CMHP College of Mental Health Pharmacy

Mental health

After completing this tutorial, you will be able to:

- Outline the considerations when advising on the choice of a medicine for a patient with a mental health condition.
- Describe strategies for swapping and stopping antidepressants and antipsychotics.
- Discuss the significant side effects associated with antidepressants and antipsychotics.
- Talk to patients with a mental health condition about their medicines and answer their questions.

Why this subject matters …

One in four people in the UK will experience a mental health problem each year. As a trainee or foundation pharmacist you will therefore be caring for patients with a mental health condition(s) whether that be as inpatients, maybe admitted to a ward for something unrelated, or as outpatients attending specialist clinics.

The types of question that you may be asked about medicines in this field can vary, but there are some common issues such as swapping antidepressants and managing side effects which will be covered in this tutorial.

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Because we're looking at frequently encountered problems, this tutorial only discusses antidepressants and antipsychotics; for guidance on drugs used in other mental health conditions such as anxiolytics and hypnotics refer to the Information sources (below).

Introduction

The number of people reporting mental health problems has been increasing in recent years. The frequency of some conditions such as depression is commonly expressed as the number of new cases annually (the incidence). For other conditions, such as schizophrenia, the frequency is given as the risk over a patient's lifetime (their lifetime prevalence). Mixed anxiety and depression is the most common problem affecting 8 people in every 100, each week. For statistics on other mental health conditions, MIND has a really clear summary and help on interpreting the figures.

To understand the impact of developing a mental health disorder upon patients' lives, you may like to listen to a psychiatric nurse discussing his own depression, or to Stephen Fry describing his bipolar disorder. You can also read a mother's experience of post-natal depression.

Swapping antidepressants

Antidepressants may need to be changed for a variety of reasons including lack of efficacy or adverse effects. Swapping between them can involve a balance of minimising the risk of a drug interaction while ensuring that the patient has adequate levels of antidepressant on board during the period of changeover. Interactions may be pharmacodynamic or pharmacokinetic in nature.

- **Pharmacodynamic** interactions may arise if the two antidepressants act upon the same neurotransmitter(s). For example swapping between two agents that increase serotonin levels can exacerbate the adverse effects of both, and, in some cases, lead to 'serotonin syndrome'. It is usually rapid in onset, occurring within the first few doses of the second drug. You can read more about this potential side effect here.

- **Pharmacokinetic** interactions may arise through effects on cytochrome p450. For example, some of the SSRIs are potent inhibitors of CYP2D6 (e.g. fluoxetine), which is involved in the metabolism of tricyclic antidepressants. Concomitant use can lead to increased plasma levels of the tricyclic and increased risk of adverse reactions (e.g. dry mouth, sedation, confusion) and potential toxicity.

  The inhibition of CYP2D6 can persist for some time after stopping an SSRI, so an interaction with a tricyclic antidepressant is still possible even when an SSRI has been discontinued.

  To avoid such interactions, cross-tapering regimens are sometimes recommended. However these aren't always appropriate – for example if the patient is suffering a severe adverse reaction, then the causative antidepressant should be discontinued immediately.

For further information on swapping antidepressants, including cross-tapering regimens, refer to the Information sources (below).

Swapping antipsychotics

Questions about changing antipsychotic drugs occur less frequently than for antidepressants, but they present similar problems with regard to interactions and loss of symptom control. Several strategies have been proposed and are outlined clearly in Information sources (below) such as Bazire's Psychotropic Drug Directory and The Maudsley Prescribing Guidelines and so will not be repeated here. Studies comparing these techniques are lacking, so when recommending a strategy consider:

- The **individual patient** concerned (e.g. the indication for switching, ability to manage a complex cross-tapering regime if being treated at home, their clinical condition).

- The **medicines** involved (e.g. risk of interactions, side effect profile, half-life, risk of discontinuation symptoms). Remember that long-acting depot formulations may remain in the body for several weeks after being stopped.

Concomitant prescription of anticholinergic medicines such as procyclidine used for extrapyramidal side effects may no longer be required with a new antipsychotic and can be gradually tapered.

Stopping psychiatric medicines

Psychiatric medicines may need to be stopped for a range of reasons such as no longer being indicated or due to side effects, for example.

Most **antidepressants** have been reported to cause a 'discontinuation syndrome' when stopped abruptly or if a few doses are missed. However it is important to realise that many patients are not affected. Paroxetine, venlafaxine and other drugs with a short half-life and inactive metabolites seem particularly likely to cause the problem. In contrast drugs such as fluoxetine with long-acting active metabolites (norfluoxetine) rarely cause discontinuation effects.

