



Nutrition Consequences of Psychotropic Medications

People suffering from a severe mental illness, including psychosis, frequently require psychotropic medications as part of their treatment.

Psychotropic Medications

The main categories of psychotropic medications include antipsychotics, antidepressants, mood stabilisers, anti-anxiety (anxiolytic) medications and cholinesterase inhibitors (for dementia). Anticholinergic agents and beta blockers may be prescribed to manage some of the adverse effects of antipsychotic medications. The drug/nutrient interactions and side effects of many psychotropic medications may impact on nutritional status to varying degrees.

Antipsychotic medications are used to treat psychotic disorders. There are two main categories of antipsychotic medications: typical, also referred to as first generation, and atypical, or second generation. The main difference between the two types of medications is the side effect profile, in particular the drug's tendency to cause extrapyramidal symptoms, especially dystonias and pseudoparkinsonism.

Metabolic side effects of antipsychotic medications

Atypical antipsychotic medications in general have a lower incidence of extrapyramidal side effects than typical antipsychotics.¹

A common side effect of atypical antipsychotics is that they are associated with weight gain.^{2,3,4} The precise mechanism through which these medications impact on weight remain unclear and requires further research. It is important to note that significant weight gain may result in poor adherence to antipsychotic medication.⁵

Possible mechanisms by which atypical antipsychotics may cause weight gain include:

- increased appetite and reduced satiety, possibly linked with neurochemical pathways (e.g. histamine receptors), including the mesolimbic dopaminergic pathway^{6,7,8,9,10,11,12}
- reduced basal metabolic rate^{13, 14}
- sedation and reduced energy expenditure¹⁵

Table 1. Weight gain, and lipid and/or glucose disturbance potential of antipsychotic medications (24)

Antipsychotic Medication	Weight gain potential	Risk of lipid and/or glucose disturbance
Chlorpromazine	Substantial	High (with limited data)
Clozapine	Substantial	High
Olanzapine	Substantial	High
Paliperidone	Intermediate	Mild
Quetiapine	Intermediate	Moderate
Risperidone	Intermediate	Mild
Thioridazine	Intermediate	High (with limited data)
Amisulpride	Low	Mild
Aripiprazole	Low	Low
Fluphenazine	Low	Low (with limited data)
Haloperidol	Low	Low
Perphenazine	Low	Low
Ziprasidone	Low	Low

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Evidence suggests that the dibenzodiazepines clozapine and olanzapine have the most significant impact on weight¹⁶ and are associated with cardiometabolic abnormalities including impaired glucose tolerance, type 2 diabetes mellitus and hyperlipidaemia.¹⁷ A Malaysian study revealed that 66.7% of participants on clozapine developed metabolic syndrome.¹⁸ Antipsychotic polypharmacy may be associated with increased cardiometabolic abnormalities; individuals treated with antipsychotic agents are directly or indirectly at increased risk of cardiometabolic abnormalities.^{20,21} Traditional risk factors such as obesity, poor diet, lack of exercise, smoking, stress and abnormalities in the hypothalamic, pituitary or adrenal systems²² are likely to account for most cases of diabetes that are observed in people with schizophrenia.²³

Gastrointestinal effects of antipsychotic medications

The anticholinergic effects of antipsychotic medications may contribute to gastrointestinal side effects such as nausea, thirst, dry mouth and constipation.

Gastro-oesophageal reflux (GORD) is commonly experienced by people taking antipsychotic medications. In addition to the medication itself, lifestyle factors such as smoking, consuming large portions, high caffeine consumption, high fat intake and over-consumption of acidic drinks, can significantly contribute to the presence and severity of GORD.^{25, 26}

Severe constipation has been described with the use of clozapine.^{27, 28} Hypersalivation is a common side effect of clozapine and, in severe cases, can interfere with eating. Chlorpromazine can cause sedation, dry mouth and constipation.¹⁶

Other side-effects of antipsychotic medications

Typical antipsychotic medications, such as haloperidol and fluphenazine, have a tendency to produce extrapyramidal side-effects. This can include dystonic reactions such as trismus (lock jaw), which involves spasm of the muscles of the jaw, tongue and floor of the mouth.²⁹ Of the atypical antipsychotics, when taken in high doses, risperidone and amisulpride can also cause these side effects.³⁰

