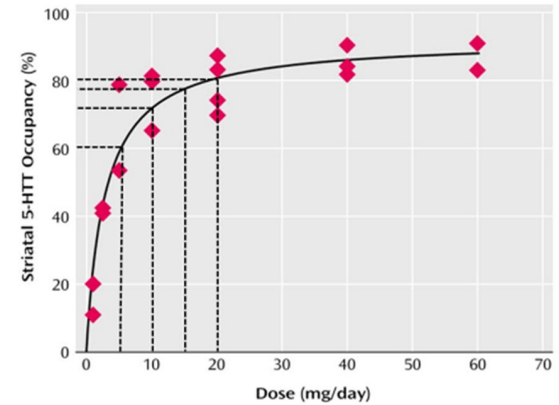




Antidepressant withdrawal effects and safe deprescribing



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Case study

- A 56 year old woman turns up to an appointment saying she is feeling anxious, can't sleep and is having panic attacks.
- She stopped 100mg of sertraline 3 weeks ago because she wanted to try going without it because of making her feel flat and groggy

Case study

- She was given antidepressants 5 years ago following the death of her mother.
- She was then lethargic and depressed and slept long hours
- She has felt fine the last 2 years but feels like she is numbed on medication, has put on weight and feels tired during the day – she wonders if it is the medication
- Symptoms came on about 2 weeks after stopping her tablet.
- She is now not sleeping, and anxious and it has gotten worse the last few days
- She feels dizzy, slightly unsteady on her feet and like things around her are 'dream-like'

Case study

- Diagnosis made of antidepressant withdrawal syndrome
 - Onset 2 weeks after dose reduction – can be delayed in onset
 - Presence of physical symptoms – dizziness, unsteadiness and derealization ('dream like' sensation) not present in anxiety/depression
 - Psychological symptoms somewhat distinct from symptoms that prompted original prescription
 - Unlikely to have recurring condition – grief/loss
- Re-started on sertraline – symptoms improved by half in 7 days, resolved in 2 weeks
- Patient offered a slower plan of reduction using a liquid formulation of medication or compounded capsules to be conducted over months

Case Study 2

- 30 year woman put on sertraline 100mg at age 19, when stressed by university
- Came off over 4 weeks under GP's instructions: half dose to 50mg for 2 weeks, take 50mg every second day for 2 weeks, stop
- Developed:
 - panic attacks, pacing, restlessness, brain zaps in her head, emotional numbness,
 - lack of sexual function, altered sensation on the right side of her body, altered sense of heat and cold, muscle spasms, bladder pain
 - Profound suicidality

Case study 2

- She attempted re-instatement of her sertraline at a dose of 5mg (test dose) 6 weeks after stopping. She had been reluctant to re-try the drug after suffering such life altering symptoms on stopping
- Her symptoms worsened on re-starting the drug and she stopped it after 3 days
- She has had ongoing symptoms for 3 months after stopping with no improvement, pacing each day and highly suicidal
- Her parents presented her to Emergency and she was admitted to an in-patient ward
- The treating team told her it was not possible that her symptoms were caused by sertraline as the drug was out of her body and withdrawal symptoms were mostly mild and brief
- They diagnosed her with a psychotic disorder and decided to restrain and medicate her with an antipsychotic because she was refusing further medication

Official guidance on antidepressant withdrawal syndrome until 2019

- NICE guidelines stated: ‘discontinuation symptoms are **usually mild and self-limiting over about one week**, but can be severe, particularly if the drug is stopped abruptly’ (NICE, CG90, 2009)
- CANMAT says “are mild to moderate in severity and resolve within a few weeks.”
- This description was influenced by a ‘consensus panel’ put together by a drug company in the 1990s, which focused on people who had used antidepressants for just 8 weeks
- They coined the euphemism ‘discontinuation symptoms’ and distributed numerous papers with the description ‘brief and mild’

Historical guidance on management of antidepressant withdrawal syndrome

- Previous NICE guidance on how to manage withdrawal symptoms says: “**gradually reduce the dose, normally over a 4-week period**, although some people may require longer periods, particularly with drugs with a shorter half-life” (NICE, CG90, 2009)
- CANMAT says: “we recommend slowly tapering the dose over several weeks or months”, no recommendation for liquids or compounded meds,
- This guidance 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: reduce dose by half for 2-4 weeks, reduce dose to quarter for 2-4 weeks (often by alternating half a tablet every second day)
- An RCT found that just 6.5% of patients are able to stop their antidepressant with this method (Eveleigh et al. 2017)

Consequence: people turn to peer support websites online for guidance



301,768 posts



mdwstrx: Lexapro taper or ...
By mdwstrx
4 minutes ago

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



Designing withdrawal support services for antidepressant users: Patients' views on existing services and what they really need

John Read ^a, Joanna Moncrieff ^{b c}  , Mark Abie Horowitz ^{b c 1}

[Show more](#) 

- 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%).

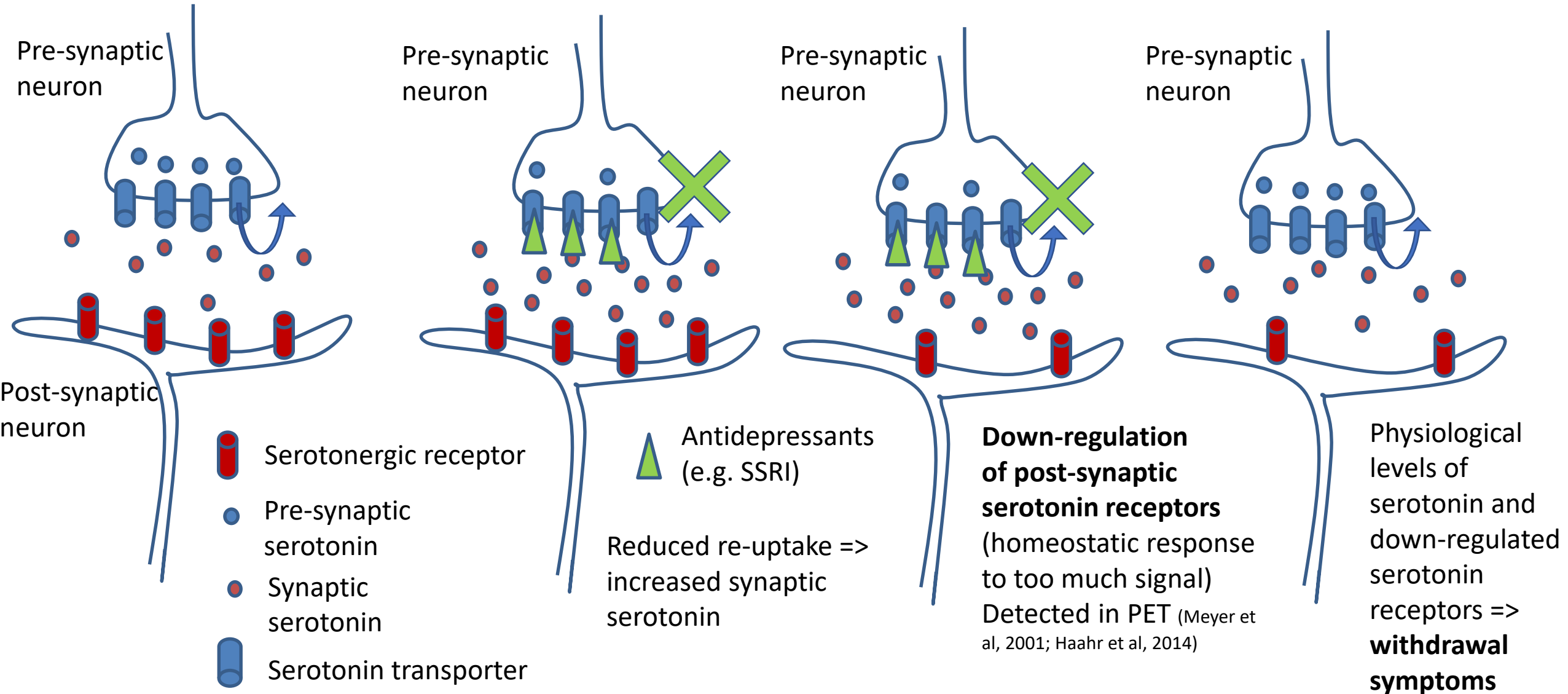
Effect of long-term antidepressant use and stopping

