

# Bipolar

## Nondrug Options for Recovery



ONWARD  
MENTAL HEALTH

Craig Wagner  
ONWARD Mental Health



See latest version of this document at [www.OnwardMentalHealth.com](http://www.OnwardMentalHealth.com) (Resources). See disclaimer\* below.



**Overview.** Bipolar disorder is a chronic mental health diagnosis that causes dramatic shifts in a person's mood, energy and their ability to think clearly. People with bipolar have high moods (mania) and commonly low moods (depression), which are more dramatic than the typical ups and downs most people experience.

People with bipolar typically transition between mania and depression and when this occurs frequently, it is called "rapid cycling". Severe bipolar may include psychotic symptoms such as hallucinations (e.g. hearing voices) or delusions.

With a disciplined and holistic recovery plan, many people live well with the condition.

Suicide is a potential danger for people with bipolar which can occur in periods of mania or depression. Although bipolar can begin at any time, it typically starts around age 25. Bipolar disorder affects men and women equally. This monograph outlines considerations for bipolar and potential non-drug therapies to evaluate with your practitioners.

**Symptoms.** Everyone's experience with bipolar is different. A bipolar diagnosis means a person must have experienced mania or hypomania, and may have experienced depression.

- **Mania.** Hypomania is a milder form of mania that doesn't include psychotic episodes. Although someone with bipolar may find an elevated mood appealing, the "high" may not be comfortable or controllable. Mania can be extreme irritability or euphoria, but can also show as agitation, sleeplessness, talkativeness or extreme pleasure-seeking or risk-taking behaviors. Most of the time, people in manic states are unaware of the negative consequences of their actions.
- **Depression.** Depression produces physical and emotional symptoms that inhibit a person's ability to function nearly every day over two weeks. It can range from severe to mild low mood. The lows of bipolar depression can be so debilitating that people may be unable to get out of bed. Typically, people with depression have difficulty falling and staying asleep, but they also may sleep far more than normal. When people are depressed, even minor decisions can seem overwhelming. Feelings of loss, personal failure, guilt or helplessness may also be present.

**There is good reason to be hopeful.** Integrative Mental Health, an emerging discipline, offers tremendous hope. It embraces the best of conventional psychiatry – including drugs when needed – and a much larger menu of proven non-drug options. There are thousands of "gold standard" studies that support the effectiveness of non-drug treatments and the significant majority of these treatments reduce mental health symptoms with little or no side effects. And more importantly, thousands of people with a bipolar diagnosis live in recovery today using these techniques – leading meaningful, productive, and joyful lives. Recovery isn't necessarily easy, but pragmatic science is on your side.

**Safety first.** Safety is the #1 priority. If someone is unable to perceive reality or is a danger to themselves or others, call 911. Hospital emergency rooms can help. Hospitals nearly always work to stabilize the individual, very often with drugs.



**Always work with trained and licensed practitioners.** We urge people not to self-diagnose or self-treat. Licensed practitioners can help select and run the most appropriate tests/evaluations and can be your guide to help you determine the specific interventions that might be best for you. When you are working with multiple doctors, make sure you coordinate your care, so each doctor is aware of what the others are doing. Also, remember that your practitioners are your trusted advisors, not your boss. Ultimately, the person with diagnosis must create their own recovery and select the treatments and approaches they will use. Although significant support and some level of paternalistic care may be needed in crisis and early recovery, increasing self-determination is seen as a necessary part of recovery.

**Consider bipolar from four perspectives.** It is often best to consider bipolar from four perspectives: 1) potential physical causes, 2) potential psychological causes, 3) wellness basics, and 4) symptom relief. Therapeutic responses based in each of these four perspectives are supported by hundreds, if not thousands, of gold standard scientific studies. The first three perspectives target known causes and influencers of depressive symptoms to help create sustainable wellness. The more that issues are addressed by the first three perspectives, the less is often needed from the fourth perspective. This is important since the fourth perspective often involves psychiatric drugs that come with a variety of potentially serious side effects and withdrawal difficulties. This multi-pronged approach often means getting two or three different practitioners involved, but sometimes they might be found in the same practice.

## **Physical perspective.**

It is important to find a practitioner skilled in the physical/biomedical causes and influencers of bipolar. These practitioners can identify an individual's unique **bio-individuality** through blood/urine and other testing, using detailed biomedical test panels (see the *biomedical test panels* on our [resources](#) page). These tests can uncover nutrient imbalances, hormonal issues, amino acid irregularities, food allergies, pathogens, inflammation, toxicities, or other physical conditions that can cause or influence mental health symptoms. Customized therapies can then be prescribed targeted at the specific issues identified in the lab results.

Perhaps the most comprehensive and proven biomedical protocol for mental health was developed by the [Walsh Institute](#), described in the book, [Nutrient Power](#), a brief [5-minute video](#), and an extended [90 minute video](#). The institute has amassed what is probably the world's largest database of mental health laboratory analyses: more than three million records from over 30,000 people with mental health issues. This database shows that umbrella mental health diagnoses, including bipolar, are composed of multiple subtypes, each requiring a different nutrient response.

Walsh has found that the most common biomedical issues with bipolar are zinc/copper imbalance, folate disorder, pyrrole disorder, methylation disorder, fatty acid imbalance, oxidative stress, and toxic metals. Walsh indicates that 72% of people with bipolar who undergo six months of customized nutrient therapy experience a significant reduction in symptoms.<sup>1</sup> With that symptom reduction, people are often able to gradually reduce psychiatric drug dosages under practitioner care. In some cases, people can be slowly tapered off of drugs altogether.

Most conventional psychiatrists do not focus on robust biomedical testing, but the good news is that practitioners in the emerging discipline of integrative mental health do. Practitioners who use robust biomedical testing have a variety of titles including integrative psychiatrist, integrative general practitioner, orthomolecular practitioner, naturopath, Functional Medicine practitioner and others.



