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978-1-108-96568-2 — Management of Complex Treatment-resistant Psychotic Disorders  
Michael Cummings, Stephen Stahl  
Frontmatter  
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## Management of Complex Treatment-Resistant Psychotic Disorders

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# Management of Complex Treatment-Resistant Psychotic Disorders

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Edited by

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## Contents

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Contributors	xi
Acknowledgements	xiii
List of Abbreviations	xv
List of Icons	xix
Introduction	xxi
Part I Treatment Strategies	1
1.01 Approaches to Positive Psychotic Symptoms	3
1.02 Use of Plasma Levels in Antipsychotic and Mood Stabilizer Treatment	12
1.03 Advantages of Long-Acting Injectable Antipsychotics	16
1.04 Approach to Treatment-Resistant Schizophrenia Spectrum Patients	22
1.05 Approach to Depressed or Suicidal Schizophrenia Spectrum Patients	34
1.06 Approach to Persistent Aggression and Violence in Schizophrenia Spectrum Psychotic Disorders	38
1.07 Approach to Bipolar Diathesis in Schizophrenia Spectrum Patients	42
1.08 Approach to Anxiety in Schizophrenia Spectrum Patients	51
1.09 Approach to Insomnia and Sleep Disturbance in Schizophrenia Spectrum Disorders	56
1.10 Approach to Psychosis in Children and Adolescents	60
1.11 Electroconvulsive Therapy and Other Non-Pharmacological Treatments	80
1.12 Approach to Substance Use Disorders in Schizophrenia Spectrum Disorders	86
1.13 Approaches to Behavioral Disturbances in Dementia and Traumatic Brain Injury Patients	98

Part II Medication Reference Tables	103
First-Generation (Typical) Antipsychotics	105
2.01 Chlorpromazine	105
2.02 Fluphenazine	109
2.03 Haloperidol	113
2.04 Loxapine	117
2.05 Perphenazine	121
2.06 Thiothixene	125
2.07 Trifluoperazine	129
Second-Generation (Atypical) Antipsychotics	133
2.08 Asenapine	133
2.09 Clozapine	137
2.10 Iloperidone	145
2.11 Lumateperone	150
2.12 Lurasidone	154
2.13 Olanzapine	159
2.14 Paliperidone	165
2.15 Quetiapine	170
2.16 Risperidone	175
2.17 Ziprasidone	180
Dopamine Partial Agonist Antipsychotics	185
2.18 Aripiprazole	185
2.19 Brexpiprazole	190
2.20 Cariprazine	195
Medications for Motor/Neurologic Adverse Effects	200
2.21 Amantadine	200
2.22 Benztropine	204
2.23 Diphenhydramine	208
2.24 Trihexyphenidyl	213
Mood Stabilizers	217
2.25 Carbamazepine	217
2.26 Lamotrigine	222
2.27 Lithium	228
2.28 Valproic Acid	233
Selective Serotonin Reuptake Inhibitor Antidepressants	238
2.29 Citalopram	238
2.30 Escitalopram	242

2.31	Fluoxetine	246
2.32	Fluvoxamine	251
2.33	Paroxetine	256
2.34	Sertraline	261
	SSRI/5HT <sub>1A</sub> Partial Agonist Antidepressants	265
2.35	Vilazodone	265
2.36	Vortioxetine	269
	Serotonin/Norepinephrine Reuptake Inhibitor Antidepressants	273
2.37	Desvenlafaxine	273
2.38	Duloxetine	277
2.39	Levomilnacipran	282
2.40	Venlafaxine	286
	Mixed Mechanism Antidepressants	290
2.41	Bupropion	290
2.42	Mirtazapine	295
2.43	Trazodone	299
	Tricyclic Antidepressants	304
2.44	Amitriptyline	304
2.45	Clomipramine	308
2.46	Desipramine	312
2.47	Doxepin	316
2.48	Imipramine	320
2.49	Nortriptyline	324
	Monoamine Oxidase Inhibitor Antidepressants	328
2.50	Isocarboxazid	328
2.51	Moclobemide	331
2.52	Phenelzine	335
2.53	Transdermal Selegiline	338
2.54	Tranlycypromine	342
	Anxiolytics	345
2.55	Alprazolam	345
2.56	Buspirone	350
2.57	Clonazepam	354
2.58	Diazepam	358
2.59	Hydroxyzine	362
2.60	Lorazepam	365