Parkinsonism may also appear in the first week or two of treatment. The main symptoms include muscle rigidity, shuffling gait and loss of pendular arm swing – a generalised poverty of movement.³⁰ Pill-rolling tremor can occur but is much less common than in primary Parkinson's Disease. These symptoms may affect the individual's ability to eat and are usually managed with medication (e.g. benztropine), reduced dosage or change in antipsychotic medication.¹⁸

Tardive dyskinesia, associated with prolonged administration of some antipsychotic medications, is a syndrome of abnormal involuntary movements often affecting the mouth and tongue, which may affect eating. Movement disorders may increase the risk of poor nutrition and malnutrition, appearing in 20 to 25% of patients on long term typical antipsychotic treatment. Larger doses of typical antipsychotic medications are associated with greater risk and in some cases the effects may be irreversible. Tardive dyskinesia has not been reported with clozapine.^{31, 32}

A higher prevalence of osteoporosis is widely reported in schizophrenia compared with the general population. The effect of antipsychotic-induced hyperprolactinemia seems to be a contributing factor for low bone mineral density. Patients with poor nutritional status, low vitamin D levels, low physical activity levels, alcohol intake and smoking may have an increased risk of developing low bone mineral density. Active management of bone loss in those with antipsychotic associated bone disease may halt or even reverse the process.^{33, 34}

Table 2. Indication and drug/nutrient interactions of antipsychotic agents³⁵

DRUG CATEGORY AND INDICATION	GENERIC NAME	BRAND NAME	DRUG – NUTRIENT/HEALTH INTERACTIONS	SIDE EFFECTS
<p>Antipsychotic agents Typical: (1st generation drugs) Psychotic illness including:</p> <ul style="list-style-type: none"> schizophrenia schizoaffective disorder some symptoms of bipolar disorder 	<ul style="list-style-type: none"> Haloperidol (decanoate) Chlorpromazine Trifluoperazine Flupenthixol Decanoate Fluphenazine Decanoate Zuclophenthixol (HCl, decanoate, acetate) Pericyazine 	<ul style="list-style-type: none"> Serenace™ Haldol™ Largactil™ Stelazine™ Fluanxol™ Modecate™ Clopixol™ Neulactil™ 	<ul style="list-style-type: none"> <u>Chlorpromazine, Trifluoperazine and Fluphenazine</u> are all phenothiazine derivatives - similar in structure to vitamin B₂; can cause deficiency by impairing formation of FAD from B₂, and consequently increase requirements for B₂ <u>Largactil</u> (phenothiazine derivative) decreases B₁₂ absorption <u>Haloperidol</u>: contradictory evidence of interaction between tea and coffee; grapefruit juice may decrease drug effect <u>Alcohol not recommended</u> 	<ul style="list-style-type: none"> <u>Chlorpromazine, Trifluoperazine, Pericyazine</u>: fatigue, extra pyramidal effects, constipation, blurred vision, weight gain <u>Fluphenazine</u>: fatigue, extra pyramidal effects, constipation, dry mouth, blurred vision <u>Haloperidol, flupenthixol, zuclophenthixol</u>: Extrapyramidal effects, fatigue <u>Most can cause</u> postural hypotension
<p>Antipsychotic agents Atypical (2nd generation drugs) Indicated as above</p>	<ul style="list-style-type: none"> Clozapine Olanzapine Risperidone Quetiapine Amisulpride Aripiprazole Paliperidone Ziprasidone 	<ul style="list-style-type: none"> Clopine™ Clozaril™ Zyprexa™ Risperdal™ Seroquel™ Solian™ Abilify™ Invega™ Zeldox™ Amipride™ Sulprix™ Lanzek™ 	<ul style="list-style-type: none"> <u>Clozapine</u>: grapefruit juice may decrease drug effect; caffeine can increase clozapine plasma level <u>Clozapine</u> may interact with nicotine, resulting in reduced Clozapine plasma levels. Hence, a reduction in cigarette smoking may lead to increased serum clozapine levels <u>Aripiprazole</u>: may interact with grapefruit juice <u>Alcohol not recommended</u> <u>Smoking</u>: Chlorpromazine, clozapine, fluphenazine, haloperidol, olanzapine and zuclophenthixol 	<ul style="list-style-type: none"> <u>Most can cause</u>: fatigue, weight gain, hypersalivation (Clozapine) or dry mouth, constipation, hypotension, headache, akathisia, blurred vision, tremor <u>Risperidone, Amisulpride Aliperidone and Ziprasidone</u> can cause extrapyramidal effects