Ensure you find a practitioner familiar with this testing in a mental health context. To help you choose a biomedical practitioner, consider the following directories:

- Walsh trained doctors - [www.walshinstitute.org/clinical-resources.html](http://www.walshinstitute.org/clinical-resources.html). Mensah Medical ([www.MensahMedical.com](http://www.MensahMedical.com)), a Walsh-trained practice based in the Chicago area, also has scheduled satellite locations in the US that they travel to periodically for patient care.
- Safe Harbor's practitioner directory. <http://www.alternativementalhealth.com/find-help/categories/practitioner>.
- Functional medicine practitioners. [www.ifm.org](http://www.ifm.org), look under "Find a Practitioner".
- APA Caucus on Integrative Psychiatry practitioner directory. [www.intpsychiatry.com](http://www.intpsychiatry.com) (Find a psychiatrist).
- Integrative Medicine for Mental Health Registry. <http://www.integrativemedicineformentalhealth.com/registry.php>.
- American College for Advancement in Medicine - [www.acam.org](http://www.acam.org).
- International Network of Integrative Mental Health - <https://inimh.org>. (FIND a Network Partner Near You)
- International College of Integrative Medicine. [www.icimed.com](http://www.icimed.com).
- American Board of Integrative Holistic Medicine. <http://www.abihm.org/search-doctors>.
- Academy of Integrative Health Medicine. [www.aihm.org](http://www.aihm.org).
- American Holistic Health Association. <http://ahha.org/holistic-practitioners>.
- Orthomolecular.org Worldwide Directory. [www.orthomolecular.org/resources/pract.shtml](http://www.orthomolecular.org/resources/pract.shtml).
- Canadian Society of Orthomolecular Medicine. <https://ionhealth.ca/public/find-a-practitioner>.
- Naturopathic Physicians (select "find a doctor"). [www.naturopathic.org](http://www.naturopathic.org).
- Find a Naturopath. [www.findanaturopath.com](http://www.findanaturopath.com).
- Canadian Association of Naturopathic Doctors. [www.cand.ca](http://www.cand.ca).
- Mad in America directory of doctors who aid psychiatric drug withdrawal. <https://goo.gl/kvstV0>.

If you cannot find a biomedical practitioner with a mental health focus that you can see face-to-face, consider tele-services through phone consults at [www.mensahmedical.com](http://www.mensahmedical.com) (call [847-222-9546](tel:847-222-9546), they are Walsh trained). In addition, certain labs provide practitioner referrals and more self-directed support to patients (e.g. DHA labs - [www.pyroluriatesting.com](http://www.pyroluriatesting.com), Great Plains Labs [www.GreatPlainsLaboratory.com](http://www.GreatPlainsLaboratory.com)). Your regular doctor can work with these labs and order tests directly from these labs.

Even without comprehensive testing, select biomedical approaches have been shown to be effective in clinical trials.

**Omega-3 Fatty Acids.** Omega-3 fatty acids are important in cellular metabolism, having anti-inflammatory properties that can improve brain function. There are three types: EPA (ethyl eicosapentaenoic acid), DHA (docosahexaenoic acid), and ALA (alpha-linolenic acid). EPA and DHA are found in fish and shellfish, while ALA is plant-based and found in flaxseed oil. A deficiency of DHA can lead to bipolar depression.



A meta-analysis found that adding omega-3 fatty acids to mood stabilizers improves bipolar depression.<sup>2</sup> Another found that additive omega-3 helped people remain in remission significantly longer than placebo.<sup>3</sup> EPA appears to be more beneficial than DHA for bipolar depression.

**Folic Acid.** Folic acid (Vitamin B9, folate, methylfolate) plays an essential role in serotonin synthesis and serves as a serotonin reuptake enhancer.<sup>i</sup> It reduces the synaptic activity at serotonin, dopamine, and norepinephrine receptors, and may provide neuroprotection.<sup>4</sup> Folate in our bodies can be compromised by smoking, alcohol, poor diet, mood-stabilizers, and statins. One study found that folic acid increases the effectiveness of lithium to control bipolar depressive symptoms.<sup>5</sup>

**Branched-chain Amino Acid drink.** Drinking a mixture of amino acids (leucine, isoleucine, and valine) specifically excluding the amino acids tyrosine and phenylalanine (a precursor to tyrosine) can depress the mood.<sup>6</sup> This drink may benefit patients with acute mania. One study of 25 patients found that those who drank it had a significant reduction in manic symptoms within six hours of treatment, and they sustained the improvements for a week after the study.<sup>7</sup>

**N-acetylcysteine (NAC).** NAC is produced by the amino acid L-cysteine and is a precursor to glutathione, the most important antioxidant in the brain. NAC has been used to treat a variety of inflammatory disorders.<sup>8</sup> Oxidative stress and imbalanced glutathione have been associated with bipolar and depression.

One trial of bipolar patients on mood stabilizers found that those who were given N-acetylcysteine (2 gm/day) showed a significant improvement in depression, mania, quality of life, and social and occupational functioning, as compared with patients taking a placebo.<sup>9</sup> A broader review found it helpful for bipolar depression.<sup>10</sup> Another study confirmed the additive benefit of NAC (one gram twice daily) to mood stabilizers for depressive symptoms but found no significant benefits for mania.<sup>11</sup>

**Magnesium.** Magnesium is the fourth most abundant mineral in the body; it contributes to more than 300 enzymatic reactions and can be found inside cells (particularly in the heart and brain) in high concentrations. Magnesium is also one of the first nutrients to disappear from food when it is processed, and one of the first nutrients to leave the body when it is stressed.<sup>12</sup> For a variety of reasons (e.g. soil depletion and food processing), the average daily intake of magnesium has plummeted from about 500mg/day in 1900 to about 200mg today. Overall, the population is deficient in magnesium.<sup>13</sup>

Although it is difficult to assess magnesium levels through blood tests, its deficiency can lead to neurological (especially neuromuscular and “restless legs”) disorders.<sup>14</sup> Common symptoms of magnesium deficiency are digestive issues, irritability, anxiety, insomnia, constipation, and calcium deficiency. Magnesium supplements are often prescribed for two or three times per day. Magnesium can also be absorbed through the skin by spending fifteen- or twenty-minutes soaking in hot water in which between one and two cups of magnesium sulfate crystals (Epsom salts) have been dissolved.<sup>15</sup>

Preliminary evidence suggests that in cases of acute bipolar mania or rapid cycling, magnesium is helpful as an additive to mood stabilizers.<sup>16</sup> In one study, magnesium and verapamil were much more effective than verapamil alone for acute mania.<sup>17</sup> In a case series, several patients remained stable on reduced psychotropics while undergoing magnesium therapy.<sup>18</sup>

**Coenzyme Q10 (Q10).** Q10 is a nutrient and naturally occurring antioxidant and anti-inflammatory found in the body and in many foods. One study found that 200mg/day Q10 improves bipolar depression after 8-weeks with a large effect-size (large improvement) compared to placebo with minimal adverse effects.<sup>19</sup> This confirms smaller studies using 800-1200mg/day dosages.<sup>20</sup>

