The Maudsley®

Deprescribing Guidelines

Antidepressants,
Benzodiazepines,
Gabapentinoids and Z-drugs

Mark Horowitz David Taylor

WILEY Blackwell

The Maudsley® Deprescribing Guidelines

The Maudsley Guidelines

Other books in the Maudsley Prescribing Guidelines series include:

The Maudsley Prescribing Guidelines in Psychiatry, 14th Edition

David M. Taylor, Thomas R. E. Barnes, Allan H. Young

The Maudsley Practice Guidelines for Physical Health Conditions in Psychiatry

David M. Taylor, Fiona Gaughran, Toby Pillinger

The Maudsley Guidelines on Advanced Prescribing in Psychosis

Paul Morrison, David M. Taylor, Phillip McGuire

The Maudsley Prescribing Guidelines for Mental Health Conditions in Physical Illness Siobhan Gee, David M. Taylor

The Maudsley® Deprescribing Guidelines

Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs

Mark Horowitz, BA, BSc(Med), MBBS(Hons), MSc, GDipPsych, PhD

Clinical Research Fellow in Psychiatry and Co-lead clinician in the Psychotropic Deprescribing Clinic North East London NHS Foundation Trust, Ilford, UK Honorary Clinical Research Fellow, Department of Psychiatry, University College London, London, UK

David Taylor, PhD, FFRPS, FRPharmS, FRCP_{Edin}, FRCPsych(Hon)

Director of Pharmacy and Pathology South London and Maudsley NHS Foundation Trust Professor of Psychopharmacology, King's College London, London, UK



This edition first published 2024 © 2024 John Wiley & Sons Ltd

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by law. Advice on how to obtain permission to reuse material from this title is available at http://www.wiley.com/go/permissions.

The right of Mark Horowitz and David Taylor to be identified as the authors of this work has been asserted in accordance with law.

Registered Offices

John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SO, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Trademarks: Wiley and the Wiley logo are trademarks or registered trademarks of John Wiley & Sons, Inc. and/or its affiliates in the United States and other countries and may not be used without written permission. All other trademarks are the property of their respective owners. John Wiley & Sons, Inc. is not associated with any product or vendor mentioned in this book.

Limit of Liability/Disclaimer of Warranty

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting scientific method, diagnosis, or treatment by physicians for any particular patient. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials or promotional statements for this work. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Cataloging-in-Publication Data Applied for ISBN: 9781119822981 (Paperback); 9781119823018 (Adobe PDF); 9781119823025 (EPub)

Cover design: Wiley

Set in 10/12pt Sabon by Straive, Pondicherry, India

Contents

	Pretace	1X
	Acknowledgements	xii
	Notes on using The Maudsley® Deprescribing Guidelines	xiii
	Abbreviations List	XV
Chapter 1	Introduction to Deprescribing Psychiatric Medications	1
-	Deprescribing as an Intervention	1
	The context for deprescribing	2
	Why deprescribe?	2 7
	Barriers and facilitators to deprescribing	11
	Withdrawal Effects from Psychiatric Medications	13
	Mis-diagnosis of withdrawal effects as relapse	13
	Pathophysiology of psychiatric drug withdrawal symptoms	16
	Clinical aspects of psychiatric drug withdrawal	19
	Specific issues in psychiatric drug withdrawal	23
	How to Deprescribe Psychiatric Medications Safely	27
	The neurobiology of tapering	28
	Practical options for prescribing gradually tapering doses	36
	Psychological aspects of tapering	43
	Tapering psychiatric drugs in practice	45
	Further topics	52
Chapter 2	Safe Deprescribing of Antidepressants	57
•	When and Why to Stop Antidepressants	57
	Adverse effects of antidepressants	66
	Discussing deprescribing antidepressants with patients	72
	Withdrawal Effects from Antidepressants	76
	Recent developments in the understanding of antidepressant withdrawal	76
	Pathophysiology of antidepressant withdrawal symptoms	80
	Clinical aspects of antidepressant withdrawal	87
	How common, severe and long-lasting are withdrawal symptoms from	
	antidepressants?	92
	Protracted antidepressant withdrawal syndrome	96

	Post-SSRI sexual dysfunction	98
	Factors influencing development of withdrawal effects	99
	Stratfiying risk of antidepressant withdrawal	105
	Distinguishing antidepressant withdrawal symptoms from relapse	107
	Distinguishing antidepressant withdrawal symptoms from new	
	onset of a physical or mental health condition	111
	Withdrawal symptoms during antidepressant maintenance treatment or	
	switching medication	113
	How to Deprescribe Antidepressants Safely	115
	Tapering antidepressants gradually	119
	Hyperbolic tapering of antidepressants	125
	Practical options in prescribing gradually tapering doses of antidepressants	131
	Psychological aspects of antidepressant tapering	140
	Tapering antidepressants in practice	143
	Managing complications of antidepressant discontinuation	153
	Tapering Guidance for Specific Antidepressants	158
	Agomelatine	159
	Amitriptyline	163
	Bupropion	168
	Citalopram	174
	Clomipramine	183
	Desvenlafaxine	188
	Dosulepin	193
	Doxepin	198
	Duloxetine	203
	Escitalopram	209
	Fluoxetine	216
	Fluvoxamine	223
	Imipramine	228
	Lofepramine	233
	Mirtazapine	238
	Moclobemide	243
	Nortriptyline	248
	Paroxetine	253
	Phenelzine	259
	Sertraline	264
	Tranylcypromine	270
	Trazodone	275
	Venlafaxine	280
	Vilazodone	288
	Vortioxetine	292
Chapter 3	Safe Deprescribing of Benzodiazepines and Z-drugs	297
	When and Why to Stop Benzodiazepines and Z-drugs	297
	Discussing deprescribing benzodiazepines and z-drugs	304
	Withdrawal Symptoms from Benzodiazepines and Z-drugs	309
	, 1	

	Physical dependence vs addiction in use of benzodiazepines and z-drugs	311
	Pathophysiology of benzodiazepine withdrawal syndrome	313
	Variety of withdrawal symptoms from benzodiazepines and z-drugs	316
	Protracted benzodiazepine withdrawal syndrome	320
	Distinguishing benzodiazepine withdrawal symptoms from return of an	
	underlying condition	323
	Withdrawal symptoms during benzodiazepine maintenance treatment	326
	How to Deprescribe Benzodiazepines and Z-drugs Safely	327
	Tapering benzodiazepines and z-drugs gradually	330
	Hyperbolic tapering of benzodiazepines and z-drugs	332
	Switching to longer-acting benzodiazepines to taper	335
	Making up smaller doses of benzodiazepines and z-drugs practically	338
		342
	Other considerations in tapering benzodiazepines and z-drugs	345
	Psychological aspects of tapering benzodiazepines and z-drugs	
	Tapering benzodiazepines and z-drugs in practice	348
	Management of complications of benzodiazepine and z-drug	250
	discontinuation	358
	Tapering Guidance for Specific Benzodiazepines and Z-drugs	362
	Alprazolam	364
	Buspirone	375
	Chlordiazepoxide	380
	Clonazepam	388
	Clorazepate	396
	Diazepam	404
	Estazolam	412
	Eszopiclone	418
	Flurazepam	423
	Lorazepam	429
	Lormetazepam	440
	Nitrazepam	446
	Oxazepam	452
	Quazepam	461
	Temazepam	467
	Triazolam	474
	Zaleplon	480
	Zolpidem	485
	Zopiclone	490
Chapter 4	Safe Deprescribing of Gabapentinoids	495
-	When and Why to Stop Gabapentinoids	495
	Discussing deprescribing gabapentinoids	504
	Overview of Gabapentinoid Withdrawal Effects	507
	Physical dependence vs addiction in use of gabapentinoids	510
	How to Deprescribe Gabapentinoids Safely	512
	Principles for tapering gabapentinoids	512
	Making up smaller doses of gabapentinoids practically	516
	making up smaller doses of gavapentinolus practically	510

viii Contents

Other considerations in tapering gabapentinoids	520
Psychological aspects of tapering gabapentinoids	523
Tapering gabapentinoids in practice	525
Management of complications of gabapentinoid discontinuation	532
Tapering Guidance for Specific Gabapentinoids	537
Gabapentin	538
Pregabalin	546
Index	553

Preface

'It is an art of no little importance to administer medicines properly; but it is an art of much greater and more difficult acquisition to know when to suspend or altogether omit them.'

