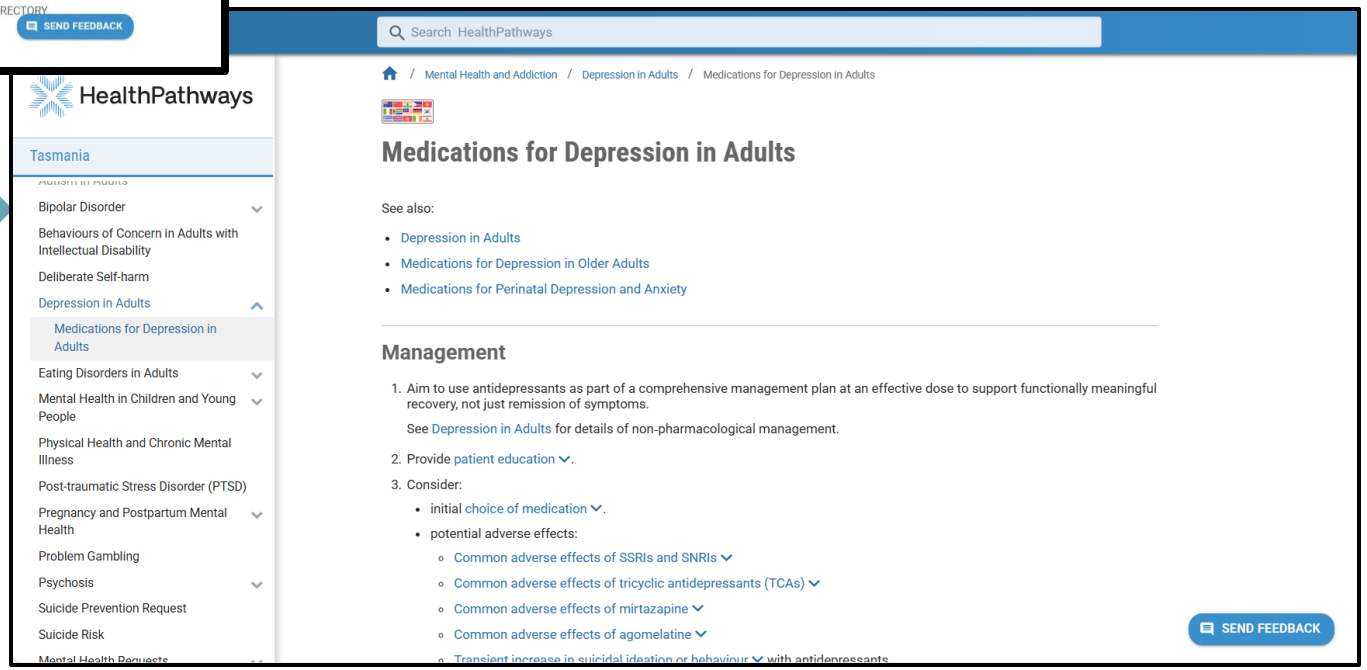


Figure Total and relative CO_2e emissions for 13 health-care expenditure categories

Malik A et al- Lancet Planetary Health 2018

Tasmanian HealthPathways



Resources

Tasmanian HealthPathways

RC PSYCH ROYAL COLLEGE OF PSYCHIATRISTS

Stopping antidepressants

This information is for anyone who wants to know more about stopping antidepressants.

It describes:

- why someone might choose to stop taking their antidepressant
- how to do so safely
- symptoms that you may get when stopping an antidepressant
- some ways to reduce or avoid these symptoms.

This patient information accurately reflects recommendations in the NICE guidance on depression in adults: www.nice.org.uk/guidance/ng222

RELEASE
REdressing Long-tErm Antidepressant uSE

Stopping Antidepressants

Depression in adults: treatment and management

NICE guideline [NG222] Published: 29 June 2022 Register as a stakeholder

RELEASE printable resources

- Stopping antidepressants
  - Stopping Antidepressants.pdf 757.6KB
- How family & friends can help
  - How family & friends can help.pdf 750.1KB
- Is now the time for me to stop antidepressants?
  - Decision Aid.pdf 178.1KB
- Letter for patients to take to pharmacist
  - Letter for patients to take to pharmacist.pdf 92.6KB

RELEASE antidepressant tapering plans

- 1 Sertraline faster.pdf 276.0KB
- 1 Sertraline slower.pdf 297.7KB
- 1 Sertraline even slower.pdf 310.2KB

Mental health prescribing by state/territory

- Data for 2022/3, shows that overall prescribing of mental-health related medications was higher in Tasmania than any other state or territory in Australia

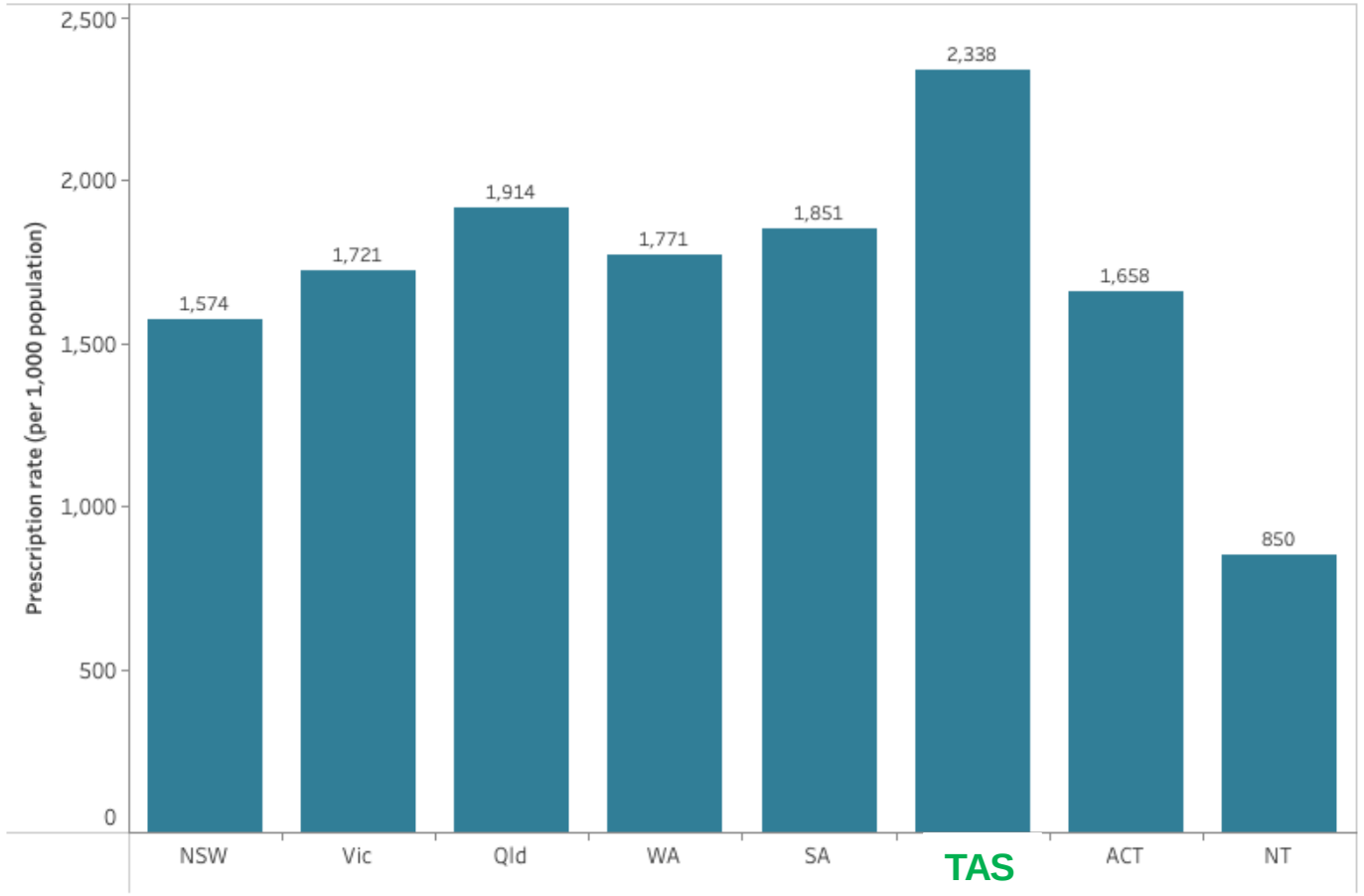


Figure PBS.3: Number of mental health-related prescriptions per 1,000 population, by states and territories and medication type, 2022–23.

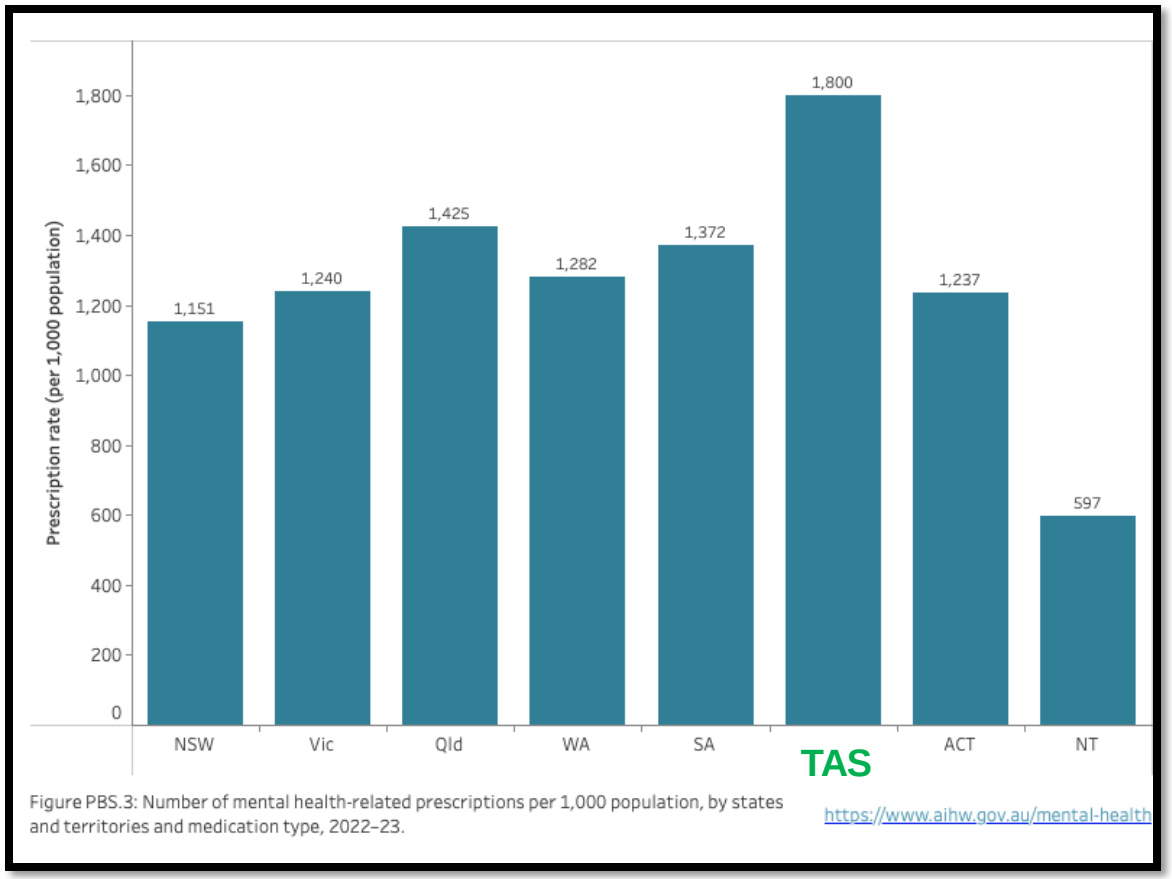
https://www.aihw.gov.au/mental-health

Source: https://www.aihw.gov.au/mental-health/topic-areas/mental-health-prescriptions

Antidepressant/anxiolytic prescribing by state/territory

- This is primarily driven by prescribing of two types of psychotropics

Antidepressants



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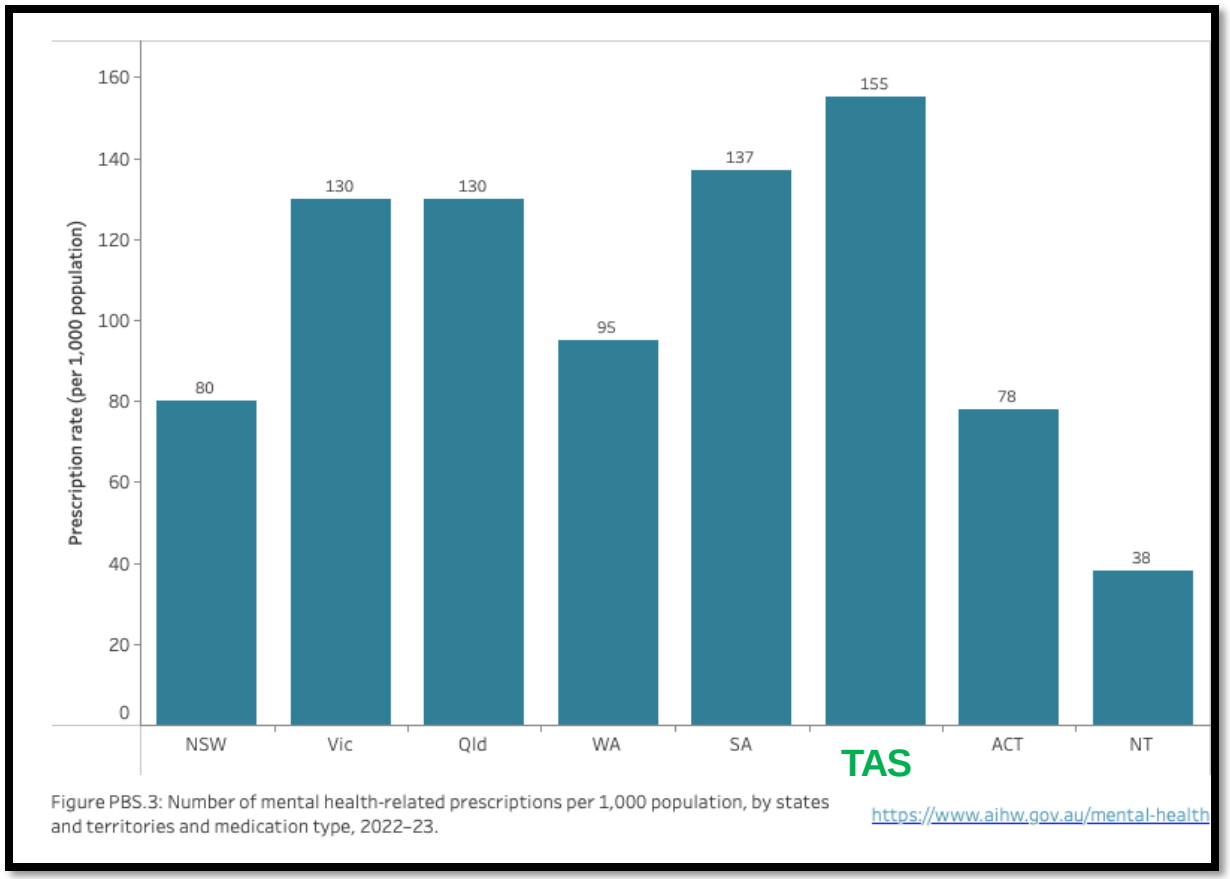
Anxiolytics