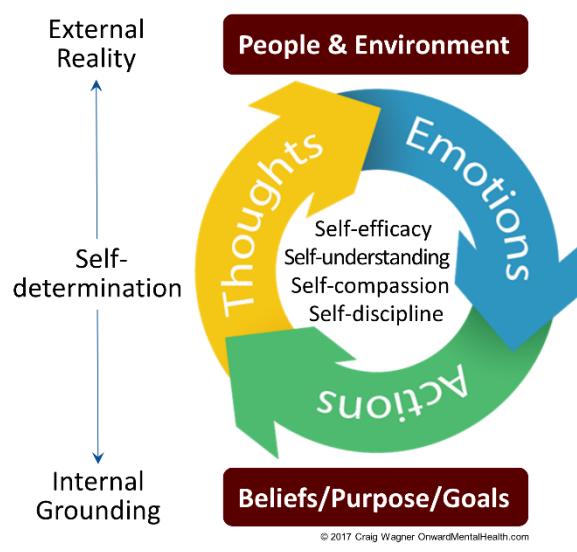


**Aspirin.** One randomized controlled trial found that treating underlying inflammation – a common denominator in mental distress – with simple aspirin provided benefit for bipolar depression on par with psychiatric drugs.<sup>21</sup>

## Psychological perspective.

An evaluation by a trained psychotherapist is important for cases of bipolar. Trauma and stress can directly cause or influence symptoms — and these may be unknown to family members and supporters. People with bipolar who receive intensive psychotherapy were 58% more likely be well in a given month and had higher rates of recovery than individuals only receiving collaborative care.<sup>22</sup> There are a variety of possible psychological interventions.

**Cognitive Behavioral Therapy (CBT).** CBT is based on the idea that thoughts drive our emotions and actions, and behaviors and emotions influence how we think. By exploring unhelpful Thought-Emotion-Action cycles people can learn how to modify them.



As a result, they become happier and more able to weather adversity and create meaningful lives for themselves.

CBT teaches people not so much how to control their world, but how to control the way they interpret and respond to their world. It is predicated on the belief that events don't cause our emotions; emotions are caused by the way we interpret and give meaning to events. CBT can help break vicious cycles of negative thinking, feelings, and behaviors that influence mental health symptoms.

CBT has proven to work on many levels for bipolar, decreasing relapse rates, depression, and mania while improving psychosocial functioning.<sup>23</sup>

CBT is generally short-term and structured, with homework between sessions. It uses a problem-solving and goal-directed approach to address mental health issues. It can be taken in many forms including face-to-face, apps, on-line tools, and group sessions. Online therapist-to-client matching services can help (One example is [www.MindQuire.com](http://www.MindQuire.com)). Versions of CBT that are not face-to-face are considerably less expensive and easier to schedule than therapist-led CBT and are as effective as face-to-face CBT therapy if therapist support is provided.

**Interpersonal and Social Rhythm Therapy (IPSRT).** IPSRT is founded upon the belief that disruptions of our circadian rhythms (our body's "clock") and sleep deprivation may influence symptoms of bipolar. IPSRT establishes daily rhythms for routines and sleep cycles, using activities and social stimulation designed to moderate moods and relieve symptoms. When IPSRT is used during acute bipolar episodes, individuals have significantly longer periods of stability,<sup>24</sup> far greater regularity in daily routines, and improved functioning at work.<sup>25</sup> Intensive psychological interventions and family involvement are important ingredients for the best outcomes in bipolar.



## The Wellness perspective.

There are a number of common-sense health practices we can adopt that often have a significant impact on mental health.

**Diet.** For those with mental health issues, maintaining a good diet is very important. Doctors and nutritionists often recommend a diet that contains plenty of fresh fruits and vegetables, sufficient fat, low-fat protein sources, probiotics for digestive health, sodium, and potassium electrolytes. The diet often recommended is one low in refined sugar, white flour, and processed foods (especially junk foods). Diligently reduce saturated fat and especially sugar in the diet is important.

A “Mediterranean diet” rich in vegetables, fruit, legumes, whole grains, lean meats, fish, heart-healthy fats and oils, with minimal animal fats and sweets is considered an excellent model. Although eating fish is healthy, nearly all fish and shellfish now contain traces of mercury, so we should eat predominantly low-mercury seafood. Nutritionists urge us to incorporate changes slowly and then maintain healthy dietary changes.

As a rule of thumb, dietitians recommend taking the time for excellent breakfasts because our blood sugar levels are lowest in the morning, so healthy breakfasts get us going. It’s better to eat dinners early in the evening and avoid eating when we feel stressed, since too much adrenalin shuts down digestion.

**Food Allergies.** Research shows that people with bipolar have a much higher risk of having antibodies associated with a gluten allergy or gluten sensitivity than the normal population.<sup>26</sup> There are blood tests than detect gluten allergies, but one common way to assess for a possible allergy is simply to start an “elimination diet”. This means completely eliminating gluten from the diet for a period of time to see if symptoms improve. Although many foods have gluten in them, with a little work, diets can be created that are reasonable. Work with a practitioner to determine if a gluten allergy or potentially other allergies (milk products and soy are the next most common) are present.

**Gut Health.** Overall gut health is important to those with bipolar, since digestive distress can cause mood changes.<sup>27</sup> Probiotics (found in yogurt, Keifer, and other sources) can improve bipolar symptoms significantly. Probiotics can also be found in capsule form, usually containing lactobacillus and bifidobacteri. Dysbiosis, an imbalance in gut bacteria, may be caused by antibiotic or alcohol use, stress, or high fat/sugar diets. The imbalance can cause intestinal permeability, sometimes called “leaky gut,” making it easier for unhealthy substances to enter the body and cause both physical and mental issues.

One study found that taking probiotics is associated with reduced bipolar hospitalizations.<sup>28</sup>

**Exercise.** Some form of consistent bodily movement daily in the form of either exercise or a Mind-Body Discipline (e.g. yoga) is often helpful. However, this should be done with caution for those who are prone to rapid cycling.