Philippe Pinel 1745–1826

This is not a book that questions the validity or effectiveness of medicines used for mental health conditions. It is a guide to the deprescribing of psychotropic medication in situations where deprescribing is, on balance, agreed to be a better option than continued prescribing. The agreement here is between prescriber and patient. The core tenet of this text is that decisions are made jointly in the patient's best interest.

Patients have expressed dissatisfaction – and sometimes outrage – with available medical assistance for stopping psychiatric medications. This has led to many tens of thousands of patients seeking advice from online peer-support forums. When surveyed, these patients report that their doctors were often unhelpful either because they recommended tapering too quickly or because they were not familiar enough with withdrawal effects to provide helpful advice.¹ Some doctors are apparently still suggesting that antidepressants do not cause withdrawal symptoms. The main requests from these patients are that health professionals are sufficiently well informed to provide personalised, flexible reduction plans and that access is provided to smaller doses to facilitate tapering (either liquid versions of medication, or specially compounded smaller dose tablets or capsules).¹ We hope this textbook will contribute to a broader understanding of these issues, a greater expertise in helping patients and a better outcome for all.

In writing this textbook we took on what some might consider an impossible task. Safely stopping psychiatric medications is not simply a matter of outlining a regimen of reducing doses for patients to follow. There are too many aspects of the drug, the individual and their lives that come into play such that adjustments inevitably need to be made, often involving a certain amount of trial and error. Yet the most common request we receive from patients and clinicians is to provide tapering schedules to guide reductions. It can be daunting to begin a journey without a map to follow. So in this book we have tried to balance specific guidance with flexibility, offering different routes to reducing doses, whilst trying to accommodate the complexity required for adjusting the course for an individual. We have also tried to acknowledge the tenets of other guidance

in this field. The advice given here is, for example, largely consistent with the UK NICE guidelines on this topic, but we aimed to provide greater detail on how to implement the broad principles outlined.

Balancing competing priorities has proved difficult. On the one hand, patients often report that they are tapered off psychiatric drugs too quickly, and on the other, patients should not be exposed for an unnecessarily long time to a drug that could be stopped more quickly. Added to this is the awareness that there is great variation from one person to another – and that we have little to guide us in predicting how an individual will react. We have therefore attempted to accommodate a wide variety of circumstances with further instructions on how to make changes from the suggested regimens.

We wrote this book partly because of our own difficulties in coming off various psychiatric drugs. Our main motivation has been that, by clarifying what is known about safe deprescribing and applying that to practice, we will spare others some of the difficult experiences we have endured. It is perhaps the book that we wished our prescribers had possessed.

It is sobering to consider that had we not experienced stopping medication first-hand we would have found it hard to believe the accounts of patients, which can seem almost fantastical in the variety and severity of symptoms (what one experienced practitioner in this field has called 'the unbelievability factor'2). We hope this book will help clinicians develop a greater appreciation for the difficulties some patients experience when trying to stop psychotropic medication.

We recognise that much of the guidance included in this book requires confirmation and clarification from further research but we also appreciate that people are already reducing and stopping their medication and that we should not let the perfect be the enemy of the good. The main messages of the textbook could be summed up in a few words: go slowly, at a rate the patient can tolerate and proceed even more cautiously for the last few milligrams, which are often the hardest to stop.

One major barrier for prescribers we have observed is a reluctance to prescribe liquid versions of drugs, compounded medication or other unlicensed (but widely used) methods to make up the smaller doses of medication necessary for optimal tapering. Often this is for good reasons like cost and complexity. However, minute doses are likely to be required for a substantial proportion of long-term users if they are to stop their medication safely. Many patients report that once a clinician has traversed this psychological moat the process of tapering off their medication becomes substantially easier.

We have also sought to empower patients in the process of coming off their drugs. Patient autonomy is increasingly highlighted in medicine (and psychiatry more widely), but in the area of deprescribing where relatively little is known and where patient experience is so central, it is even more important. We have observed that patients soon become the experts in understanding what rate they can tolerate in reducing their medications and we hope that clinicians will support patients in this process. An old adage from another area of medicine – 'Pain is what the patient says it is' – might be borrowed here. Withdrawal is what the patient says it is.

On this topic, we have also included in this textbook the voices of patient experts and advocates who have been instrumental in drawing attention to the problems many patients face in withdrawal, and in working out innovative approaches to minimise risks. Some of these patient experts have medical training, and some have published

research in academic journals. Their experience of being both patients and, in some cases, clinicians brings unique insight into the process.

When discussing withdrawal syndromes from psychiatric drugs, the concepts of addiction or misuse and abuse often arise. However, we have emphasised throughout this textbook that physical dependence is a predictable physiological response to chronic use of psychotropic medication. This inevitably and predictably leads to a withdrawal syndrome on stopping or reducing the dose and does not indicate addiction, misuse or abuse.

This book has been written so that it may be read from cover to cover but it is also designed to be sampled as needed by the busy clinician. To this end, there are 'quick start' guides for tapering specific drugs that are designed to be intelligible largely independent of the rest of the book. The chapters on individual drug classes outline the issues specific to each class but also to tapering in general, given some commonalities. This deliberate design has necessitated some degree of repetition, the reasons for which we hope the reader will understand.

We would like to pay special tribute to Adele Framer for sharing the wisdom gained from years of supporting patients to safely stop antidepressants and other psychiatric drugs in peer-led forums, combining lived experience with academic knowledge. Also, Nicole Lamberson and Christy Huff, medical professionals with lived experience, for contributing their long experience in helping people to safely stop benzodiazepines via peer-led forums. We would also like to thank Bryan Shapiro for his help putting together the section on gabapentinoids, and Andrea Atri Mizrahi and Ivana Clark for their tireless efforts in assembling and checking for accuracy substantial parts of the drugspecific guidance. Lastly we would like to record our appreciation for the support of Robin Murray in our work in the field of deprescribing.

Mark Horowitz
David Taylor
London
November 2023

References

- Read J, Moncrieff J, Horowitz MA. Designing withdrawal support services for antidepressant users: patients' views on existing services and what they really need. *Journal of Psychiatric Research* 2023. https://www.sciencedirect.com/science/article/pii/S0022395623001309.
- Frederick B. Recovery and Renewal: Your Essential Guide to Overcoming Dependency and Withdrawal from Sleeping Pills, Other 'Benzo'
 Tranquilisers and Antidepressants, rev. edn. London: RRW Publishing, 2017.

Acknowledgements

We thank the following for their contributions to *The Maudsley® Deprescribing Guidelines*

Adele Framer

Alex Macaulay

Andrea Atri Mizrahi

Anna Lembke

Britain Baker

Bryan Shapiro

Christian Müller

Christy Huff

Constantin Volkmann

Daniel Cohrs

Ivana Clark

James Richard O'Neill

Jessica Overton

Laura Nininger Devlin

Louise Bundock

Mary Ita Butler

Michael O'Connor

Nicole Lamberson

Robin Murray

Samuel Bruneau-Dubuc

Tom Stockmann

Notes on using The Maudsley® Deprescribing Guidelines

The main aim of *The Guidelines* is to provide clinicians with practically useful advice on the deprescribing of psychotropic agents in commonly encountered clinical situations. The advice contained in this handbook is based on a combination of literature review, clinical experience and expert contribution, including from patient experts and advocates. We do not claim that this advice is necessarily 'correct' or that it deserves greater prominence than the guidance provided by other professional bodies or special interest groups. We hope, however, to have provided guidance that helps to assure the safe, effective and economical use of medicines in psychiatry, including when they are no longer required.