A Before Medication

B Medication introduced

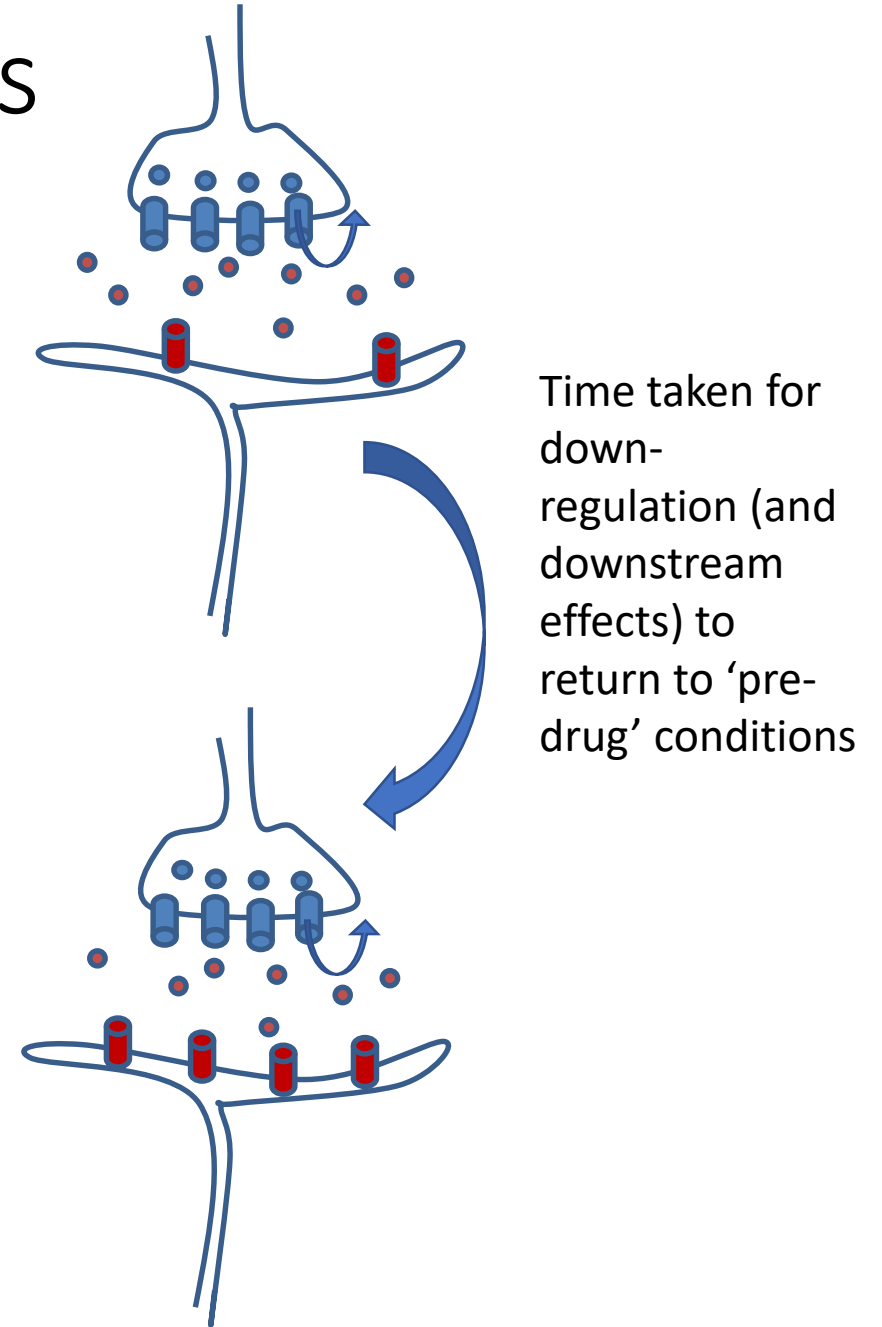
C Long term medication

D Medication stopped



Duration of withdrawal symptoms

- In 7 out of 10 studies identified, withdrawal symptoms went for longer than weeks
- Some surveys found patients had withdrawal symptoms 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 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
- Long-term use of antidepressants can cause long-term changes to the brain (identified on PET scanning even after short-term use) – also seen in animal studies



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 etc – 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

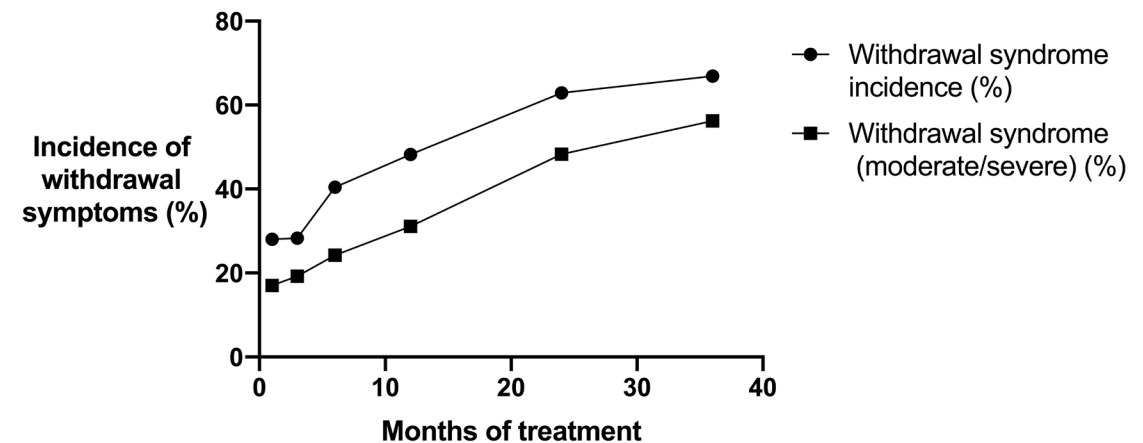
Mis-diagnosing antidepressant withdrawal effects as relapse

- 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

- This 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, 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
- Withdrawal symptoms can last for months or years after the drug has left the system – this is because this is how long it takes adaptations in the brain to resolve
- Unpublished survey in IAPT: 40% of patients wish to stop antidepressants but unable to do so because of difficulty stopping (extrapolates to 2 million people+ in England trapped on drugs)

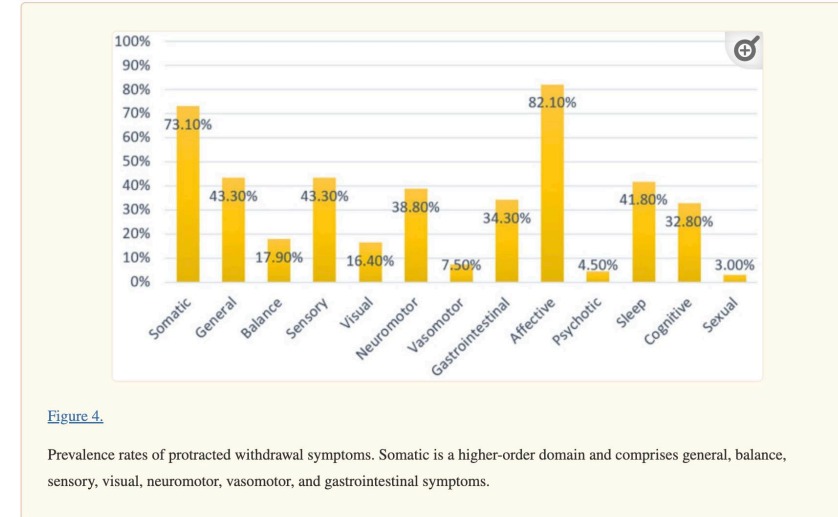
Relationship between duration of antidepressant use and incidence of withdrawal syndrome



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)

low points I considered suicide.' 'I continue to fight to get my life back, I could write a novel on the amount of suffering I have endured thanks to SSRI use. It has effected (sic) every part of my life, I can't work, I am not able to be active and even worse I can't get help because the prescribers are in the dark about the true harms of the drugs they prescribe.' 'Before I was put in this situation I was a "normal" person doing



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.”

How to minimise withdrawal symptoms by safely tapering

Why deprescribe antidepressants?

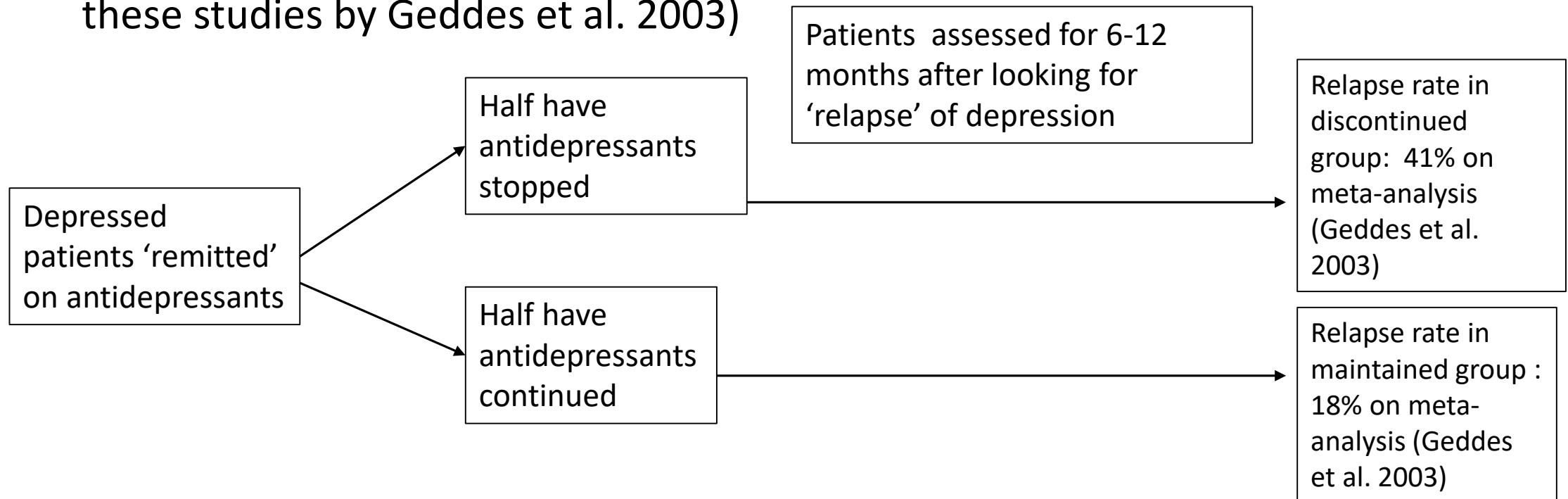
- Medication no longer needed
 - Stressor resolved (many patients prescribed these drugs in the context of divorce, job loss, physical health problem, death in family, etc – with relapse unlikely)
 - Alternative coping skills developed
 - Use for longer than guidelines recommend (mostly recommend 6-12 months for uncomplicated depression or anxiety)
- 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

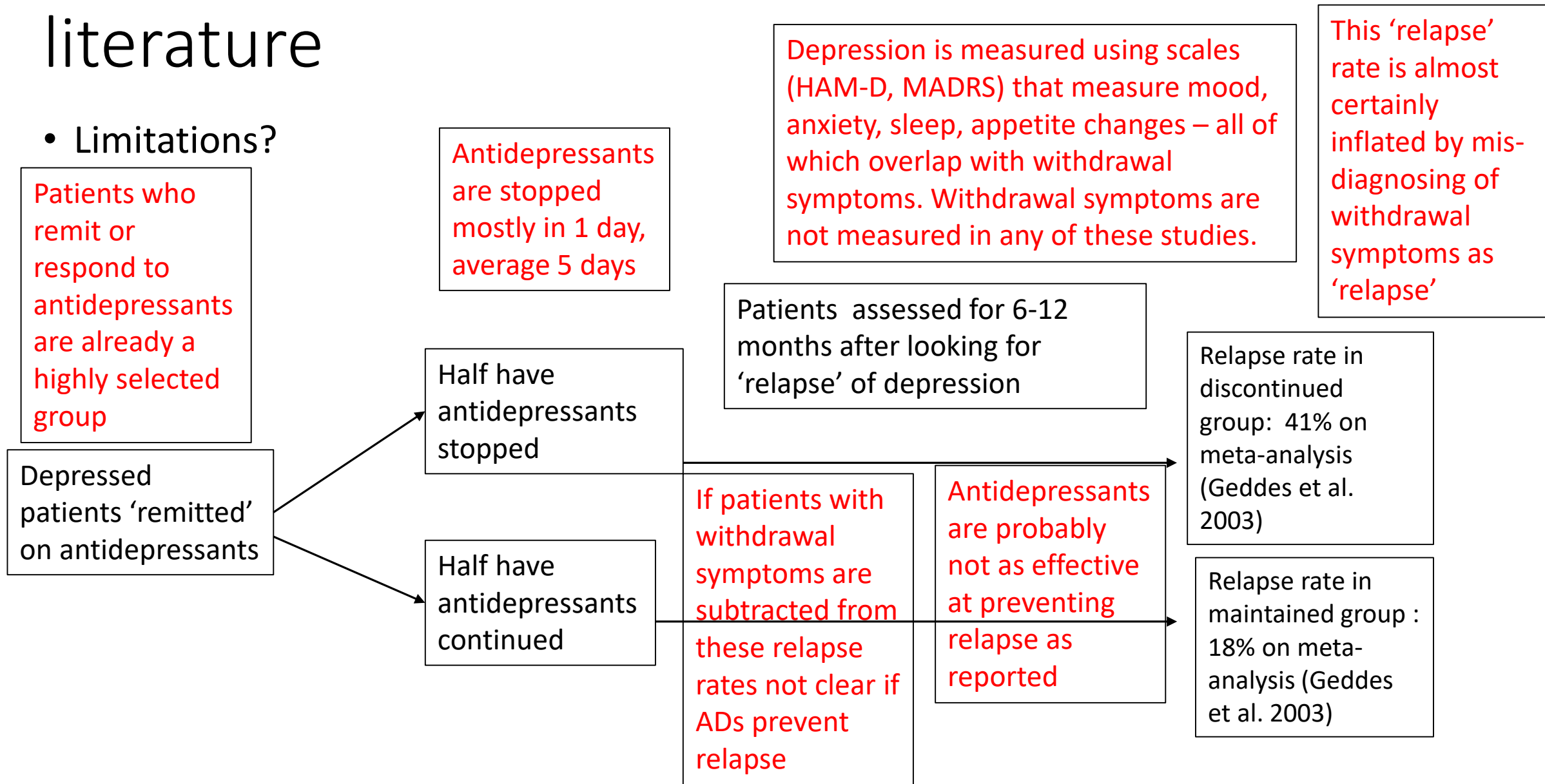
Evidence for long-term use of antidepressants