**Light Therapy.** Bright light therapy is based on the idea that sunlight can strongly influence mood. The therapy consists of sitting in front of a device called a light therapy box, which emits bright light that mimics natural outdoor light. Trials have found that bright light therapy can improve bipolar depression.<sup>29</sup>

Therapy, in which complete darkness is used as a mood stabilizer for bipolar, is roughly the opposite of light therapy for depression. Data is limited, but one small study shows that being in complete darkness from 6:00 p.m. to 8:00 a.m. over three days can reduce rapid cycling manic symptoms.<sup>30</sup>



Instead of complete darkness, wearing amber colored glasses (which block blue light often emitted by computer screens and TVs) may be similarly effective.<sup>31</sup>

**Sleep.** Our bodies and minds align to a natural daily rhythm, called a circadian rhythm, influenced by sunlight. Regular good sleep is an important part of this rhythm. Over 70% of people with bipolar appear to have sleep issues, and these can impact mental health. It is often important to get into a consistent pattern of sleep for those with bipolar. This can be done with good sleep hygiene (e.g. going to bed only when sleepy, avoiding caffeine and sugar prior to bed, avoiding computer/tablet/screen use within a few hours of bed), going for a walk before bed, etc.

Although sleep hygiene is a critical component in mental health, short bursts of sleep *deprivation* appear to be one of the most fast-acting antidepressants known. Treatment can be a single instance or repeated instances of sleep deprivation, either all night or partial the second half of the night. Sleep deprivation must be done under supervision, since it has been associated with an increased incidence of psychiatric disorders.<sup>32</sup> In one study, 70% of patients with bipolar depression improved rapidly with sleep deprivation and Light Therapy combined, and 57% remained depression-free at the nine-month follow-up.<sup>33</sup>

There are also insomnia therapies including melatonin, a hormone.

**Substance avoidance.** Avoiding caffeine, alcohol, marijuana and other mood-altering substances is often important.

## Symptom relief perspective.

The most common treatment for bipolar is a combination of psychiatric drugs (called polypharmacy) that may include antipsychotics, prescription lithium (lithium carbonate), anticonvulsants, antidepressants, and benzodiazepines.

One study found that 72% of bipolar patients were taking 2 or more drugs, 55% were on 3 or more, and 36% were on 4 or more. It isn't unusual for people with bipolar to take as many as 6 different drugs.

Bipolar drugs have been well-studied in hundreds of gold standard trials, individually, and sometimes in drug pairs. Their benefits come with a variety of risks and limitations (see infographic on next page).

**A gut-check on your odds of success with drugs.** Many studies show that bipolar drugs *work* - they produce better symptom relief than sugar pills. But to make informed trade-off decisions on bipolar care, we need to consider the *odds* they'll work. Surprisingly, those odds are fairly slim - about 1 in 5.

An example is helpful. Consider trials testing lithium, the gold standard treatment for bipolar mania. Results show that about 31% of people see substantial improvement (>50% mania symptom reduction) in 1-2 months without treatment. Another 53% get modest or no relief with or without lithium. The remaining 16% (less than 1 in 5) see substantial symptom improvement in 1-2 months *attributable* to the lithium they take.

The implications are clear. First, you may be in the fortunate 16%, so dismissing drugs is dismissing the possibility that they might help you. Second, if you don't like the 1 in 5 odds, you can work with practitioners well-trained in nondrug options to evaluate, select, and experiment with the ones most appropriate for you.



**Bipolar Drugs**  
*Benefits, Risks, and Limitations*  
Summary of gold-standard evidence of attributable benefit and harm<sup>1</sup>

**BIG Picture Trade-offs**

- PARTIAL RELIEF**  
Bipolar drugs offer partial but inconsistent symptom relief that varies by person.
- STABILIZATION**  
Drugs can reduce the frequency of manic and depressive episodes.
- DRUG LOAD**  
2-5 drug combos are prescribed for bipolar.<sup>2</sup> High drug load is linked to higher suicide rates and worse outcomes.<sup>3</sup>

**REWARD**  **RISK**

- CRISIS USE**  
Bipolar drugs can sedate during suicidality and dangerous behavior.
- LOW RECOVERY**  
On drugs alone, people rarely recover<sup>4</sup> and have symptoms half the year.<sup>7</sup>
- NON-CURATIVE**  
Bipolar drugs can reduce symptoms but don't cure or address causes.
- SIDE EFFECTS**  
Sexual dysfunction, organ damage, diabetes, cognitive impairment, tremors, and addiction may occur.
- UNCERTAINTY**  
Bipolar drug combo testing is "practically nonexistent".<sup>4</sup> Prescribing is largely trial and error.<sup>5</sup>

**DRUG Pros-Cons**

**01 Lithium**

**Risks:** Kidney impact with long-term use.<sup>11</sup>  
**Limitations:** Little secure evidence it helps acute bipolar depression.<sup>4</sup>

**Side effects (frequency):** Weight gain (75%), excess urination (70%), tremors (42%), sexual dysfunction (37%), chronic kidney disease (33%), hypothyroidism (14%).

**FDA black box warning:** Dosages are near toxic levels.

**02 Anticonvulsants** (e.g. Lamictal, Depakote, Topamax, Carbamazepine)

**How well do the top 3 anticonvulsants work?**<sup>12</sup>

Drug	Acute Mania	Acute Depression	Mood Stabilizer
Lamotrigine	20%	13%	17%
Valproate	20%	13%	17%
Carbamazepine	25%	-	-

**Limitations:** Little secure evidence they help acute depressive symptoms.  
**Suicide:** Use increases risk.<sup>17</sup>

**Side effects (frequency):** Much less than other mood drugs but... altered liver enzymes (13%), tremors (10%), rash (10%). Less frequent nausea and weight gain.

**FDA black box warnings for lethal rash, liver damage, pancreatitis, fetal risk, and anemia.**<sup>18</sup>

**03 Antipsychotics** (e.g. Abilify, Clozaril, Latuda, Seroquel, Risperidol)

**Risks:** Dose-proportional brain shrinkage, diabetes (3%). Use associated with worse long-term recovery in schizophrenia.

**Side effects (frequency):** Weight gain (90%), sexual dysfunction (66%), fatigue (35%), tremors (17%), sedation (13%), metabolic syndrome (13%).

**FDA black box warning for elevated risk of death in elderly.**<sup>19</sup>

**04 Benzodiazepines** (e.g. Valium, Xanax, Ativan, Librium, Clonazepam)

**Benefits:** Reduces agitation, anxiety, restlessness, and acute mania.<sup>21</sup>  
**Prescribing:** Fast acting. Very short-term use. Guidelines limit to 1-28 days.<sup>21</sup>  
**Long term:** 20% use it long-term despite evidence it worsens symptoms and increases mood relapse risk.<sup>22</sup>

**Side effects (frequency):** Fatigue (50%), sexual dysfunction (33%). Raises risk of dementia and cognitive decline.<sup>23</sup>  
**Suicide:** Use increases risk.<sup>23</sup>

**Use is controversial.**<sup>24</sup> DEA controlled drug. May be addictive as prescribed. Withdrawal syndrome (30%) may last months/years.<sup>25</sup>

**FDA black box warning:** Can be fatal if taken with opioids.<sup>26</sup>

**05 Antidepressants** (e.g. Prozac, Celexa, Paxil, Zoloft, Lexapro)

**For depression:** 17% of people improve substantially due to taking one in an FDA-approved combo with an antipsychotic...<sup>27</sup> ...but 35% see large weight gain.<sup>28</sup>

**Ineffective when used with lithium and anticonvulsants:** Widely considered over-prescribed. None are FDA-approved stand-alone for bipolar (weak evidence).