Note that the term 'withdrawal' is often used by patients, but less preferred by some experts due to its association with substance misuse.

Discontinuation symptoms usually appear within a few days of stopping therapy and they may be mild and self-limiting. However they can also be quite broad ranging and patients may think that they are suffering a relapse of their depression. If no action is taken, discontinuation symptoms are likely to subside after several weeks. Gradual dose reduction rather than abrupt withdrawal helps to reduce the risk of discontinuation symptoms.

For example, sudden discontinuation of paroxetine can cause dizziness, sensory disturbances (e.g. electric shock sensations), sleep disorders, agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, and palpitations. An extended discontinuation period with careful step down is likely to be required and use of the liquid formulation will make final dose reductions more practical and comfortable. Letting the patient control the timeframe and addressing their anxieties may make for a more successful discontinuation.

Any antidepressant suspected of causing a serious side effect should be stopped immediately (e.g. arrhythmias).

A discontinuation syndrome may also occur in neonates born to mothers who have been taking antidepressants close to delivery.

Questions about stopping **antipsychotics** are less common, but the same principles of tapering apply, to avoid discontinuation symptoms and to help identify early signs of any relapse.

Restarting psychiatric medicines

You might be asked about when and how to restart psychiatric medicines after a temporary discontinuation, such as if the patient has suffered a serious side effect, taken an overdose or been non-adherent.

For some medicines, the product manufacturer gives specific advice in the SmPC (e.g. clozapine) but in most cases such guidance is lacking. In these situations, you will usually need to consider the clinical condition of the patient, the length of time the patient has been without therapy, and the side effect and pharmacokinetic profile of the medicine. A patient who has been without medication for more than a few days may need to be initiated on therapy again 'from scratch' such as with methadone where tolerance is lost within a few days.

For example, you might be asked about a patient with schizophrenia who has forgotten to take their quetiapine for a week. Re-starting the patient on a dose similar to their old maintenance dose seven days ago risks side effects such as postural hypotension because the amount of drug left in their system will be low. However, if you treat the patient with the low doses usually used to initiate therapy it will take longer to control the patient's symptoms. You will need to balance safety (side effects and ability to monitor patient) versus their clinical condition (severity of symptoms, dangers to themself and others). What you recommend should also take into account the level of support available to the patient (e.g. healthcare professionals, carers) and the patient's views given that they will not be naive to the medicine.

Choosing psychiatric medicines

You may be asked to help choose the right medicine to treat a patient with a mental health condition. The diverse range of unwanted effects that psychiatric drugs can have, and their potential to interact with other medicines, means that the choice is not always straightforward.

Their side effect profile can make treatment choice difficult in many patient groups including those with heart disease and epilepsy, and in women who are pregnant or breastfeeding. The potential drug interactions are many; common scenarios include the use of antidepressants in patients taking serotonergic agents such as the triptans or tramadol, and combining medicines that are known to prolong the QT-interval. As with any long-term treatment, patients need to be aware of the perceived benefits and risks and should be involved in the decision-making process if they are able. Refer to the Information sources (below) for treatment recommendations in all these special populations.

Lucy's experience below highlights the importance of keeping the individual patient at the centre of your decision-making when choosing a medicine for a mental health condition.

Choosing a medicine case study

Lucy is a 27-year-old woman who experienced a stillbirth 6 months ago after unexpectedly falling pregnant. She sits and weeps for long periods of time and has been unable to talk to anyone about how she feels. Although her mother is alive and well, she lives 200 miles away. She currently lives with her husband.

Lucy has epilepsy and currently takes sodium valproate. Investigations suggest that valproate was unlikely to have caused the stillbirth.

Her appetite is poor, she has lost 2 stone in weight and her sleep is disrupted, often waking at 4am thinking how cruel the world is and how she might as well end it all. She cannot cope with her job as a nursing assistant and is not looking after her home or doing any cooking. She constantly argues with her husband who thinks that enough time has passed now and she should be able to get back to work.

1. What do you think might be Lucy's diagnosis?
2. What aspects of her story made you think this was her diagnosis?

Lucy visits her GP and is prescribed amitriptyline 25mg at night for a month. Four days later she is admitted to an acute psychiatric ward following an attempted overdose. She has no past psychiatric history.