Please Note: Drugs such as **Haloperidol, Clozapine, Quetiapine, Aripiprazole, Paliperidone and Ziprasidone** are associated with cytochrome P450 isoenzymes and there is **potential for interaction** with foodstuffs associated with the CYP 3A4 enzyme such as: **caffeine, liquorice, grapefruit, and possibly cranberry.**

³⁵Information from Nutrition Consultants Australia. Drug-Nutrient Interactions: The Manual. 2015

Antidepressants and other medications used in psychiatry

Of all drugs in the sedative and anti-depressant categories (Tables 3 and 4), mirtazapine, sodium valproate, and lithium carbonate are the most likely to lead to weight gain.² Weight gain associated with tricyclic antidepressants correlates positively with dosage and duration of treatment.³⁶

- See Table 3 for **use, side effects and drug/nutrient interactions of antidepressant medications**
- See Table 4 for **side effects and drug/nutrient interactions of mood stabilizers and other medications used in psychiatry**

Monoamine oxidase inhibitors (MAOI)

MAOI antidepressant medications are not commonly prescribed because of the risk of a hypertensive crisis associated with the consumption of tyramine rich foods. Patients prescribed these medications should follow a low tyramine diet to avoid this.³⁷ Severe medication interactions can also occur with other classes of drugs, including some over-the-counter medications such as cough and cold remedies.³⁰

There has been debate regarding which foods need to be avoided by people taking MAOIs and whether overly restrictive diets are necessary. Furthermore, MAOIs and their associated restrictive diets may be potentially harmful due to reduced compliance issues.³⁷

Other interactions with some antidepressant medications / mood stabilisers

Amitriptyline, escitalopram, SNRI, NaSSA, NaRI and RIMA medications are associated with cytochrome P450 isoenzymes and there is potential for interaction with foods associated with the CYP 3A4 enzyme. These include caffeine, liquorice, grapefruit and possibly cranberry.³⁸

Tricyclic antidepressants may cause anticholinergic adverse effects similar to those described above under 'Gastrointestinal effects of antipsychotics'.

Lithium can impair the uptake or release of iodine by the thyroid. Lithium requires daily sodium intake as restriction may enhance the renal tubular reabsorption of lithium with potential lithium toxicity.^{39,40}

Table 3: Use, side effects and drug/nutrient interactions of antidepressant medications³⁵