**Risks:** Dose-proportional brain shrinkage, diabetes (3%). Use associated with worse long-term recovery in schizophrenia.

**Side effects (frequency):** Sexual dysfunction (58%), withdrawal difficulties (56%),<sup>29</sup> fatigue (21%), weight gain (15%).

**Risks:** Diabetes,<sup>30</sup> mania (2.6X),<sup>31</sup> rapid cycling (3.8X),<sup>32</sup> and adult suicide (2X).<sup>33</sup>

**Use is controversial.**<sup>34</sup> Prescribed 30-81% of time<sup>35</sup> despite studies and expert consensus offering little support.<sup>36</sup>

**FDA black box warning for INCREASED suicide risk in young people.**<sup>37</sup>

**Conventional Bipolar Care** vs **Integrative Mental Health**

**A paradigm shift is available today, embraced by many practitioners...**  
It uses the best of drug therapy and evidence-based nondrug options. It reduces symptoms so drug dosages and their side effects can be reduced. It often targets causative factors.<sup>41</sup> It often supports sustainable wellness. Not a panacea, but nondrug options have few side effects<sup>42</sup> and are crucial to long-term recovery.<sup>43</sup>

**Drugs aren't the savior nor the enemy.**  
They are one option with pros and cons.  
**Integrative practitioners offer many others.**

**Choose Wisely.** 

For more information on antidepressants, see: [Infographic](#).  
www.OnwardMentalHealth.com/infographics

OnwardMentalHealth.com

Version 1, 01/2019

**Drugs cause side effects and elevated risk.** Bipolar drugs come with side effects (86% of people who take antidepressants experience side effects<sup>34</sup> while 94% of people who take antipsychotics do<sup>35</sup>).

Some of the most troublesome are chronic kidney disease with lithium, tremors, nausea, cognitive decline, sedation, sizable weight gain, sexual dysfunction, addiction (with benzodiazepines) and withdrawal difficulties. The infographic gives a sense of some of the major side effects for each of the five bipolar drug classes.

**Polypharmacy Risk.** Most people with bipolar take 2-5 psychiatric drugs (polypharmacy),<sup>36</sup> a practice that boosts symptom relief somewhat, but at considerable additional risk.

Unfortunately, the sheer number of individual bipolar drugs makes drug combination testing practically nonexistent.<sup>37</sup> This creates an uncomfortable reality: although psychiatry seeks evidence-based care, it ventures beyond the evidentiary base for all but the simplest bipolar prescribing.<sup>38</sup> And straying from the evidence creates grim results: longer hospital stays,<sup>39</sup> increased suicide,<sup>40</sup> and a rise in drug-related illness.

Even if we are comfortable with this added risk, the benefits come with diminishing return. The benefit of multiple drugs is nearly always less than the sum of the parts, and in some cases add-on drugs provide no benefit at all (as we will see with antidepressants).

Antipsychotic polypharmacy – taking two or more antipsychotics at once – is considered one of the riskiest forms of polypharmacy. In fact, the American Psychiatric Association (APA) launched a campaign targeting antipsychotic over-use. The APA's CEO and Medical Director cautioned, "...Physicians and patients together should be thinking carefully. Are the medications really needed and are there downsides and negative consequences for overuse?"<sup>41</sup>

This caution is well-placed: those on two or more antipsychotics for bipolar have almost triple the risk of requiring medical care, with no improvement in functioning.<sup>42</sup> And the greater the number of antipsychotics taken concurrently, the shorter the expected life-span.<sup>43</sup> Despite this evidence, 10% of people with bipolar are on two or more antipsychotics.

**The evidence on antidepressants.** The largest-ever federally funded trial for bipolar depression found that antidepressants *don't work* (*don't outperform sugar pills*) when added to mood stabilizers.<sup>44</sup> And most people taking bipolar drugs are on mood stabilizers.<sup>45</sup> Gold-standard meta-analyses and systematic reviews in 2001, 2008, 2011, 2012, 2013, 2014, and 2016 all reached variations of the same conclusion: antidepressants don't work for bipolar.<sup>46</sup>



One meta-analysis concluded: "Existing evidence of efficacy does not support the short-term or long-term application of antidepressant therapy in patients with bipolar."<sup>47</sup> Another warns that the research "suggests an unfavorable risk / benefit relationship for long-term antidepressant treatment in bipolar disorder".<sup>48</sup>

The poor results with antidepressants collide with a prescribing reality: 30-81% of people treated for bipolar depression are taking antidepressants.<sup>49</sup> This disconnect is considered the largest controversy in bipolar care.

To attempt to resolve it, an expert task force was convened in 2013. They found insufficient evidence to make any broad statements supporting antidepressants. Bottom line: antidepressant prescribing for bipolar depression is extremely common, but the best available research and expert consensus don't support it.

A variety of contributing factors influence this situation:

- Although many prescribing guidelines have changed across the world to reflect consensus opinion, some have not.
- A bias toward drug solutions limits the options even when viable nondrug options are available.
- Antidepressant withdrawal symptoms, a reality for over half the people who take them, often make it hard to get off of antidepressants once started.

Researchers have sought to find some aspect of bipolar for which antidepressants provide a compelling solution. But none has been found.

Stand-alone antidepressants aren't recommended nor FDA-approved since they can promote mania and switching.<sup>50</sup> Add-on antidepressants to mood stabilizers provide no benefit.<sup>51</sup> One antidepressant (fluoxetine) helps depression when combined with an antipsychotic (olanzapine), but the solution is almost as likely to harm as help.<sup>52</sup> Short-term use for bipolar II may provide value, but it can easily slide to long-term use because of antidepressant withdrawal difficulties. Long-term use may reduce the risk of new depression but it increases mood fluctuations<sup>53</sup> and the lifetime risk of polarity change and mixed episodes.<sup>54</sup>

### Final Thoughts.

I leave you with the following perspectives:

**Drugs aren't the savior nor the enemy.** Blur your eyes and look at the earlier infographic. An expanse of red will wash over your retinas. But there are also swaths of green. Yes, not a lot of big numbers on the green, but green. Many people confirm that drugs help them reside more often in a place of safety and stability from which they can build their recovery. Unfortunately, 75-85% of the time, people don't see substantial improvement due to a bipolar drug they take. There is far more to healing than can be included in the chemistry of a pill.



