# Orthomolecular Psychiatric Treatments Are Preferable to Mainstream Psychiatric Drugs: A Rational Analysis

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**Abstract** *Although mainstream psychiatric drugs (MPDs) can help to quickly stabilize patients having mental breakdowns or suicidal crises, there are rational reasons for clinicians to consider orthomolecular psychiatric treatment (OPT). The practice of orthomolecular medicine encourages clinicians to diagnose accurately and recommend safer and more effective treatments than MPDs for the following reasons: (1) OPT utilizes substances that are normally present in the human body whereas MPDs are xenobiotics and not normally present in the human body; (2) OPT supports and nourishes the brain and body opposed to MPDs that induce abnormal brain states and can produce worrisome, problematic, toxic and sometimes even disabling psychological and somatic side effects; and (3) OPT is not associated with physiological dependence, withdrawal symptoms, or significant long-term harm whereas MPDs are. Even if there are questions about the author's interpretation of published data or his personal biases, we should still be concerned and re-evaluate the current practice of placing vulnerable patients on MPDs for long periods of time. We need a mental health system that is life-affirming, not life-impeding, and sufficiently open-minded and conscientious to consider seriously the recognized merits of OPT.*

## Introduction

Although mainstream psychiatric drugs (MPDs) can help to stabilize patients during mental episodes or breakdowns (e.g., first psychotic episode, disabling depression and acute mania), there are rational reasons why clinicians may wish to consider using orthomolecular medicine to reduce patients' needs for MPDs and/or to facilitate the eventual reduction of doses to ameliorate side effects. MPDs might themselves be responsible for the protracted course of psychiatric illness and debility since recurrences and/or relapses might be attributable to the iatrogenic effects of medications.[1] In this paper, I will demonstrate why orthomolecular psychiatric treatment (OPT) is a safer and more effective treatment option than MPDs for the following reasons: (1) OPT utilizes optimal doses of substances that are normally present in the human body as opposed to MPDs that are xenobiotics and are not normally present in the human body; (2) OPT supports and nourishes the brain and body as opposed to MPDs that induce abnormal brain states and produce worrisome and sometimes disabling psychologic and somatic side effects; and (3) OPT is not associated with physiological dependence, withdrawal symptoms, and significant long-term harm whereas MPDs have been associated with dependence and can cause worrisome symptoms during with-

drawal. They can also cause harm when vulnerable patients are experiencing symptoms and side effects during episodes of illness. In comparison to OPT, this paper asserts that MPDs are unnatural agents that induce abnormal brain states, produce iatrogenic symptoms or even cause harm and have been associated with chronic long-term debility.

## Support for Orthomolecular Psychiatric Treatment

### OPT Uses Optimum Doses of Naturally Occurring Substances to Correct Defective Enzyme-Catalyzed Reactions and Helps to Restore Normal Brain Metabolism

Common sense dictates that an orthomolecule, i.e., a micronutrient naturally and normally present in the human body, such as vitamins, minerals, amino acids, and essential fatty acids, would be more health-promoting than synthetic prescription medications. OPT therapy provides the optimal molecular environment for the brain and other tissues by improving the patient's intake of essential nutrients, such as vitamins (and their metabolites), minerals, trace elements, macronutrients, as well as other naturally-occurring metabolically active substances.

OPT should be preferable to using MPDs for the treatment of psychiatric disorders. Arguments in support of OPT have been previously published by Pauling and others.[2-4] Pauling argued that since the human race is characterized by genetic heterogeneity, enzyme concentrations in the tissues of individual patients can be expected to differ tremendously by factors of 2, 10, or even 100. It is therefore reasonable to consider that mental status changes might arise, in part, due to defective enzyme-catalyzed reactions, associated with biochemical individuality as well as deficiencies of precursors and sub-optimal levels of enzyme co-factors. The saturating capacity would be much greater for defective enzymes that have diminished combining capacity for their respective substrates. A defective enzyme-catalyzed reaction could therefore be corrected by increasing the concentration of its substrate and co-factors through the use of optimal doses of particular orthomolecules.