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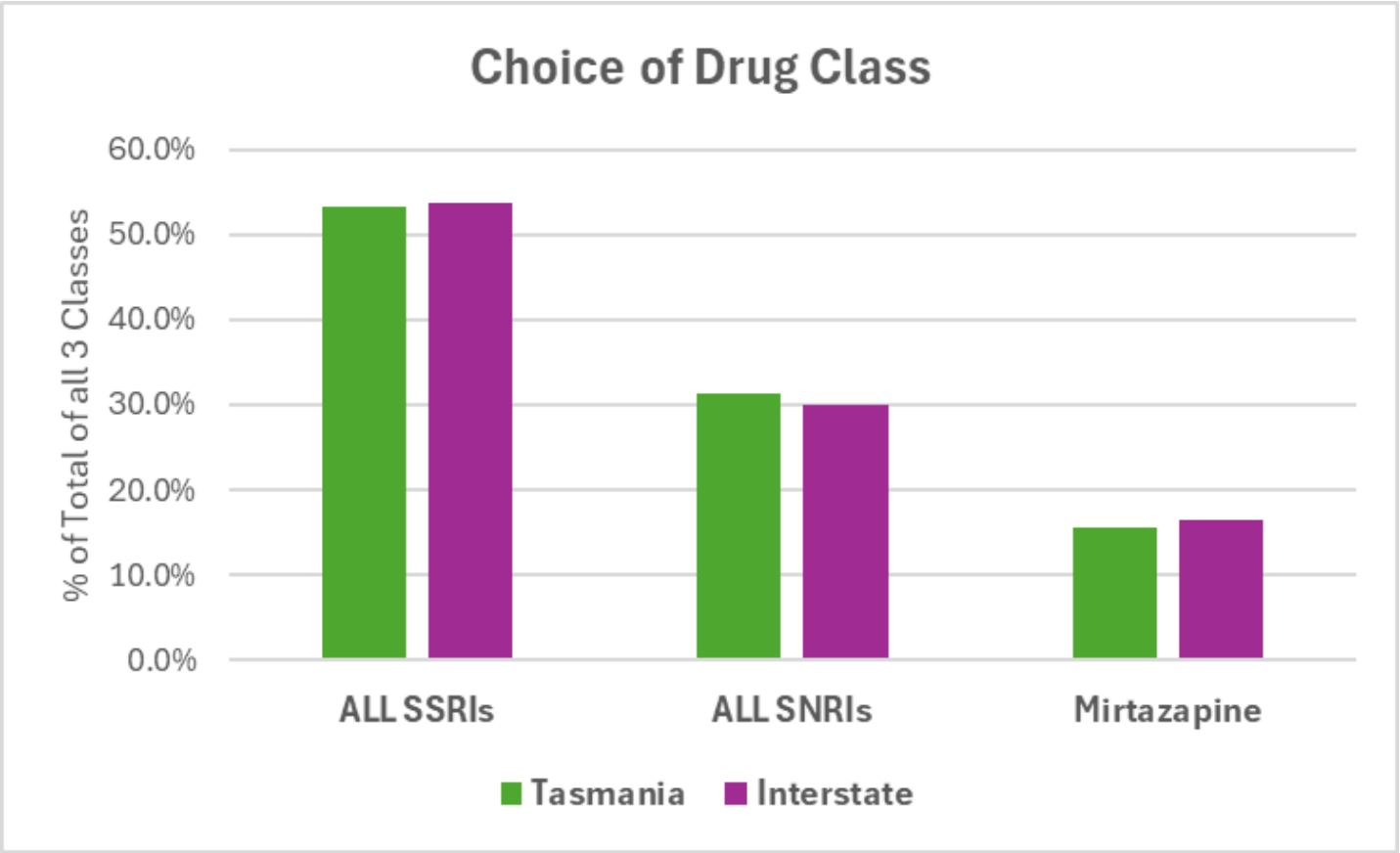
Source: https://www.aihw.gov.au/mental-health/topic-areas/mental-health-prescriptions

Drug class choice in Tasmania and Interstate

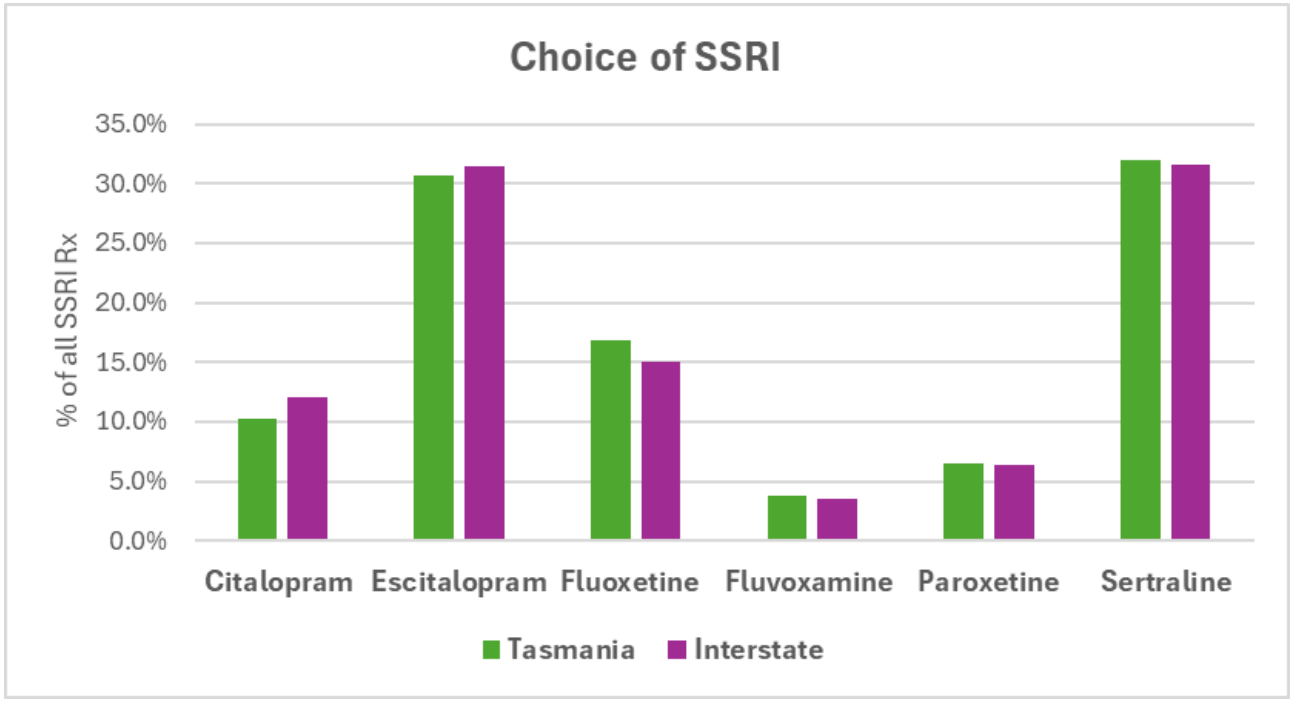
- The profile of drug classes used is very similar

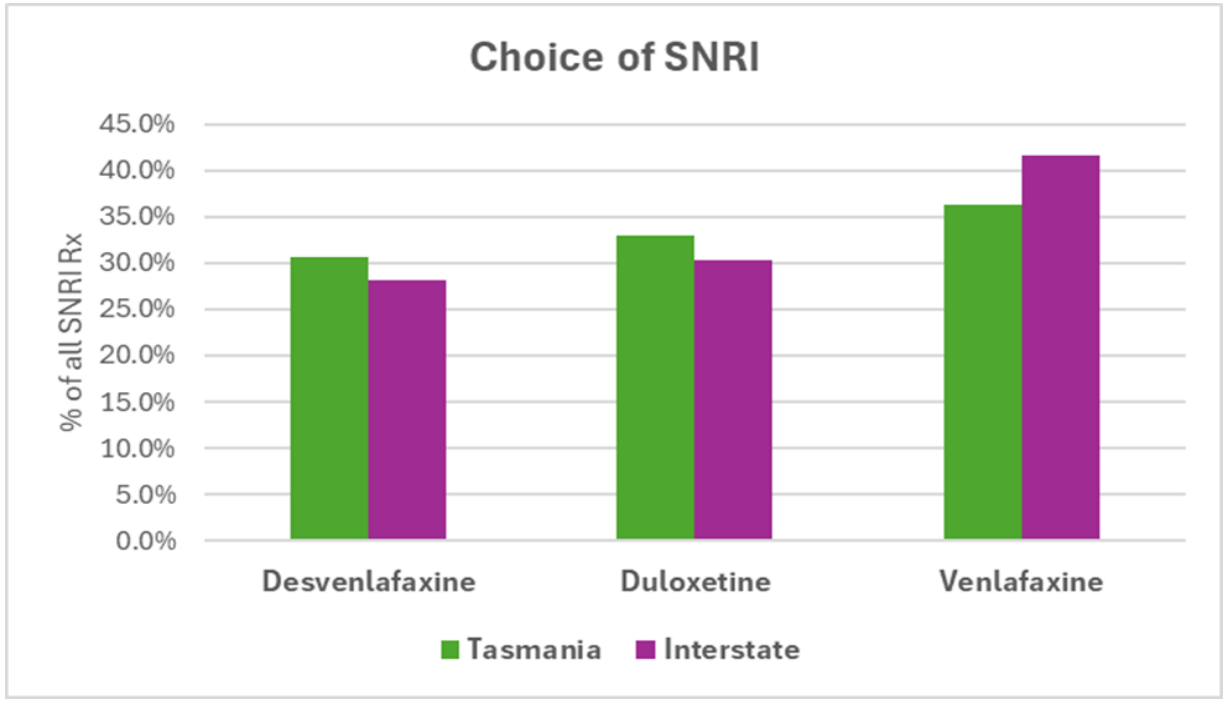


*Source: http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

SSRI and SNRI choice in Tasmania and Interstate

- The choice of specific SSRIs and SNRIs is also very similar





*Source: http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

Antidepressant prescribing in Tasmania

- More recent data* for the year to June 2024, shows over half a million PBS prescriptions were dispensed for SSRIs, SNRIs and mirtazapine alone in Tasmania
- This would suggest that approximately 1 in 12 Tasmanians are taking one of these classes of antidepressant
- Looking at individual drugs, the 4 most widely prescribed were:
  - Sertraline ~87k Rx
  - Escitalopram ~84k Rx
  - Mirtazapine ~79k Rx
  - Venlafaxine ~58k Rx

***Source:** http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp*

Presenters

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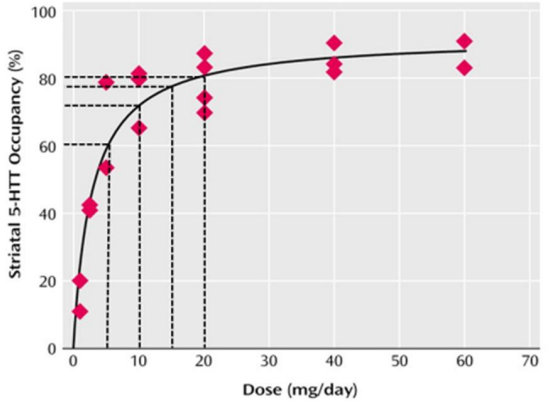

Antidepressant withdrawal effects and safe deprescribing

Dr Mark Horowitz BA, BSc, MBBS, MSc, PhD (IoPPN, KCL)
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Clinical Research Fellow in Psychiatry (UCL, NELFT)
Lead clinician – Psychotropic drug Deprescribing Clinic (NELFT)
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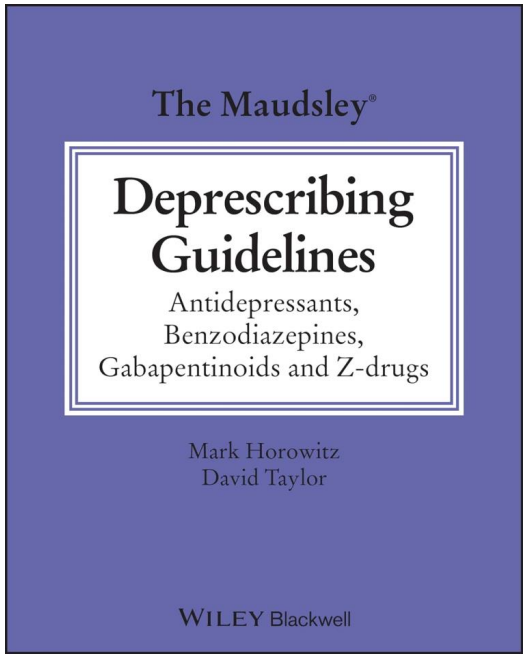


NELFT NHS
NHS Foundation Trust

KING'S College LONDON

UCL

Patient montage

Australian antidepressant use

- 1 in 7 people (1 in 6 adults) in Australia on an antidepressant, about 3 million people
- Average duration of use is 4 years
- Most guidelines recommend 6-12 months of use for an episode of anxiety or depression
- Oz amongst highest users of antidepressants in OECD
- Sertraline and escitalopram now in top 10 most prescribed drugs in Oz
- 1.5 fold more women than men
- 2-fold increase for older people
- More likely to be prescribed to poorer, inner regional regions

Long-standing Australian guidance on antidepressant withdrawal

- Historically (TG, RANZCP, etc): “Discontinuation symptoms are usually mild and last 1 to 2 weeks (but can last a month or longer in some patients).”
- This description was influenced by papers produced by drug companies in the 1990s, which focused on people who had used antidepressants for 8 - 12 weeks
- At a consensus panel organised by an antidepressant manufacturer the euphemism ‘discontinuation symptoms’ was coined and numerous papers with the description ‘brief and mild’ were distributed to clinicians