- 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)

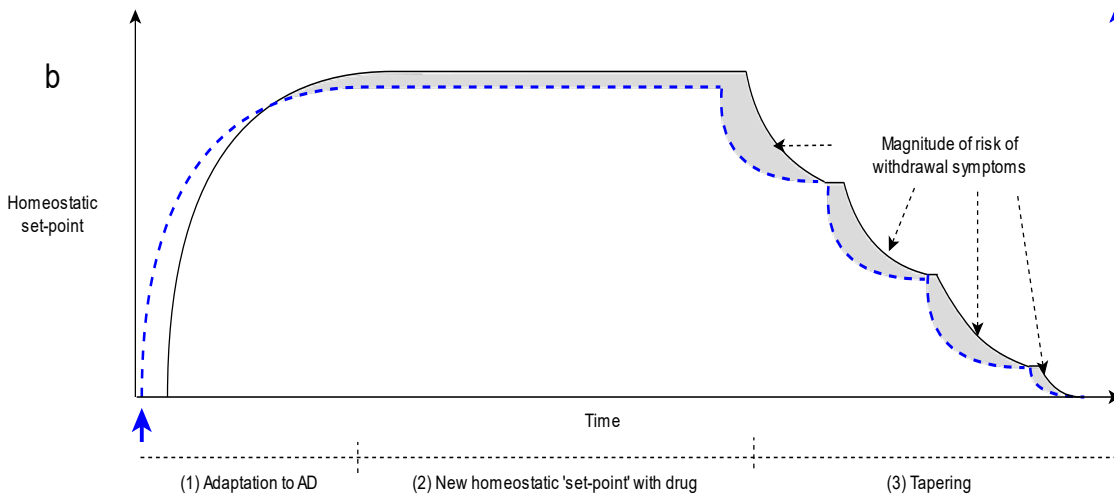
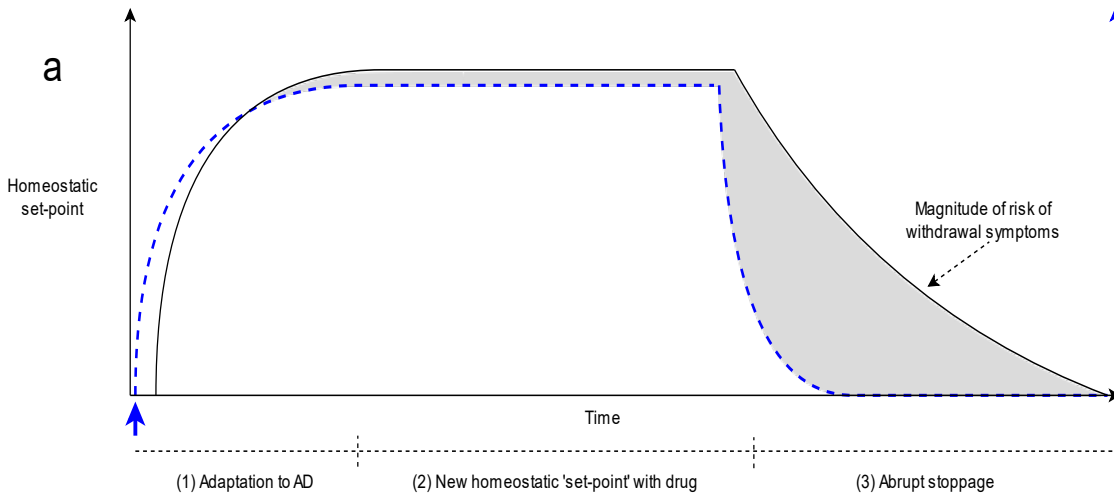


Limitations to the relapse prevention literature

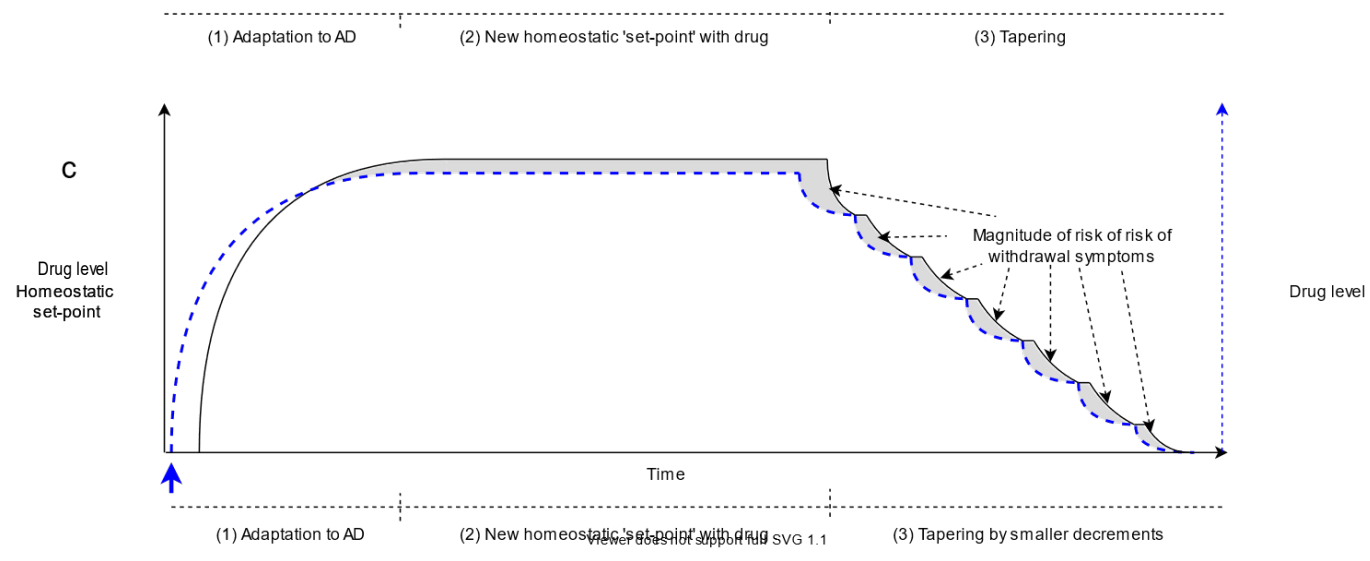
- Limitations?



Why taper



- The brain adapts to a drug
- When the drug is stopped the brain 'misses' the drug -> withdrawal effects
- Stopping a drug abruptly causes the greatest change and worst withdrawal effects
- Stopping in gradual steps reduces withdrawal effects
- Withdrawal effects last for as long as it takes the brain to re-adjust to the absence of medication
- From brain scanning this can take months or years in some patients



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 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