DRUG CATEGORY	INDICATION	GENERIC NAME	BRAND NAME	DRUG – NUTRIENT/HEALTH INTERACTIONS	SIDE EFFECTS
Tricyclic Antidepressants (TCAs)	<ul style="list-style-type: none"> Depression OCD Panic disorder Generalised anxiety disorder 	Amitriptyline Doxepin Imipramine Nortriptyline Clomipramide Dosulepin	Tryptanil™ Sinequan™ Tofranil™ Allegron™ Aventyl™ Anafranil™ Placil™ Dothep™	<ul style="list-style-type: none"> <u>Amitriptyline</u> - associated with CYP 3A4 isoenzyme. Interacts with alcohol <u>All</u>: avoid alcohol 	<ul style="list-style-type: none"> Dry mouth Constipation Sedation Weight gain Low blood pressure
Selective Serotonin Reuptake Inhibitors (SSRIs)	<ul style="list-style-type: none"> Depression OCD Panic disorder Generalised anxiety disorder 	Fluoxetine Sertraline Citalopram Paroxetine Escitalopram Fluvoxamine	Prozac™ Zoloft™ Cipramil™ Aropax™ Lexapro™	<p>SSRIs may interact with tryptophan; regular monitoring of sodium levels recommended whilst prescribed</p> <ul style="list-style-type: none"> <u>Sertraline</u>: interacts with grapefruit juice <u>Escitalopram</u>: associated with CYP 3A4 isoenzyme <u>All</u>: avoid alcohol 	<ul style="list-style-type: none"> Loss of appetite Diarrhea or constipation Nausea, indigestion Insomnia Sexual dysfunction
Serotonin Noradrenaline Reuptake Inhibitor (SNRI)	<ul style="list-style-type: none"> Major depression Generalised anxiety disorder 	Venlafaxine Duloxetine Desvenlafaxine	Efexor–XR™ Cymbalta™ Pristiq™	<p><u>SNRI</u></p> <ul style="list-style-type: none"> Associated with CYP 3A4 isoenzyme May interact with tryptophan 	<ul style="list-style-type: none"> Nausea Headache Hypertension Dizziness Fatigue
Noradrenaline and Specific Serotonin Antagonist (NaSSA)	<ul style="list-style-type: none"> Major depression Generalised anxiety disorder 	Mirtazapine	Avanza™ Mirtazon™ Axit™	<p><u>NaSSA</u></p> <ul style="list-style-type: none"> Associated with CYP 3A4 isoenzyme Avoid alcohol 	<ul style="list-style-type: none"> Weight gain Fatigue
Noradrenaline Reuptake Inhibitor (NaRI)	<ul style="list-style-type: none"> Major depression 	Reboxetine	Edronax™	<p><u>NaRI</u></p> <ul style="list-style-type: none"> Associated with CYP 3A4 isoenzyme Interacts with tryptophan 	<ul style="list-style-type: none"> Dry mouth Constipation Insomnia
Irreversible Monoamine Oxidase Inhibitor (MAOI)	<ul style="list-style-type: none"> Major depression 	Phenelzine Tranylcypromine	Nardil™ Parnate™	<ul style="list-style-type: none"> Interacts with tyramine Interaction with alcohol Possible interaction with vitamin B₆ 	<ul style="list-style-type: none"> Risk of hypertensive crisis and other drug interactions Constipation Dry mouth Postural hypotension
Reversible MAOI (RIMA)	<ul style="list-style-type: none"> Depression and Social Anxiety 	Moclobemide	Amira™ Aurorix™ Clobemix™ Manerix™	<ul style="list-style-type: none"> Associated with CYP 3A4 isoenzyme Avoid alcohol Does not react with tyramine as severely as MAOI but caution should still be taken 	<ul style="list-style-type: none"> Dry mouth Headache Insomnia Nausea Dizziness

Table 4: Side effects and drug/nutrient interactions of mood stabilisers and other medications used in psychiatry³⁵