We hope also to have made clear precisely the sources of information used to inform the guidance given. Please note that some of the recommendations provided here involve the use of unlicensed formulations of some drugs in order to facilitate tapering. Note also that, while we have endeavoured to make sure all quoted doses are correct, clinicians should always consult statutory texts before prescribing. Users of *The Deprescribing Guidelines* should also bear in mind that the contents of this handbook are based on information available to us in November 2023. Much of the advice contained here will become out-dated as more research is conducted and published.

No liability is accepted for any injury, loss or damage, however caused.

Notes on inclusion of drugs

The Deprescribing Guidelines originate in the UK but are intended for use in other countries outside the UK. With this in mind, we have included in this edition those drugs in widespread use throughout the Western world in November 2023. These include drugs not marketed in the UK, such as desvenlafaxine, vilazodone, amongst several others. Many older drugs or those not widely available are either only briefly mentioned or not included on the basis that these drugs were not in widespread use at the time of writing. This book was written to have worldwide utility, although it retains a mild emphasis on UK practice and drugs.

Contributors' Conflict of Interest

Most of the contributors to *The Deprescribing Guidelines* have not received funding from pharmaceutical manufacturers for research, consultancy or lectures, although some have. Readers should be aware that these relationships inevitably colour opinions on such matters as drug selection or preference. However, in the case of a textbook that advises on stopping psychiatric drugs, and that generally recommends not using medications to treat withdrawal from another, such conflicts may be less pertinent than in other circumstances. As regards direct influence, no pharmaceutical company has been allowed to view or comment on any drafts or proofs of *The Deprescribing Guidelines*, and none has made any request for the inclusion or omission of any topic, advice or guidance. To this extent, *The Deprescribing Guidelines* have been written independent of the pharmaceutical industry.

Abbreviations List

% CI	percentage confidence	DSM-III-R	Diagnostic and Statistical Manual of Mental
ADHD	attention deficit hyperactivity disorder		Disorders 3rd revised edition
AMPA	α-amino-3-hydroxy-5-methyl- 4-isoxazolepropionic acid	DSM-V	Diagnostic and Statistical Manual of Mental
APA BDD	American Psychiatric Association body dysmorphic disorder		Disorders 5th revised
BIND	benzodiazepine-induced neurological dysfunction	EMA	European Medicines Agency
BNF BZD	British National Formulary benzodiazepine	EMPOWER	Eliminating Medications Through Patient
BzRAs	benzodiazepine receptor	ER	Ownership of End Results extended release
CABG	agonists coronary artery bypass graft	FDA	US Food and Drugs
CANMAT	Canadian Network for Mood and Anxiety	FND	Administration functional neurological
	Treatments		disorder
CBT	cognitive behavioural	GABA	gamma-aminobutyric acid
	therapy	$GABA_A$	gamma-aminobutyric acid
CBT-I	cognitive behavioural		type A receptor
	therapy for insomnia	GAD	generalised anxiety disorder
CFS	chronic fatigue syndrome	GMC	General Medical Council
CNS	central nervous system	GP	general practitioner
COPD	chronic obstructive pulmonary disease	HAM-A	Hamilton Anxiety Rating Scale
CR	controlled release	HAM-D	Hamilton Depression
CSM	Committee on the Safety of		Rating Scale
	Medicines	HPA	hypothalamic-
DAT	dopamine transporter		pituitary-adrenal
DAWSS	Discriminatory	IBS	irritable bowel syndrome
	Antidepressant Withdrawal	ICD-10-CM	The International
	Symptom Scale		Classification of Diseases,
DESS	discontinuation-emergent		10th Revision, Clinical
	signs and symptoms		Modification

IR LOID	immediate-release	PPWS	persistent post-withdrawal
LGIB MADRS	lower gastrointestinal bleeds Montgomery-Åsberg	PSSD	syndrome post-SSRI sexual dysfunction
MADKS	Depression Rating Scale	PTSD	post-traumatic stress disorder
MAO	monoamine oxidase	PWS	persistent withdrawal
MAOI	monoamine oxidase inhibitor	1 W 3	symptoms
MB-CT	mindfulness based cognitive	RCPsych	Royal College of
WID CI	therapy	reor syen	Psychiatrists
MDD	major depressive disorder	RCT	randomised controlled trial
MDMA	3,4-methylenedioxymetham	RIMA	reversible inhibitor of
	phetamine		monoamine oxidase A
MHRA	Medicines and Healthcare	RLS	restless leg syndrome
	Products Regulatory Agency	RO	receptor occupancy
MMSE	Mini Mental State	RPS	Royal Pharmaceutical
	Examination		Society
MUS	medically unexplained	SAD	social anxiety disorder
	symptoms	SARI	serotonin antagonist and
NaSSAs	noradrenaline and specific		reuptake inhibitors
	serotonergic antidepressants	SERT	serotonin transporter
NET	noradrenaline transporter	SIADH	syndrome of inappropriate
NEWT	North East Wales NHS Trust		secretion of antidiuretic
NGO	non-governmental		hormone
	organisation	SMD	standardised mean difference
NHS	National Health Service	SmPC	summary of product
NICE	National Institute for Health		characteristics
	and Care Excellence	SNRI	serotonin and norepinephrine
NIDA	National Institute on Drug		reuptake inhibitor
	Abuse	SR	sustained-release
NMDA	N-methyl-D-aspartate	SSRI	selective serotonin reuptake
NNT	number needed to treat	OTTO DD	inhibitor
NPS	National Prescribing Service	STOPP	Screening Tool of Older
OCD	obsessive compulsive disorder	TO A	Persons' Prescriptions
ODV	O-desmethylvenlafaxine	TCAs	tricyclic antidepressants
ONS	Office of National Statistics	TI	The Therapeutics Initiative
OR	odds ratio	TIA	transient ischaemic attack
PAWS	post-acute withdrawal	UGIB	upper gastrointestinal bleeds
DD	syndrome	WHO	World Health Organization
PD PET	panic disorder	XR or XL	extended-release
PEI	positron-emission tomography	Z-drugs	nonbenzodiazepine
FIL	patient information leaflet		sedative-hypnotics

Introduction to Deprescribing Psychiatric Medications

Deprescribing as an Intervention

Deprescribing is the planned and supervised process of reducing or stopping medication for which existing or potential harms outweigh existing or potential benefits.¹ The term 'deprescribing' originates from geriatric medicine where polypharmacy in frail patients can cause more harm than benefit.¹ Deprescribing is increasingly recognised to be a key component of good prescribing – reducing doses when they are too high, and stopping medications when they are no longer needed.² This process cannot occur in a vacuum of theoretical concerns but should take into account the patient's health, current level of functioning and, importantly, their values and preferences.¹ Deprescribing seeks to apply best practice in prescribing to the process of stopping a medication. It requires the same skill and experience as for the process of prescribing from prescribers, as well as support from pharmacists and other healthcare staff to obtain the best results. Importantly, it should place patients at the centre of the process to ensure medicines optimisation.³

There has historically been little attention paid to deprescribing in psychiatry. There is a dearth of research into a structured approach to stopping psychiatric medication, with the exception of some early studies examining stopping benzodiazepines¹ and in some specific populations, like people with learning disabilities. The focus of research efforts has been predominantly the prescribing of psychiatric medications – for example, there are estimated to be about 1,000 (published and unpublished) studies on starting antidepressants and only 20 on stopping them.⁴ Concern about this imbalance is not specific to psychiatry with other medical specialties, such as cardiology, also engaging in a re-appraisal of long-term medication continuation, with support for developing strategies for repeated risk–benefit analyses over time.⁵