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

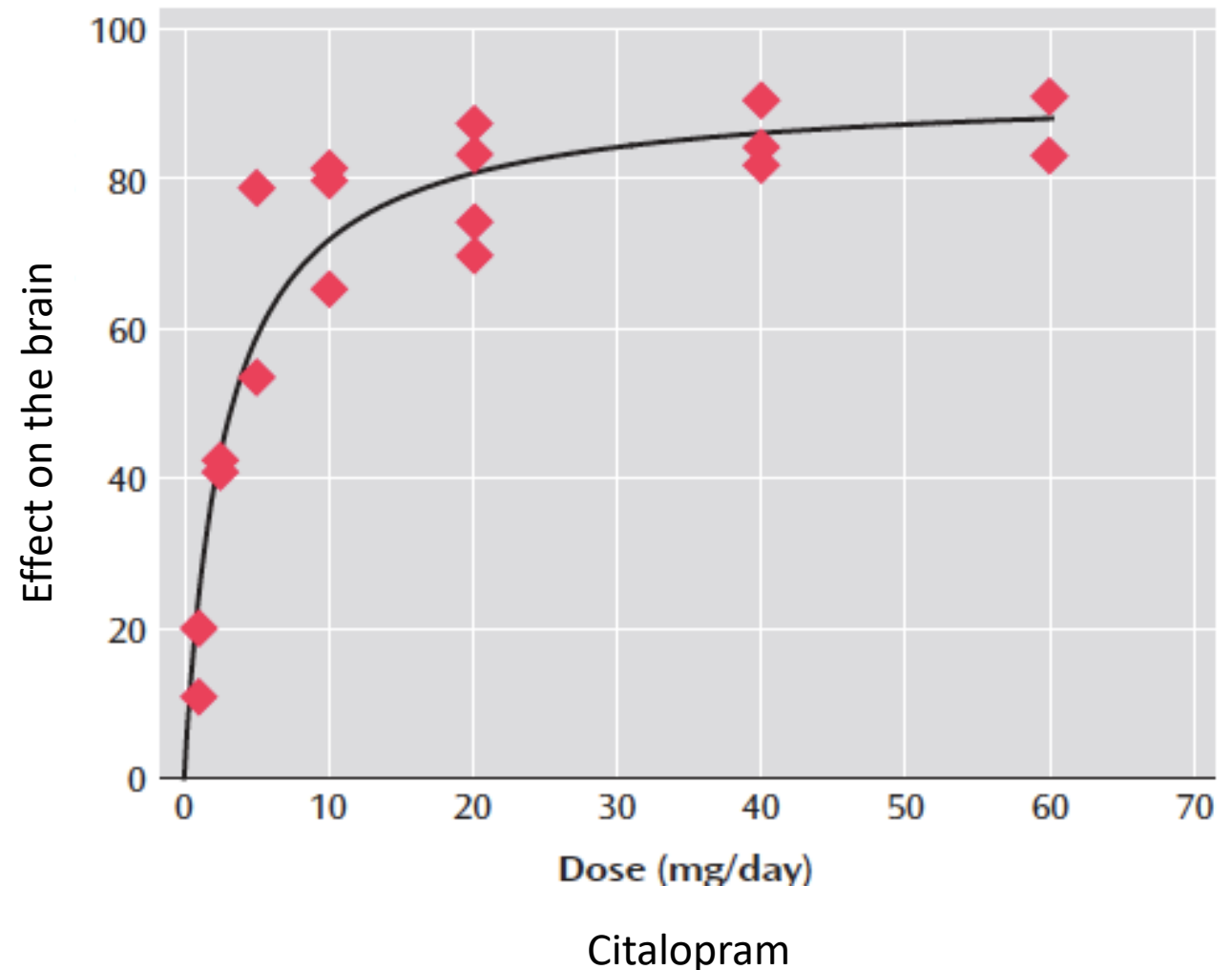
THE LANCET
Psychiatry

PERSONAL VIEW | VOLUME 6, ISSUE 6, P538-546, JUNE 01, 2019

Tapering of SSRI treatment to mitigate withdrawal symptoms

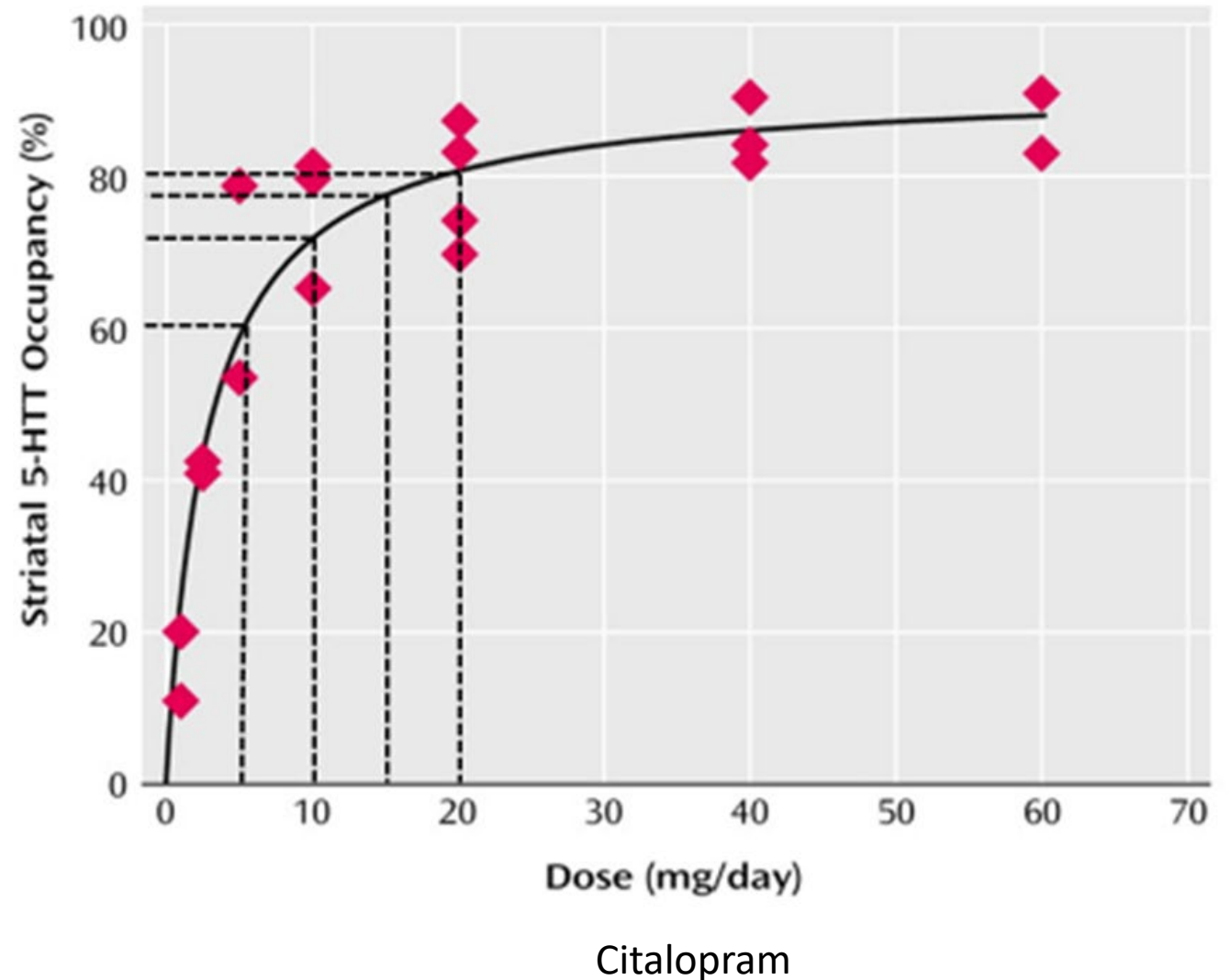
Mark Abie Horowitz, PhD · Prof David Taylor, PhD

Published: March 05, 2019 · DOI: [https://doi.org/10.1016/S2215-0366\(19\)30032-X](https://doi.org/10.1016/S2215-0366(19)30032-X) · [Check for updates](#)



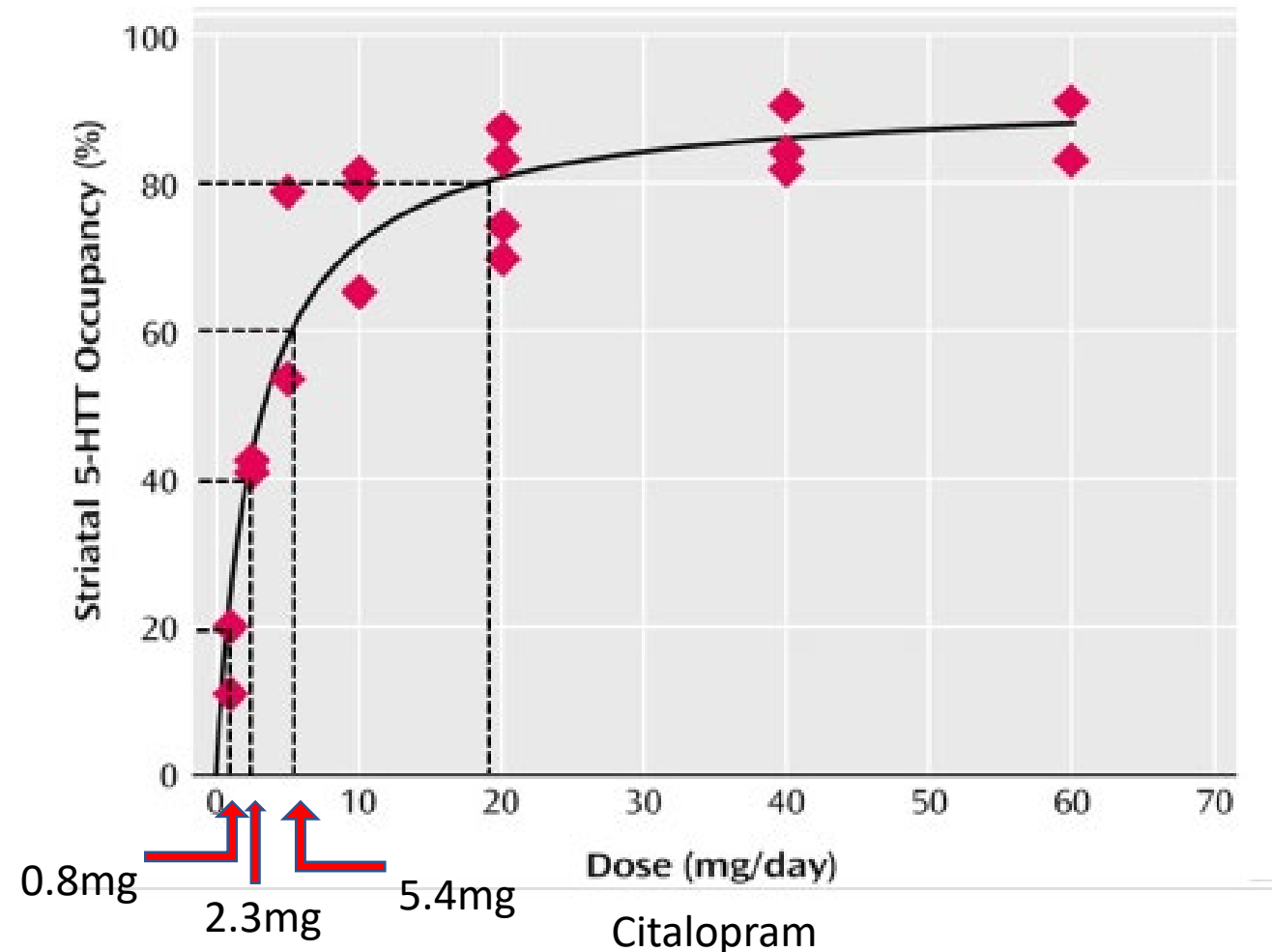
What happens when you taper linearly?