In a 2002 publication,[5] the need for large doses of orthomolecules was deemed necessary as a means to increase coenzyme concentrations and to correct defective enzymatic activity in fifty human genetic diseases. The authors of this study went further by stating that the "examples discussed here are likely to represent only a small fraction of the total number of defective enzymes that would be responsive to therapeutic vitamins." Therefore, it is reasonable to prescribe orthomolecules to psychiatric patients as a therapeutic treatment aimed at "normalizing" altered brain function resulting from deficiencies of essential nutrients and from defective enzyme-coenzyme reactions.

### OPT Utilizes Naturally Occurring Substances that Offset Deficiencies in the Cerebral Spinal Fluid and/or in Other Tissues of the Body

Pauling also discussed the possibility that cerebrospinal fluid (CSF) concentrations of vital orthomolecules could be grossly diminished while concentrations in the blood and lymph remained essentially normal.[2,3] He hypothesized that localized cerebral deficiencies might result from decreased rates of transfer (i.e., decreased permeability) of vital orthomolecules across the blood-brain barrier, increased rates of their destruction within the CSF, or from other (unknown) factors. Other authors have speculated that exposures to toxic chemicals (i.e., alcohol, industrial solvents or halogenated hydrocarbons) might block the entry of specific orthomolecules into the brain, leading to CSF deficiencies.[6] This phenomenon of a localized cerebral deficiency has been described in reports documenting neuropsychiatric improvements from therapeutic vitamin $B_{12}$ supplementation among subjects having normal vitamin $B_{12}$ levels in the serum, but deficient levels within the CSF.[6,7] It is conceivable that the therapeutic administration of many orthomolecules might correct for micronutrient deficiencies within the CSF, and therefore "normalize" altered brain function

among patients with psychiatric disorders.

Even if one does not consider the relationship between nutrition and the "health" of the CSF, it is well-established that deficiencies of orthomolecules can lead to mental status changes resulting from many factors, such as poor diet and lifestyle habits,[8,9] concomitant disease (i.e., malabsorption), and prescription drugs (i.e., drug-induced nutrient depletions or compromised nutrition due to side effects like loss of appetite[10]). When micronutrient deficiencies arise they typically follow a fairly predictable course (**Table 1,** below),[11] which invariably would impact the CSF and other tissues, and likely cause a deficiency or some perturbation within some or all of these compartments of the body.

Even though clinical symptoms can be recognizable at any point along this continuum (from stages 1-3), they can be hidden to the untrained clinician who might not be cognizant that there is a relationship between common neuropsychiatric presentations (e.g., cognitive impairment, depression, psychosis, and even mania) and micronutrient inadequacy. Neuropsychiatric presentations might reflect long-latency deficiency disease states as a result of poor nutritional intakes for many years.[4] **Table 2**, (p.20) highlights mental status changes associated with common micronutrient deficiencies.[12-14] Overall, the therapeutic administration of orthomolecules should have significant value in reversing many neuropsychiatric presentations when related to inadequate micronutrient status.

## OPT Improves Short-Term (and Likely, Long-Term) Therapeutic Outcomes Among Patients with Mental Disorders

Readers of this journal are well aware that decades of case reports have documented successful patient outcomes from using OPT either alone or in combination with MPD treatment for mood, thought, attention and other mental disorders. Outside of this journal, many published case reports document successful recoveries from the use of OPT, which include, for example: (1) fibromyalgia syndrome[15] (via micronutrients to offset mitochondrial myopathy); (2) schizophrenia[16] (via a low-carbohydrate, ketogenic diet that ameliorated the patient's psychotic symptoms as a result of gluten avoidance and/or modulation of the disease at a cellular level); and (3) recent onset of psychotic disorder, hypertension and seizures in a 16-year old patient[17] (via intramuscular injections of vitamin $B_{12}$ as the only therapy administered).