The context for deprescribing

Over-prescription in psychiatry

Despite evidence of benefit for psychiatric drug treatment, there have been concerns raised regarding over-prescription. 1 in 6 people in western countries are prescribed an antidepressant in any given year, with rates rising a few per cent each year.^{4,6} These increasing prescription numbers are mostly caused by longer periods of prescribing – the median duration of use of antidepressants is now more than 2 years in the UK and more than 5 years in the USA.⁶ Some commentators have suggested that the increasing duration of prescriptions in part reflect the difficulty people have in stopping these medications due to withdrawal effects.⁷ In practice, 30–50% of patients do not have evidence-based reasons for the continued prescription of antidepressants, ⁸⁻¹⁰ prompting calls to action to reduce associated risks.^{6,11} There have been similar concerns about the high rates of antipsychotic use in conditions other than serious mental illness, ¹² as well as a reconsideration of their open-ended use in psychotic conditions for all patients. ^{13,14} There are long-standing worries about levels of benzodiazepine and z-drug prescribing, ^{15,16} and more recent concerns about gabapentinoid prescribing. ¹⁷

High rates of medication prescribing has also gained governmental attention in the UK,¹⁷ with a particular focus on psychiatric drugs. A government report has noted that 1 in 4 adults in the UK are prescribed at least one dependence forming medication each year, with some patients having difficulties stopping these medications.¹⁸ One central concern is that short-term symptom control might be prioritised over long-term functional outcomes, especially as most studies guiding treatment protocols measure symptomatic outcomes over short time periods rather than functional outcomes (or other outcomes often valued by patients) over longer time periods.^{13,19,20}

Alongside this disquiet regarding over-prescription there has been renewed scrutiny of the effectiveness of some psychiatric medications. There is some consensus in the UK and Europe that benzodiazepines and z-drugs have limited effectiveness in the long term, with guidance recommending against long-term treatment for anxiety and insomnia, 21 matched by guidance in the USA from some health management organisations.¹⁵ Preliminary studies have recently found similar outcomes in the treatment of selected patients with first-episode psychosis with or without antipsychotics in the context of comprehensive psychosocial support, ^{22,23} and non-drug treatment for serious mental illness has attracted increasing interest, including a large randomised controlled trial (RCT).²⁴ There have been calls from clinicians and patients for 'minimal medication' options for the treatment of psychotic conditions, such as have been established in Norway and parts of the USA.²⁵ There has continued to be debate regarding the efficacy of antidepressants^{26,27} with arguments being made for their use in selected populations. ²⁸ Concerns have emerged regarding the efficacy and safety of gabapentinoids.¹⁷ In some countries there has been a shift away from a drug-centric approach in some patient groups - for example, in England and Wales the National Institute for Health and Care Excellence (NICE) now recommends that mild depression should not be treated with antidepressants as a first-line treatment, and suggests eight equally effective (and costeffective) non-pharmacological treatment options for severe depression, alongside medication options.29

In addition to the above, there has also been significant critical attention directed towards the relapse prevention properties of psychiatric drugs.^{30,31} All psychiatric drug classes are recognised to cause withdrawal effects when stopped that may be misinterpreted as relapse of the initial condition necessitating treatment.³² These withdrawal symptoms are often ignored in discontinuation studies examining relapse prevention properties.^{30,33,34} As a result there have been questions raised as to whether the relapse prevention properties of psychiatric drugs have been over-stated by misclassification of withdrawal effects as relapse,^{30,33,34} indicating we should be cautious in our interpretation of these studies.

Research and guideline establishment in deprescribing

In recent years interest in psychiatric deprescribing has increased exponentially. Numerous studies have been conducted or are ongoing exploring reducing and stopping antipsychotics in first and multi-episode psychotic conditions, in Taiwan, France, Denmark, the Netherlands, England, Australia and Germany, including the establishment of an international research consortium. ¹⁴ Some of these studies are examining gradual reductions, or hyperbolic dose reductions specifically. ^{14,35} Alongside this there are studies looking at how to help patients stop antidepressants – in the UK, ³⁶ the Netherlands ³⁷ and in Australia ³⁸ – as well as several published studies looking at substitutions for antidepressant treatment like preventative cognitive therapy or mindfulness-based cognitive therapy. ^{39–41}

There has been increasing interest in the process of stopping medication based on the pharmacological properties of the drugs,^{42–45} as well as in the practical means for making gradual dose reduction (for example, using compounded tablets in very small doses).^{46–48} There has also been increased focus on the non-pharmacological aspects of reducing and stopping medication – the positive and negative impact on people's lives, as well as the barriers and the facilitators.^{1,49–52}

In parallel, there has been increasing institutional interest in deprescribing in some countries. In the UK, in recent years, there has been guidance issued by the Royal College of Psychiatrists on how to safely stop antidepressants,⁵³ as well as guidance from NICE on how to stop antidepressants, benzodiazepines, z-drugs, opioids and gabapentinoids.⁵⁴ Similar guidance on how to stop antipsychotics has been called for.⁵⁵ In England, the National Health Service (NHS) has introduced structured medication reviews to reduce the use of unnecessary medication, including some psychiatric drugs,⁵⁶ and the Department of Health and Social Care has been tasked with upscaling deprescribing capacity in the NHS.¹⁸

Many clinicians report an interest in deprescribing and in receiving training for its practice. In total, 75% of UK clinicians working in first-episode psychosis services thought that early discontinuation of antipsychotic medication was beneficial for most patients.⁵⁷ In patients with multiple psychotic episodes English psychiatrists reported that they would feel comfortable supporting about 20% of their patients to discontinue their antipsychotics, with a minority of psychiatrists comfortable to support greater proportions.⁵⁸ In a survey 68% of GPs expressed a desire for more training on the withdrawal effects of antidepressants.⁵⁹ As mentioned, in Norway, government directives have led to the establishment of 'drug-free' wards, in which deprescribing is a central activity.²⁵ There are several dedicated psychiatric drug deprescribing services established around the world situated either in public or private healthcare settings or run by

NGOs partnered with health systems.⁶⁰ Indeed, several academics and psychiatrists have written about their own experience stopping psychiatric medication, often with the theme that this process was far more difficult than the published literature or their training had intimated.⁶¹⁻⁶³

Patient knowledge and advocacy

This rise in academic, professional and institutional interest in psychiatric drug deprescribing has lagged behind decades of interest in the topic by patient groups who have sought ways to rationalise (and generally reduce) their medication in the relative absence of professional help. This movement seems driven by the subjectively unpleasant effects and physical health consequences from being on such medications.^{64–67} It is noteworthy that much of the academic work now being conducted in deprescribing borrows from the expertise developed by patient groups. 44,48,62,66 Groups of patients (often supported by clinicians) have created guidance and advice on the topic of deprescribing in various guides and websites. 64,66,68 Manuals like The Ashton Manual (written by the clinical pharmacologist Professor Heather Ashton) are widely used in peer-led withdrawal communities, 69 and this manual has influenced NICE guidance on withdrawing from benzodiazepines.⁷⁰ Alongside this there has been substantial patient advocacy for more clinical services for deprescribing, which has been part of the driving force in the shift of interest to this topic, ^{64,71-73} as well as increasing media attention to the issue of how to safely stop psychiatric medications and the adverse consequences of stopping too rapidly.74-78

