The Maudsley®

# Prescribing Guidelines for Mental Health Conditions in Physical Illness

Siobhan Gee
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# The Maudsley® Prescribing Guidelines for Mental Health Conditions in Physical Illness

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WILEY Blackwell

This edition first published 2025


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

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*Library of Congress Cataloging-in-Publication Data is applied for*

Paperback ISBN: 9781394192403

Cover Design: Wiley

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

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# Preface

More than 40% of people diagnosed with a serious mental illness have at least one concurrent physical illness. Prescribing medicines to treat the psychiatric condition can be complex in these circumstances. The prescriber will need to consider both the potential for prescribed medication to adversely affect any physical health condition and the possibility of altered response because of the presence of physical illness. Choice of medication in the physically unwell patient can be further complicated by a host of other factors. Some patients, for example, cannot take medicines orally, some are at the end of life, some may be on renal replacement therapy, and so on.

The challenges of managing mental health medicines in patients with complex physical comorbidity are faced daily in liaison psychiatry (also known as consultative psychiatry or consultation-liaison psychiatry). As the global population ages and the prevalence of psychiatric conditions continues to increase, these challenges are also increasingly faced by psychiatrists working in all specialisms, both acute and chronic, inpatient and outpatient. This book aims to help the clinician navigate these prescribing scenarios and to be of use not only to psychiatrists but general physicians too.

The importance of treating psychiatric conditions in people with physical illness cannot be overstated. There is no doubt that for every physical illness, the presence of mental ill health adversely affects both morbidity and mortality. We hope this book will not only enable the choice of safe and effective medication in physically unwell patients, but also engender confident prescribing for mental illness, even in the face of severe physical illness.

*Siobhan Gee*
*David M. Taylor*
*July 2024*

# Acknowledgements

The following have contributed to the 1st edition of the *Maudsley® Prescribing Guidelines for Mental Health Conditions in Physical Illness*.

John Archer
Grainne D'Ancona
Mary-Jane Docherty
Petrina Douglas-Hall
Alexa Duff
Nicola Kalk
Cathrine McKenzie
Calum Moulton
Larissa Ryan
Mark Samaan
Esha Sharma
Clare Thomson
Jessica Webb
Hayley Wells

Particular thanks go to colleagues based within the Mind & Body Programme at King's Health Partners who obtained funding from the Maudsley Charity in 2019 to facilitate the development of these guidelines. The work of the Mind & Body Programme continues at King's Health Partners to provide integrated mental and physical healthcare that aims to improve care and outcomes for patients in South East London. For more information, please contact mindandbody@slam.nhs.uk.

# Abbreviations

| | |
|---|---|
| ACE | angiotensin-converting enzyme |
| ADHD | attention deficit hyperactivity disorder |
| APD | automated peritoneal dialysis |
| ARF | acute respiratory failure |
| ATP | adenosine triphosphate |
| BD | bis die (twice a day) |
| BMI | body mass index |
| BNP | B-type natriuretic peptide |
| BP | blood pressure |
| cAMP | cyclic adenosine monophosphate |
| CAPD | continuous ambulatory peritoneal dialysis |
| CCV | central compartment volume |
| CHD | coronary heart disease |
| CNS | central nervous system |
| COPD | chronic obstructive pulmonary disorder |
| CRP | C-reactive protein |
| CYP | cytochrome P |
| DSM-5 | *Diagnostic and Statistical Manual 5* |
| ECG | electrocardiogram |
| ECHO | echocardiogram |
| ECT | electroconvulsive therapy |
| ENRICHD | enhancing recovery in coronary heart disease |
| EPSE | extrapyramidal side effect |
| FBC | full blood count |
| FDA | Food and Drug Administration |
| GABA | gamma-aminobutyric acid |
| GI | gastrointestinal |
| HDAC9 | histone deacetylase 9 |
| IBD | inflammatory bowel disease |
| ICS | inhaled corticosteroid |
| ICU | intensive care unit |
| IL | interleukin |
| IM | intramuscular |