Australian guidance on management of antidepressant withdrawal syndrome

- RANZCP: for those with ‘risk factors’, reduce to minimum effective, half dose for a week, reduce by dividing tablets every 2 weeks, then stop. No guidance for venlafaxine or duloxetine.
- Identical guidance in the UK was based on one study that showed that abruptly stopping caused too severe withdrawal effects (Rosenbaum et al., 1998), and that 4 weeks was considered a reasonable time by the committee (i.e. no evidence)
- Most common approach in practice: reduce dose by half for 2 weeks, reduce dose to quarter for 2 weeks (often by alternating half a tablet every second day)
- Recent RCT found that 40% of patients on ADs >1-2 years who did not meet guidelines for ongoing use, low risk of withdrawal can come off by tapering over 2-4 months (ie slower than guidelines in Oz suggest).
- Leaves at least 60% of patients trapped on their medications with current approaches

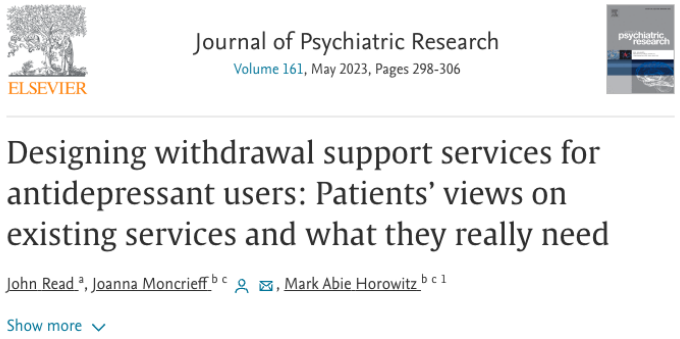
Consequence: people turn to peer support websites online for guidance

750,000 hits a month

150,000 hits a month

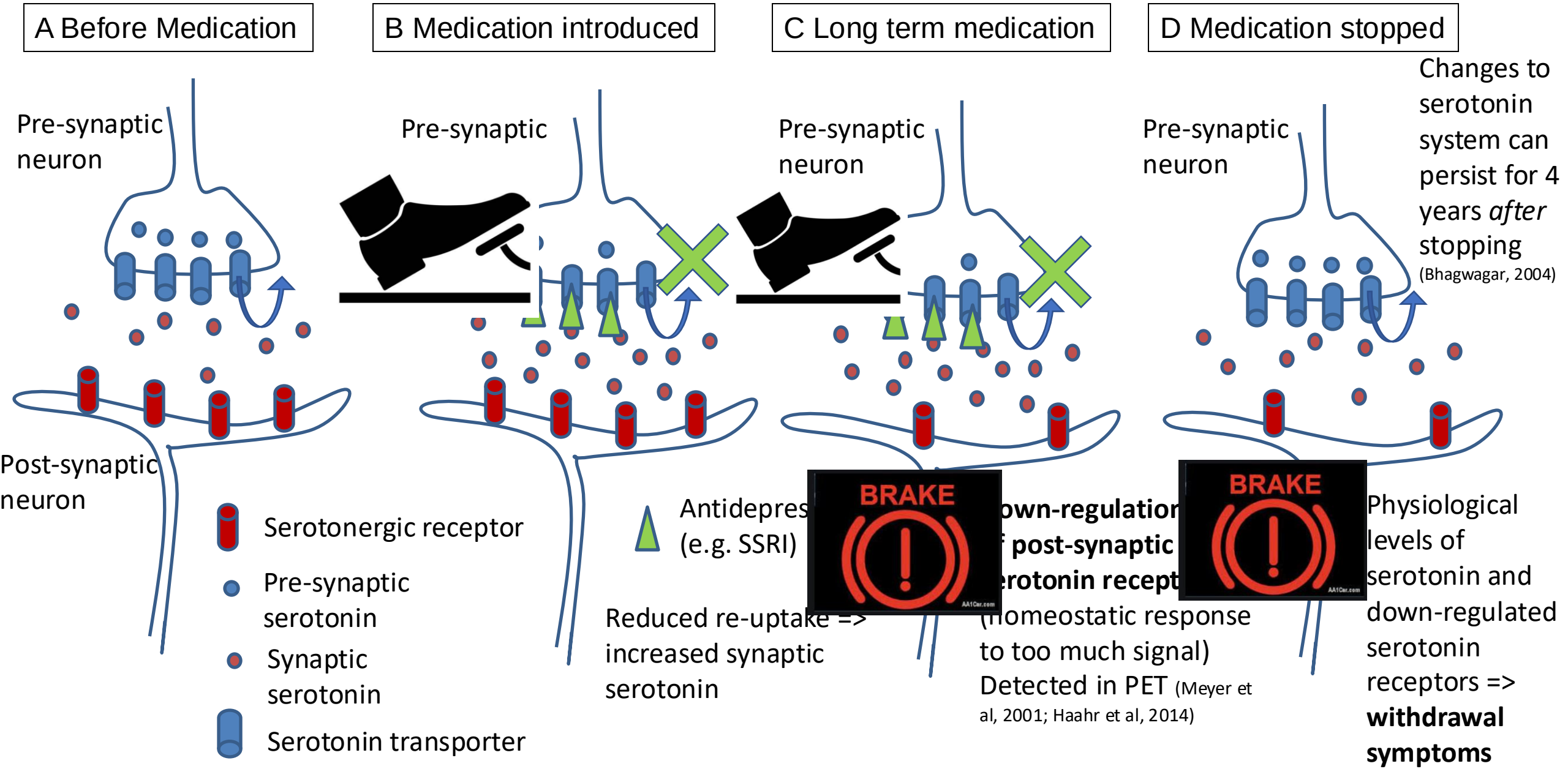
- Commonest story: my doctor told me to stop taking my antidepressant over between 0 and 4 weeks
- The effects were so horrendous that I had to go back on them.
- The doctor told me there shouldn't be a problem with coming off them, so that it must be my original condition coming back, diagnosed me with relapse, informed me I should be on this drug life-long
- But it felt different to my original condition eg I had dizziness/brain zaps/panic attacks for the first time
- So I have lost faith in my doctor. The advice on this website was more helpful than my doctor.
- Coming off much more slowly than they suggest – **at 10% of the most recent dose every month (so that reductions become smaller and smaller as the total dose lowers** - has made the process much easier (although still not easy).

Patients' experience and what they want



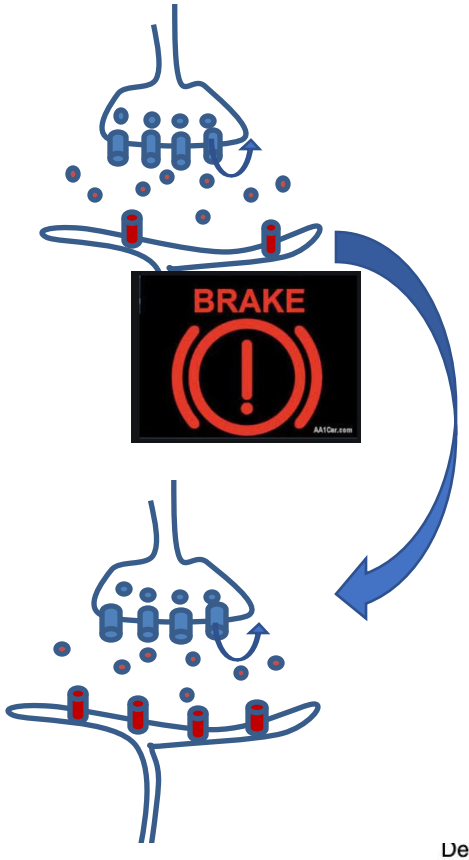
- 71% of respondents found their doctors' advice unhelpful. Main reasons:
  - 'Recommended a reduction rate that was too quick for me',
  - 'Not familiar enough with withdrawal symptoms to advise me' and
  - 'Suggested stopping antidepressants would not cause withdrawal symptoms'
- The most common tapering period suggested by doctors was 2 weeks and 4 weeks
- What patients wanted:
  - 'Access to smaller doses (e.g. tapering strips, liquid, smaller dose tablets) to ensure gradual reduction' (88%) and
  - 'A health professional providing a personalised, flexible reduction plan' (79%).

Effect of long-term antidepressant use and stopping

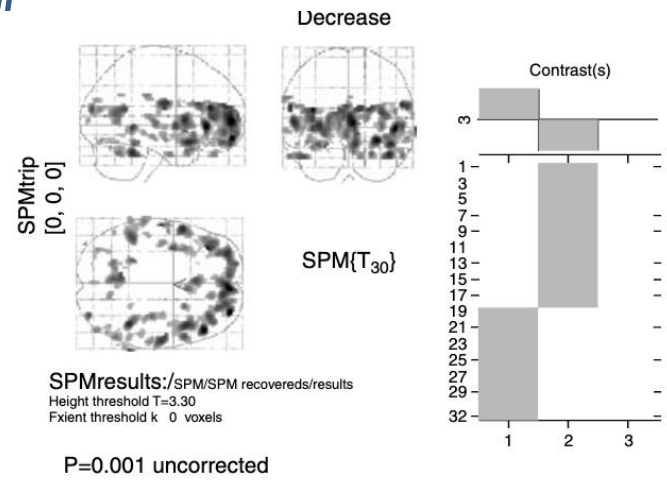


Duration of withdrawal symptoms

- In many studies, withdrawal symptoms went for months or years
- How can symptoms last so long after the drug is out of the body?
- It is the time taken for adaptations (changes) to the drug to resolve that determines the length of the time for withdrawal – not how long it take the drug to be eliminated from the body (sound analogy)
- Long-term use of antidepressants can cause long-term changes to the brain that might account for long-term symptoms:
  - In patients there are changed to the serotonin system (reduced receptors) that has been detected for up to 4 years after stopping (Bhagwagar, 2004)
  - In animal studies (Renoir, 2013) there are changes to the hormonal system and serotonin system that persist for more than a year (in human equivalent time) after stopping



Time taken for down-regulation (and downstream effects) to return to 'pre-drug' conditions



Antidepressant withdrawal syndrome

- Physiological symptoms that occur on stopping – or reducing the dose – of an antidepressant
- They can manifest in either psychological or physical symptoms (these drugs affect multiple bodily systems)
- Occur because changes (adaptation) to the brain caused by the drug use take time to resolve
- Withdrawal symptoms do not require addiction (compulsion/craving etc) but only adaptation (often called physical dependence – though this term has become conflated with addiction unfortunately) - addiction involves craving, compulsive use etx – not relevant to antidepressants
- Caffeine, etc cause physical dependence which predicts withdrawal on stopping (no need for ‘high’, misuse, abuse, etc) – as for antidepressants.
- The greater the degree of adaptation (high dose, longer use, etc) the greater the withdrawal effects – the ‘flip-side’ of withdrawal is tolerance which is seen with antidepressants (‘poop out’ in America, lessening of some side effects, drug effect wearing off)

Antidepressant withdrawal syndrome

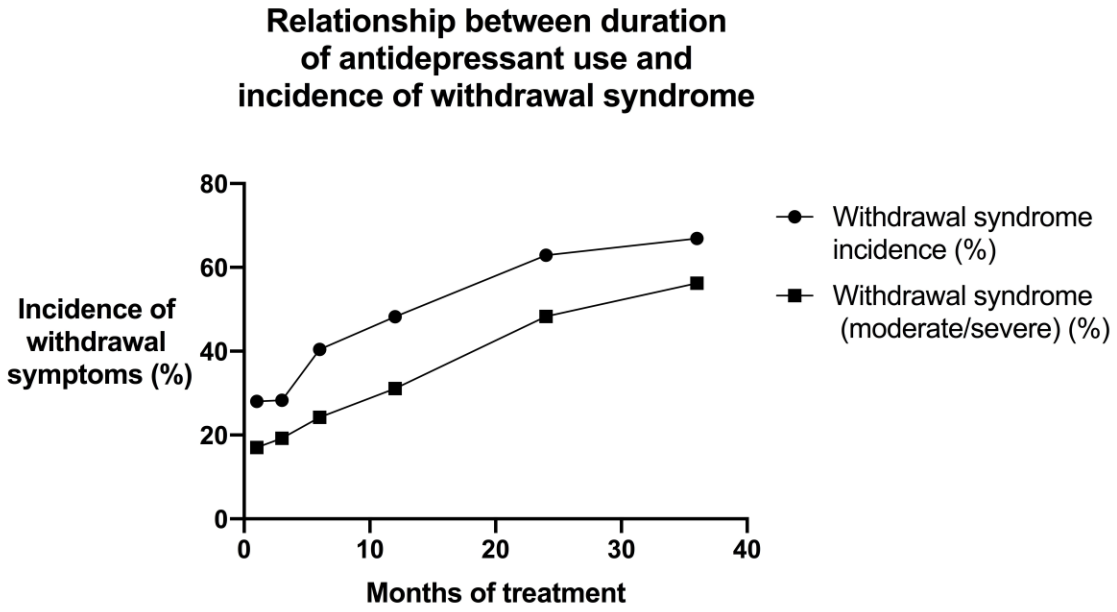
- Most common withdrawal symptoms are (Fava et al. 2015) :
  - **Dizziness**, insomnia, impaired concentration, fatigue
  - Headache, tremor, tachycardia, nightmares
  - Affective symptoms: *depressed mood*, irritability, *anxiety, panic attacks*
  - Sensory symptoms: 'Electric-shock' sensations in the head (often on moving eyes), or in limbs
  - Gastrointestinal symptoms: nausea, vomiting, diarrhoea
  - Increase in suicide attempts in the 2 weeks after stopping an antidepressant (Valuck et al., 2009)
  - Akathisia – this is most recognised as a side effect of long-term antipsychotic use but can occur in withdrawal from antidepressants (and other psychiatric drugs) – involving pacing, a sense of terror, often described as the 'feeling like the nervous system is on fire' – high risk of suicide. Often mis-diagnosed as agitated depression, mania when clinicians are not familiar

Mis-diagnosing antidepressant withdrawal effects as relapse

- Reported to occur by patients often but not studied in detail
- We surveyed 1400 people out of the 180,000 on peer support websites for tapering off antidepressants (and other similar drugs) – main reason given for being there
- Withdrawal symptoms can include *anxiety, depressed mood, insomnia, appetite changes* (even in people with no underlying mental health condition e.g. those prescribed for migraine)
- Easy to confuse with relapse of depression or anxiety (especially when withdrawal thought to only be 'mild and brief')
- Clues to distinguish withdrawal from relapse:
  - Quick onset, but can be delayed (?perhaps because of slower dissociation from central compartment)
  - Specific symptoms (dizziness, electric shock, other symptoms not present in baseline condition)
  - Often quick resolution on re-instatement of antidepressant (hours, day or two)
- Can also be mis-diagnosed as chronic fatigue syndrome, medically unexplained syndrome, neurological disorder, onset of a new psychiatric disorder, etc

How common, severe and long-lasting are withdrawal symptoms

- A review found from an average of 14 trials that measured incidence that **about half of patients (56%) experienced withdrawal symptoms** (Davies and Read, 2018)
- In surveys, about half (46%) of patients reported that their symptoms were ‘severe’
- The longer patients take antidepressants the more likely they are to experience withdrawal symptoms and for those symptoms to be severe