References

- 1. Gupta S, Cahill JD. A Prescription for 'Deprescribing' in Psychiatry. Psychiatric Services 2016; 67: 904–7.
- 2. Farrell B, Mangin D. Deprescribing is an essential part of good prescribing. Am Fam Physician 2019; 99: 7-9.
- Department of Health and Social Care. Good for you, good for us, good for everybody: a plan to reduce overprescribing to make care better and safer, support the NHS, and reduce carbon emissions. 2022.
- Davies J, Read J. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: are guidelines evidencebased? Addict Behav 2019; 97: 111–21.
- Rossello X, Pocock SJ, Julian DG. Long-term use of cardiovascular drugs: challenges for research and for patient care. J Am Coll Cardiol 2015; 66: 1273–85.
- 6. Kendrick T. Strategies to reduce use of antidepressants. Br J Clin Pharmacol 2021; 87: 23-33.
- 7. Healy D, Aldred G. Antidepressant drug use and the risk of suicide. Int Rev Psychiatry 2005; 17: 163-72.
- 8. Cruickshank G, MacGillivray S, Bruce D, Mather A, Matthews K, Williams B. Cross-sectional survey of patients in receipt of long-term repeat prescriptions for antidepressant drugs in primary care. *Ment Health Fam Med* 2008; 5: 105–9.
- Ambresin G, Palmer V, Densley K, Dowrick C, Gilchrist G, Gunn JM. What factors influence long-term antidepressant use in primary care? Findings from the Australian diamond cohort study. J Affect Disord 2015; 176: 125–32.
- Eveleigh R, Grutters J, Muskens E, et al. Cost-utility analysis of a treatment advice to discontinue inappropriate long-term antidepressant use in primary care. Fam Pract 2014; 31: 578–84.
- 11. Wallis KA, Donald M, Moncrieff J. Antidepressant prescribing in general practice: a call to action. Aust J Gen Pract 2021; 50: 954-6.
- 12. Byng R. Should we, can we, halt the rise in prescribing for pain and distress? Br J Gen Pract 2020; 70: 432-3.
- 13. Murray RM, Quattrone D, et al. Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics? Br J Psychiatr 2016; 209: 361–5.
- Sommer IEC, Horowitz M, Allott K, Speyer H, Begemann MJH. Antipsychotic maintenance treatment versus dose reduction: how the story continues. Lancet Psychiatry 2022; 9: 602–3.
- 15. Kaiser Permanente. Benzodiazepine and z-drug safety guideline expectations for Kaiser Foundation Health Plan of Washington Providers. 2019. https://wa.kaiserpermanente.org/static/pdf/public/guidelines/benzo-zdrug.pdf (accessed 19 October 2022).
- Davies J, Rae TC, Montagu L. Long-term benzodiazepine and z-drugs use in the UK: a survey of general practice. Br J Gen Pract 2017; doi:10.3399/bjgp17X691865.

- Horowitz MA, Kelleher M, Taylor D. Should gabapentinoids be prescribed long-term for anxiety and other mental health conditions? Addict Behav 2021; 119: 106943.
- 18. Public Health England. Dependence and withdrawal associated with some prescribed medicines. An evidence review. 2019. www.gov.uk/government/publications/prescribed-medicines-review-report (accessed 25 May 2021).
- 19. Wunderink L, Nieboer RM, Wiersma D, Sytema S, Nienhuis FJ. Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation or maintenance treatment strategy long-term follow-up of a 2-year randomized clinical trial. JAMA Psychiatry 2013; 70: 913–20.
- 20. Moncrieff J. Antipsychotic maintenance treatment: time to rethink? PLoS Med 2015; 12: 1-7.
- National Institute for Health and Care Excellence (NICE). Generalised anxiety disorder and panic disorder in adults: management. NICE clinical guideline CG113 2011. www.nice.org.uk/guidance/cg113/chapter/2-Research-recommendations#the-effectiveness-of-physical-activity-compared-with-waiting-list-control-for-the-treatment-of-gad (accessed 19 October 2022).
- 22. Morrison AP, Pyle M, Maughan D, et al. Antipsychotic medication versus psychological intervention versus a combination of both in adolescents with first-episode psychosis (MAPS): a multicentre, three-arm, randomised controlled pilot and feasibility study. Lancet Psychiatry 2020; published online 23 July. doi:10.1016/S2215-0366(20)30248-0.
- Francey SM, O'Donoghue B, Nelson B, et al. Psychosocial intervention with or without antipsychotic medication for first-episode psychosis: a randomized noninferiority clinical trial. Schizophr Bull Open 2020; 1. doi:10.1093/schizbullopen/sgaa015.
- 24. Pilling S, Clarke K, Parker G, et al. Open dialogue compared to treatment as usual for adults experiencing a mental health crisis: protocol for the ODDESSI multi-site cluster randomised controlled trial. Contemp Clin Trials 2022; 113: 106664.
- Cooper RE, Mason JP, Calton T, Richardson J, Moncrieff J. Opinion piece: the case for establishing a minimal medication alternative for psychosis and schizophrenia. Psychosis 2021; 13: 276–85.
- Horowitz M, Wilcock M. Newer generation antidepressants and withdrawal effects: reconsidering the role of antidepressants and helping patients to stop. Drug Ther Bull 2022; 60: 7–12.
- Munkholm K, Paludan-Müller AS, Boesen K. Considering the methodological limitations in the evidence base of antidepressants for depression: a reanalysis of a network meta-analysis. BMJ Open 2019; 9: e024886.
- Stone MB, Yaseen ZS, Miller BJ, Richardville K, Kalaria SN, Kirsch I. Response to acute monotherapy for major depressive disorder in randomized, placebo controlled trials submitted to the US Food and Drug Administration: individual participant data analysis. BMJ 2022; 378: e067606.
- National Institute for Health and Care Excellence (NICE). Depression in adults: treatment and management | Guidance | NICE. 2022; published online June. www.nice.org.uk/guidance/ng222 (accessed 16 July 2022).
- Récalt AM, Cohen D. Withdrawal confounding in randomized controlled trials of antipsychotic, antidepressant, and stimulant Drugs, 2000– 2017. Psychother Psychosom 2019; 88: 105–13.
- Cohen D, Récalt A. Discontinuing psychotropic drugs from participants in randomized controlled trials: a systematic review. Psychother Psychosom 2019; 88: 96–104.
- Cosci F, Chouinard G. Acute and persistent withdrawal syndromes following discontinuation of psychotropic medications. Psychother Psychosom 2020; 89: 283–306.
- 33. Hengartner MP. How effective are antidepressants for depression over the long term? A critical review of relapse prevention trials and the issue of withdrawal confounding. Ther Adv Psychopharmacol 2020; 10: 2045125320921694.
- Horowitz MA, Taylor D. Distinguishing relapse from antidepressant withdrawal: clinical practice and antidepressant discontinuation studies. BJPsych Advances 2022; 28: 297–311.
- 35. Moncrieff J, Lewis G, Freemantle N, et al. Randomised controlled trial of gradual antipsychotic reduction and discontinuation in people with schizophrenia and related disorders: the RADAR trial (Research into Antipsychotic Discontinuation and Reduction). BMJ Open 2019; 9:
- 36. Kendrick T, Geraghty AWA, Bowers H, et al. REDUCE (Reviewing long-term antidepressant use by careful monitoring in everyday practice) internet and telephone support to people coming off long-term antidepressants: protocol for a randomised controlled trial. *Trials* 2020; 21:
- Vinkers CH, Ruhé HG, Penninx BW. Antidepressant discontinuation: in need of scientific evidence. J Clin Psychopharmacol 2021; 41: 512–5.
- 38. RELEASE: REdressing Long-tErm Antidepressant uSE in general practice. 2021; published online 4 September. https://medical-school.uq.edu.au/release (accessed 3 October 2022).
- Breedvelt JJF, Warren FC, Segal Z, Kuyken W, Bockting CL. Continuation of antidepressants vs sequential psychological interventions to prevent relapse in depression: an individual participant data meta-analysis. JAMA Psychiatry 2021; 78: 868–75.
- Huijbers MJ, Wentink C, Simons E, Spijker J, Speckens A. Discontinuing antidepressant medication after mindfulness-based cognitive therapy: a mixed-methods study exploring predictors and outcomes of different discontinuation trajectories, and its facilitators and barriers. BMJ Open 2020; 10: e039053.
- 41. Kuyken W, Hayes R, Barrett B, et al. Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. *Lancet* 2015; 386: 63–73.
- Horowitz MA, Jauhar S, Natesan S, Murray RM, Taylor DM. A method for tapering antipsychotic treatment that may minimize the risk of relapse. Schizophr Bull 2021; 47: 1116–29.
- 43. Horowitz MA, Taylor D. How to reduce and stop psychiatric medication. Eur Neuropsychopharmacol 2021; 55: 4-7.
- 44. Horowitz MA, Taylor D. Tapering of SSRI treatment to mitigate withdrawal symptoms. Lancet Psychiatry 2019; 6: 538–46.
- 45. Horowitz MA, Moncrieff J, de Haan L, et al. Tapering antipsychotic medication: practical considerations. Psychol Med 2021; 1-4.