In three review publications, the results of many short-term intervention trials (normally, around 12 weeks or less) demonstrate therapeutic benefits from single orthomo-

**Table 1.** Micronutrient Deficiency Stages

| | |
|---|---|
| **Stage 1** | Micronutrient body stores begin to be depleted. Micronutrient urinary excretion decreases, while homeostatic mechanisms maintain a normal level of the micronutrient in the blood. |
| **Stage 2** | Depletion is more marked. As the micronutrient urinary excretion declines, there is a corresponding drop in its concentration in the blood and other tissues. The result is a lowering of micronutrient metabolites and/or dysfunction of dependent enzymes. Occasionally, hormone concentrations will decrease and may be accompanied by observable physiological alterations. |
| **Stage 3** | Presence of morphological and/or functional disturbances. They are initially reversible, and then irreversible. Patients might present with nonspecific signs and symptoms. Unless they are adequately treated, death will eventually result. |

**Table 2.** Mental Status Changes Associated with Common Micronutrient Deficiencies

| | |
|---|---|
| B-Complex Deficiencies ($B_1$, $B_2$, $B_3$, $B_6$, $B_{12}$ and folic acid are the most common) | Agitation, Apathy, Cognitive Impairment, Delirium, Dementia, Depression, Dizziness, Emotional Lability, Faintness, Fatigue, Insomnia, Irritability, Mania, Memory Impairment, Mood Swings, Nervousness, Pain Sensitivity, Psychosis, Restless Legs, Rigidity, Somnolence, and Weakness |
| Vitamin D Deficiency | Anxiety, Depressed Mood, Insomnia, Nervousness and Weakness |
| Mineral Deficiencies (calcium and magnesium are the most common) | Agitation, Amnesia, Apathy, Behavioural Disturbances, Cognitive Impairment, Delirium, Depression, Dizziness, Fatigue, Hyperactivity, Irritability, Insomnia, Nervousness, Neurological Problems, Psychosis, Restlessness, Tremor and Weakness |
| Trace Mineral Deficiencies (chromium, zinc, selenium, and copper are the most common) | Amnesia, Apathy, Cognitive Impairment, Fatigue, Irritability and Psychosis |
| Essential Fatty Acids Deficiency | Alterations in Thought and Mood, Anxiety, Fatigue and Neurotic Fears |

lecular and multiple orthomolecular supplementation among patients having mental disorders.[4,18,19] In several of the reviewed intervention trials, patients provided with orthomolecules and MPDs fared better than patients given only MPDs.[20-26] A major criticism of OPT is the claimed dearth of clinical trials demonstrating benefits, yet these review articles clearly document successful short-term outcomes from using OPT in more than 80 intervention trials.

While rigorous long-term studies documenting the benefits from OPT is lacking, the therapeutic effects of OPT would likely sustain over time. Since the brain and body depend on a constant supply of micronutrients (i.e., achieved through dietary modifications and/or micronutrient supplementation), it seems plausible that the provision of optimal doses of OPT would facilitate improved mental and physical health over time. These effects would be cumulative, in that they would mitigate other risks of increased morbidity (e.g., nutrient insufficiency, hypertension, obesity, and immune dysfunction) and early mortality (e.g., diabetes, heart disease, and infectious disease) – for optimal nutrition is a sound and reasonable way to improve the quality (i.e., healthspan) and the duration (i.e., lifespan) of a person's existence.

For example, a depressed patient might be prescribed an optimal daily dose (4,000 IU) of vitamin $D_3$ (cholecalciferol) by a clinician who uses OPT. While this intervention might positively impact depression by improving this patient's sense of wellbeing[27] (note: not all intervention trials have shown benefit on depression[28]), the addition of this amount of vitamin $D_3$ would also reduce hypovitaminosis D-related ill health (i.e., many types of cancer, cardiovascular diseases, autoimmune diseases, diabetes mellitus types 1 and 2, specific bacterial and viral infections, and all-cause mortality rates),[29] and therefore

improve the health and increase the lifespan of the depressed patient.

### OMT is Not Associated with Physiological Dependence, Withdrawal Symptoms, or Long-Term Harm

Our bodies demand a constant supply of micronutrients found in foods and through supplementation. If the body's needs are not met, the individual will suffer from the consequences of micronutrient insufficiency, and in more extreme cases, malnutrition. Based on these facts, the body is physiologically dependent on receiving a complete "sum" of micronutrients on a daily basis; otherwise, signs and symptoms of nutritional inadequacy will manifest and cause a myriad of physical and psychological perturbations. This healthy physiological dependency, described here, is not the same as the unhealthy physiological dependency that results from tapering down or stopping MPDs.