Protracted antidepressant withdrawal syndrome

- Withdrawal syndromes that can last for months or years increasingly recognised for antidepressants (Hengartner, 2020; Guy, 2020; Cosci 2020)
- These can be debilitating and involve neurological, psychological and other bodily symptoms (similar to symptoms for acute withdrawal)
- People can be bed-bound, lose jobs, relationships, experience financial difficulties
- Very poor recognition by medical community, due to limited education, who generally perceive it as relapse (despite numerous distinguishing features) or other physical conditions (Guy et al, 2020)
- Now, 100,000s of people on peer support sites looking for support for these problems because they can't get suitable help from their medical providers (White et al 2020, Read et al 2023)

		Experienced any severity of this symptom BEFORE starting antidepressants	Experienced new onset or worsening of this symptom AFTER stopping
Psychological	Impaired concentration	41.4%	93.0%
	Worsened mood	57.3%	92.5%
	Feeling suicidal	29.6%	60.7%
	Emotional numbing	42.6%	74.1%
Neurological	Electric shocks ('brain zaps')	5.6%	76.8%
	Akathisia/internal sensation of buzzing and tension	11%	63.5%
	Increased sensitivity to light, sound	22.3%	79.2%
	Tinnitus	17.6%	60.7%
	Vivid dreams	27.9%	73.4%
Somatic	Nausea	15.2%	71.1%
	Muscular problems		
	Dizziness/light-headedness	17.9%	88.7%
	Fatigue	61.5%	93.0%
	Diarrhoea	24.4%	73.7%
	Sexual numbing/ unpleasant genital arousal	28.3%	66.1%

0-33%
34-66%
67-100%

Moncrieff et al, JAD Reports, 2024

Updates in official guidance on withdrawal

- For the last two decades the NICE guidelines has described withdrawal effects from antidepressants as “brief and mild” “lasting a week or two”
- In 2019 the Royal College of Psychiatrists reported that patients should be informed of “the potential in some people for **severe and long-lasting withdrawal symptoms** on and after stopping antidepressants”
- NICE in 2021: “[Withdrawal symptoms] can last longer (in some cases, several weeks, occasionally **several months**) and can sometimes be severe, particularly if the antidepressant medication is stopped suddenly.”
- Minimal update to TG/other guidelines

How to minimise withdrawal symptoms by safely tapering

Why deprescribe antidepressants?

- Medication no longer needed
  - Stressor resolved (many patients prescribed these drugs in the context of divorce, job loss, physical health problem, death in family, etc – with relapse unlikely)
  - Alternative coping skills developed
  - Use for longer than guidelines recommend (mostly recommend 6-12 months for uncomplicated depression or anxiety): 30-50% of patients do not meet criteria for ongoing use (Kendrick, 2021)
- Improve quality of life by removing unwanted effects (harms outweigh benefits)
  - Sexual side effects > 50%
  - Emotional numbing >50% (main reason people come to our clinic)
  - Fatigue, impaired memory, concentration
  - Insomnia, worsened anxiety or depression (tardive dysphoria)
  - Weight gain (30%)

Why deprescribe antidepressants? 2

- Avoid health consequences. In long-term observational data all are increased in antidepressant users (with debate about the degree attributed to antidepressants or underlying condition):
  - Strokes; Obesity; Falls; Cardiovascular disease; Osteoporosis; Premature mortality
- Patient wishes to stop
  - Desire to pursue alternative strategies
  - Woman wishes to become pregnant (antidepressants increase risk of foetal abnormality 2.5 to 3-fold (from low base rate))
- Reduce pill burden, interactions with other medication

The serotonin hypothesis of depression


Molecular Psychiatry www.nature.com/mp

SYSTEMATIC REVIEW OPEN

Check for updates

The serotonin theory of depression: a systematic umbrella review of the evidence

Joanna Moncrieff[1,2✉], Ruth E. Cooper[3], Tom Stockmann[4], Simone Amendola[5], Michael P. Hengartner[6] and Mark A. Horowitz[1,2]

- It is now broadly held by academic psychiatrists that the serotonin/monoamine hypothesis is not supported
- The Royal College of Psychiatrists said: “the old idea that ADs [antidepressants] correct a chemical imbalance in the brain is an over-simplification and we do not support this view”. Their leaflet on depression no longer mentions low serotonin as a potential cause of depression
- Prominent psychiatric thought leaders have rejected it
  - The American Psychiatric Association has said “Additional experience has not confirmed the monoamine depletion hypothesis”
  - Prominent UK academic psychiatrists have said “the serotonin theory of depression has not been clearly substantiated” (Cowen and Browning, 2015)
  - Reference to chemical imbalance in depression removed from RANZCP website

Why deprescribe antidepressants? Barriers

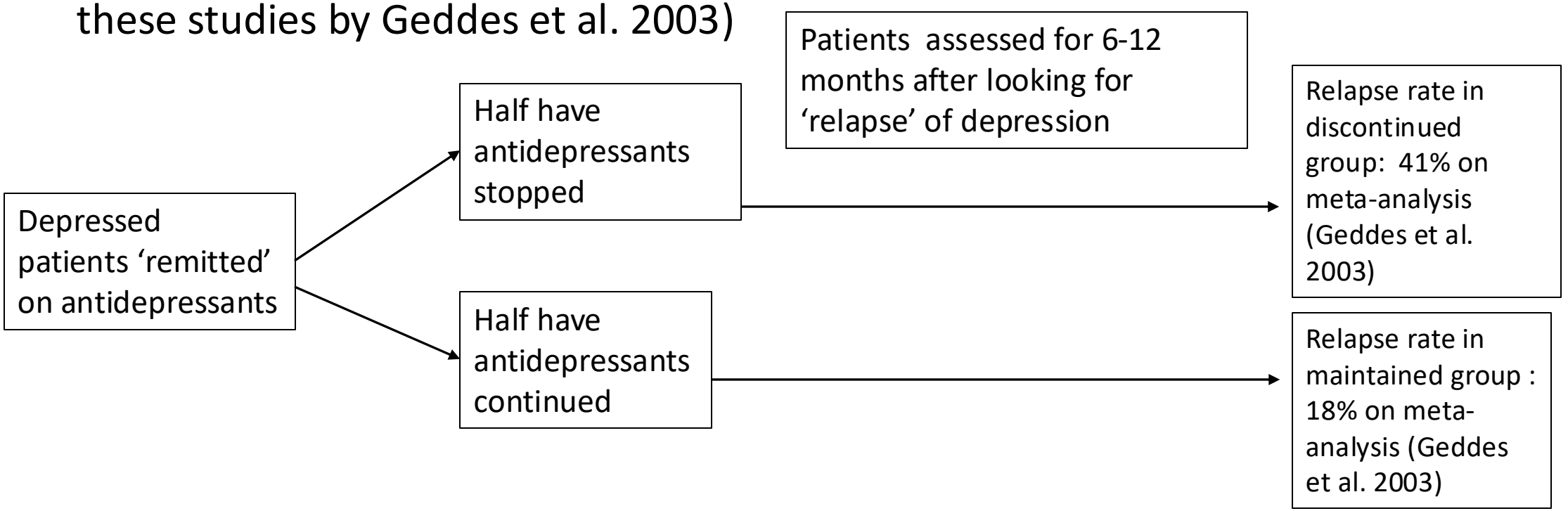
- Many patients continue antidepressants because they believe that antidepressants correct a chemical imbalance (e.g. low serotonin)
  - 85% of Australian public believes depression is caused by a ‘chemical imbalance’ (Pilkington, 2013)
  - Belief that antidepressants rectify this chemical imbalance prominent barrier to stopping no longer indicated antidepressants (Eveleigh et al, 2019)
  - Other unproven biological explanations for mechanisms of action exist (neurogenesis, inflammation, etc)
  - Obvious, plausible explanation for effect exists….

Emotional numbing/blunting

- Reported by 50-70% of people on antidepressants in surveys (Read and Williams, 2018; Goodwin et al 2017)
- Reduced intensity of negative and positive emotions
- May be related to genital numbing reported by many people on antidepressants
- If you chew up many antidepressants they will numb the mouth
- Some suggest it is the depression causing the numbing but recent high-profile study finding emotional numbing in healthy volunteers (no MH issues) given antidepressants (Langley et al 2023) – and this impaired emotional learning processes
- This effect may provide relief from strong emotions in the short term but may have consequences to relationships, quality of life
- It is the number one reason patients give for wanting to stop their antidepressants

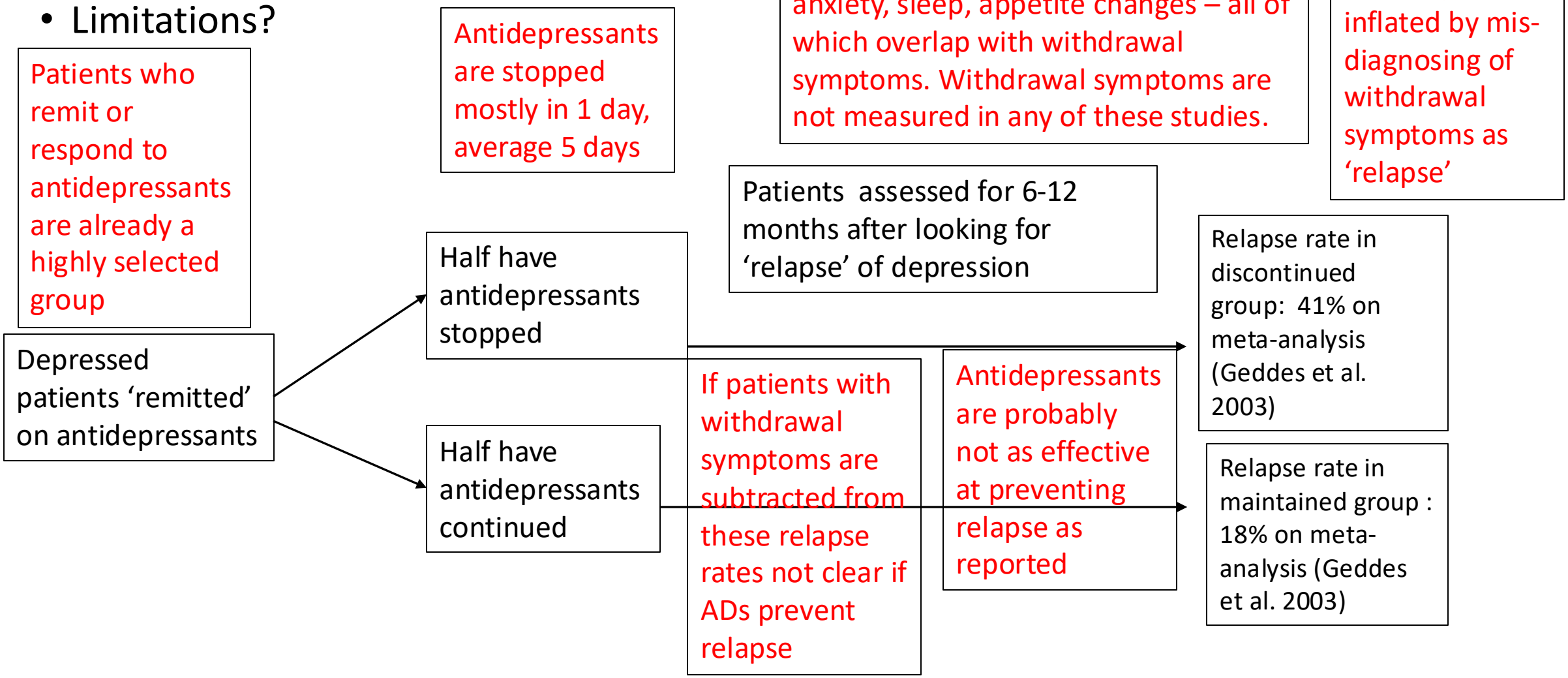
Evidence for long-term use of antidepressants

- There is a recommendation to “continue antidepressants for at least 2 years if they are at risk for relapse” in the NICE depression guidelines
- This advice is based on discontinuation studies (in particular, a meta-analysis of these studies by Geddes et al. 2003)



Limitations to the relapse prevention literature

- Limitations?



Royal College of Psychiatrists guidance on ‘Stopping antidepressants’

- Published in October 2020
- Recommends patients who have been on antidepressants for more than a few weeks weeks taper off over **“months or longer”**
- Suggest going down to **very small doses (<1mg) before stopping**
- Recommends going down in **smaller and smaller sized reductions**
- Rate **titrated to the individual**’s ability to tolerate the process

RC PSYCH
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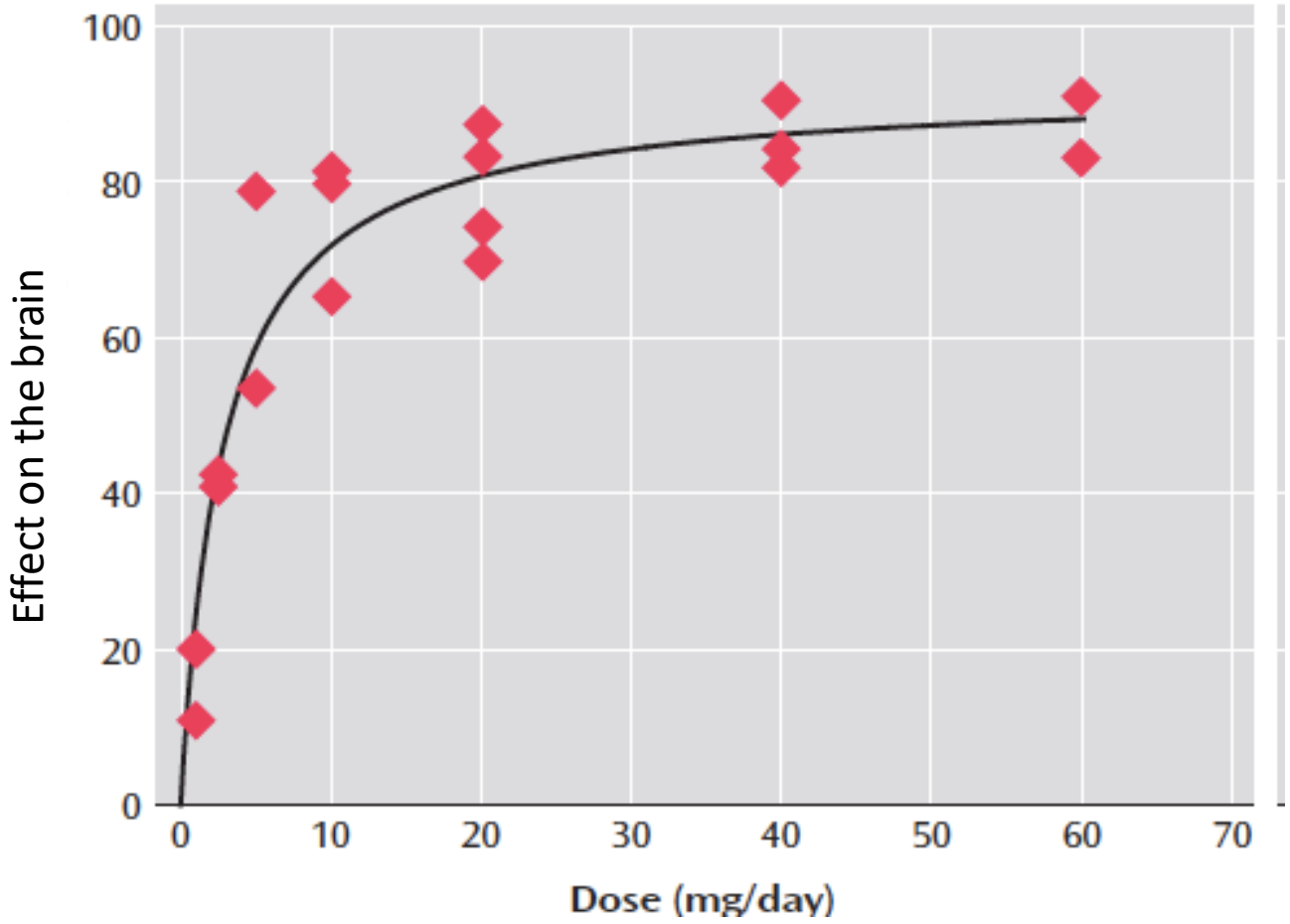
Stopping antidepressants