3. Comment on the appropriateness of the prescription.
4. Which antidepressant would you recommend for Lucy and why?
5. What events in her life may be causing or exacerbating her condition?
6. How might you encourage adherence with a new antidepressant treatment regimen?
7. Are there any other medicines management considerations?

When you've thought about the answers to these questions, read on to see some suggestions.

Choosing a medicine case study suggested answers

1. What do you think might be Lucy's diagnosis?
Post-natal depression as her illness started within 12 months of giving birth.

2. What aspects of her story made you think this was her diagnosis?
Low mood – sitting and weeping for long periods
Suicidal ideation
Early morning wakening with negative thoughts
Lack of motivation to do any cooking or look after the home
Weight loss
Symptoms for more than two weeks

3. Comment on the appropriateness of the prescription.
a) NICE recommend a generic SSRI for most patients requiring antidepressant treatment. Although the sedative effects of tricyclics may appear to be beneficial in patients with poor sleep, they are associated with a range of other adverse effects such as dry mouth, constipation and blurred vision. Postural hypotension can increase the risk of falls and reduced reaction times may present extra hazards for driving.

b) The therapeutic dose of amitriptyline for depression is around 150mg. Lucy has been started on 25mg daily which is below the usual initial dose of 50mg daily.

c) Lucy has epilepsy and although all antidepressants decrease the seizure threshold to some extent, amitriptyline is one of the most pro-convulsive.

d) Tricyclics are also toxic in large doses (e.g. overdose). No risk assessment appears to have been undertaken to establish whether the patient is likely to attempt self-harm.

e) Furthermore, there is an interaction to consider. Amitriptyline levels are increased by valproate, and the pharmacokinetics of valproate can be affected by amitriptyline.

4. Which antidepressant would you recommend for Lucy, and why?
As above, NICE recommend a generic SSRI first-line for most patients requiring antidepressant treatment. Of these the most suitable options for Lucy would be sertraline or citalopram due to the lack of interactions with anticonvulsants, and because they are less likely to reduce seizure threshold at therapeutic doses. Mirtazapine might be an appropriate second choice should Lucy not respond to sertraline/citalopram or be intolerant of side effects.

5. What events in her life may be causing or exacerbating her condition?
Trauma of the stillbirth
Husband not obviously supportive
Mother lives over 200 miles away so is geographically distant
Co-morbidity (epilepsy)
Social circumstance (feels isolated)
Pressure at work

6. How could you encourage adherence to an appropriate treatment regimen?
If you have the opportunity to talk to Lucy you could inform her about antidepressant treatment including: how it may contribute to helping her feel better, the time to onset of action, the need

to continue for at least 6 months after recovery if this is her first episode and the possible withdrawal effects if treatment is stopped suddenly. Consider providing some written information to support these points such as Choice and Medication leaflets (see Information sources below). You could also ask if involving her husband in the treatment plan would be helpful.

7. Are there any other medicines management considerations?
Yes – the valproate and pregnancy prevention programme. This needs to be picked up almost certainly at a separate meeting and with the person who manages Lucy's epilepsy. At this stage simply advising that valproate is no longer routinely recommended as an epilepsy treatment for women who are of childbearing potential is sufficient. This may not be easy as in her current state of mind she may feel the stillbirth was punishment for being on this drug. Remind Lucy that valproate wasn't to blame for what happened but her epilepsy treatment will need to be reviewed. This is a regulatory requirement.

As further learning you may like to listen to Sarah's story of experiencing a stillbirth.

Managing side effects

You may be asked for advice on how to manage side effects in patients taking psychiatric medicines. Compared to other therapeutic areas, the medicines used in mental health are particularly likely to be linked to groups of related adverse effects or syndromes, rather than individual complaints.

Extrapyramidal side effects

For example, certain antipsychotics can cause well-established patterns of extrapyramidal side effects. These are characterised by movement disorders such as:

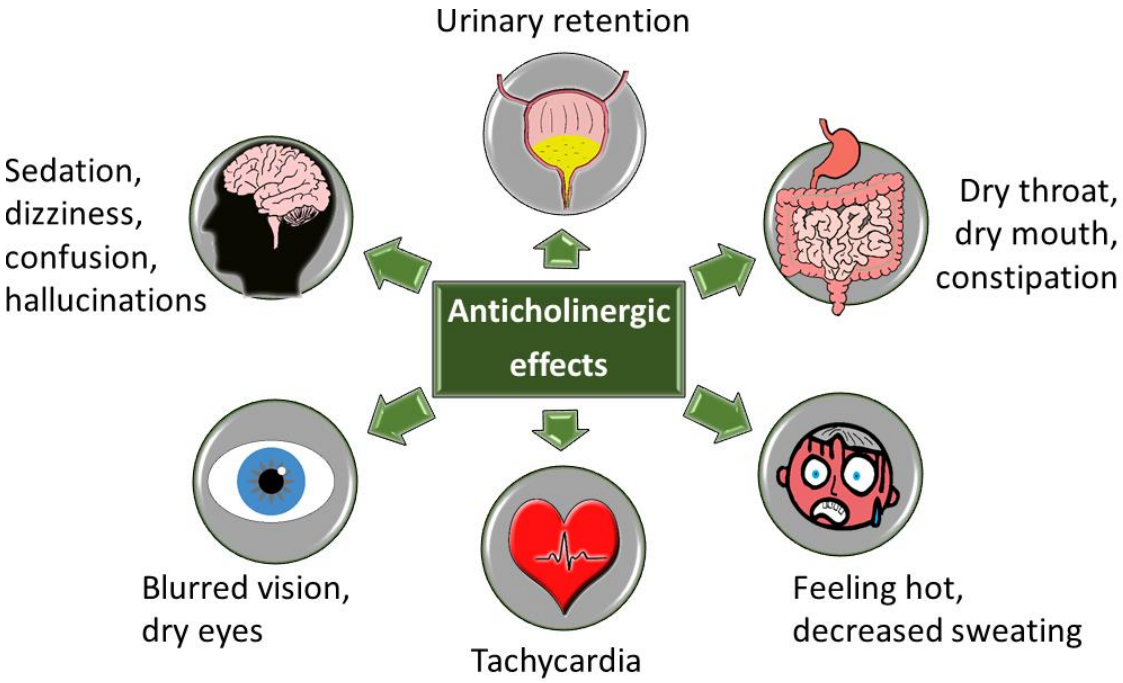
- Acute dystonia (involuntary muscle contraction)
- Akathisia (increased restlessness often in lower limbs, feeling of 'unease' and irritability)
- Parkinsonism (bradykinesia, tremor, rigidity)
- Tardive dyskinesia (typically presents as repetitive mouth movements)

If some of these terms are unfamiliar to you, there are US videos describing acute dystonia, akathisia, and tardive dyskinesia that may help you. They describe the presentation of these conditions, but the treatments and terminology sometimes represent US rather than UK practice.

Anticholinergic burden

Acetylcholine is a neurotransmitter that mediates activities such as peristalsis, bladder emptying, slowing of the heart, saliva production, control of body temperature, and focusing of the eye. It is also found in the brain where, amongst other actions, acetylcholine helps alertness, concentration, and learning. Given the widespread role of acetylcholine in controlling basic body functions, medicines with anticholinergic properties can cause a broad range of side effects.

Many medicines have anticholinergic side effects, also known as antimuscarinic effects, which are additive when more than one of these types of drug is taken together. Mental health medicines such as tricyclic antidepressants, many antipsychotics, and procyclidine can all cause these symptoms, as well as medicines used for non-mental health reasons such as hyoscine, oxybutynin, carbamazepine, and older antihistamines like chlorphenamine.