- 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.**



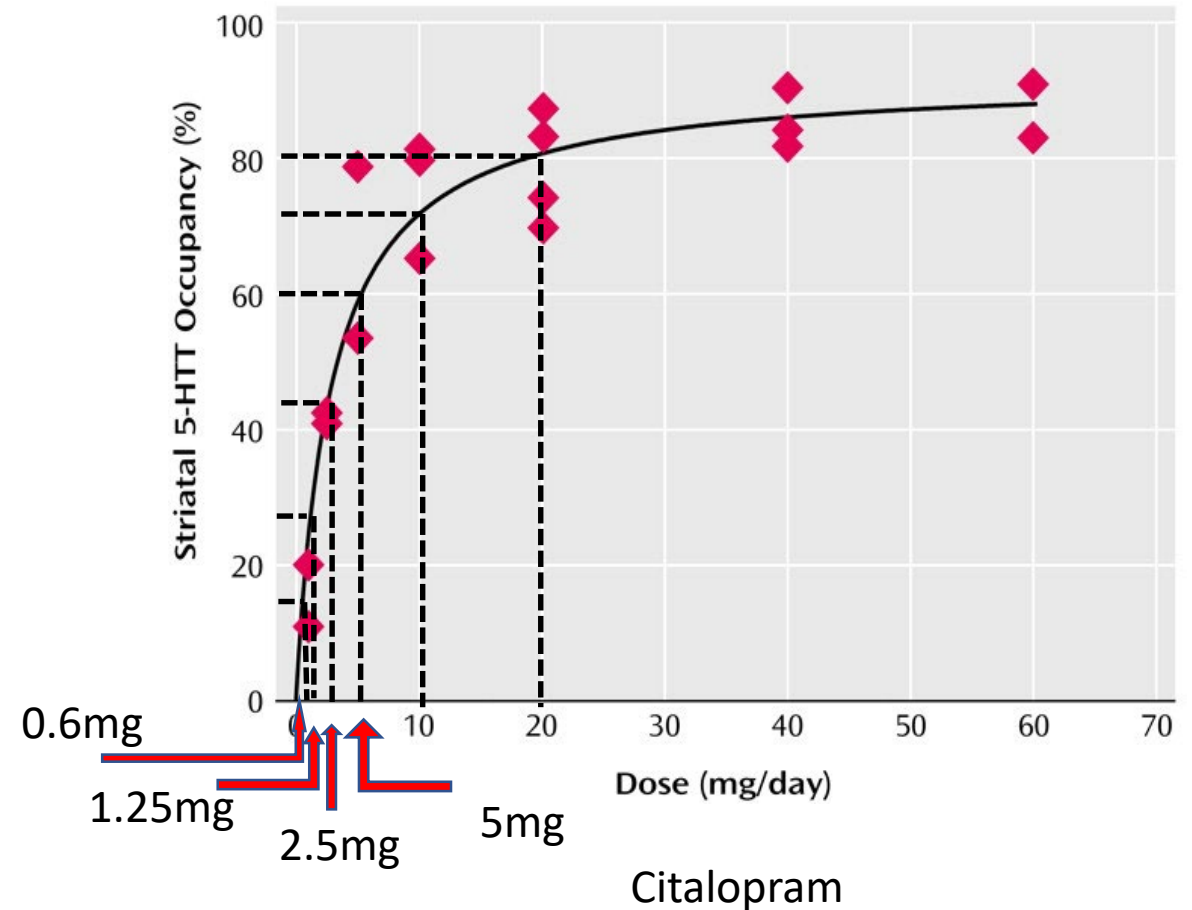
What happens when you taper by fix amounts of effect on the brain? Hyperbolic dose decrease

- 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



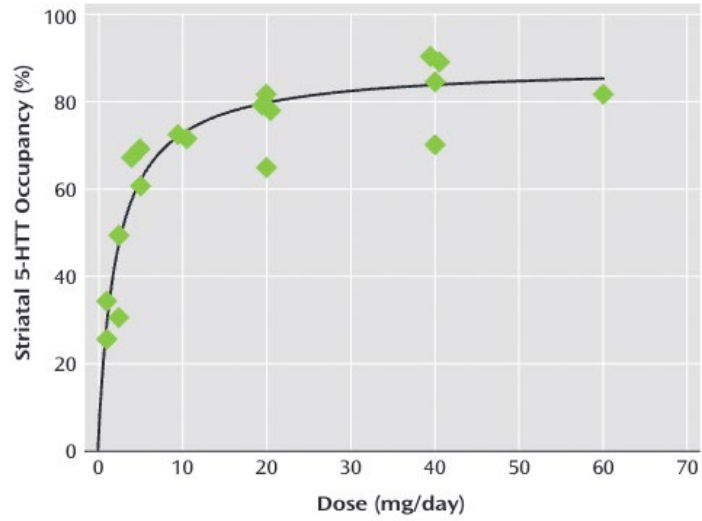
What happens when you taper by fixed amounts of effect on the brain? Proportionate dose decrease

- 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

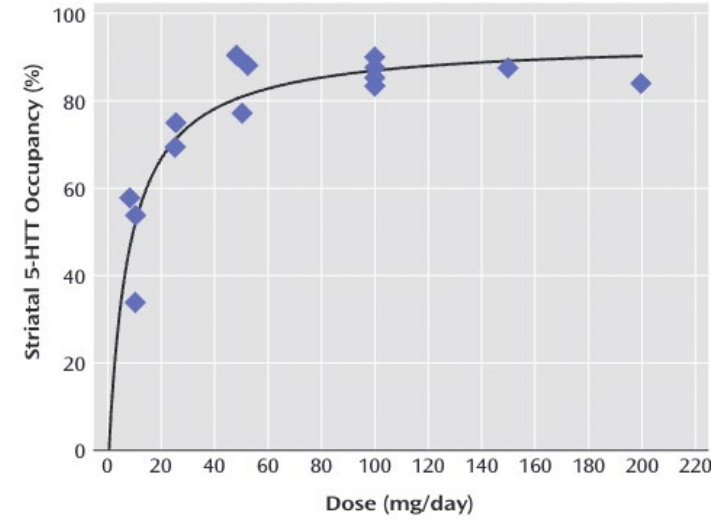


True for all antidepressants

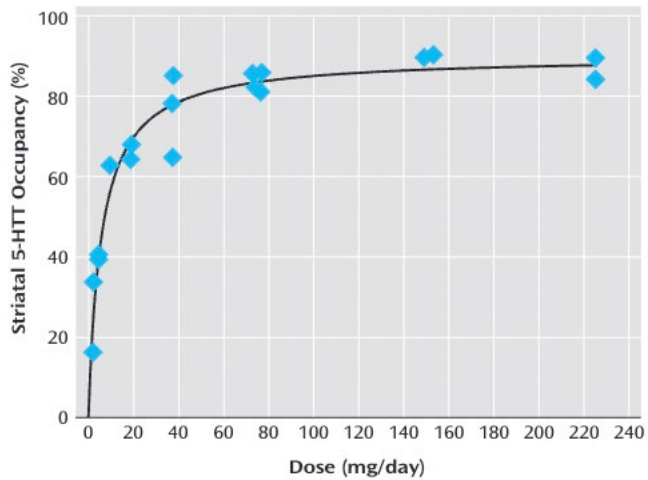
Fluoxetine



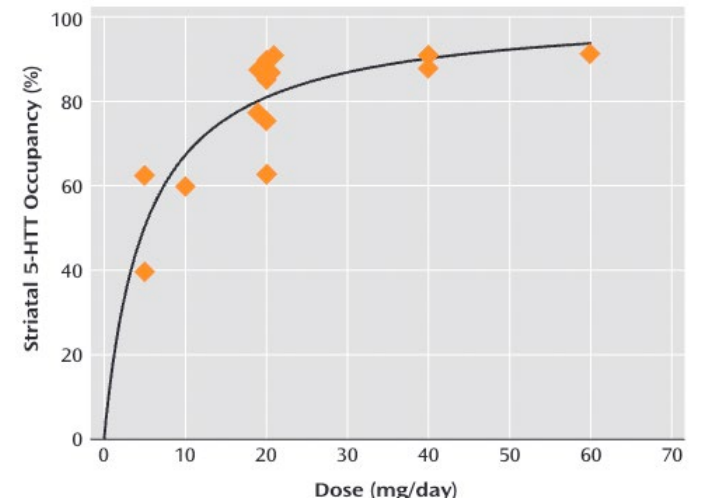
Sertraline



Venlafaxine



Paroxetine



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)

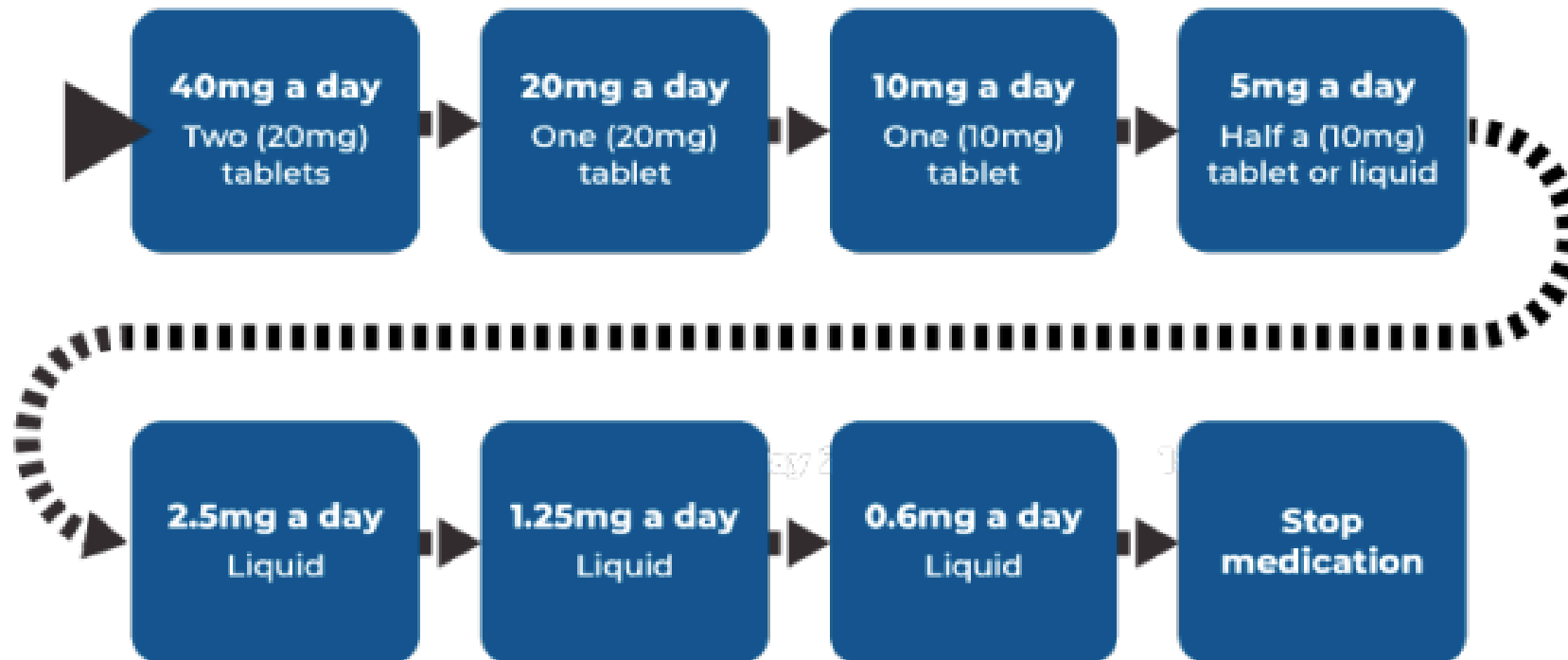


Stopping antidepressants

A rapid reduction schedule (RCPsych, 2020)