When patients have compromised micronutrient intake because of an insufficient diet, radical dietary changes, and/or stopping their micronutrient supplementation, they can present with a wide variety of neuropsychiatric manifestations when their depletion of certain micronutrients exceeds their individual thresholds (e.g., as in vitamin $B_{12}$-deficient mania,[30] obsessive-compulsive disorder,[31] and psychosis[32]). Their changed mental states, heretofore, can result from a "lack" of essential micronutrients and not from instability induced by the discontinuation of a MPD.

With respect to harm, the use of hugely excessive doses of micronutrients can cause worrisome symptoms, but usually any such harm is self-limited and will reverse itself soon after the micronutrient dosage is reduced or discontinued. Essentially, there are no risks of long-term harm associated with the use of micronutrients. To illustrate this, I offer several examples from the published literature. The first example involves a schizophrenic patient who developed hepatitis following large doses (nine grams/day) of niacinamide.[33] This patient had no evidence of clinical hepatitis when taking 2,000-3,000 mg/day of niacinamide, but did develop clinical hepatitis when the dose was increased to 9,000 mg daily. The nausea and vomiting, as well as abnormal liver function tests, resolved after the patient discontinued the vitamin for three weeks.

The second example involves vitamin $B_6$ (in the form of pyridoxine hydrochloride). Studies in dogs have shown neurotoxicity leading to peripheral neuropathy, with ataxia, muscle weakness and loss of balance after having been administered vitamin $B_6$ 200 mg/kg body weight for 40-75 days.[34] In dogs it has even been possible to have a more acute onset of swaying gait and ataxia within nine days after vitamin $B_6$ taking 300 mg/kg body weight.[35] In humans, there are reports of sensory neuropathy following very large doses of vitamin $B_6$. Seven patients in one report had ataxia and severe sensory nervous system dysfunction after taking 2-7 g/day of vitamin $B_6$ for several months.[36] Four of the patients were severely affected, but they all improved following cessation of the vitamin even though some patients did have residual nerve damage. Weakness was not part of their clinical presentation and the central nervous system was clinically spared.

In an experimental study of five human volunteers, daily doses of either 1 or 3 g of vitamin $B_6$ was given until laboratory and/or clinical abnormalities resulted.[37] Electrophysiological and clinical abnormalities occurred simultaneously in all subjects, but occurred earlier in those taking higher daily doses of the vitamin. Upon stopping the vitamin, symptoms progressed for an additional 2-3 weeks before remitting. Most reports of sensory neuropathy following vitamin $B_6$ therapy involve daily doses larger than one gram.[38] Review articles typically mention that safe daily doses are between 200-500 mg,[38,39] even though there are recent randomized trials showing no evidence of harm when large doses are used to treat medication-induced side effects (1,200 mg/day for five days among patients with acute neuroleptic-induced akithisia[40,41] and 1,200 mg/day for 12 weeks among patients with tardive dyskinesia[42]). These examples are representative of the relative safety of OMP since the

negative effects caused by excessive doses of micronutrients are mostly reversible, and are not associated with long-term impairment.

Another way to assess harm from OPT is to review data pertaining to mortality. The American Association of Poison Control Centers has been collecting data on the fatalities associated with numerous products (i.e., vitamin supplements, medications, household cleaning products, etc) for decades. Only 13 deaths were linked to vitamins from 1983 to 2011,[43] but this data does not prove causality for it merely ascribes fatal outcomes to the use of vitamins.

Finally, OPT is unlikely to cause death since the therapeutic indexes (TIs) of the majority of orthomolecules tend to be extremely large. The TI represents an estimate of treatment safety. A very safe treatment would be expected to have a very large toxic dose in comparison to a much smaller effective dose. TI is calculated by determining the ratio of the LD50 (i.e., the dose required to produce a lethal effect in 50% of the population) to the ED50 (i.e., the median effective dose at which 50% of the population exhibits a specified therapeutic effect).[44] Of course, the actual TIs of medications and vitamins are not calculated with exact precision, but are extrapolated from experimental studies, animal studies, drug trials, and accumulated clinical experience.