**Don't wait for the paradigm shift.** Most psychiatrists focus their practice on drug therapy, so you often need to expand your practitioner team to explore nondrug options. Fortunately, there is a vanguard of mental health practitioners that can help. Some are aligned with the emerging evidence of bio-individuality that informs individualized nutrient therapy, shown broadly effective in open label trials. Others see the correlation between bipolar and childhood trauma and are helping address sources of enduring pain. Others are aligned with expert consensus and are creating de-prescribing plans that slowly ween people off psychiatric drugs when needed. And professionals in peer support, mindfulness, mind-body disciplines, and more are providing valuable recovery support.

**Nondrug options aren't a panacea.** Although there is growing gold-standard evidence that supports them, it's much smaller than for drugs. Nondrug options may take longer to show benefit, they require greater personal commitment, most aren't covered by insurance, and practitioners are scarce. They aren't miracles. However, their ability to address causative factors of distress, support core wellness, and minimize exposure to the risks and side effects of bipolar drugs, make them essential and a pragmatic source of hope.

The more effort that is applied in addressing the first three perspectives outlined above (physical, psychological and wellness basics), the less psychiatric drugs are often needed. And the less we depend on psychiatric drugs, the less we must contend with their side effects and withdrawal difficulties.

**Build a better plan with your practitioners.** Carefully evaluate the evidence on your current bipolar drugs. Answer the APA's question, "Are the medications really needed and are there downsides and negative consequences for overuse?" If you make adjustments, do so slowly under practitioner care.

If psychiatric drugs are required, it is often best to seek the *minimum effective dosages* – no larger a dose than is needed to substantially reduce symptoms. This is done through experimentation in one of two ways. If the person is not yet on the drug, a low dose can be given and potentially slowly increased if needed to gain suitable symptom relief. If the person is already on the drug, a very slow tapering technique can be used to find the balance point between symptom relief and side effects. Any drug tapering should be done only under practitioner guidance and done very slowly to avoid relapse.

But – and this is my central point – *don't limit yourself to bipolar drugs*. Explore evidence-based nondrug options. Avoid drug myopia. Trust your own experience. Your recovery may well depend on it.

**Things to avoid.** Some practitioners recommend avoiding supplements for calcium, chromium picolinate, glutamine , SAM-e, vanadium, St. John's Wort, and ginseng for people with bipolar. When therapies are used to reduce the depressive symptoms of bipolar, caution should be exercised to avoid the onset of mania.

Also avoid Electroconvulsive Therapy (ECT). ECT is the most controversial therapy in all of psychiatry. It subjects the brain to intense electrical shock that induces a grand mal seizure. It is generally ineffective in the mid- to long-term, although ECT can significantly reduce depressive symptoms during treatment and for a short period after. Most trials show that real ECT is only marginally better than sham ECT, and this advantage can fade quickly. ECT relapse is common with symptoms often return to pretreatment levels. ECT comes with troubling cognitive side effects: some memory loss occurs in nearly all cases; larger and persistent memory loss in about one-quarter to one-half of the cases; and very severe cognitive dysfunction more rarely. The cognitive impact of ECT seems cumulative: future shocks must be larger than previous ones, and the more powerful and frequent the shocks, the greater the side effects.



There are a variety of more recently developed therapies that apply electrical impulses to the brain that use significantly lower electrical charges, show benefit, and appear to have no adverse cognitive side effects.

**Get started.** Integrative mental health offers significant hope for mental health recovery by offering you a remarkably diverse set of options that include, but go well beyond, medication. Although there are no silver bullets in mental health, working with integrative mental health practitioners can help open the door to sustainable wellness. These practitioners can help you determine which of the above approaches are most likely to help you, based on thorough testing and evaluation, and a review of your personal history. They can then work with you to experiment with your chosen approaches in a priority order, since the only way to know your individual response to an approach is to try it.

As first steps, watch a short [video](#) of William Walsh, PhD on the methods and results of Nutrient Therapy for bipolar. Engage a practitioner trained in the diagnosis and treatment of the biomedical issues of mental health (see [biomedical practitioner finder](#)). Check out Safe Harbor's [Free Mental Health Strategies](#) – 80 budget-minded nondrug mental health options. Or consider the [27 broad evidence-based nondrug options](#) that span all diagnoses. There is far more available than most people realize.

I hope you find this information valuable. If we can be of assistance, please don't hesitate to contact us.

Take care and good luck,

Craig Wagner

President, [Onward Mental Health](#)

*\*Disclaimer. Onward Mental Health ([www.OnwardMentalHealth.com](http://www.OnwardMentalHealth.com)) and its representatives provide insight on non-drug mental health alternatives. This information is for educational purposes only. We don't give medical advice or make specific therapy recommendations for individuals. This paper and other referenced material are not intended to replace practitioner guidance. Always work with appropriate practitioners to determine the best care for you which may include psychiatric drugs. Although we take care and seek transparent accuracy, this paper is not exhaustive and some errors may be included. Providing links to directories and other information does not constitute endorsement or full agreement. See [www.OnwardMentalHealth.com](http://www.OnwardMentalHealth.com) for further disclaimer information and terms of use for this information. 1.9.2019*

---

Footnotes for the Bipolar Drug Infographic can be found at: [www.OnwardMentalHealth.com/infographics](#)

<sup>1</sup> Walsh W, Nutrient Power Heal Your Biochemistry and Heal your Brain, Skyhorse Publishing, 2014, <http://goo.gl/DxolvQ>.

<sup>2</sup> Sarris J, Omega-3 for bipolar disorder: meta-analyses of use in mania and bipolar depression, J Clin Psychiatry, 2012, PMID: [21903025](#).

<sup>3</sup> Stoll AL et al. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. Arch Gen Psych, 1999, PMID: [10232294](#).

<sup>4</sup> Walsh W, Advanced Nutrient Therapies for Bipolar Disorders with Dr. Walsh, Natural Treatments for Bipolar, video, <https://goo.gl/l6h8Y5>.