Citalopram

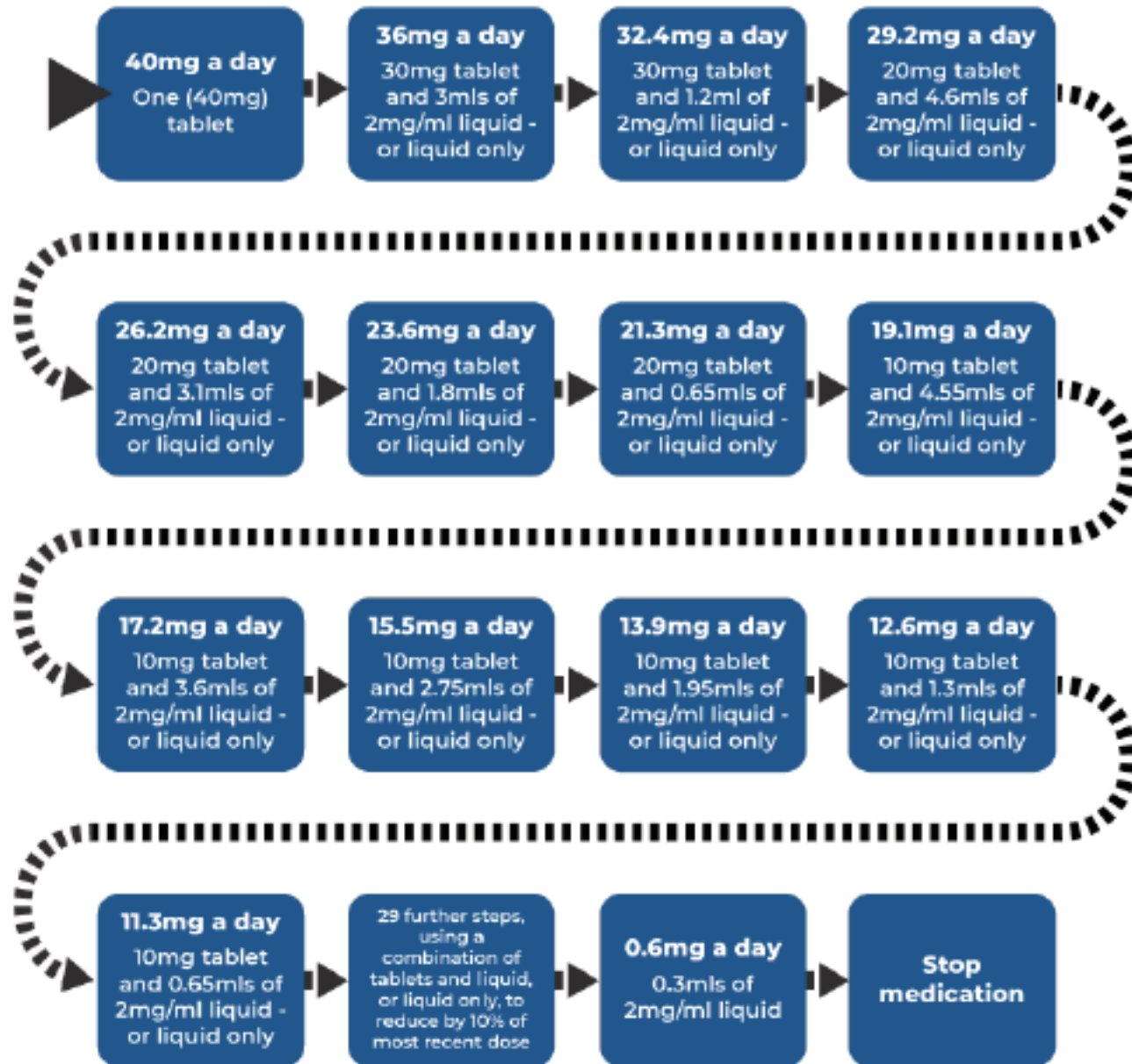
Reduction of dose by 50%, every 2-4 weeks. Some people may need to reduce more slowly.



- 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



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Guideline

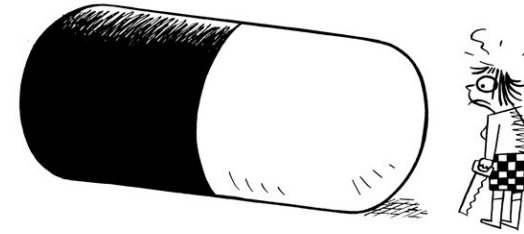
Depression in adults

Draft for consultation, November 2021

- 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 will be required – available for most antidepressants in UK – using small syringes
- 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 $\frac{1}{4}$ of peak levels



Good luck with
the tapering of
your medication



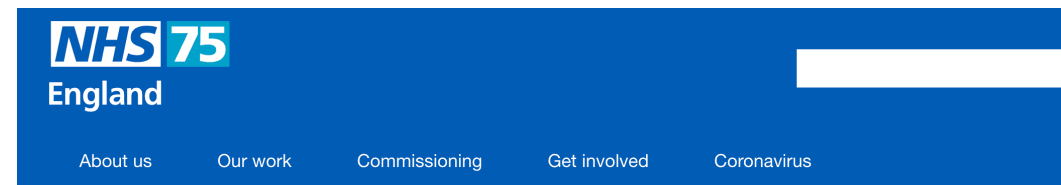
Sigmund copyright 2018 Peter de Wit

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NHS England commissioning framework for prescribed drug dependence

- In March 2023, NHS England released a commissioning framework, including an Action to:
- ‘ensure appropriate commissioning of services for patients taking medication associated with dependence and withdrawal symptoms [including antidepressants], **including services for patients wishing to reduce or stop these medications**”



Optimising personalised care for adults prescribed medicines associated with dependence or withdrawal symptoms

Medication optimization for antidepressants

National medicines optimisation opportunities 2023/24

7. Addressing inappropriate antidepressant prescribing

- One of the identified aims of the NHS is to reduce inappropriate antidepressant prescribing - i.e. longer than guidelines recommend or where harms outweigh benefits or the person wants to stop
- They have recommended specialist services to help people stop and also to care for those with protracted and severe withdrawal syndromes

What success looks like

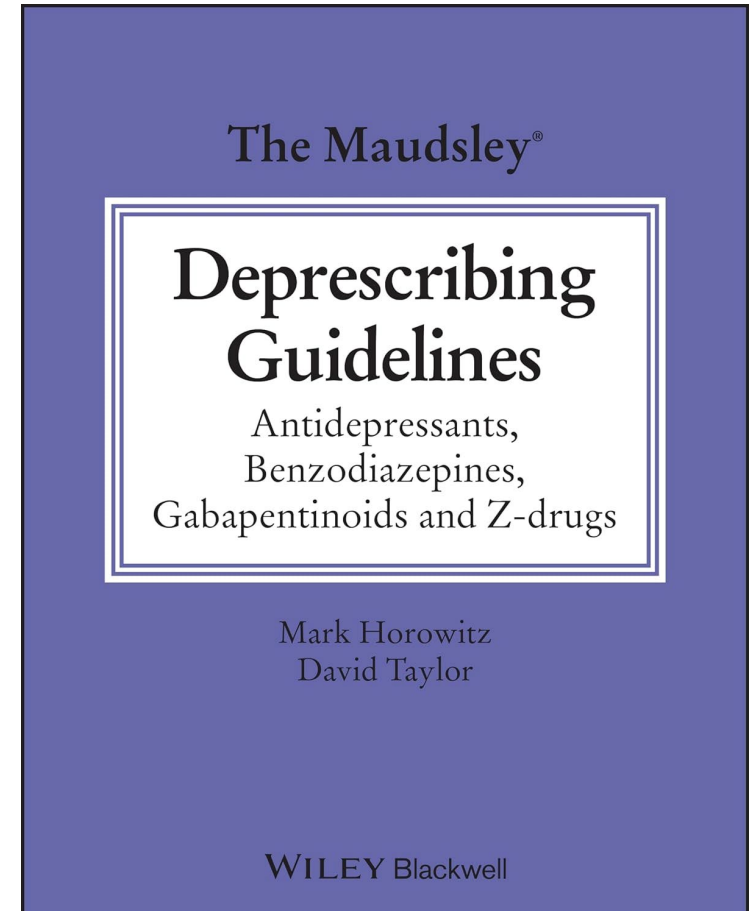
- Use of antidepressants in line with NICE guidance on treatment and management of depression.
- ICB commissioned services in place to support people suffering from protracted and severe problems associated with antidepressant withdrawal.



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 Canada 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
<u>Duration of use^a</u>	
■ 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
<u>Antidepressant type</u>	
■ 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
<u>Dosage</u>	
■ Minimum therapeutic dosage or lower	0 points
■ Greater than the minimum therapeutic dosage	1 point
<u>Past experience of withdrawal symptoms</u>	
■ 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

Rules of thumb for tapering

- In very broad terms:
 - FAST: 50% dose reductions every month (made on the previous month's dose) are very quick, only few will tolerate
 - MODERATE: 25% dose reductions every month (made on the previous month's dose) are moderate, some will tolerate
 - SLOW: 10% dose reductions every month (made on the previous month's dose) are slow, many will tolerate
 - VERY SLOW: 5% dose reductions (or less) every month (made on the previous month's dose) will be required by some patients (e.g. long-term paroxetine, venlafaxine, etc).

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.

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



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Citalopram, escitalopram, paroxetine or sertraline tablets

Can be crushed and/or dispersed in water, or crushed and given with soft food. The tablets are film-coated and contents may taste bitter or unpleasant. Crushed sertraline and paroxetine tablets may have a local anaesthetic effect on the tongue.

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.