Management of the antidepressant withdrawal syndrome

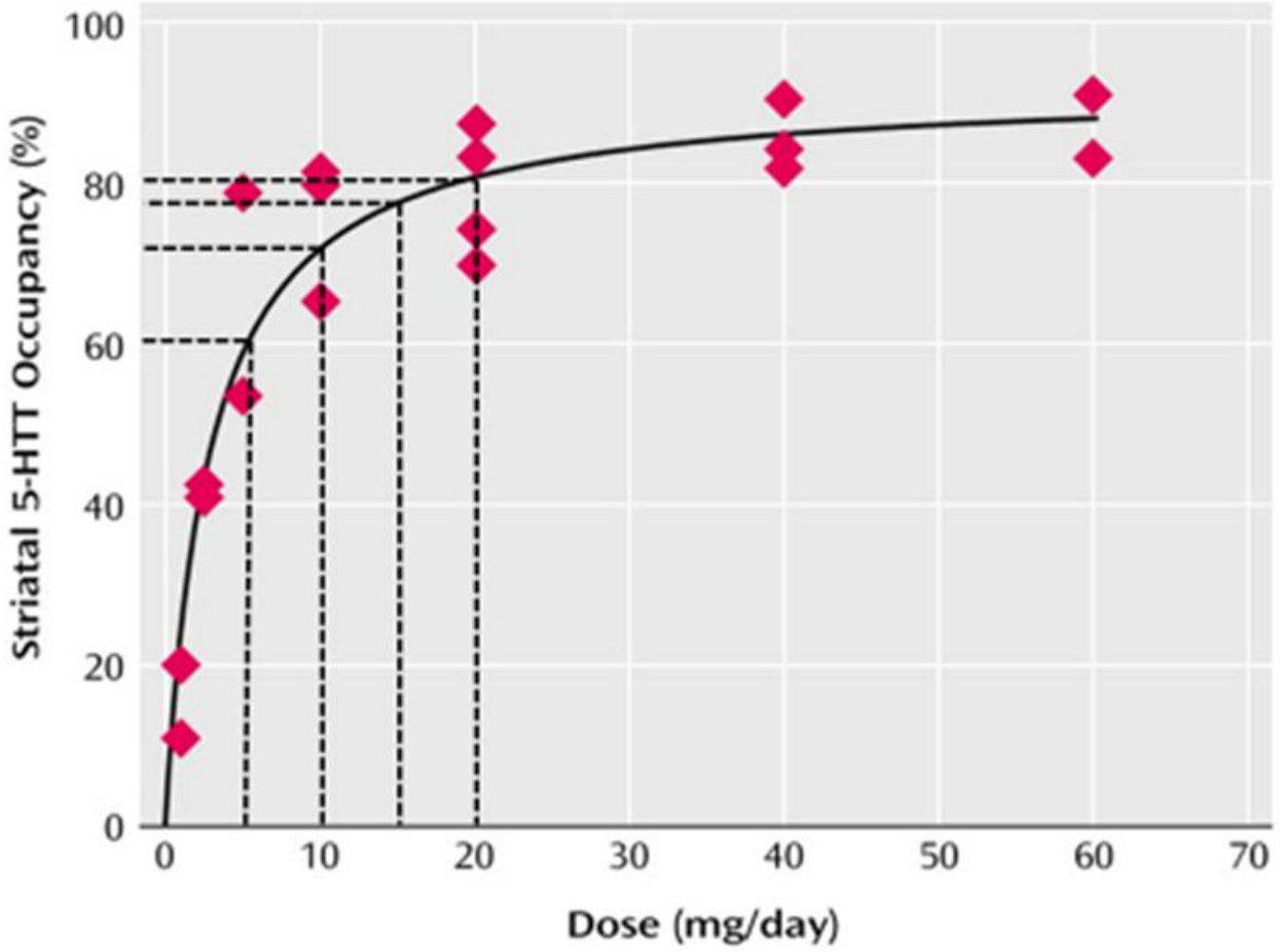
- We used brain imaging (PET) data of antidepressant action to develop rational tapering guidance for antidepressants
- E.g. Citalopram's effect on the serotonin transporter, its major target
- This also applies to all other psychiatric medications



Citalopram

What happens when you taper linearly?

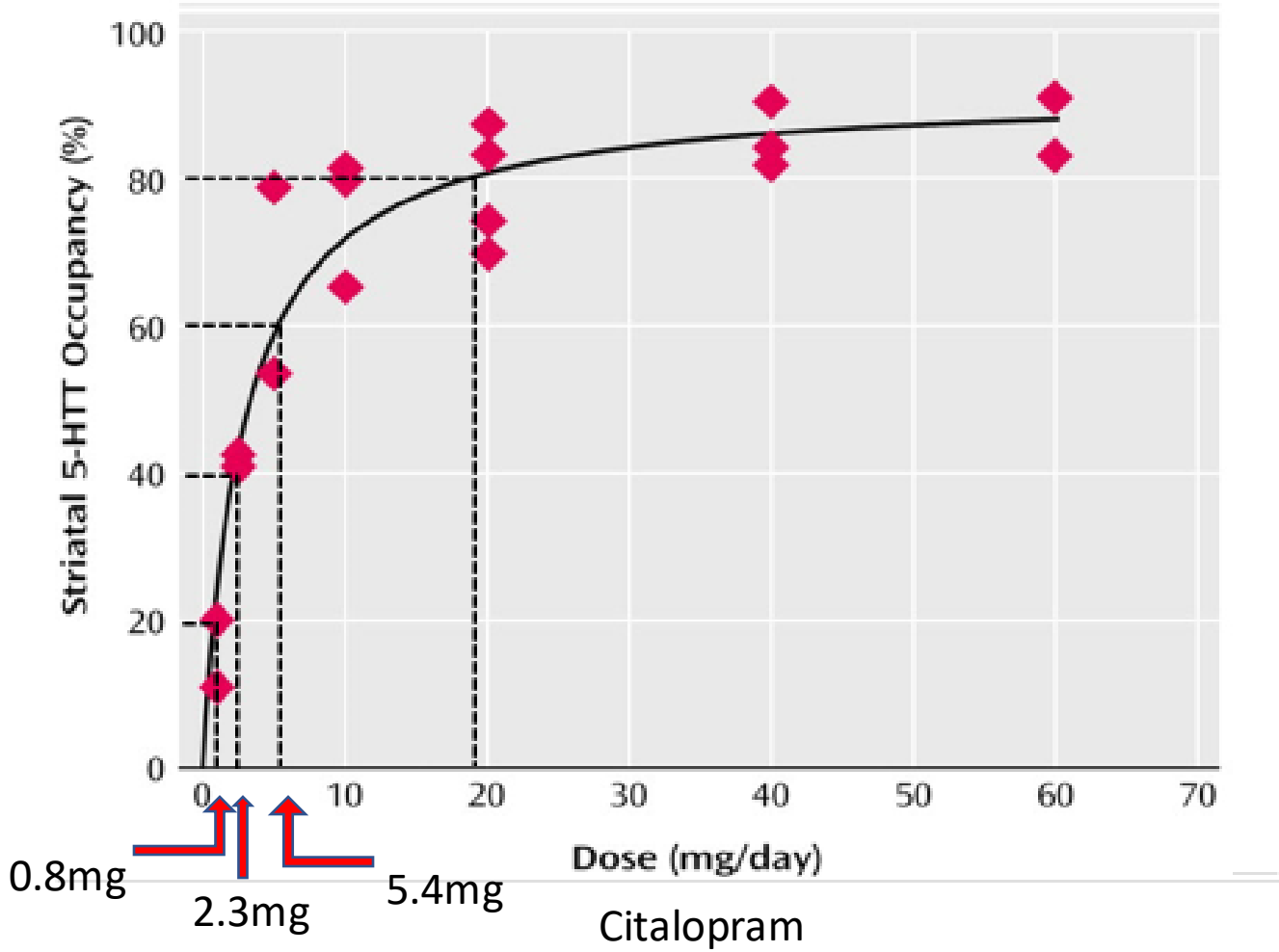
- Citalopram linear taper
- 20mg to 15mg -> 3% change
- 15mg to 10mg -> 6% change
- 10mg to 5mg -> 13% change
- 5mg to 0mg -> 58% change
- This correspond to the increasingly severe withdrawal symptoms reported by patients as dose gets lower
- 10mg is smallest tablet available. Sometimes split in half to make 5mg
- **Most common tapering by clinicians is: 20mg, 10mg, 5mg, stop.**



Citalopram

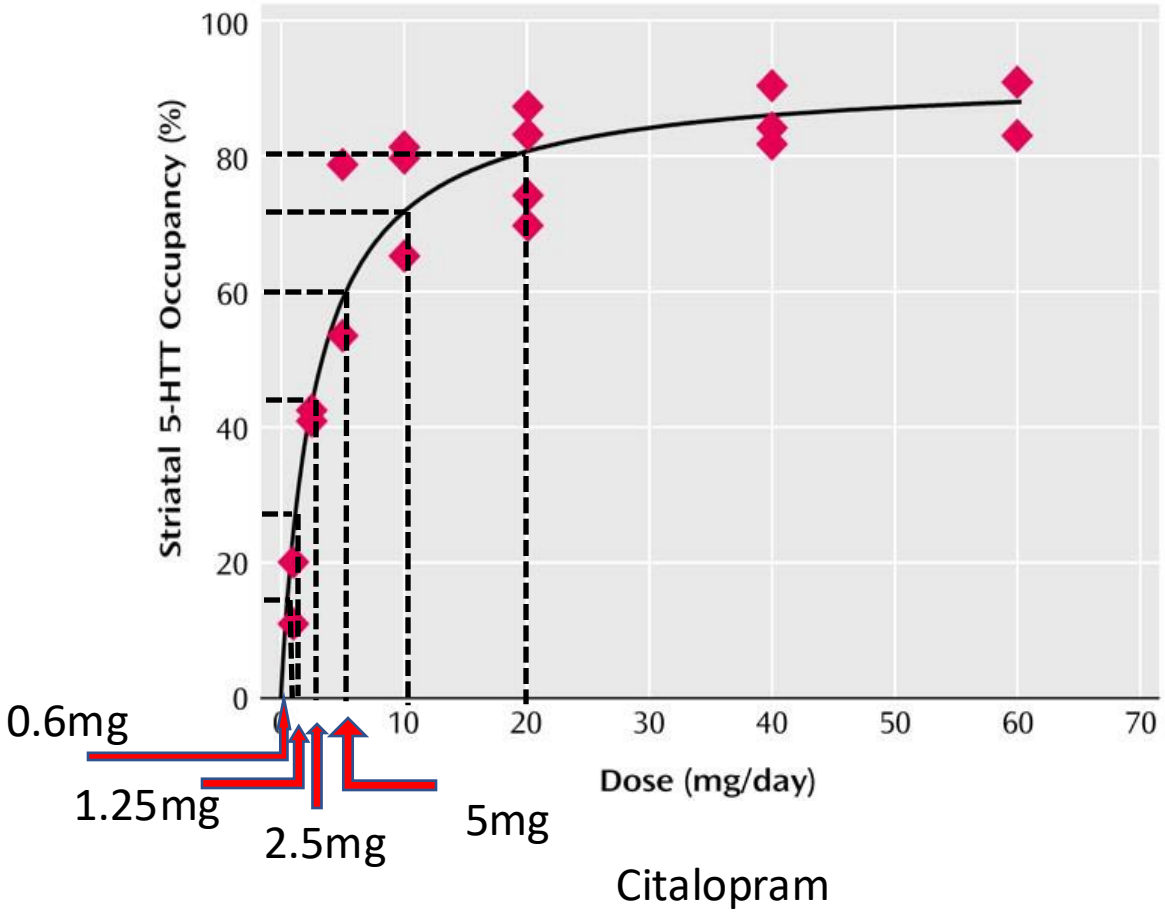
What happens when you taper by fix amounts of effect on the brain? Hyperbolic dose decrease

- Tapering according to equal change in effects at the serotonin transporter
- Yields hyperbolically reducing regimen
- Final dose before stopping will need to be very small



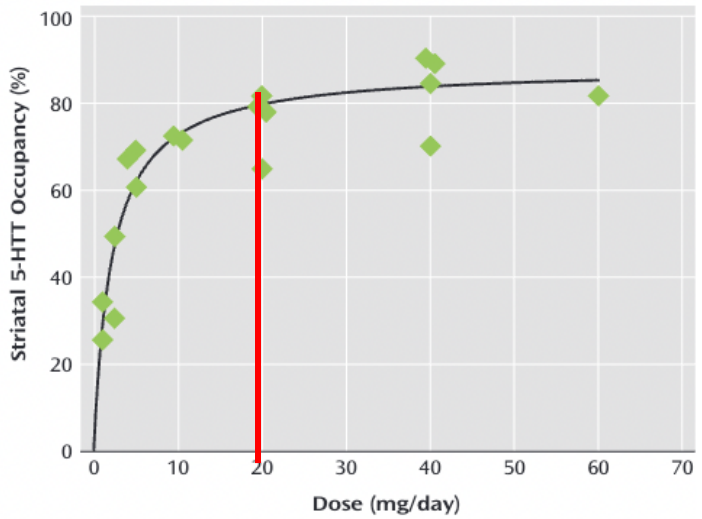
What happens when you taper by fixed amounts of effect on the brain? Proportionate dose decrease