<sup>5</sup> Coppen A et al, Folic acid enhances lithium prophylaxis. J Affect Disord. 1986, PMID: [2939126](#).

<sup>6</sup> Barrett S et al, Acute phenylalanine/tyrosine depletion: A new method to study the role of catecholamines in psychiatric disorders, Primary Psychiatry, 2004.

<sup>7</sup> Scarna A et al, Effects of a branched-chain amino acid drink in mania, British J of Psychiatry, 2003, PMID: [12611783](#).

<sup>8</sup> Lake J, Integrative Treatment of Bipolar Disorder: A Review of the Evidence and Recommendations, Psych Times, 2013, <http://goo.gl/7IGU7U>.



<sup>9</sup> Sarris J, Mischoulon D, Schweitzer I. Adjunctive nutraceuticals with standard pharmacotherapies in bipolar disorder: a systematic review of clinical trials. *Bipolar Disord.* 2011, PMID: [22017215](#).

<sup>10</sup> Dean O, Giorlando F, Berk M. N-acetylcysteine in psychiatry: current therapeutic evidence and potential mechanisms of action. *J Psychiatry Neurosci.* 2011, PMCID: [PMC3044191](#).

<sup>11</sup> Berk M et al, N-acetyl cysteine for depressive symptoms in bipolar disorder—a double-blind randomized placebo-controlled trial. *Biol Psychiatry.* 2008, PMID: [18534556](#).

<sup>12</sup> Greenblatt James, Integrative Psychiatrist <http://vimeo.com/49454442>

<sup>13</sup> Greenblatt J, Magnesium: the missing ink in mental health?, 2016, Integrative Medicine for Mental Health, <https://goo.gl/epKm3o>.

<sup>14</sup> Swaminathan R, Magnesium Metabolism and its Disorders, *Clin Biochem Rev.* 2003, PMCID: [PMC1855626](#).

<sup>15</sup> Fredricks, R, Healing & Wholeness Complementary and Alternative Therapies for Mental Health, All Things Well Publications, 2008.

<sup>16</sup> Chouinard G et al, A pilot study of magnesium aspartate hydrochloride (Magnesiocard) as a mood stabilizer for rapid cycling bipolar affective disorder patients. *Prog Neuropsychopharmacol Biol Psych.* 1990, PMID: [2309035](#).

<sup>17</sup> Giannini AJ et al, Magnesium oxide augmentation of verapamil maintenance therapy in mania. *Psychiatry Res.* 2000, PMID: [10699232](#).

<sup>18</sup> Heiden A et al. Treatment of severe mania with intravenous magnesium sulphate as a supplementary therapy, *Psychiatry Res.* 1999, PMID: [10708270](#).

<sup>19</sup> Mehrpooya M et al, Evaluating the Effect of Coenzyme Q10 Augmentation on Treatment of Bipolar Depression: A Double-Blind Controlled Clinical Trial, *J Clin Psychopharmacol.* 2018, PMID: [30106880](#), <https://goo.gl/B87R2P>.

<sup>20</sup> Forester B et al, Coenzyme Q10 Effects on Creatine Kinase Activity and Mood in Geriatric Bipolar Depression. *J Geriatr Psych Neurol.* 2012, PMCID: [PMC4651420](#); Forester BP et al, Antidepressant effects of open label treatment with Coenzyme Q10 in geriatric bipolar depression. *J Clin Psychopharmacol.* 2015, [PMC4414830](#).

<sup>21</sup> Haarman B et al, Aspirin for recurrence prevention in bipolar disorder- promising, yet clinically understudied?, *Bipolar Disord.* 2018, PMID: [30472767](#), <https://goo.gl/Zc9qWB>.

<sup>22</sup> Sachs GS et al, Effectiveness of Adjunctive Antidepressant Treatment for Bipolar Depression, *N Engl J Med.* 2007, PMID: [17392295](#).

<sup>23</sup> Chiang KJ et al, Efficacy of cognitive-behavioral therapy in patients with bipolar disorder: A meta-analysis of randomized controlled trials, *PLoS One,* [PMC5417606](#).

<sup>24</sup> Nusslock R, Interpersonal Social Rhythm Therapy (IPSRT) for Bipolar Disorder Review and Case Conceptualization, 2011, <http://goo.gl/cSaL6p>.

<sup>25</sup> IPSRT.org, Current Research, copied 4/8/15 from <https://www.ipsrt.org/currentResearch>.

<sup>26</sup> Dickerson F, Markers of gluten sensitivity and celiac disease in bipolar disorder, *Bipolar Disorders.* 2011, PMID: [21320252](#).

<sup>27</sup> Pataracchia R, Orthomolecular Treatment for Depression, Anxiety & Behavior Disorders, Naturopathic Med Research Clinic, 2008. <http://goo.gl/g26VUR>

<sup>28</sup> Dickerson F et al, Adjunctive probiotic microorganisms to prevent rehospitalization in patients with acute mania: A randomized controlled trial, *Bipolar Disord.* 2018, PMID: [29693757](#).

<sup>29</sup> Samuelson K, Bright light therapy at midday helped patients with bipolar disorder, 2017, <https://goo.gl/exe4xC>.

<sup>30</sup> Barbini B et al, Dark therapy for mania: a pilot study, *Bipolar Disord.* 2005, PMID: [15654938](#).

<sup>31</sup> Phelps J, Dark therapy for bipolar disorder using amber lenses for blue light blockade, *Med Hypotheses.* 2008, PMID: [17637502](#)

<sup>32</sup> Neckelmann D et al, Chronic insomnia as a risk factor for developing anxiety and depression, *Sleep.* 2007, PMID: [17682658](#)

<sup>33</sup> Benedetti F et al, Combined total sleep deprivation and light therapy in the treatment of drug-resistant bipolar depression: acute response and long-term remission rates. *J Clin Psychiatry.* 2005, PMID: [16401154](#).