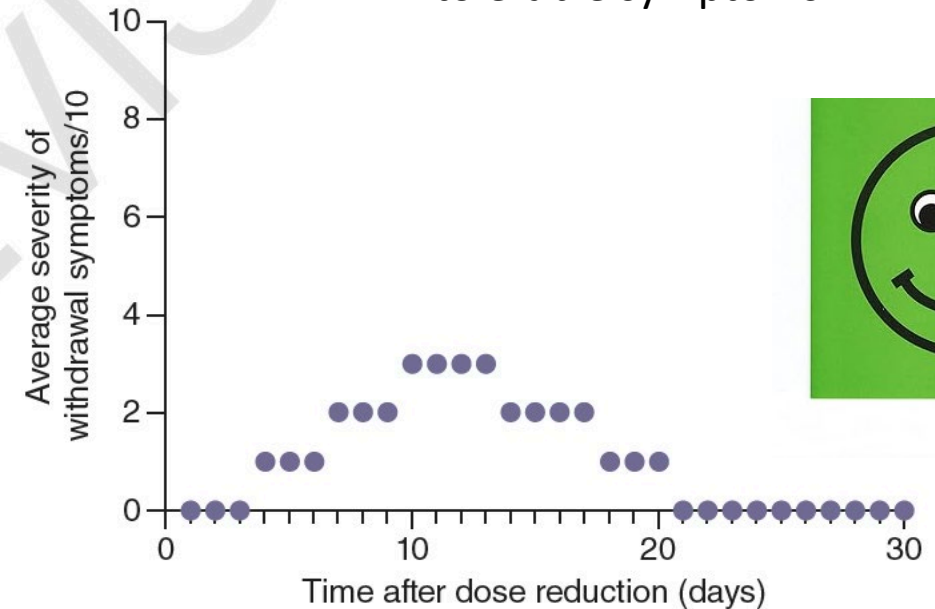
Adjusting the taper to an individual

Miss Y, Citalopram, April 2021.

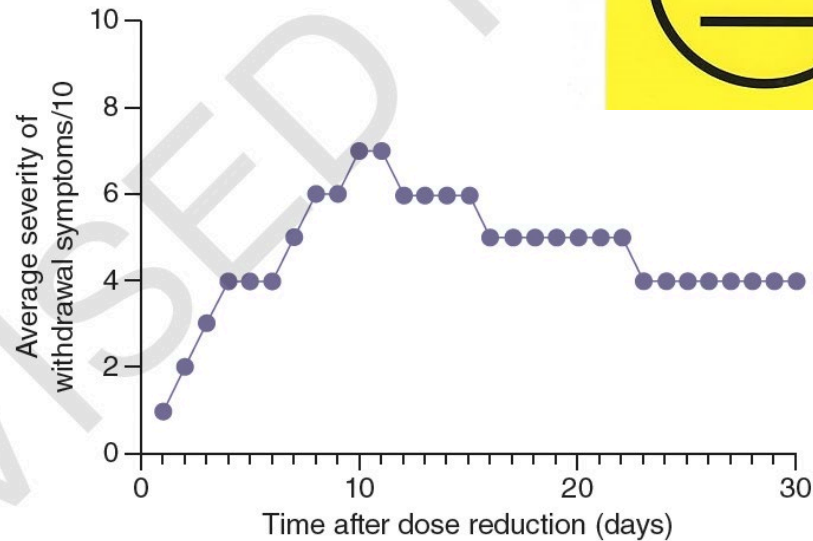
Day	Dose (mg)	Anxiety /10	Dizziness /10	Insomnia /10	Overall symptom /10
1	20	1	0	0	1
2	20	1	0	0	1
3	20	1	0	0	1
4	20	1	0	0	1
5	15	1	0	0	1
6	15	1	0	0	1
7	15	2	1	1	2
8	15	2	1	2	2
9	15	2	1	2	2
10	15	3	2	2	3
11	15	3	2	3	3
12	15	4	3	3	4
13	15	4	3	4	4
14	15	4	3	4	4
15	15	4	4	3	4
16	15	4	4	3	4
17	15	3	3	2	3
18	15	3	3	2	3
19	15	3	3	2	3
20	15	2	2	2	2
21	15	2	2	2	2
22	15	2	2	1	1
23	15	1	1	1	1
24	15	1	1	1	1
25	15	1	1	1	1

Record of withdrawal symptoms

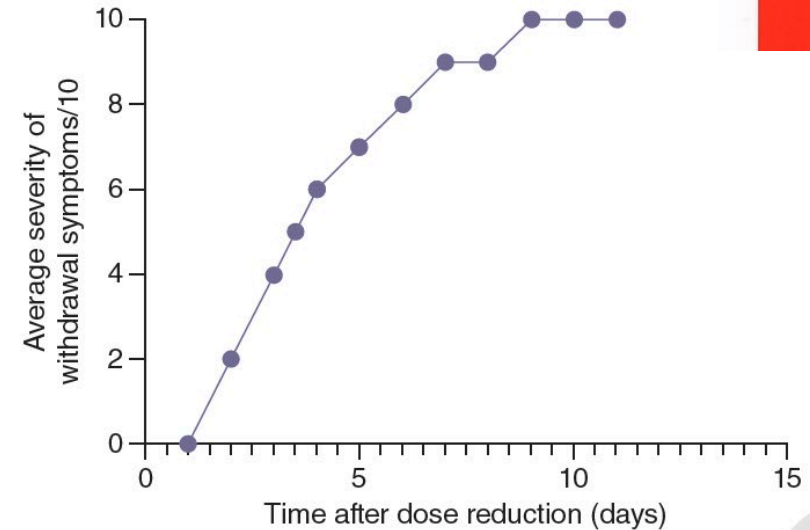
Withdrawal symptoms in graph form (to view) - 'tolerable symptoms'



Adjusting the taper to an individual - 2



Moderately severe withdrawal symptoms -> wait longer before next reduction + taper more gradually



Severe withdrawal symptoms -> return to previous dose, wait to stabilize + taper much more gradually

Adjusting the taper to an individual - 3

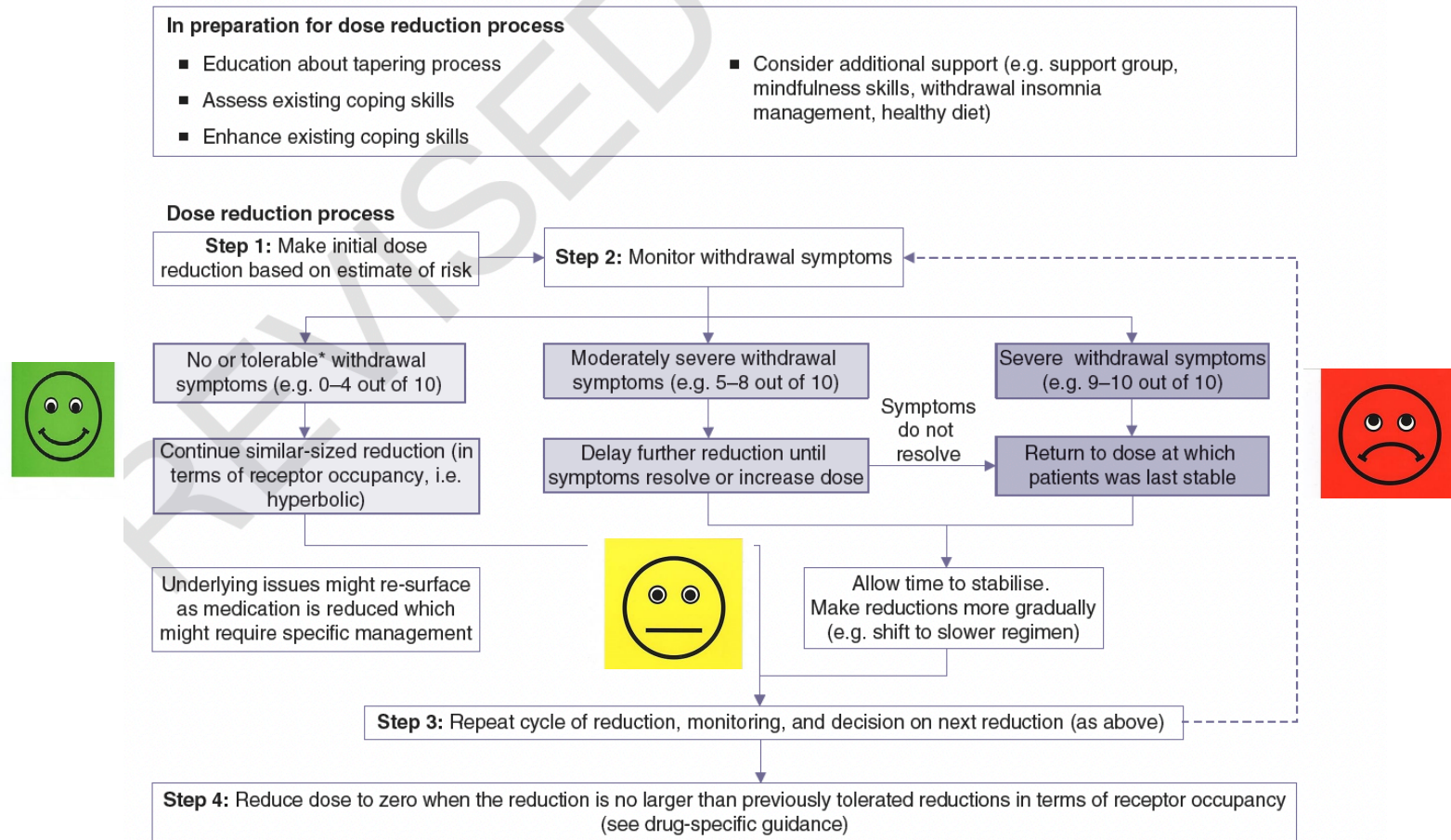


Figure 2.9 An overview of the process of tapering antidepressants.

*What constitutes tolerable symptoms will vary between patients but are generally symptoms that do not overly interfere with their lives.