It can be inferred that the TIs of vitamins and other orthomolecules would be generally quite large since the amount needed to produce a therapeutic effect would be much less than the amount needed to produce a lethal effect. For example, the estimated TI of vitamin $B_6$ is 12,791(LD50/ED50 = 5500 mg per kg/0.43 mg per kg). This was calculated by using LD50 data from a material data sheet[45] and ED50 data from a published study.[46] Thus, the TI for vitamin $B_6$ (and for the majority of micronutrients and other orthomolecules) is extremely high suggesting that in a given patient, a much smaller dose would be prescribed for therapeutic purposes compared to an inconceivably large "toxic" dose that might result in death.

## Evidence Against MPDs

### MPDs are Xenobiotics that Induce Abnormal Brain States

The brain depends on a constant supply of nutrition, oxygen, and other naturally-occurring substances to ensure their proper functioning. The proper functioning of the brain is not dependent on MPDs. These xenobiotic substances are not normally found in the brain and body. An emerging body of literature advocates for a drug-centred model of drug action as opposed to the outdated disease-centred model that espouses MPDs as correcting some known and well-validated disease process.[47]

For example, in the disease-centred model a depressed patient would be offered antidepressant medication as a means to correct some abnormal brain state (i.e., serotonin deficiency), which is then offset (i.e., helped) by the drug's action upon the underlying disease process (i.e., increasing serotonin within the central nervous system). In the drug-centred model, a depressed patient would be offered a medication to possibly induce a favourable "altered" mental state, which does not arise because the drug corrected some underlying disease process, but results from the consequences of being in a drug-induced altered state. This drug-centred model is a more accurate way to understand how MPDs function because the evidence that mental disorders are associated with deficiencies or excesses of specific neurochemicals is inadequate[48] (e.g., proof is lacking for some of the major theories of mental illness, such as the monoamine hypothesis of depression[49] and the dopamine hypothesis of schizophrenia[50]).

Given the inherent problems with the disease-centred model of drug action, the obvious question arises: "What then do MPDs actually do?" Simply put, all MPDs are psychoactive and in being psychoactive they "… induce complex, varied, often unpredictable physical and mental states that patients typically experience as global, rather than distinct therapeutic effects and side effects."[47] Patient should be told that these drug-induced altered states might be useful, for some altered states might suppress unwanted manifestations of mental disorders; however, alterna-

tively, these altered states might be harmful, for some altered states might induce unwanted or even unexpected physical and/or mental manifestations.[47,49] In reality the alteration in mental state induced by MPDs is not natural, and the ability of MPDs to favourably impact symptoms of mental distress is largely unpredictable. Notwithstanding their potential benefit, it is not entirely clear if "therapeutic" drug effects are merely the result of a poorly understood science of drug-induced psychological toxicity.[51] To further illustrate this, I offer an excerpt from Breggin's book, *Brain Disabling Treatments in Psychiatry*:

"The brain does not welcome psychiatric medications as nutrients. Instead, the brain reacts against them as toxic agents and attempts to overcome their disruptive impact. For example, when Prozac induces an excess of serotonin in the synaptic cleft, the brain compensates by reducing the output of serotonin at the nerve endings, by reducing the number of receptors in the synapse that can receive the serotonin, and by increasing the capacity of the transport system to remove serotonin from the synapse. Similarly, when antipsychotic drugs such as Risperdal, Zyprexa, or Haldol reduce reactivity in the dopaminergic system, the brain compensates, producing hyperactivity in the same system by increasing the number and sensitivity of dopamine receptors. All of these compensatory reactions create new abnormalities in brain function, sometimes causing irreversible disorders, such as antipsychotic drug-induced tardive dyskinesia."[52]

MPDs are xenobiotic substances which do not support the brain; instead, they artificially affect biochemical and physiological processes within the human organism, creating a chemical imbalance or an abnormal brain state with the hope that this "altered" state affords patients with fewer disabling psychiatric symptoms and improved functionality.