Sedatives	370
2.61 Diphenhydramine	370
2.62 Eszopiclone	371
2.63 Hydroxyzine	375
2.64 Lorazepam	376
2.65 Oxazepam	377
2.66 Temazepam	381
2.67 Zaleplon	385
2.68 Zolpidem	389
Circadian Regulators	393
2.69 Melatonin	393
2.70 Ramelteon	397
2.71 Tasimelteon	401
Stimulants	404
2.72 Atomoxetine	404
2.73 Dextroamphetamine	408
2.74 Lisdexamfetamine	415
2.75 Methylphenidate	421
2.76 Mixed Amphetamine Salts	427
Histaminic Stimulants	434
2.77 Armodafinil	434
2.78 Modafinil	440
Cognitive Agents	446
2.79 Dextromethorphan/Quinidine	446
2.80 Donepezil	452
2.81 Galantamine	458
2.82 Memantine	465
2.83 Rivastigmine	469
$\alpha_2$ -Adrenergic Agonists	476
2.84 Clonidine	476
2.85 Guanfacine	482
Appendices	487
3.01 Optimal Antipsychotic Plasma Concentration Ranges	489
3.02 Optimal Mood Stabilizer Plasma Concentration Ranges	490

3.03	Formulas for Correcting QT Interval	491
3.04	Common Cytochrome P450 Inducers and Inhibitors	492
3.05	Management of Constipation	493
3.06	Child-Pugh Hepatic Function Scoring	495
3.07	Loading of Lithium and Valproic Acid	496
3.08	Treatment of Prolactin Elevation	497
3.09	A Select List of Foods High in Tyramine	499
3.10	Medications That Present Risk for Serotonin Syndrome When Combined with Monoamine Oxidase Inhibitor	501
3.11	Selected Treatment of Psychomotor Agitation Algorithm	502
	Index	508



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## Abbreviations

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AChE	acetylcholinesterase
Ach-EIs	acetylcholinesterase inhibitors
AD	Alzheimer's disease
ADHD	attention deficit hyperactivity disorder
AED	antiepileptic drugs
AHR	adjusted hazard ratio
AL <sub>NCD</sub>	aripiprazole lauroxil nanocrystal
ANC	absolute neutrophil count
ASD	autism spectrum disorder
AV	atrioventricular block
BDNF	brain derived neurotrophic factor
BEN	benign ethnic neuropenia
BLT	bright light therapy
BMI	body mass index
BPH	benign prostatic hypertrophy
BPRS	Brief Psychiatric Rating Scale
BuChE	butylcholinesterase
CBT	cognitive behavioral therapy
CGI	clinical global impression
CI	confidence interval
CMA	chromosomal microarray
CNS	central nervous system
CNV	copy number variants
COPD	chronic obstructive pulmonary disease
COS	childhood-onset schizophrenia
CPAP	continuous positive airway pressure
CR	controlled release
CYP	cytochrome P450
DBS	deep brain stimulation
DLB	dementia with Lewy bodies
DLPFC	dorsolateral prefrontal cortex
DN-RIRe	dopamine and norepinephrine reuptake inhibitor and releaser
DRESS	drug reaction with eosinophilia and systemic symptoms
D-RI	dopamine reuptake inhibitor
ECT	electroconvulsive therapy
EOS	early-onset schizophrenia
EPS	extrapyramidal adverse effects
ER	extended-release
FDA	US Food and Drug Administration

FGA	first-generation antipsychotic
GABA	gamma-aminobutyric acid
GABA-PAM	gamma-aminobutyric acid positive allosteric modulator
GAD	generalized anxiety disorder
GC	gas chromatography
GI	gastrointestinal
HR	hazard ratio
HTN	hypertension
IM	intramuscular
IR	immediate-release
LAI	long-acting injectable
LVD	left ventricular dysfunction
LVH	left ventricular hypertrophy
MAOI	monoamine oxidase inhibitor
MCCB	MATRICES Consensus Cognitive Battery
MOAS	Modified Objective Aggression Scale
MS	mass spectroscopy
NAMI	National Alliance on Mental Illness
NDD	neurodevelopmental disorders
NMDA	N-methyl-D-aspartate
NMS	neuroleptic malignant syndrome
NNH	number needed to harm
N-RA	norepinephrine receptor agonist
NSAID	nonsteroidal anti-inflammatory drug
OCD	obsessive-compulsive disorder
ODD	oppositional-defiant disorder
OR	odds ratio
OSAHS	obstructive sleep apnea/hypopnea syndrome
PANSS	Positive and Negative Symptoms Scale
PDMP	prescription drug monitoring program
PFC	prefrontal cortex
PGP	P-glycoprotein
PM	poor metabolizers
PMDD	primary major depressive disorder
PT	protime
PTSD	post-traumatic stress disorder
RAS	reticular activating system
RCT	randomized controlled trial
RTMS	repetitive transcranial magnetic stimulation
SAD-BT	schizoaffective disorder, bipolar type
SANS	Scale for the Assessment of Negative Symptoms
SGA	second-generation antipsychotic
SIADH	syndrome of inappropriate antidiuretic hormone secretion