Other psychiatric drugs

Tapering other psychiatric drugs

- “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”

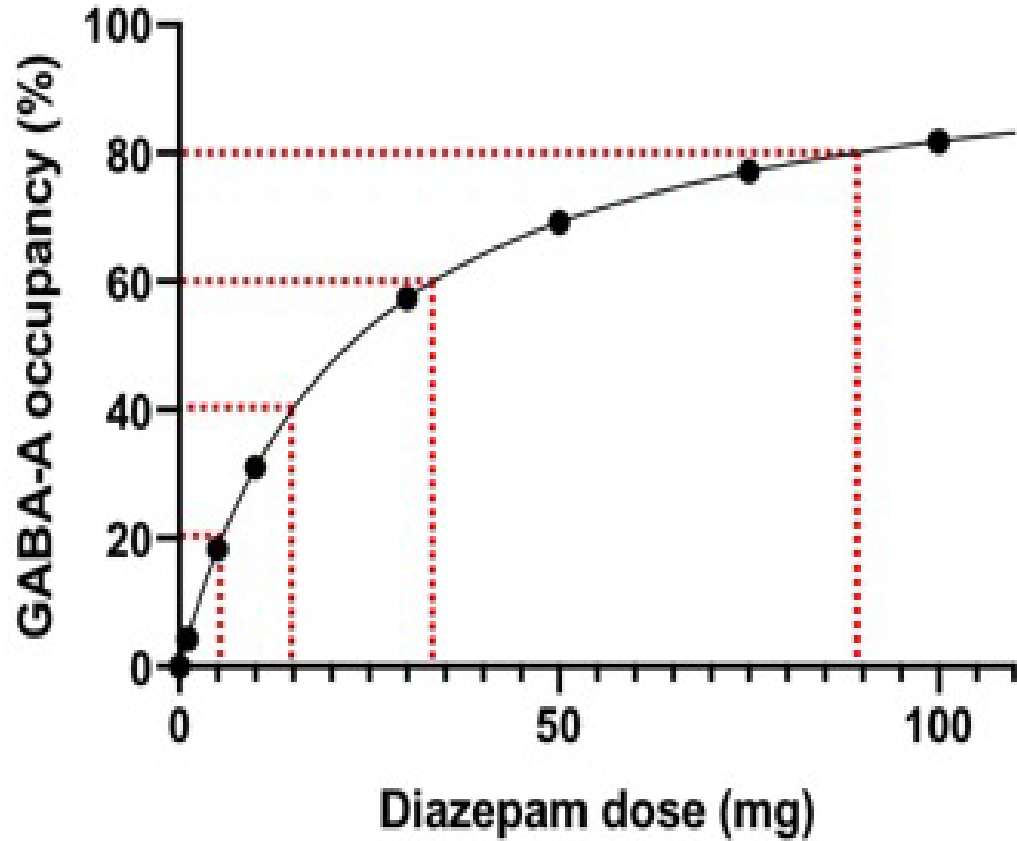
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Guideline

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

Draft for consultation, October 2021

C



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*.

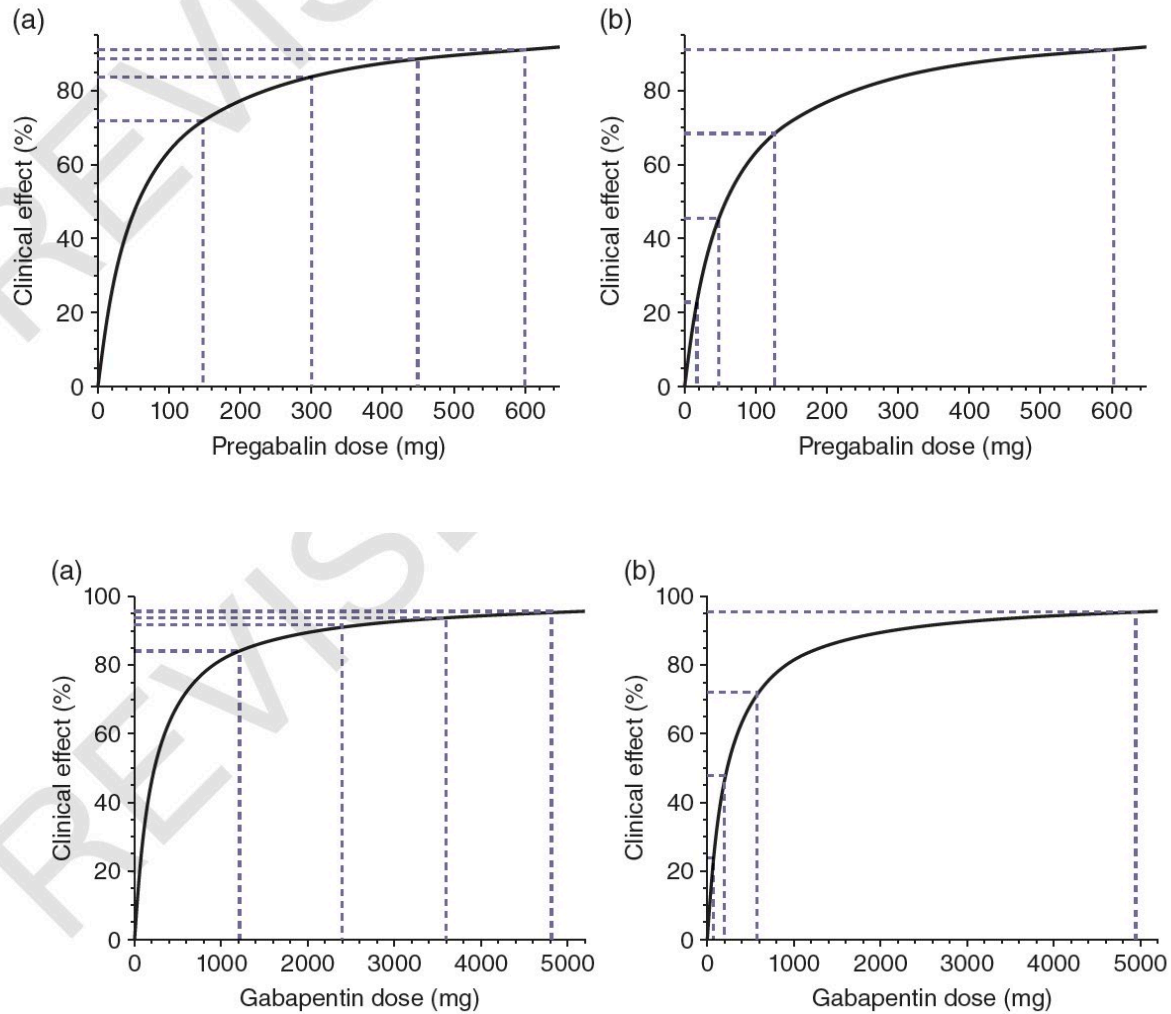
Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form	Step	RO (%)	AM (mg)	PM (mg)	Total daily dose (mg)	Form
1	70.8	30	30	60	Use tablets	13	36.2	7	7	14	Use tablets
2	69	25	30	55	Use tablets	14	32.7	6	6	12	Use tablets
3	66.9	25	25	50	Use tablets	15	28.8	5	5	10	Use tablets
4	64.6	20	25	45	Use tablets	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											

Including guidance on when to switch shorting acting benzodiazepines to diazepam

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											

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

Take home messages 1

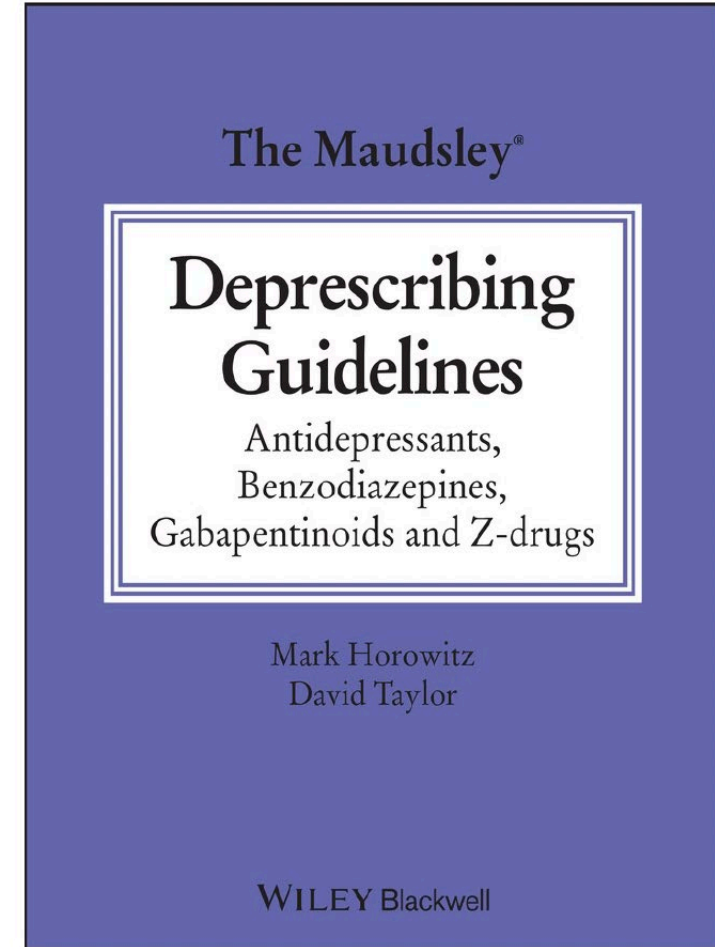
- Feeling anxious or depressed when reducing/stopping antidepressants is not necessarily a sign of relapse – these symptoms are common in withdrawal (and can be very familiar)
- Withdrawal effects are usually mild and brief after short term use but can be severe, prolonged and debilitating after longer term use
- Withdrawal effects can be delayed by weeks or longer in onset
- Protracted withdrawal syndrome can consist of psychological and somatic symptoms which persist for months or longer with significant implications – almost always mis-diagnosed
- Tapering antidepressants over much longer periods (months or sometimes years) than usual practice (weeks) is more likely to be successful

Take home messages - 2

- Make reductions by smaller and smaller amounts as total dose gets lower (called proportionate or hyperbolic tapering)
- Some patients will need to go down to very small doses before stopping eg a fraction of a mg for many antidepressants
- In order to make these small reductions patient will need access to liquid versions of drugs or other small compounded doses
- The rate of tapering should be modified based on the ability of the patient to tolerate reductions (i.e. withdrawal symptoms)
- With the exception of fluoxetine the short half-life of antidepressants means that every other day dosing risks withdrawal symptoms – it is better to take the same dose every day
- Same principles apply to other psychiatric drug classes

Thank you for listening

- Questions?
- My email for any further questions:
m.horowitz@ucl.ac.uk



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References

- Davies, J. and Read, J. (2019) 'A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guidelines evidence-based?', *Addictive Behaviors*. Elsevier, 97(August), pp. 111–121. doi: 10.1016/j.addbeh.2018.08.027.
- Groot PC, van Os J. How user knowledge of psychotropic drug withdrawal resulted in the development of person-specific tapering medication. *Therapeutic Advances in Psychopharmacology*. 2020 Jan 10;10:204512532093245.
- Horowitz, M. A. and Taylor, D. (2019) 'Tapering of SSRI treatment to mitigate withdrawal symptoms', *The Lancet Psychiatry*. Elsevier Ltd, 6(6), pp. 538–546. doi: 10.1016/S2215-0366(19)30032-X.
- National Institute for Health and Care Excellence. Depression in adults:Guideline (Draft for consultation, November 2021) [Internet]. [cited 2021 Dec 2]. Available from: <https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0725/documents>
- NICE. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults [Internet]. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults - draft guideline. 2021 [cited 2021 Nov 9]. Available from: <https://www.nice.org.uk/guidance/GID-NG10141/documents/draft-guideline>
- Royal College of Psychiatrists. Stopping antidepressants. 2020. <https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/stopping-antidepressants>
- Royal College of Psychiatrists Position statement on antidepressants and depression. 2019. https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps04_19---antidepressants-and-depression.pdf?sfvrsn=ddea9473_5