- Hyperbolic reductions roughly approximated by *proportional* reductions
  - e.g., 5 halvings (50% reductions): 20mg, 10mg, 5mg, 2.5mg, 1.25mg, 0.6mg, 0mg
- Slower reductions required for many: such as 10% of the last dose/month

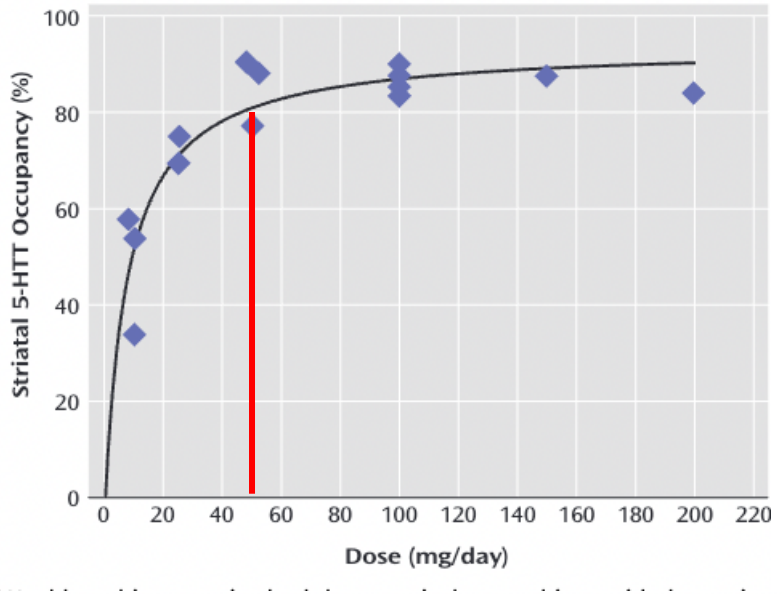


True for all antidepressants

Fluoxetine

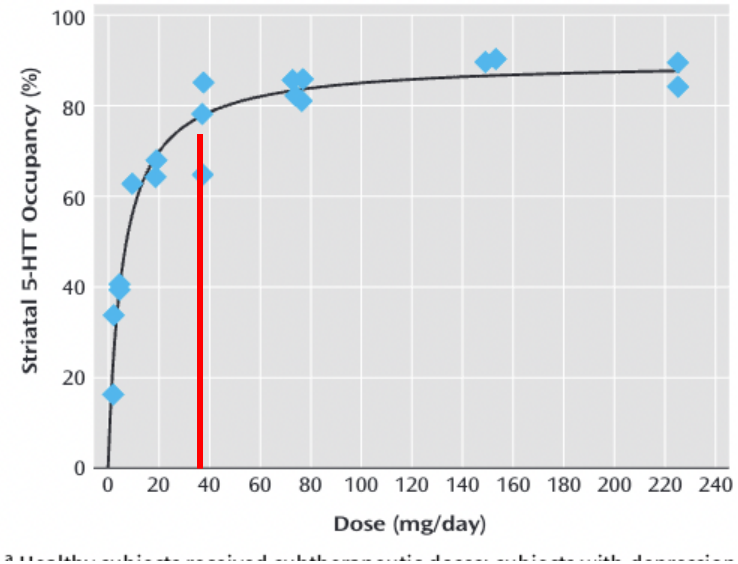


Sertraline

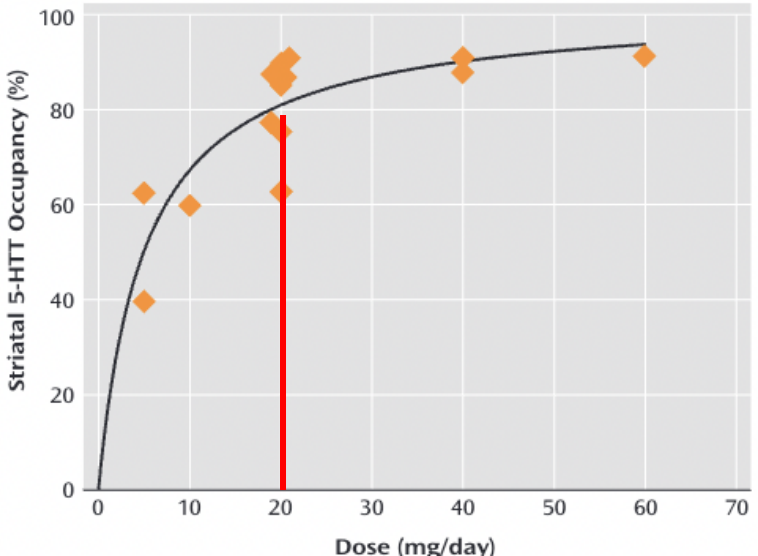


Red line= The smallest available tablet or capsule in Australia

Venlafaxine



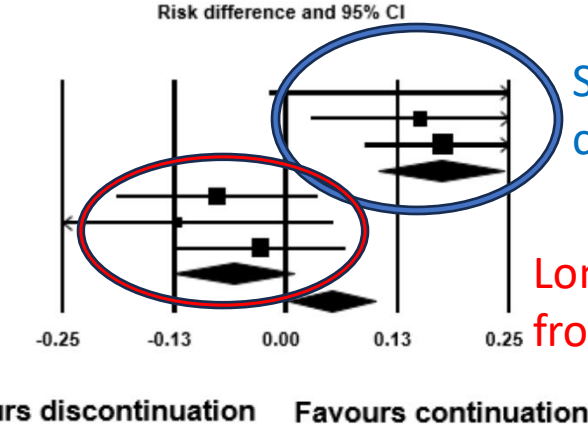
Paroxetine



Evidence for gradual tapering

- A meta-regression of 13 antidepressant discontinuation studies found that the length of taper correlated highly with risk of relapse (p=0.00001) (Gotzsche and Demasi, 2023)
- In the three trials that tapered over about 6 months no difference in relapse rates from maintenance (MT) (17% difference for rapid tapering vs MT) (Gotzsche and Demasi, 2023)

Length of taper	Study name	Statistics for each study: Risk difference	Standard error	Variance	Lower limit	Upper limit	Z	P
Short	Cook 1986	0.333	0.180	0.032	-0.019	0.685	1.857	0.063
Short	Huijbers 2016	0.151	0.062	0.004	0.028	0.273	2.411	0.016
Short	Lewis 2021	0.176	0.045	0.002	0.088	0.264	3.913	0.000
Overall		0.174	0.036	0.001	0.104	0.244	4.862	0.000
Long	Bockting 2018	-0.077	0.057	0.003	-0.190	0.035	-1.342	0.179
Long	Kuyken 2008	-0.121	0.089	0.008	-0.296	0.054	-1.359	0.174
Long	Kuyken 2015	-0.028	0.048	0.002	-0.123	0.067	-0.585	0.558
Overall		-0.059	0.034	0.001	-0.126	0.008	-1.733	0.083
Overall		0.052	0.025	0.001	0.004	0.100	2.106	0.035

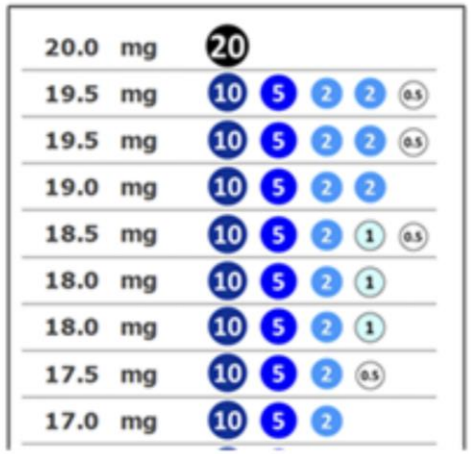


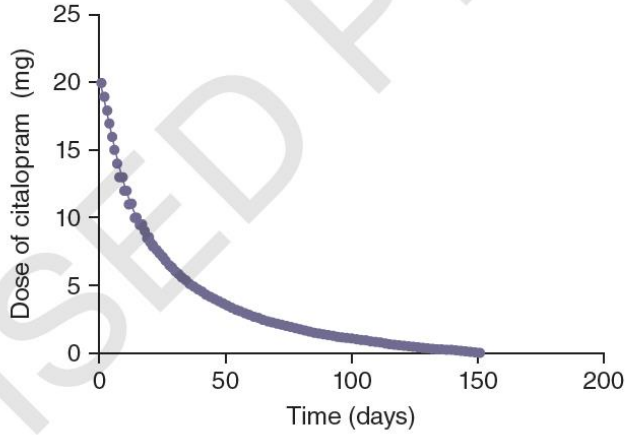
Short tapering – favours continuation

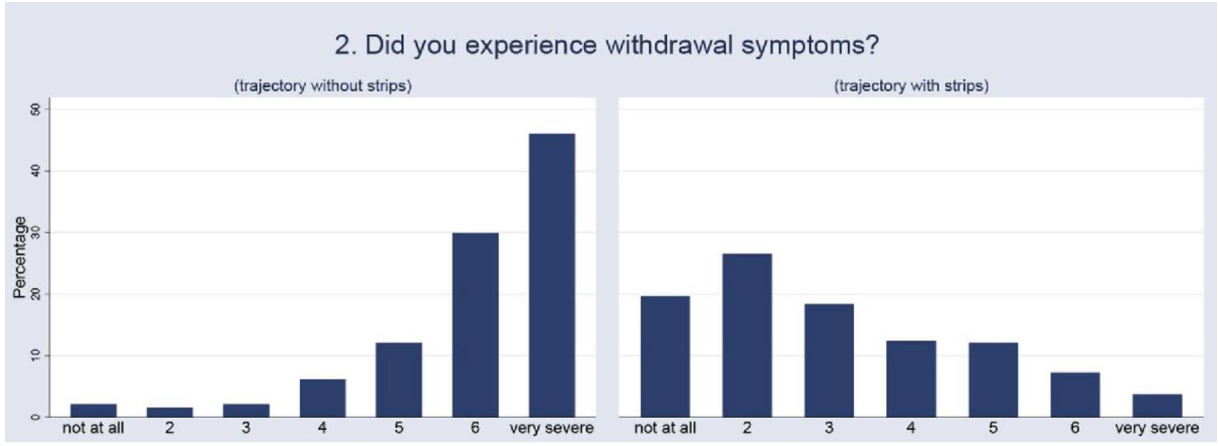
Long tapering (6 months) – no diff from continuation

Evidence for gradual, hyperbolic tapering

- In one study of 895 patients where two-thirds had been unable to stop antidepressants in usual quick linear taper 71% were able to stop with a hyperbolic taper over months (Groot and van Os, 2018)







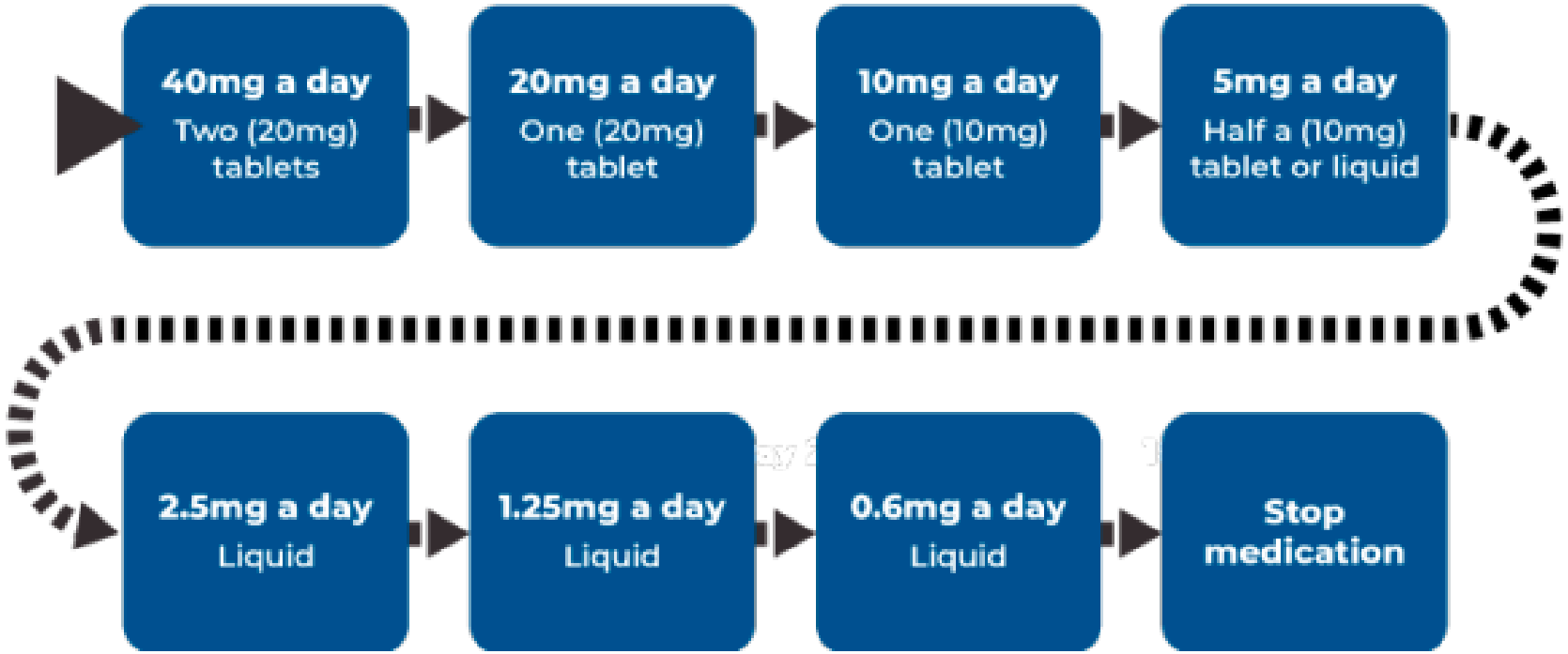
Royal College of Psychiatrists guidance on ‘Stopping antidepressants’

- Importantly, recommends individualizing rate of reduction to the rate that can be *tolerated by the patient*
- If withdrawal symptoms become too severe, then reduction should be *halted or dose increased until symptoms resolve*. Then reduction should proceed at a *slower pace*
- Many patients can only reduce their dose at *10% of the most recent dose per month* (which means reductions get smaller and smaller)

A rapid reduction schedule (RCPsych, 2020)