- Groot PC, van Os J. Successful use of tapering strips for hyperbolic reduction of antidepressant dose: a cohort study. Ther Adv Psychopharmacol 2021; 11: 20451253211039330.
- Groot PC, van Os J. Outcome of antidepressant drug discontinuation with taperingstrips after 1–5 years. Ther Adv Psychopharmacol 2020; 10: 204512532095460.
- Groot PC, van Os J. How user knowledge of psychotropic drug withdrawal resulted in the development of person-specific tapering medication. Ther Adv Psychopharmacol 2020; 10: 204512532093245.
- 49. Maund E, Dewar-Haggart R, Williams S, et al. Barriers and facilitators to discontinuing antidepressant use: a systematic review and thematic synthesis. J Affect Disord 2019; 245: 38–62.
- Moncrieff J, Gupta S, Horowitz MA. Barriers to stopping neuroleptic (antipsychotic) treatment in people with schizophrenia, psychosis or bipolar disorder. Ther Adv Psychopharmacol 2020; 10: 2045125320937910.
- 51. Gupta S, Cahill JD, Miller R. Deprescribing antipsychotics: a guide for clinicians. BJPsych Advances 2018; 24: 295-302.
- 52. Karter JM. Conversations with clients about antidepressant withdrawal and discontinuation. Ther Adv Psychopharmacol 2020; 10: 2045125320922738.
- 53. Burn W, Horowitz M, Roycroft G, Taylor D. Stopping antidepressants. Stopping Antidepressants. 2020. www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/stopping-antidepressants (accessed 19 October 2022).
- 54. National Institute for Health and Care Excellence (NICE). Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | Guidance | NICE. www.nice.org.uk/guidance/ng215/chapter/Recommendations (accessed 27 June 2022).
- 55. Cooper RE, Grünwald LM, Horowitz M. The case for including antipsychotics in the UK NICE guideline: 'Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults,' Psychosis 2020; 12: 89–93.
- National Health Service. Network contract directed enhanced service: structured medication reviews and medicines optimisation: guidance.
 2022.
- 57. Thompson A, Singh S, Birchwood M. Views of early psychosis clinicians on discontinuation of antipsychotic medication following symptom remission in first episode psychosis. *Early Interv Psychiatry* 2016; 10: 355–61.
- 58. Long M, Stansfeld J, Kikkert M, et al. Views and practice of antipsychotic discontinuation among 241 UK psychiatrists: a survey. (in preparation).
- Read J, Renton J, Harrop C, Geekie J, Dowrick C. A survey of UK general practitioners about depression, antidepressants and withdrawal: implementing the 2019 Public Health England report. Ther Adv Psychopharmacol 2020; 10: 204512532095012.
- Cooper RE, Ashman M, Lomani J, Moncrieff J, Guy A. "Stabilise-reduce, stabilise-reduce": A survey of the common practices of deprescribing services and recommendations for future services. PLoS One. 2023. Available: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0282988
- 61. Stockmann T. What it was like to stop an antidepressant. Ther Adv Psychopharmacol 2019; 9: 2045125319884834.
- 62. Horowitz M. Stopping antidepressants: what is the best way to come off them? Evidently Cochrane. 2021; published online 4 June. www. evidentlycochrane.net/stopping-antidepressants-what-is-the-best-way-to-come-off-them/ (accessed 3 October 2022).
- 63. Taylor D. Truth withdrawal. Open Mind. 1999; September/October.
- 64. Inner Compass Initiative. The Withdrawal Project. 2021. https://withdrawal.theinnercompass.org/ (accessed 19 October 2022).
- 65. White E, Read J, Julo S. The role of Facebook groups in the management and raising of awareness of antidepressant withdrawal: is social media filling the void left by health services? Ther Adv Psychopharmacol 2021; 11: 2045125320981174.
- Framer A. What I have learnt from helping thousands of people taper off psychotropic medications. Ther Adv Psychopharmacol 2021; 11: 204512532199127.
- 67. Witt-Doerring J, Shorter, K. Online communities for drug withdrawal: what can we learn? *Psychiatr Times* https://cdn.sanity.io/files/0vv8moc6/psychtimes/a601f0899ba233e43e83ac7a649028b77df79749.pdf/PSY0418_PDF%20w%20Classifieds.pdf (accessed 19 October 2022).
- 68. Hall W. Harm reduction guide to coming off psychiatric drugs and withdrawal. The Icarus Project and Freedom Center, 2012.
- 69. Ashton H. Benzodiazepines: How They Work & How to Withdraw, The Ashton Manual. 2002. Available: http://www.benzo.org.uk/manual/bzcha01.htm (accessed 7 October 2022)
- Scenario: Benzodiazepine and z-drug withdrawal. https://cks.nice.org.uk/topics/benzodiazepine-z-drug-withdrawal/management/benzodiazepine-z-drug-withdrawal/ (accessed 7 October 2022).
- 71. Akathisia Alliance for Education and Research. https://akathisiaalliance.org/about-akathisia/ (accessed 17 September 2022).
- 72. International Institute for Psychiatric Drug Withdrawal. https://iipdw.org/ (accessed October 7, 2022).
- 73. APPG for Prescribed Drug Dependence. http://prescribeddrug.org/ (accessed 7 October 2022).
- 74. Carey B. How to quit antidepressants: very slowly, doctors say. *The New York Times*. 2019; published online 6 March. www.nytimes. com/2019/03/05/health/depression-withdrawal-drugs.html (accessed 7 October 2022).
- Carey B, Gebeloff R. Many people taking antidepressants discover they cannot quit. The New York Times. 2018; published online 7 April. www.nytimes.com/2018/04/07/health/antidepressants-withdrawal-prozac-cymbalta.html (accessed 7 October 2022).
- 76. Boseley S. Antidepressants: is there a better way to quit them? *The Guardian*. 2019; published online 22 April. www.theguardian.com/lifeandstyle/2019/apr/22/antidepressants-is-there-a-better-way-to-quit-them (accessed 7 October, 2022).
- 77. Aviv R. The Challenge of Going Off Psychiatric Drugs. The New Yorker. 2019; published online March 29. www.newyorker.com/magazine/2019/04/08/the-challenge-of-going-off-psychiatric-drugs (accessed 7 October 2022).
- 78. Piore A. Antidepressants work better than sugar pills only 15 percent of the time. Newsweek. 2022; published online 21 September. www.newsweek.com/2022/09/30/antidepressants-work-better-sugar-pills-only-15-percent-time-1744656.html (accessed 7 October 2022).

Why deprescribe?

A variety of clinical scenarios may warrant deprescribing. These include:

- high-dose prescribing,
- polypharmacy (drug-drug interactions, effects on adherence, and medical risk in vulnerable populations).
- inappropriate prescribing (wrong drug, dose or duration),
- patient preference,
- harms outweighing benefits,
- condition improved, resolution of stressors or alternative coping strategies developed.