| | |
|---|---|
| INR | international normalised ratio |
| IV | intravenous |
| LABA | long-acting beta-2 agonist |
| LAMA | long-acting muscarinic antagonist |
| MAO | monoamine oxidase |
| MAOI | monoamine oxidase inhibitor |
| MDMA | 3,4-methylenedioxymethamphetamine |
| MI | myocardial infarction |
| MIND-IT | myocardial infarction and depression intervention trial |
| MOOD-HF | mood and mortality in depressed heart failure patients |
| NaCl | sodium chloride |
| NaSSA | noradrenaline and specific serotonergic antidepressant |
| NG | nasogastric |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| NJ | nasojejunal |
| NMDA | N-methyl-d-aspartate |
| NNT | number needed to treat |
| NOAC | non-vitamin K antagonist oral anticoagulant |
| NRT | nicotine replacement therapy |
| NSAID | non-steroidal anti-inflammatory drug |
| NT-pro BNP | N-terminal pro B-type natriuretic peptide |
| OD | omni die (once a day) |
| PEG | percutaneous endoscopic gastrostomy |
| QTc | QT interval adjusted for heart rate |
| RASS | Richmond Agitation Sedation Scale |
| RCT | randomised controlled trial |
| SABA | short-acting beta-2 agonist |
| SADHART-CHF | sertraline against depression and heart disease in chronic heart failure |
| SAMA | short-acting muscarinic antagonist |
| SC | subcutaneous |
| SIADH | syndrome of inappropriate antidiuretic hormone secretion |
| SL | sublingual |
| SMI | serious mental illness |
| SNRI | serotonin and noradrenaline reuptake inhibitor |
| SSRI | selective serotonin reuptake inhibitor |
| STAR*D | Sequenced Treatment Alternatives to Relieve Depression programme |
| TCA | tricyclic antidepressant |
| TDS | ter die sumendum (three times a day) |
| TNF | tumour necrosis factor |
| UC | ulcerative colitis |
| UK | United Kingdom |
| USA | United States of America |
| Vd | volume of distribution |

# Chapter 1

# Cardiac Disease

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Siobhan Gee and David M. Taylor.

## INTRODUCTION

The influence of psychiatric symptoms on the functioning of the heart was first described in 1628 by Sir William Harvey, the English physician who discovered the cardiac circulatory system. Since then, numerous studies have proven him correct, finding mental illness to be a significant predictor of cardiac mortality across the spectrum of cardiac diseases. Treatment of the mental illness is therefore vital not only for relief of psychiatric symptoms, but also for optimal treatment of the cardiac disease.

Few data are available to compare efficacy of drugs for mental illness within individual physical illnesses, such as heart failure or coronary heart disease, and even fewer for patients who have more than one concurrent physical illness. When extrapolating data from studies in patients without cardiac disease, it should be noted that populations studied in these trials are different (e.g. cardiac disease patients tend to be older than populations with general depression). Perhaps more importantly, the biological symptoms of mental illnesses that are measured by standard rating scales may not appear to improve on addition of psychiatric drugs because of the overlap of these physical symptoms with ongoing symptoms of the heart disease (e.g. fatigue, insomnia). Failure to demonstrate response to a drug on a rating scale is of little importance in clinical practice (symptoms are the target) but is relevant if trial data are used to make decisions about drug choice. Conversely, it is also possible that illnesses such as depression or anxiety – specifically in the context of heart disease – are biologically distinct from general depression. Consequently, drug treatments may not be effective for this reason.

## HEART FAILURE

### Depression and anxiety in heart failure

As many as one in five patients with heart failure suffer from depression, more than doubling the mortality risk and trebling the risk of non-compliance with medical treatment recommendations[1]. Clinically significant symptoms of anxiety are also commonly reported in patients with heart failure (30%)[2]. Symptoms of heart failure and those of anxiety may overlap, increasing the apparent prevalence. A clear link between anxiety and mortality in heart failure has not been fully established, but an increased risk is evident for patients with other cardiac disorders such as coronary artery disease[3]. Of course, depression and anxiety may co-exist, and together they increase the risk of both cardiac rehospitalisation and mortality in patients with heart failure[4].