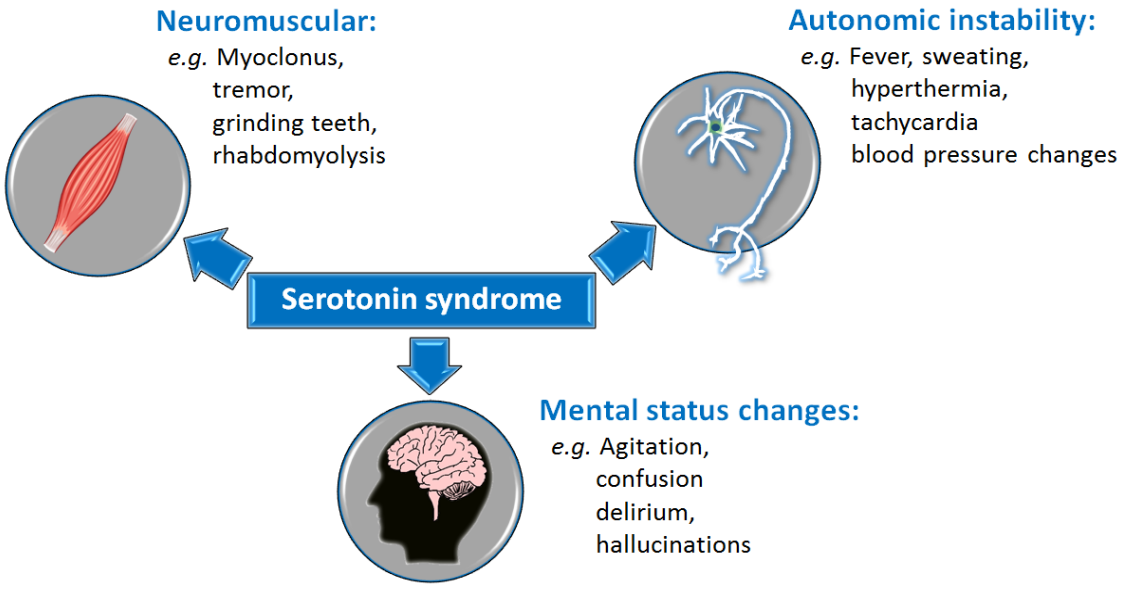
As you can see, anticholinergic side effects are numerous and quite diverse, and they may present in ways which make a drug-related cause not immediately obvious. The dizziness and sedation due to these medicines may cause **falls** in the elderly, for example, and dry mouth may contribute to **dental decay**. Importantly, anticholinergic medicines may also contribute to the development of **cognitive impairment** and symptoms easily mistaken for onset of **dementia** in older patients. For these reasons, anticholinergic medicines must be used with care in this population and avoided when possible.

Two UK websites allow you to calculate an **anticholinergic burden score** for individual patients by estimating the ability of all their medicines to block the actions of acetylcholine. Take a look at one or both of these now: ACB Calculator and Medichec.

We have also written a short, separate tutorial on managing the side effects of anticholinergic medicines. It's intended for clinicians in a primary care setting, but it's a good way to refresh your knowledge of this important topic.

Serotonin syndrome

Medicines that boost the activity of serotonin can cause this syndrome, often when two or more are taken together but sometimes when large doses of a single serotonergic medicine are taken. Some common medicines known to cause serotonin syndrome include most antidepressants, St John's Wort, tramadol, triptans, pethidine, and lithium. The resulting excess of serotonin causes a range of symptoms affecting muscles, mental state, and the autonomic nervous system as illustrated below:



Serotonin syndrome shares many symptoms in common with **neuroleptic malignant syndrome** (NMS) which, as its name suggests is caused by antipsychotic (neuroleptic) medicines. Whilst the serotonin syndrome is caused by pro-serotonin medicines, the neuroleptic malignant syndrome is precipitated by dopamine antagonists. This can be an important way of differentiating between the two syndromes as they both can cause symptoms such as sweating, tachycardia, and changes in mental state. Another important difference is that serotonin syndrome tends to cause muscle spasms (clonus), whilst NMS typically presents with extreme muscle rigidity.

In practice NMS is very rare and diagnosis should only be made when other circumstances (e.g. infection alongside extrapyramidal symptoms) have been ruled out. This is because future antipsychotic treatment becomes very difficult once a diagnosis of NMS has been made.

Other important side effects

Another example of a group of related adverse effects is the **Syndrome of Inappropriate AntiDiuretic Hormone** secretion (SIADH). Antidepressants, antipsychotics and carbamazepine are amongst the many medicines that can stimulate the over-secretion of antidiuretic hormone which causes significant fluid retention, resulting in hyponatraemia. This triggers symptoms such as weakness, weight gain, cramps, vomiting and anorexia. It can lead to confusion, coma and death so it's important to pick this problem up early.

Dopamine inhibits prolactin release and so dopamine antagonists such as antipsychotics have the potential to increase prolactin plasma levels. **Hyperprolactinaemia** may lead to unwanted milk production and disturbed menstrual periods, and is associated with reduced bone mineral density and increased risk of fractures in the longer-term.

Weight gain is common with many psychiatric medicines and this together with a severe and enduring mental health condition such as schizophrenia or depression can predispose to **diabetes**. Additionally olanzapine is known to contribute to insulin resistance**.** Collectively this patient group is prone to the adverse outcomes associated with metabolic syndrome and so attention to regular physical healthcare is to be encouraged.

At this stage of your career, you're not expected to remember all the details of the various syndromes that we've presented in these pages, but it is important to be aware that they may occur and to be on the alert for patterns of side effects when caring for patients who take these medicines for their mental health.