High-dose prescribing, polypharmacy, inappropriate prescribing

It is widely agreed that high-dose prescribing and polypharmacy can, in many instances, produce more harm than benefit.¹ For many psychiatric conditions, including major depressive disorder, there is no clear advantage to high-dose pharmacotherapy, although the risks of adverse effects can increase as a function of dose.² The lower range of licensed doses is thought to achieve an optimal balance between efficacy, tolerability and acceptability in acute treatment.² The potential harms of high-dose antipsychotic prescribing and psychiatric drug polypharmacy are also well recognised.¹ Additionally, potentially inappropriate prescribing of psychiatric medication occurs commonly – including chronic polypharmacy for patients with personality disorders, in which guidance generally recommends avoiding pharmacological treatment or employing it for short-term use.³ Deprescribing may be warranted for long-term benzodiazepine and z-drug use, which is generally officially frowned upon,⁴ and in the substantial proportion of patients on antidepressants with no evidence-based reason for ongoing treatment (for example, the antidepressant may have had no beneficial effect or it might have been effective but has been continued for too long).⁵

Patient preference

In an era in which medical treatment in general is moving towards patient-centred treatment and away from paternalism, patient preference should be a central consideration, unless a patient is legally required to comply with treatment via a community treatment order.^{6,7} Many patients report that their clinicians decline to help them reduce or stop their medication.⁸ In some cases this can lead to patients following more risky options like stopping abruptly, the technique most likely to lead to aversive outcomes. Many people feel compelled to seek advice from online peer-support communities instead of their clinicians because of their clinicians' reluctance to support deprescribing, or lack of knowledge of how to do so.^{8,9} Clinicians and patients may have different priorities with clinicians concerned with risk of relapse, symptom control and potential legal consequence for aversive outcomes, while patients may prioritise fulfilling social roles or quality of life, over being symptom free (although there is wide variation on this matter).¹⁰ Negotiating a balance between differing priorities amongst patients and clinicians may be beneficial for outcomes, including treatment alliance and adherence to treatment recommendations in general.⁷

Harms outweigh benefits

For a portion of patients the benefits of medication will be outweighed by adverse effects.

Limited benefits

In some people the medication may never have been particularly effective but has continued because of inertia, a lack of attention to deprescribing or a desire not to 'rock the boat'. ^{11,12} Even in short-term trials the number needed to treat (NNT) for many forms of psychiatric medication is 6–10 or more meaning many patients are not helped by a specific effect of the medication to an appreciable degree. For some patients the medication may have been initially helpful, but through the development of tolerance to the drug this benefit has diminished. ^{13,14} This is well recognised for benzodiazepines and z-drugs, is also an issue for gabapentinoids, ¹⁵ and has also been somewhat controversially implicated in the long-term use of antidepressants, ^{16,17} and antipsychotics. ^{18,19}

Many medications are continued after initial symptoms have resolved with the intention of preventing future relapse. However, as above, there are significant concerns about the certainty of the evidence for the prophylactic properties for psychiatric drugs. These discontinuation studies often stop psychiatric drugs abruptly or rapidly, do not take into account withdrawal effects, which are likely to be mis-classified as relapse in the discontinuation arms of these trials. This phenomenon would provide an exaggerated estimation of the relapse prevention properties of psychiatric drugs, and should lead us to be more cautious in interpreting the extent of the relapse prevention properties of some long-term psychiatric medications.

Adverse effects

The myriad adverse effects from psychiatric drugs range from weight gain and other metabolic consequences, particularly noted for atypical antipsychotics, to more subtle effects such as impaired capacity for feeling, memory or concentration caused by many psychiatric drug classes. Sexual side effects are very common, especially with selective serotonin reuptake inhibitors (SSRIs), where they occur in half or more of patients^{24,25} and other adverse effects often thought to be short term have been found to persist.²⁶ There are also risks of long-term use such as possible cortical loss with antipsychotic treatment, 19,27 increased risk of dementia for some medications, 28,29 as well as falls and increased mortality, especially as people age. 30,31 Extra-pyramidal side effects from firstgeneration antipsychotics and tremor from lithium can be aversive.1 When substantial benefits to a patient are provided by psychiatric drugs, these risks may be acceptable, but in other cases the balance of harms and benefits may not be favourable. As patients age the risks may increase owing to impaired metabolism of drugs and greater frailty, while the benefits may decrease, due to tolerance and perhaps the improvement of their condition over time. Lastly, withdrawal effects are particularly associated with increased duration of medication use; one reason to stop medication earlier rather than later.^{32,33}

Mental health condition improved or alternative coping

For some patients the original condition for which they were prescribed medication will have resolved or improved over time. The most obvious example is the circumstance in which a stressor that precipitated depression or anxiety has resolved, with a

corresponding improvement in the patient's condition. Even conditions often considered life-long such as psychotic conditions or affective disorders can improve with time – as reported in several cohorts of patients, ^{19,34,35} with up to 40% of people with psychotic conditions being well and on no or little medication years after first diagnosis. ^{19,36} The behaviours diagnosed as personality disorders generally improve over time; ³⁷ patients may have found more stable personal or professional circumstances and maturity may limit emotional instability. For some patients, especially those who are stable, medication may have less benefit than during more active periods of their condition. Or patients may have developed or be interested in pursuing alternative approaches to managing their mental health conditions. As one example, NICE has identified a dozen treatments that are as effective (and cost-effective) as antidepressants in the treatment of depression. ³⁸

References

- 1. Taylor D, Barnes T, Young A. The Maudsley Prescribing Guidelines in Psychiatry, 114th edn. Hoboken, NJ: Wiley-Blackwell; 2021.
- 2. Furukawa TA, Cipriani A, Cowen PJ, Leucht S, Egger M, Salanti G. Optimal dose of selective serotonin reuptake inhibitors, venlafaxine, and mirtazapine in major depression: a systematic review and dose-response meta-analysis. *Lancet Psychiatry* 2019; 6: 601–9.
- National Institute for Health and Care Excellence (NICE). Borderline personality disorder: recognition and management. Cg78 2009; 1–40.
- 4. Byng R. Should we, can we, halt the rise in prescribing for pain and distress? Br J Gen Pract 2020; 70: 432–3.
- 5. Kendrick T. Strategies to reduce use of antidepressants. Br J Clin Pharmacol 2021; 87: 23–33.
- 6. Gupta S, Cahill JD, Miller R. Deprescribing antipsychotics: a guide for clinicians. BJPsych Advances 2018; 24: 295-302.
- 7. Gupta S, Cahill JD. A prescription for 'Deprescribing' in Psychiatry. Psychiatric Services 2016; 67: 904-7.
- 8. White E, Read J, Julo S. The role of Facebook groups in the management and raising of awareness of antidepressant withdrawal: is social media filling the void left by health services? *Ther Adv Psychopharmacol* 2021; 11: 2045125320981174.
- Framer A. What I have learnt from helping thousands of people taper off psychotropic medications. Ther Adv Psychopharmacol 2021; 11: 204512532199127.
- Crellin NE, Priebe S, Morant N, et al. An analysis of views about supported reduction or discontinuation of antipsychotic treatment among people with schizophrenia and other psychotic disorders. BMC Psychiatry 2022; 22: 185.
- 11. Gupta S, Cahill J, Miller R. Deprescribing in Psychiatry 2019; 1-16.
- Maund E, Dewar-Haggart R, Williams S, et al. Barriers and facilitators to discontinuing antidepressant use: a systematic review and thematic synthesis. J Affect Disord 2019; 245: 38–62.
- 13. Peper A. A theory of drug tolerance and dependence I: a conceptual analysis. J Theor Biol 2004; 229: 477-90.
- 14. Baldessarini RJ, Ghaemi SN, Viguera AC. Tolerance in antidepressant treatment. Psychother Psychosom 2002; 71: 177-9.
- Horowitz MA, Kelleher M, Taylor D. Should gabapentinoids be prescribed long-term for anxiety and other mental health conditions? Addict Behav 2021; 119: 106943.
- Kinrys G, Gold AK, Pisano VD, et al. Tachyphylaxis in major depressive disorder: a review of the current state of research. J Affect Disord 2019; 245: 488–97.
- Fava GA. May antidepressant drugs worsen the conditions they are supposed to treat? The clinical foundations of the oppositional model of tolerance. Ther Adv Psychopharmacol 2020; 10: 2045125320970325.
- 18. Chouinard G, Samaha AN, Chouinard VA, et al. Antipsychotic-induced dopamine supersensitivity psychosis: pharmacology, criteria, and therapy. Psychother Psychosom 2017; 86: 189–219.
- 19. Murray RM, Quattrone D, et al. Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics. *British Journal of Psychiatry* 2016; 209: 361–5.
- Récalt AM, Cohen D. Withdrawal confounding in randomized controlled trials of antipsychotic, antidepressant, and stimulant drugs, 2000– 2017. Psychother Psychosom 2019; 88: 105–13.
- Cohen D, Récalt A. Discontinuing psychotropic drugs from participants in randomized controlled trials: A systematic review. Psychother Psychosom 2019; 88: 96–104.
- Hengartner MP. How effective are antidepressants for depression over the long term? A critical review of relapse prevention trials and the issue of withdrawal confounding. Ther Adv Psychopharmacol 2020; 10: 2045125320921694.
- 23. Baldessarini RJ, Tondo L. Effects of treatment discontinuation in clinical psychopharmacology. Psychother Psychosom 2019; 88: 65–70.
- Higgins A, Nash M, Lynch AM. Antidepressant-associated sexual dysfunction: impact, effects, and treatment. Drug Healthc Patient Saf 2010;
 141–50.
- 25. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. J Clin Psychopharmacol 2009; 29: 259-66
- Bet PM, Hugtenburg JG, Penninx BWJH, Hoogendijk WJG. Side effects of antidepressants during long-term use in a naturalistic setting. Eur Neuropsychopharmacol 2013; 23: 1443–51.