Citalopram

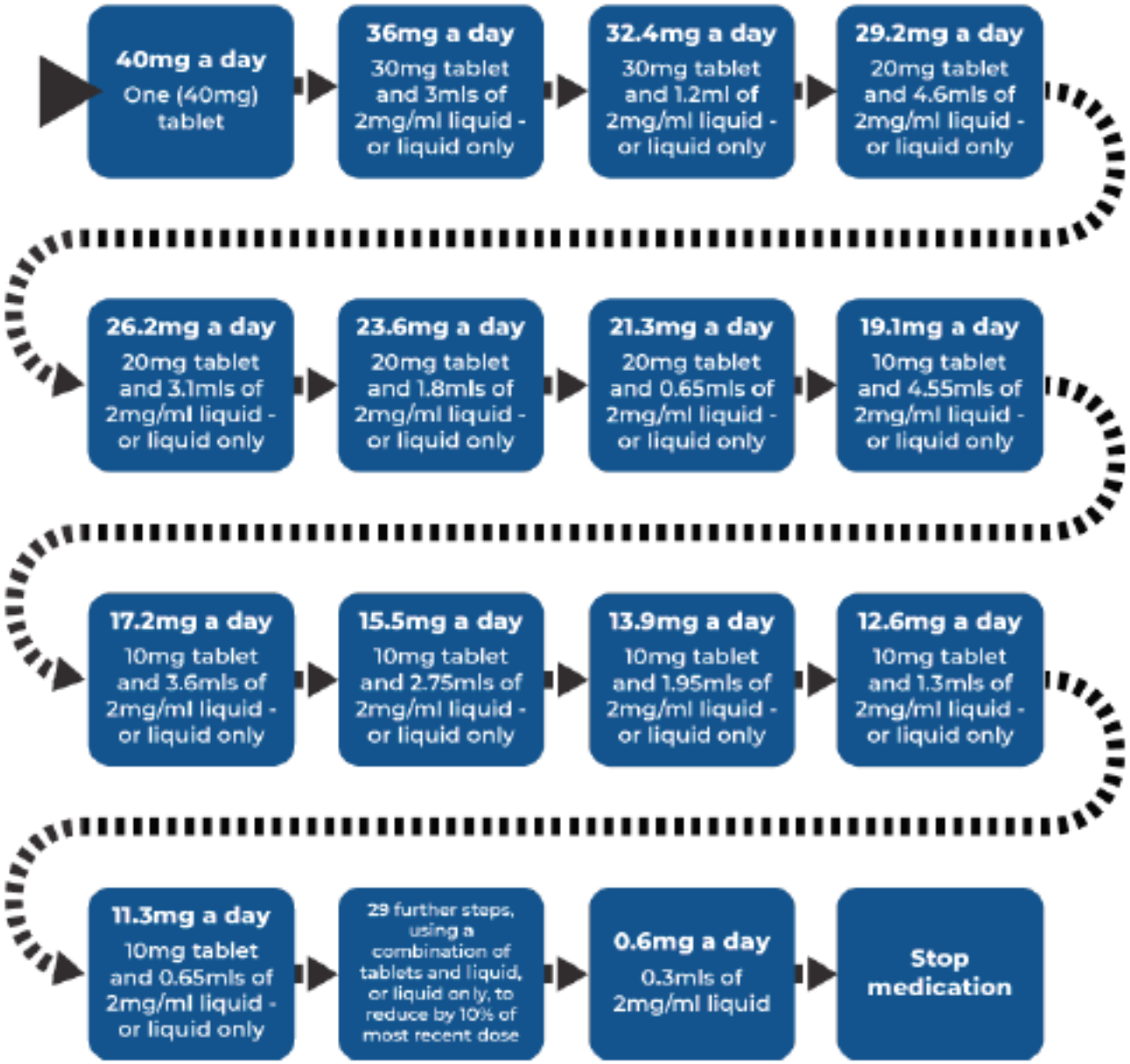
Reduction of dose by 50%, every 2-4 weeks. Some people may need to reduce more slowly.



- Total time required: 3-6 months

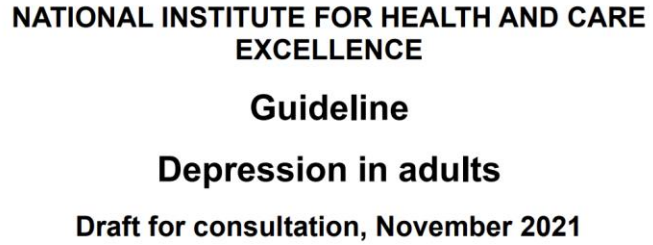
Paroxetine

Reduction by 10% of the last dose, every 2-4 weeks using tablets and liquid. Some people may need to reduce more slowly. (Updated October 2020)



- Reduce dose by 10% of the dose every 2-4 weeks
- Calculated on the last dose, so that the reductions get smaller and smaller as the total dose decreases
- Reduce down to 0.6mg before stopping
- Approximate duration: 2-3 years (often what people take)

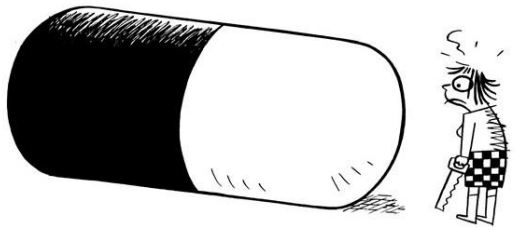
NICE guidelines



- Update to Depression guidelines published in June 2022, including guidance on stopping antidepressants, including (my italics and bolding):
  - "slowly reduce the dose to zero in a step-wise fashion, at each step prescribing a ***proportion*** of the previous dose (for example, *50% of the previous dose*)"
  - "Consider using smaller reductions (for example, 25%) as the dose becomes lower"
  - "if, once very small doses have been reached, slow tapering cannot be achieved using tablets or capsules, consider using ***liquid preparations*** if available"
  - "*ensure the speed and duration of withdrawal is led by and agreed with the person taking the prescribed medication, ensuring that any withdrawal symptoms have resolved or are tolerable before making the next dose reduction"*
  - "recognise that withdrawal [the process of discontinuation] may take weeks or *months* to complete successfully" [It can take years in some patients].

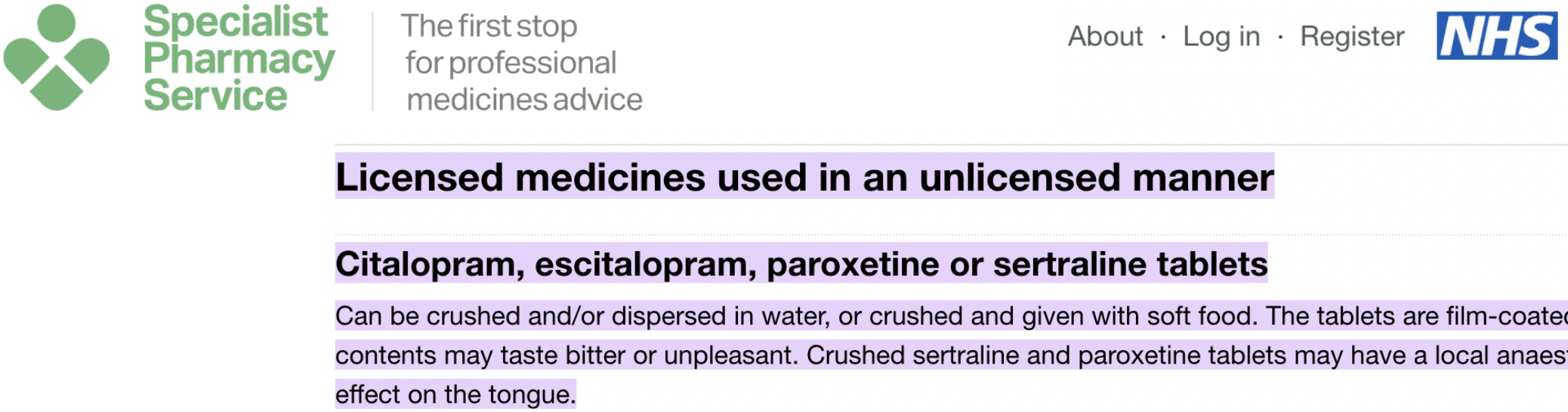
How to make these small doses?

- Tablet cutters will be needed to divide tablets – into halves and quarters
- Liquid preparations can be used – but only currently available for escitalopram in Oz
- Compounded medications (e.g. tapering strips)
- Don’t skip doses (except for fluoxetine) – can precipitate withdrawal effects because of large changes in plasma levels – most antidepressants have half-lives of 24 hours and so every second day dosing will mean that levels fall to ¼ of peak levels
- Switching to fluoxetine based on a manufacturer’s study. Fluoxetine has substantial withdrawal effects (incidence: 50%), cannot be stopped abruptly, switching process more difficult than textbooks suggest. Might be considered in some circumstances



Off-label options for tapering

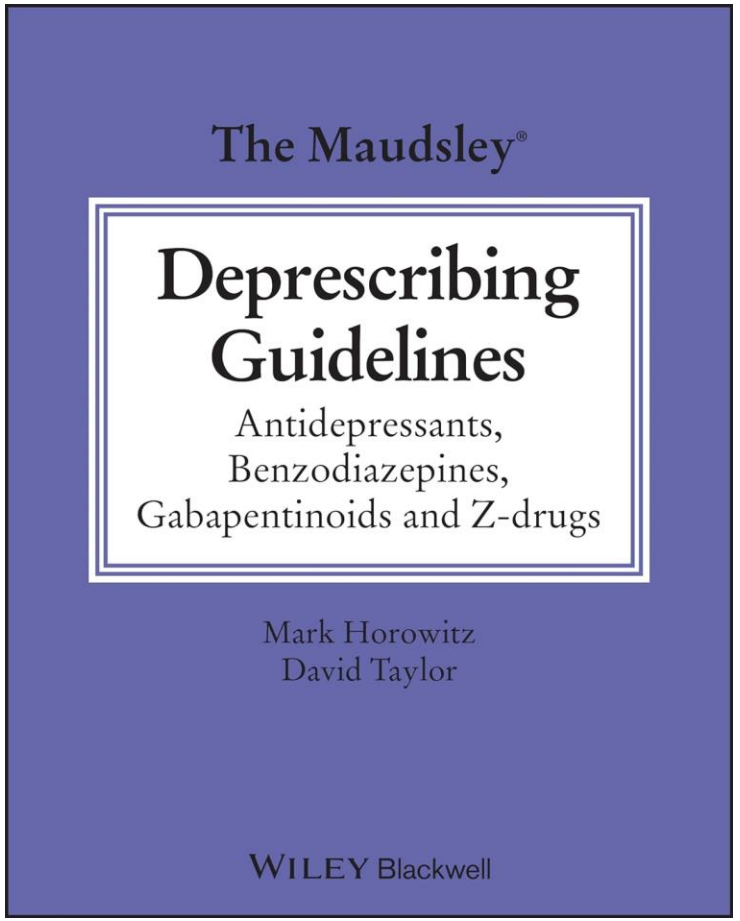
- There are also ’off-label’ options such as compounding pharmacies, opening up capsules to count beads
- Or crushing tablets (or opening capsules) and dispersing them in water. This is recommended by pharmaceutical authorities in the UK for example for giving small doses of medication to children
- Manufacturers could make liquids as they have in the UK



Maudsley Deprescribing Guidelines:

Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs

- Companion to the Maudsley Prescribing Guidelines, written with the primary author Professor David Taylor from Maudsley Psychiatry
- We set out with this clinical handbook to cover all the information a GP, psychiatrist, pharmacist, nurse, etc would need:
  - To recognize withdrawal effects from these drugs classes
  - To distinguish withdrawal effects from relapse
  - To be able to safely taper each specific antidepressant, etc with fast, moderate and slow schedules as well as advice on how tailor it for an individual
  - Covers all the formulations of medications available in Australia to safely taper with licensed and off-label uses



Guidance for stratifying risk

Table 2.11 Preliminary tool for evaluation of risk of withdrawal for an individual patient, adapted from Horowitz et al. 2022.[1]

Determinant of withdrawal risk	Weighting
Duration of use[a]	
■ Short term (1–6 months)	0 points
■ Intermediate term (6–12 months)	1 point
■ Long term (1–3 years)	2 points
■ Very long-term use (>3 years)	3 points
Antidepressant type	
■ Lowest risk (e.g. agomelatine)	0 points
■ Low risk (e.g. vortioxetine, trimipramine, dosulepin)	1 point
■ Moderate risk (e.g. SSRIs: citalopram, escitalopram, sertraline, fluvoxamine, fluoxetine; TCAs: amitriptyline, nortriptyline, clomipramine, imipramine; other: bupropion)	2 points
■ High risk (e.g. SNRIs: desvenlafaxine, duloxetine, venlafaxine; MAOIs: phenelzine, moclobemide; Other: paroxetine, mirtazapine)	4 points
Dosage	
■ Minimum therapeutic dosage or lower	0 points
■ Greater than the minimum therapeutic dosage	1 point
Past experience of withdrawal symptoms	
■ Stopped antidepressant in past with no withdrawal symptoms/unknown	0 points
■ Mild to moderate withdrawal symptoms	1 point
■ Severe withdrawal symptoms	2 points
■ Very severe withdrawal symptoms	3 points

[a] Note that very short-term use (<4 weeks) is not normally associated with significant risk of withdrawal.
MAOI monoamine oxidase inhibitor, SSRI selective serotonin reuptake inhibitor, SNRI serotonin and norepinephrine reuptake inhibitor, TCA tricyclic antidepressant

Table 2.12 Estimation of risk category for withdrawal for an individual patient, adapted from Horowitz et al. 2023.[1]

Risk category	Low	Medium	HIgh	Very high
Point score	0	1–4	5–8	≥ 9

Table 2.22 Estimation of tapering rate based on risk of withdrawal symptoms (see Tables 2.11 and 2.12).

Evaluation of risk	Initial tapering trajectory (see individual drug sections)	Initial dose reduction equivalent (approximately)*
Low risk = 0 points	Faster[a]	50% reduction
Medium risk = 1–4 points	Moderate[b]	25% reduction
High risk = 5–8 points	Slower[c]	10% reduction
Very high risk ≥ 9 points	Slowest[d]	5% reduction (or less)

For example, a person using 20mg citalopram for 4 years who has had moderate trouble when missing doses in the past would score 3 + 2 +1 + 1 = 7 points and start with a slower taper

Example of citalopram tapering regimen (faster)

A. **Faster taper** with up to 10 percentage points of SERT between each step – with reductions made every 2–4 weeks.*

Step	RO (%)	Dose (mg)	Volume**	Step	RO (%)	Dose (mg)	Volume**
1	79	40	Use tablets	6	37	2	0.4mL
2	75	20	Use tablets	7	27	1.2	0.24mL
3	68	10	Use tablets	Switch to citalopram **0.4mg/mL dilution**			
4	57	5	Use ½ tablets	8	17	0.7	1.4mL
Switch to citalopram **4mg/mL dilution**				9	7	0.3	0.6mL
5	47	3	0.6mL	10	0	0	0

RO = receptor occupancy

*The time between each decrease may be shortened to ~~one~~ week if the patient is able to make the first couple of reductions with no withdrawal symptoms. The interval between reductions should never be less than ~~one~~ week because this might increase the risk of relapse, even in the absence of withdrawal effects.[14,15]

**Note: citalopram drops come as citalopram hydrochloride which are 25% more bioavailable than citalopram hydrobromide (the tablet form) i.e. 8mg in liquid version is equivalent to 10mg in tablet form because they come as different salts.[1] Therefore the volume required is multiplied by 0.8 to get the required value.