- 34 Hu et al, Incidence and duration of side effects and those rated as bothersome with selective serotonin reuptake inhibitor treatment for depression: patient report versus physician estimate, *J Clin Psychiatry*. 2004, PMID: [15291685](#)
- 35 Lindström E et al, Patient-rated versus clinician-rated side effects of drug treatment in schizophrenia. Clinical validation of a self-rating version of the UKU Side Effect Rating Scale (UKU-SERS-Pat), *Nord J Psychiatry*. 2001, PMID: 11860666. <https://goo.gl/YzWtff>.
- 36 Weinstock LM et al, Medication burden in bipolar disorder: a chart review of patients at psychiatric hospital admission. *Psychiatry Res.* 2014, PMCID: [PMC3968952](#)
- 37 Alda M et al, Is Monotherapy as Good as Polypharmacy in Long-Term Treatment of Bipolar Disorder?, *Can J Psychiatry*. 2009, PMID: 19961659, hEps://[goo.gl/ZqpHbq](https://goo.gl/ZqpHbq),
- 38 Kingsbury S, Psychiatric Polypharmacy: The Good, the Bad, and the Ugly, *Psychiatric Times*, 1007, hEp:// [goo.gl/KIlsId](https://goo.gl/KIlsId).
- 39 Kingsbury S, Psychiatric Polypharmacy: The Good, the Bad, and the Ugly, *Psychiatric Times*, 1007, hEp://[goo.gl/KIlsId](https://goo.gl/KIlsId).
- 40 Gazalle FK et al, Polypharmacy and suicide attempts in bipolar disorder, *Rev Bras Psiquiatr*, 2007, PMID: 17435926, hEps://[goo.gl/4nC2S1](https://goo.gl/4nC2S1). “
- 41 Sharfstein SS, Big Pharma and American Psychiatry: The Good, the Bad, and the Ugly, *Psych News* 2005, hEp://[goo.gl/lzjQSW](https://goo.gl/lzjQSW). James Scully (MD, APA Medical Director and CEO), excerpt from a video of him speaking to the APA's par.cipa.on in the Choosing Wisely® campaign, 2013, hEps://[vimeo.com/74481474](https://vimeo.com/74481474), copied 2015. WaEs V, APA Joins Campaign Urging Doctors, Pa.ents to Choose 'Wisely', *Psychiatric News*, 2013, hEps://[goo.gl/WQqbFF](https://goo.gl/WQqbFF).
- 42 Brooks JO et al, Safety and tolerability associated with second-generation antipsychotic polytherapy in bipolar disorder: findings from the Systema.c Treatment Enhancement Program for Bipolar Disorder, *J Clin Psychiatry*. 2011, PMID: 20868629.
- 43 Waddington JL, Mortality in schizophrenia. An psycho.c polypharmacy and absence of adjunc.ve an.cholinergics over the course of a 10-year prospec.ve study, *Br J Psychiatry* 1998, PMID: 9926037. Joukamaa M et al, Schizophrenia, neuroleptic medica.on and mortality. *Br J Psychiatry*, 2006, PMID: 16449697.
- 44 National Institute of Mental Health (NIMH), Study Sheds Light on Medication Treatment Options for Bipolar Disorder, NIMH Archive, hKps://[goo.gl/q5YGxx](https://goo.gl/q5YGxx).
- 45 Greil W et al, Pharmacotherapeutic trends in 2231 psychiatric inpatients with bipolar depression from the International AMSP Project between 1994 and 2009. *J Affect Disord* 2012, PMID: 22134044.
- 46 Systematic reviews and meta-analyses finding no value of antidepressants over placebo. Nemerooff CB et al, Double-blind, placebo-controlled comparison of imipramine and paroxetine in the treatment of bipolar depression, *Am J Psychiatry*. 2001, PMID: [11384898](#). <https:// goo.gl/z4r9ya>. National Institute of Mental Health (NIMH), Study Sheds Light on Medication Treatment Options for Bipolar Disorder, 2007, NIMH Archive, <https:// goo.gl/q5YGxx>. Ghaemi S et al, Long-term antidepressant treatment in bipolar disorder: meta-analyses of benefits and risks, *Acta Psychiatr Scand*. 2008, PMCID: [PMC2718794](#). Sidor MM et al, Antidepressants for the acute treatment of bipolar depression: a systematic review and meta-analysis, *J Clin Psychiatry*. 2011, PMID: [21034686](#), <https:// goo.g/xtwCya>. Amit B et al, Antidepressant Treatment for Acute Bipolar Depression: An Update, *Depress Res Treat*. 2012, PMCID: [PMC3272786](#); Zhang Y et al, Antidepressants for bipolar disorder: A meta-analysis of randomized, double-blind, controlled trials, *Neural Regen Res*. 2013, PMCID: [PMC4146170](#), McInerney S et al, Review of Evidence for Use of Antidepressants in Bipolar Depression, *Primary Care Companion CNS Disord*. 2014, PMCID: [PMC4321017](#). McGirr A et al, Safety and efficacy of adjunctive second-generation antidepressant therapy with a mood stabiliser or an atypical antipsychotic in acute bipolar depression: a systematic review and meta-analysis of randomised placebo-controlled trials, *Lancet Psychiatry*. 2016, PMID: [28100425](#), <https:// goo.g/TzYB1A>.
- 47 Zhang Y et al, Antidepressants for bipolar disorder: A meta-analysis of randomized, double-blind, controlled trials, *Neural Regen Res*. 2013, PMCID: [PMC4146170](#).
- 48 Ghaemi S et al, Long-term antidepressant treatment in bipolar disorder: meta-analyses of benefits and risks, *Acta Psychiatr Scand*. 2008, PMCID: [PMC2718794](#).
- 49 Greil W et al, Pharmacotherapeutic trends in 2231 psychiatric inpatients with bipolar depression from the International AMSP Project between 1994 and 2009. *J Affect Disord* 2012, PMID: [22134044](#).
- Baldessarini RJ et al. Patterns of psychotropic drug prescription for U.S. patients with diagnoses of bipolar disorders. *Psychiatr Serv* 2007, PMID: [17215417](#);
- Goodwin G et al, Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology, *Journal of Psych*



<sup>50</sup> Liu B, Efficacy and safety of long-term antidepressant treatment for bipolar disorders – A meta-analysis of randomized controlled trials, J Affective Dis, 2017, [PMID: 28715727](#).

<sup>51</sup> National Institute of Mental Health (NIMH), Study Sheds Light on Medication Treatment Options for Bipolar Disorder, NIMH Archive, <https://goo.gl/q5YGxx>.

<sup>52</sup> Ketter TA et al, Balancing benefits and harms of treatments for acute bipolar depression, J Affect Disord. 2014, [PMID: 25533911](#), <https://goo.gl/YnCpz1>.

<sup>53</sup> Ghaemi S et al, Long-term antidepressant treatment in bipolar disorder: meta-analyses of benefits and risks, Acta Psychiatr Scand. 2008, [PMCID: PMC2718794](#).

<sup>54</sup> McInerney S et al, Review of Evidence for Use of Antidepressants in Bipolar Depression, Primary Care Companion CNS Disord. 2014, [PMCID: PMC4321017](#).