- 27. Voineskos AN, Mulsant BH, Dickie EW, et al. Effects of antipsychotic medication on brain structure in patients with major depressive disorder and psychotic features: neuroimaging findings in the context of a randomized placebo-controlled clinical trial. JAMA Psychiatry 2020; published online 26 February. doi:10.1001/jamapsychiatry.2020.0036.
- Coupland CAC, Hill T, Dening T, Morriss R, Moore M, Hippisley-Cox J. Anticholinergic drug exposure and the risk of dementia: a nested case-control study. JAMA Intern Med 2019; 179: 1084–93.
- 29. Richardson K, Fox C, Maidment I, et al. Anticholinergic drugs and risk of dementia: case-control study. BMJ 2018; 361: k1315.
- Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ 2011; 343: d4551.
- 31. Guina J, Merrill B, Benzodiazepines I: upping the care on downers: the evidence of risks, benefits and alternatives. J Clin Med Res 2018; 7: 17.
- 32. National Institute for Health and Care Excellence (NICE). Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | Guidance | NICE. www.nice.org.uk/guidance/ng215/chapter/Recommendations (accessed 27 June 2022).
- 33. Horowitz MA, Framer A, Hengartner MP, Sørensen A, Taylor D. Estimating risk of antidepressant withdrawal from a review of published data. CNS Drugs 2023; 37: 143–57.
- Morgan C, Lappin J, Heslin M, et al. Reappraising the long-term course and outcome of psychotic disorders: the AESOP-10 study. Psychol Med 2014; 44: 2713–26.
- Larsen-Barr M, Seymour F, Read J, Gibson K. Attempting to discontinue antipsychotic medication: withdrawal methods, relapse and success. Psychiatry Res 2018; 270: 365–74.
- McGorry P, Alvarez-Jimenez M, Killackey E. Antipsychotic medication during the critical period following remission from first-episode psychosis. JAMA Psychiatry 2013; 70: 898.
- 37. Paris J. Personality disorders over time: precursors, course and outcome. J Pers Disord 2003; 17: 479-88.
- 38. National Institute for Health and Care Excellence (NICE). Depression in adults: treatment and management | Guidance | NICE. 2022; published online June. www.nice.org.uk/guidance/ng222 (accessed 16 July 2022).

Barriers and facilitators to deprescribing

There are numerous factors that can facilitate or hinder deprescribing. A narrative review outlined these factors with regard to stopping antidepressants, many of which are applicable to a variety of drug classes (Table 1.1).¹ Some of these factors can be addressed through education and support, as discussed in subsequent chapters. Additionally, there are many institutional factors that act as barriers to deprescribing: while deprescribing can produce benefits for patient health and well-being, as well as health services (e.g. reduced adverse effect burden) in the long term, in the short term it often involves greater resources (e.g. increased contact, monitoring and support), which can act as a deterrent.²

Importantly, previous experience of stopping medication – either planned or, more usually, spontaneously by the patient, often abruptly or rapidly – with negative consequences can deter patients and clinicians from wishing to trial this process again.² The sometimes alarming presentations with severe symptoms after drug cessation that have generally been interpreted as relapse can strongly re-enforce the impression of a need for medication. However, there is some evidence now that these presentations – even when they are delayed for some time after drug cessation – may in fact represent withdrawal effects or the consequence of withdrawal effects, sometimes called withdrawal-associated relapse (e.g. genuine relapse as a consequence of withdrawal effects such as insomnia).^{3,4} There is further evidence, presented in subsequent chapters, that in at least some of these cases a more gradual, structured and pharmacologically informed approach to reduction may minimise or avoid some of the more negative aspects of this process.²

Domain	Parriore	Escilitators
Table 1.1	Barriers and facilitators for patie	nts to stop psychiatric medications. Adapted from [1] (2019).

Domain	Barriers	Facilitators
Psychological and physiological factors	 Stressful life circumstances Aversive experience of discontinuation in past leading to deterioration (withdrawal effects or relapse) Lack of effective coping strategies Physical dependence on psychiatric medications (leading to withdrawal effects) 	 Confidence in ability to discontinue Life circumstances stable Well-informed about approach to tapering
Perceived cause of mental health condition	 Long-term (perhaps life-long) condition requiring long-term treatment Primarily biochemical (or other biological) cause 	■ Primarily life circumstances
Fears	Fear of relapseFear of withdrawal effects	 Fear of 'addiction', physical dependence Fear of adverse effects and long-term health complications
Personal goals/ motivations	 Self-identity as 'disabled' Stopping as threat to stability Benefit of continuing to others around them Cure is not possible, only management 	 Self-identity as 'healthy' Desire to function without psychiatric medication Feeling better Dislike having to take a psychiatric medication

12

Domain	Barriers	Facilitators
Perception of psychiatric medications	Positive effectNatural or benignLack of concern over adverse/side effects	IneffectualUnacceptable adverse/side effectsUnnaturalUnhappy about long-term use
Information about the discontinuation process	 Inadequate information about the discontinuation process, and risks and benefits of this 	 Information on how to safely discontinue and what to expect
Support network (friends, family, professionals)	■ Pressure to stay on medication	■ Support to come off medication

References

- Maund E, Dewar-Haggart R, Williams S, et al. Barriers and facilitators to discontinuing antidepressant use: a systematic review and thematic synthesis. J Affect Disord 2019; 245: 38–62.
- Moncrieff J, Gupta S, Horowitz MA. Barriers to stopping neuroleptic (antipsychotic) treatment in people with schizophrenia, psychosis or bipolar disorder. Ther Adv Psychopharmacol 2020; 10. doi: 10.1177/2045125320937910.
- 3. Horowitz MA, Jauhar S, Natesan S, Murray RM, Taylor DM. A method for tapering antipsychotic treatment that may minimize the risk of relapse. Schizophr Bull 2021; 47: 1116–29.
- Framer A. What I have learnt from helping thousands of people taper off psychotropic medications. Ther Adv Psychopharmacol 2021; 11. doi: 10.1177/2045125321991274.