There are several factors that may give rise to the link between depression and anxiety, and poor cardiac outcomes in heart failure. These include biological changes that occur in association with the mental health condition (inflammation, autonomic dysfunction, alterations in the ability of platelets to aggregate, and endothelial dysfunction[2]). Adherence to medicines for the treatment of the heart failure or comorbidities may be affected, as may maintenance of a healthy lifestyle (smoking cessation, diet, exercise).

There are few data relating to the efficacy of pharmacotherapy in depression specifically with comorbid heart failure. The most well-known studies are SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) and MOOD-HF (Mood and Mortality in Depressed Heart Failure patients). SADHART-CHF demonstrated safety (although not efficacy) of sertraline[5], and MOOD-HF[6] the same for escitalopram. There are no randomised trials examining the pharmacological treatment of anxiety in heart failure patients.

## Psychosis and bipolar disorder in heart failure

Patients with serious mental illness (SMI – schizophrenia, bipolar disorder, and severe depression) have a reduced life expectancy compared with the non-SMI population[7]. Cardiovascular disease is a significant contributor to this[8]. Lifestyle interventions are as important in this population as they are in the general population[9]. Antipsychotics and mood stabilisers (lithium and mood-stabilising antiepileptics) commonly cause weight gain, hyperglycaemia, and hyperlipidaemia. Despite this, patients who take them have an overall reduction in cardiac (and all-cause) mortality[10]. This may be a direct beneficial effect of reduction in psychiatric symptoms, improved adherence to healthy lifestyle choices, and/or better compliance with physical health treatments. Heart failure outcomes in patients who have SMI are therefore strongly linked to the outcome of their mental illness, making effective treatment of the psychiatric symptoms a priority. This is an important factor when weighing the risks and benefits of individual psychiatric medication choice. Medication that is perceived as safer in heart failure but less effective for the mental disorder may not actually be the optimal choice for overall cardiac outcomes[11].

## Antidepressants

In general, SSRIs are considered first-line antidepressants, and this is also true for patients with heart failure. Of the SSRIs, sertraline[12,13] is generally well tolerated and efficacious in non-heart failure populations[14]. It has few drug interactions, less propensity than citalopram to prolong the QTc, and has been studied in patients with heart failure (it is safe, but efficacy is unproven)[5]. Escitalopram has also demonstrated safety (although not efficacy) in patients with heart failure[6], but is more often associated with QT prolongation[15] than sertraline (although this association is disputed[16]).

Other options carry some cautions. Mirtazapine is consistently shown to promote appetite, probably due to $\alpha_2$ receptor blockade and affinity for $H_1$, $D_1$, and $D_2$ receptors[17], and is therefore less desirable in conditions such as heart failure where excess weight can be detrimental to clinical outcomes. Citalopram may be more likely than other antidepressants to prolong the QT interval and is not recommended for use in uncompensated heart failure[18]. SNRIs (venlafaxine and duloxetine) are associated with dose-dependent increases in blood pressure[19] (see section on hypertension), and venlafaxine and fluoxetine may also cause prolonged QT, particularly in combination with ivabradine[20]. Tricyclic antidepressants (TCAs) are generally avoided in patients with cardiac disease due to their effects on cardiac contractility, their proarrhythmic effects (due to blockade of cardiac sodium and potassium channels), and their potential to worsen ischaemic heart disease.

Hyponatraemia is a risk with all antidepressants in the first month of treatment. Depending on the patient's risk profile, the diuretic dose may need to be adjusted. If hyponatraemia persists, the dose of sacubitril may need to be reduced or stopped. Mirtazapine and agomelatine may be less commonly associated with hyponatraemia (but are not completely without risk). Close monitoring of sodium levels is recommended, especially in the first few weeks of treatment[21] and if patients have additional risk factors for developing hyponatraemia.

**Recommendation:** sertraline.