SJS	Stevens-Johnson syndrome
SNP	single-nucleotide polymorphisms
SNRI	selective serotonin-norepinephrine reuptake inhibitor
SR	sustained-release
SSRI	selective serotonin reuptake inhibitor
TBI	traumatic brain injury
TCA	tricyclic antidepressant
TDCS	transcranial direct current stimulation
TEN	toxic epidermal necrolysis
TEOSS	Treatment of Early Onset Schizophrenia Spectrum Disorders
TGA	third-generation antipsychotic
THC	tetra-hydro-cannabidiol
TMN	tuberomammillary nucleus
TPC	temporoparietal cortex
TRS	treatment-resistant schizophrenia
TSH	thyroid stimulating hormone
tVNS	transcutaneous vagal nerve stimulation
VHA	Veterans Health Administration
VNS	vagal nerve stimulation
VPA	valproic acid

## List of Icons

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Clinical pearls of information based on the clinical expertise of the author



References



Basic Information



Classifications



How the drug works, mechanism of action



Plasma Concentrations and Treatment Response



Typical Treatment Response



Pre-Treatment Workup and Initial Laboratory Testing



Monitoring



Dosing and Kinetics



Warnings and precautions regarding use of the drug



Drug interactions that may occur



Medical Precautions and Contraindications



Do Not Use in patients with



Recommended Absolute Neutrophil Count Monitoring

## Introduction

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Increasingly, individuals living with psychotic illnesses are experiencing homelessness, incarceration and associated trauma. Forensic populations are exploding. As people cycle through jails, prisons and the streets, their disorders are going untreated while social stress exacerbates their conditions. As a result of these social determinants, clinical presentations are growing more complex, less categorical and harder to treat. Current guidelines capture the ideal treatment of straightforward presentations in clinically sterile settings. Caretakers working on the front lines often have to move beyond these extant guidelines, an exercise that can feel risky and isolating. This is a book for prescribers on the front lines of treating complex, often treatment-resistant patients.

To address the uncertainty of working with refractory patients in our large forensic hospital system, the California Department of State Hospitals created a psychopharmacology resource network. This network of prescribers, led by the authors of this book, has overcome the isolation experienced by clinicians in our system by developing and communicating best practices beyond previous guidelines. This team has evolved a process of education and consultation by blending the practical application of sophisticated evidence-based knowledge with vast experience in the pharmacological treatment of a very complex and difficult patient population.

The ideal trajectory for an individual who develops a schizophrenia spectrum disorder is early intervention with medication and psychoeducation, followed by close monitoring of optimal psychopharmacology, housing support and vocational therapy. The reality we see is a course of inability to access care, worsening psychotic symptoms, substance abuse, homelessness, and repeated criminal justice contacts as a result of the aforementioned factors. From criminal justice involvement flows trauma, inconsistent psychopharmacology and acquisition of criminogenic risk factors [1]. From these factors flows aggression, alienation and a deepening of the disenfranchisement that began the cycle. Today's complex, treatment-resistant patients require interventions at the level of most of these factors. But the cycle can only be broken with appropriate and effective psychopharmacology.

The goal of the authors is to further widen the network of prescribers working in the most challenging psychiatric environments with the most challenging patients. The authors attempt this by presenting systematic treatment strategies based on current evidence and extensive experience. The focus will be on those medications and strategies they've found especially useful in treating treatment-resistant, severe psychotic illness.

In Chapter 1, approaches to positive psychotic symptoms are explored with straightforward algorithms. In Chapter 2, the authors share the necessity and utility of plasma drug levels in guiding psychopharmacological intervention. Chapter 3 discusses the advantages of using long-acting injectable antipsychotic medication and provides useful initiation strategies. Chapter 4 takes a deep dive into the concept of treatment resistance and reviews the evidence for various strategies. Chapter 5 discusses strategies for working with depressed or suicidal patients who are also living with schizophrenia spectrum disorders. Chapter 6 is an overview of how to address aggression in this population. Chapter 7 addresses the approach to bipolar

diathesis in schizophrenia. Chapter 8 provides guidance when an individual living with schizophrenia is also suffering from anxiety. Chapter 9 focuses on sleep disturbances. Psychosis in children and adolescents is addressed in Chapter 10. Chapter 11 is an exploration of electroconvulsive therapy, along with other non-pharmacological treatments in this select patient population. Chapter 12 describes how to approach substance use disorders among these patients. Part I rounds out with strategies to mitigate behavioral disturbances, as well as how to address dementia and traumatic brain injury.

Part II of this book provides a practical and easy to follow prescribers guide for the agents discussed throughout the book based upon the well-known format used in Dr. Stahl's best-selling psychopharmacology prescribers guide [2]. Part III of the book provides further reference material on everything from how to manage constipation to how to load medications.

I am humbled and grateful for the work our psychopharmacology team has done to standardize and improve the care of our most complex, treatment-resistant patients. They have found methodologies to approach patients previously thought to be impossible to treat. I am confident the reader will benefit from the knowledge and experience reflected in this book and will join our network of clinical expertise.

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## References

1. Warburton, K. (2016). *Violence in Psychiatry*. New York: Cambridge University Press.
2. Stahl, S. M. (2020). *Stahl's Essential Psychopharmacology Prescribers Guide*. 7th ed. New York: Cambridge University Press.