A slower taper for citalopram for people with greater difficulties

B. **Moderate taper** with up to 5 percentage points of SERT between each step – with reductions made every 2–4 weeks.

Step	RO (%)	Dose (mg)	Volume*	Step	RO (%)	Dose (mg)	Volume*
1	79	40	Use tablets	11	38	2	0.4mL*
2	75	20	Use tablets	12	34	1.6	0.32mL*
3	70	15	Use ½ tablets**	13	30	1.3	0.26mL*
4	68	10	Use tablets	14	26	1	0.2mL*
5	64	7.5	Use ¾ tablets**	Switch to citalopram **0.4mg/mL dilution***			
Switch to citalopram **4mg/mL dilution***				15	21	0.8	1.6mL*
6	60	5.5	1.1mL*	16	17	0.6	1.2mL*
7	55	4.5	0.9mL*	17	13	0.4	0.8mL*
8	51	3.6	0.72mL*	18	8.5	0.25	0.5mL*
9	47	2.9	0.58mL*	19	4.3	0.1	0.2mL*
10	43	2.4	0.48mL*	20	0	0	0
See further steps in the right-hand column							

RO = receptor occupancy

*Note: citalopram drops come as citalopram hydrochloride which are 25% more bioavailable than citalopram hydrobromide (the tablet form) i.e. 8mg in liquid version is equivalent to 10mg in tablet form because they come as different salts.[1] Therefore the volume required is multiplied by 0.8 to get the required value.

**Alternatively, this dose could be made up with a liquid preparation.

Tapering other psychiatric drugs

NICE
National Institute for Health and Care Excellence

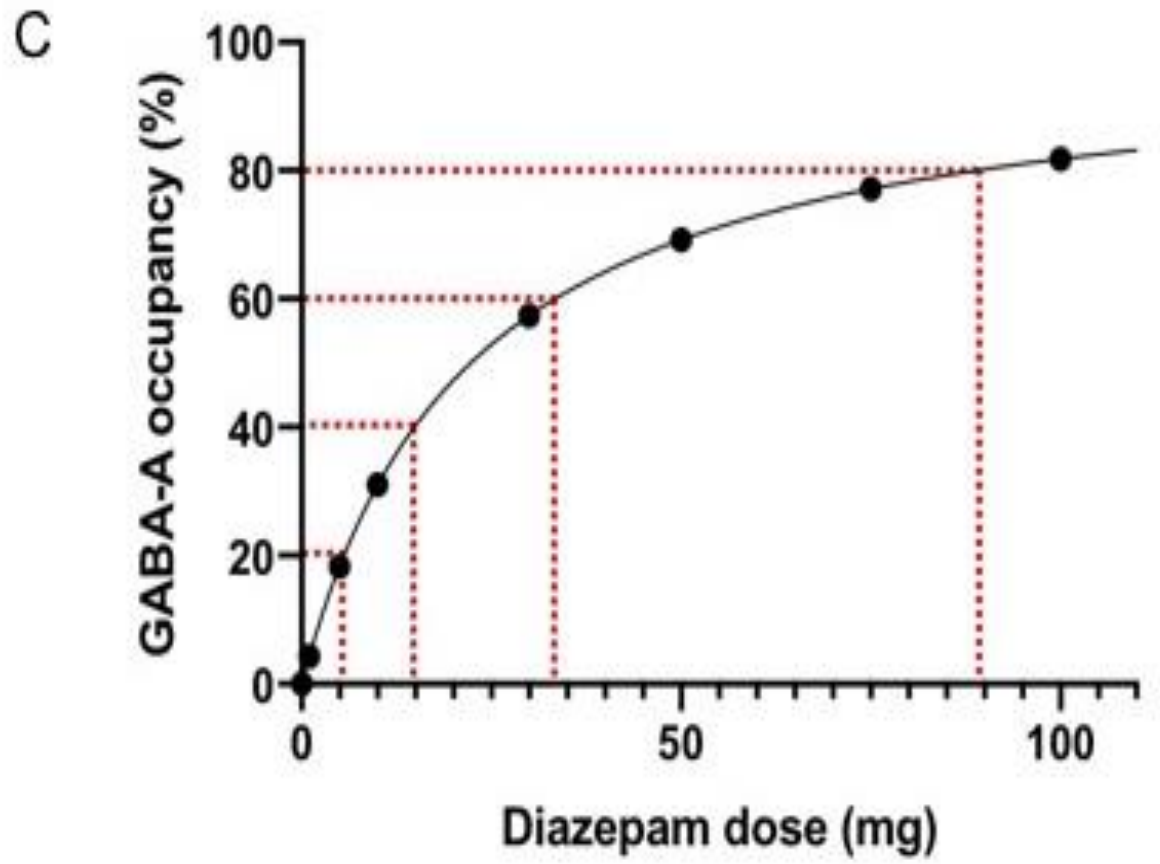
- “for opioids, benzodiazepines, Z-drugs and antidepressants, suggest a slow, stepwise rate of *reduction* ***proportionate*** *to the existing dose,* ***so that decrements become smaller as the dose is lowered***, unless rapid withdrawal is needed”

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults

Draft for consultation, October 2021



Going from 1mg to 0mg of diazepam causes as big a reduction in effect on the brain as going from 100mg to 75mg. So reductions Have to get smaller and smaller as you go down to lower doses. People often need weeks between doses

Diazepam Dosage (mg)	GABA-A occupancy (%)
200	90.0
100	81.8
75	77.1
50	69.2
37.5	62.7
25	52.9
12.5	35.9
10	31.0
5	18.3
2	8.2
1	4.3
0.5	2.2
0	0

A. **A faster taper** with up to 5 percentage points of $GABA_A$ occupancy between each step – with reductions made every 1–4 weeks*.

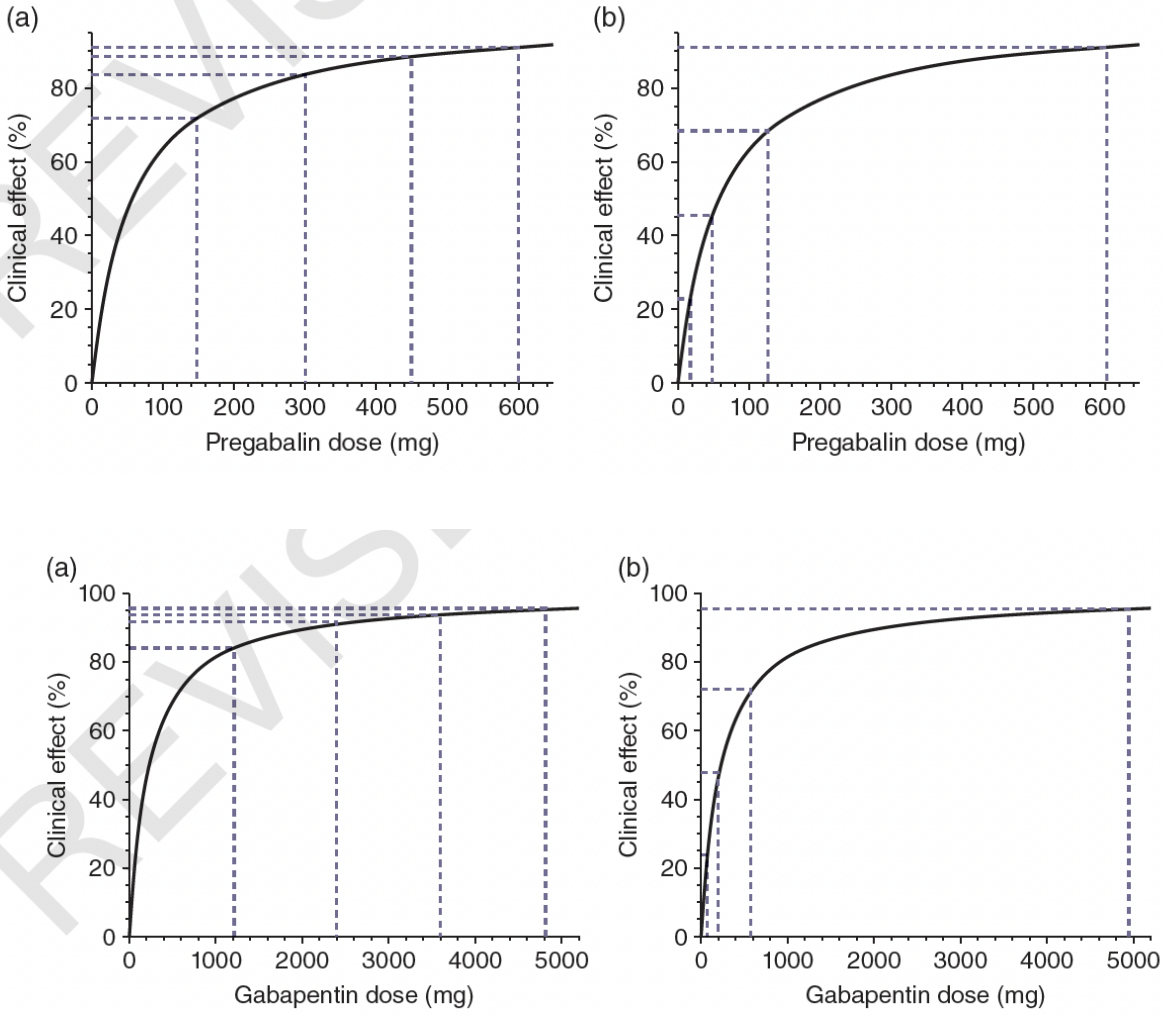
Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form	Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form
1	70.8	30	30	60	Use tablets	13	36.2	7	7	14	Use tablets
2	69	25	30	55	Use tablets	14	32.7	6	6	12	Use tablets
3	66.9	25	25	50	Use tablets	15	28.8	5	5	10	Use tablets
4	64.6	20	25	45	Use tablets	16	24.5	4	4	8	Use tablets
5	61.8	20	20	40	Use tablets	17	22.1	3	4	7	Use ½ tablets**
6	59.3	18	18	36	Use tablets	18	19.5	3	3	6	Use ½ tablets**
7	56.4	16	16	32	Use tablets	19	16.8	2	3	5	Use ½ tablets**
8	53.1	14	14	28	Use tablets	20	13.9	2	2	4	Use tablets
9	49.3	12	12	24	Use tablets	21	10.8	1	2	3	Use ½ tablets**
10	44.7	10	10	20	Use tablets	22	7.5	1	1	2	Use ½ tablets**
11	42.2	9	9	18	Use tablets	23	3.9	0.5	0.5	1	Use ¼ tablets**
12	39.3	8	8	16	Use tablets	24	0	0	0	0	
See further steps in the right-hand column											

B. **A moderate taper** with up to 2.5 percentage points of $GABA_A$ occupancy between each step – with reductions made every 1–4 weeks.

Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form*	Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form
1	70.8	30	30	60	Use tablets	23	34.5	6.5	6.5	13	Use ¼ tablets*
2	69.4	28	28	56	Use tablets	24	32.7	6	6	12	Use tablets
3	67.8	26	26	52	Use tablets	25	30.8	5.5	5.5	11	Use ¼ tablets*
4	66	24	24	48	Use tablets	26	28.8	5	5	10	Use tablets
5	64	22	22	44	Use tablets	27	26.7	4.5	4.5	9	Use ¼ tablets*
6	61.8	20	20	40	Use tablets	28	24.5	4	4	8	Use tablets
7	60.6	19	19	38	Use tablets	29	23.3	3.5	4	7.5	Use ¼ tablets*
8	59.3	18	18	36	Use tablets	30	22.1	3.5	3.5	7	Use ¼ tablets*
9	57.9	17	17	34	Use tablets	31	20.8	3	3.5	6.5	Use ¼ tablets*
10	56.4	16	16	32	Use tablets	32	19.5	3	3	6	Use ½ tablets*
11	54.8	15	15	30	Use tablets	33	18.2	2.5	3	5.5	Use ¼ tablets*
12	53.1	14	14	28	Use tablets	34	16.8	2.5	2.5	5	Use ¼ tablets*
13	51.3	13	13	26	Use tablets	35	15.4	2	2.5	4.5	Use ¼ tablets*
14	49.3	12	12	24	Use tablets	36	13.9	2	2	4	Use tablets
15	47.1	11	11	22	Use tablets	37	12.4	1.5	2	3.5	Use ¼ tablets*
16	44.7	10	10	20	Use tablets	38	10.8	1.5	1.5	3	Use ¼ tablets*
17	43.5	9.5	9.5	19	Use ¼ tablets*	39	9.2	1	1.5	2.5	Use ¼ tablets*
18	42.2	9	9	18	Use tablets	40	7.5	1	1	2	Use ½ tablets*
19	40.8	8.5	8.5	17	Use ¼ tablets*	41	5.7	0.5	1	1.5	Use ¼ tablets*
20	39.3	8	8	16	Use tablets	42	3.9	0.5	0.5	1	Use ¼ tablets*
21	37.8	7.5	7.5	15	Use ¼ tablets*	43	2	0	0.5	0.5	Use ¼ tablets*
22	36.2	7	7	14	Use tablets	44	0	0	0	0	
See further steps in the right-hand column											

Including guidance on when to switch shorting acting benzodiazepines to diazepam

Gabapentinoid tapering



A. **A faster taper** with up to 10 percentage points of 'clinical effect' between each step – with reductions made every 2–4 weeks*.

Step	CE (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form
1	91	300	300	600	Tablets or capsules
2	83	150	150	300	Tablets or capsules
3	79	100	125	225	Tablets or capsules
4	72	75	75	150	Tablets or capsules
5	63	50	50	100	Tablets or capsules
6	56	37.5	37.5	75	Use ½ tablets**
7	46	25	25	50	Tablets or capsules
8	39	18.75	18.75	37.5	Use ¾ tablets**
9	30	12.5	12.5	25	Use ½ tablets**
Switch to pregabalin **20mg/mL solution**					
10	24	9	9	18	0.45mL AM and PM
11	17	6	6	12	0.3mL AM and PM
12	9	3	3	6	0.15mL AM and PM
13	0	0	0	0	

Other drug classes

- The relationship between dose of drug and effect on target receptors is hyperbolic for all psychiatric drug classes and so the same principles of hyperbolic tapering will apply to all these classes as well:
  - mood stabilisers,
  - antipsychotics,
  - stimulants (although generally easier to stop),
  - opioids
  - Also physical health meds: beta blockers, PPIs, etc

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