Talking to patients

Whether you are working in the dispensary, on the wards, or maybe answering calls from your Trust's medicines helpline, you could be asked questions from patients about medicines they take for their mental health. They may vary from how to manage side effects, or whether they can take other medicines concomitantly, or breastfeed their infant.

If you are counselling a patient newly started on an antidepressant for example, key points to cover may include;

- It may take several weeks for symptoms to start to improve after initiating an antidepressant, but that side effects can occur earlier.
- How to manage anticipated side effects (e.g. dietary advice if constipation occurs, taking medicines after food if nausea is problematic, or using sips of cool water to help with a dry mouth).
- If side effects are not tolerable then they should seek advice from their healthcare professional, who might decide to switch to an alternative antidepressant.
- Treatment may need to be continued for some months after recovery to reduce the risk of relapse.
- Antidepressants are not addictive (there is no desire to seek higher doses as there may be with substance misuse) but if treatment is stopped then it must be done gradually and under the supervision of a doctor to reduce the risk of discontinuation effects.

Suggested questions

The diverse range of clinical problems in patients with mental health conditions means that it's not possible to provide a shortlist of suitable questions to ask when problem solving. However, if you are being asked to recommend the preferred choice of therapy for an individual patient, then two particularly helpful questions are:

- Ask the prescriber what he or she would usually use.
- Find out whether the patient has tried anything before, and if it was successful and/or tolerated.

This will give you a starting point for problem solving and help to rule out less clinically appropriate options.

Other tutorials on this site such as the questions sections on Adverse reactions or Interactions may help you in certain circumstances. Of course, you'll want to check the patient's drug history and medical history, and if you're being asked about the use of a specific medicine you'll need the indication, dose, frequency, route of administration and expected duration of treatment. So, our guide to general questions to ask when problem solving may also help you.

Information sources

The Maudsley Prescribing Guidelines and Bazire's Psychotropic Drug Directory are both excellent reference handbooks that cover the most commonly asked questions (e.g. swapping and stopping antidepressants, drug choice in special patient groups). Updated frequently, they are normally amongst the first resources to check if you're not sure where to look. You may have access to the e-book of The Maudsley Guidelines at your hospital, but the Psychotropic Drug Directory is not available online or in electronic form.

The TRIP database will signpost you to specialist psychiatry resources such as the Royal College of Psychiatrists and the British Association for Psychopharmacology, as well as more general guidance from NICE and SIGN.

Use the Clinical Knowledge Summaries for evidence-based reviews of how to manage common mental health conditions such as depression, insomnia, and obsessive-compulsive disorder.

SPS has some guidance on commonly encountered scenarios (e.g. depression in patients with heart disease, using antidepressants in patients with epilepsy, switching between antidepressants, which medicines can cause serotonin syndrome, managing antidepressant-induced hyponatraemia).

Also on the SPS website, UKDILAS offers guidance about psychotropic medicines in breastfeeding mothers. There are links to this here.

The Choice and Medication website offers patient friendly information leaflets about mental health conditions and the treatments available to help make informed decisions about choosing the right medicine. Choice and Medication is commercially available on subscription to healthcare organisations for licensed access by staff and service users. Check with your local mental health Trust if they have access, although a personal subscription to the website is available.

Check whether you have any local guidelines or speak to your clinical experts such as your local mental health pharmacist.

Next steps in learning...

If you have an interest in mental health and caring for patients who suffer from psychiatric illness, then consider joining the College of Mental Health Pharmacy. It's an opportunity to network with colleagues with similar interests, share expert resources, receive training, and keep up-to-date.

The Midlands Mental Health Clinical Pharmacist Network has produced a detailed workbook for use by healthcare professionals new to psychiatry, and their supervisors. Approved by the College of Mental Health Pharmacy, Introduction to Mental Health and Therapeutics covers a range of core and more specialist conditions as well other considerations such as legal frameworks.

BMJ Learning has a range of e-learning around mental health. Click on the 'Browse Courses' tab then select 'Psychiatry'. The MHRA also has a series of e-learning modules on psychiatry drugs including antipsychotics, SSRIs and benzodiazepines.

CPPE has a number of resources to support your learning which you can find by entering 'mental health' into the search box on any page of the CPPE website.

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In collaboration with the Royal Pharmaceutical Society, CPPE have also written several medicines optimisation briefings, including one on schizophrenia, dementia and depression.