DRUG CATEGORY AND INDICATION	GENERIC NAME	BRAND NAME	DRUG – NUTRIENT/HEALTH INTERACTIONS	SIDE EFFECTS
<p>Mood Stabilisers</p> <p>All are primarily anticonvulsant drugs, except Lithium Carbonate</p> <p>Used in:</p> <ul style="list-style-type: none"> • Bipolar disorder • Depression (augment antidepressants) 	<p>Lithium Carbonate</p> <p>Sodium Valproate</p> <p>Carbamazepine</p> <p>Lamotrigine</p> <p>Topiramate</p> <p>Gabapentin</p>	<p>Lithicarb™</p> <p>Quilonum™</p> <p>Epilim™</p> <p>Tegretol™</p> <p>Lamictal™</p> <p>Topamax™</p> <p>Neurontin™</p>	<ul style="list-style-type: none"> • <u>Lithium</u> decreases iodine uptake by the thyroid. Requires daily sodium intake due to renal competition for re-absorption • <u>Sodium Valproate</u> competitively inhibits biotin absorption, decreases carnitine absorption, may interact with salicylates, interacts with alcohol, decreases vitamin D metabolism, and may decrease folate availability • <u>Lamotrigine</u>: decreases vitamin D metabolism and may decrease folate availability • <u>Topiramate</u>: avoid alcohol, folate and vitamin K status 	<ul style="list-style-type: none"> • <u>Lithium</u>: weight gain, thirst, nausea, vomiting, diarrhoea, metallic taste, fatigue, fine tremor • <u>Sodium Valproate</u>: Weight gain, sedation, some nausea and vomiting, indigestion • <u>Carbamazepine</u>: Weight gain, sedation, dry mouth • <u>Lamotrigine</u>: sedation
<p>Anti-anxiety agents (minor tranquilizers)</p> <p>Used in:</p> <ul style="list-style-type: none"> • Insomnia • Anxiety • Agitation 	<p>Oxazepam (SH)</p> <p>Diazepam (AA)</p> <p>Temazepam (SH)</p> <p>Lorazepam (AA)</p> <p>Alprazolam (AA)</p> <p>Triazolam (SH)</p> <p>Nitrazepam (SH)</p>	<p>Serepax™</p> <p>Valium™</p> <p>Normison™</p> <p>Temaze™</p> <p>Ativan™</p> <p>Xanax™</p> <p>Halcion™</p> <p>Mogadon™</p> <p>Alodorm™</p>	<ul style="list-style-type: none"> • Caffeine may decrease drug effect • Contradictory evidence of the effect of grapefruit juice • Additive sedative effect with alcohol 	<ul style="list-style-type: none"> • Dizziness • Sleepiness • Ataxia • Headache
<p>Anticholinergics</p> <p>Used to treat antipsychotic drug side effects such as muscle stiffness</p>	<p>Benztropine</p> <p>Benzhexol</p> <p>Biperiden</p>	<p>Benztrop™</p> <p>Artane™</p> <p>Akineton™</p>	<ul style="list-style-type: none"> • <u>ALL</u>: avoid alcohol • <u>Benzotropine</u>: alkaline urine decreases drug excretion • <u>Benzhexol</u>: may interact with large caffeine intake to cause euphoria, administer at a different time from magnesium 	<ul style="list-style-type: none"> • Blurred vision • Constipation • Dry mouth • Urinary retention • Dizziness • Drowsiness
<p>Beta Blockers</p> <p>Management of akathisia, restlessness, tremor</p>	<p>Propranolol</p> <p>Oxprenolol</p>	<p>Deralin™</p> <p>Inderal™</p> <p>Trasicor™</p> <p>Corbeton™</p>	<ul style="list-style-type: none"> • <u>Propranolol</u>: may interact with alcohol; may interact with theophylline (theophylline is contained trace amounts in some foods including cocoa, tea and guarana) • <u>Oxprenolol</u>: Can cause elevated triglycerides. • <u>All beta-blockers can interact with sulphonylureas</u> (anti-diabetic drugs) to decrease BGLs. Additionally, beta-blockers can mask some of the signs of hypoglycaemia (tachycardia, tremor) so patients should be aware of this 	<ul style="list-style-type: none"> • Fatigue • Cold extremities • Depression • Nightmares

Summary

In summary, side effects are generally more pronounced with antipsychotic agents compared to antidepressants and mood stabilisers. The nutritional consequences may be quite pronounced and distressing for the person taking these medications. Side-effects, in particular rapid weight gain, may contribute to medication non-compliance and increased cardiovascular risk. Dietitian interventions can play a key role in managing these side effects, including preventing and managing weight gain and cardiometabolic risks.

Further reading

- <https://www.choiceandmedication.org/wadoh/>
- <http://www.dietitians.ca/Dietitians-Views/Health-Care-System/Mental-Health.aspx>
- www.clozaril.com
- Clinical Research Unit for Anxiety and Depression: www.crufad.org
- www.drugs.com
- www.medicbnet.com
- <http://www.medicines.org.au>
- MIMS Online (only accessible via subscription. E.g. via university library or possibly your employer)
- National Institute of Mental Health (US site): www.nimh.nih.gov
- <http://www.pbs.gov.au/html>
- www.webmd.com
- www.zyprexa.com
- Therapeutic Guidelines or Australian Medicines Handbook (available through subscription eg. Clinicians Health Channel)

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