## MPDs Do Not Improve Therapeutic Outcomes Among Patients with Mental Disorders

When reviewing studies on all the major classes of psychotropic medication, many short-term studies (around 12 weeks or less) document beneficial responses from MPDs. However, none of this data sufficiently proves that MPDs help patients to live more fulfilling lives in the long-run. The results of these studies merely show that the psychoactive effects of MPDs moderate symptoms as per changes on specific clinical-rating scales.[47] Any psychoactive substance will moderate symptoms, but rarely do the clinical trials used to evaluate MPDs determine if these favourable changes in clinical-rating scales equate to an improved quality and quantity of life.

For example, MPDs with chemical properties that presumably "calm" an overexcited nervous system, can moderate disturbances of agitation and over-arousal, and therefore the clinical-rating scale will likewise demonstrate benefit. Does this benefit, however, really translate into better long-term functionality? In their chapter on the risks and benefits of psychiatric drugs, Sparks, Cohen and Antonuccio stated: "Without longer follow-up, conclusions about effectiveness in real life cannot be determined" and the "…initial effects of drug treatment must be weighed in terms of long-term tolerability and impact beyond symptom remission."[53]

When investigators have evaluated MPDs over periods of time longer than 12 weeks, many such trials have yielded negative results suggesting that tolerability and symptom remission do not sustain over time. A well-known example of this is the 6-year $35 million National Institutes of Mental Health (NIMH)-funded study (i.e., STAR*D) that had data on almost 2,900 depressed participants (ages 18-75) and evaluated the impact of MPD augmentation or switching strategies, i.e., either a different selective serotonin reuptake inhibitor (SSRI) or cognitive behaviour therapy when a traditional regimen of a single SSRI had failed.[54] This study was unblinded and non-placebo-controlled, and was designed to be naturalistic and emulate conditions experienced in everyday clinical practice. Among the participants who received citalopram (denoted as Level 1), 28% experienced side effects ranging from moderate to intolerable.[55] Among the par-

ticipants who were augmented or switched (denoted as Level 2), 51% experienced side effects ranging from moderate to intolerable.[56] For all levels in this study, 24% dropped out due to MPD intolerability.[57] In addition, the 12-month follow-up data on participants who either remitted or responded showed a relapse rate of 58%.[58] The other finding from the STAR*D was that the average remission rate was 28% and 25% for Levels 1 and 2 respectively, and 14% and 13% for the remaining levels. None of these studies demonstrate "real" effectiveness since the typical placebo response in antidepressant trials is 30%.[59]

With respect to antipsychotic medication, the data on long-term outcomes is also disappointing. Many patients with either schizophrenia or bipolar disorder are often told that they will need antipsychotic medication for life; otherwise, their functionality will be severely impaired. These vulnerable patients are often pressured into feeling that they can never be normal unless they take medication for the duration of their life. In the NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), the primary outcome measure was stoppage of MPD for any reason.[60] The reasoning for this primary outcome is that MPD compliance is very much associated with the patient's experience of side effects. Some 1,400 participants across 57 USA sites were included in this triple-blind study, meaning the clinicians, raters, and patients were unaware of which MPD the patients were taking. In CATIE there was no placebo group, which allowed clinicians to decide upon therapeutic dosages, as well as including additional MPDs (excluding antipsychotic medication) if necessary. This was a real-world study since CATIE compared how well the second-generation antipsychotic medications (SGAs) compared to one another, and how well they compared to a first-generation antipsychotic (FGA) medication (i.e., perphenazine).

The results from CATIE showed that for the majority of patients, antipsychotic medication does not improve quality of life and induces objectionable side effects. Some 74% of CATIE patients stopped their MPD before 18 months due to a lack of efficacy and intolerable side effects (1,061 of the 1,432 patients who received at least one dose).[60] The investigators of this report also noted that this drop-out rate is similar to drop-out rates from prior antipsychotic drug trials.[60] For one-third of CATIE patients, psychosocial functioning improved only modestly at 12 months.[61] The range of moderate to adverse events was 42-69%, the hospitalization rates ranged from 11-20%, and weight gain of more than 7% happened in 14-36% of patients.[62] The CATIE investigators concluded that the superiority for SGAs was greatly overstated, and that aggressive marketing contributed to a false sense of effectiveness despite the absence of solid empirical evidence.[63]

With respect to the treatment of bipolar disorder, data once again from the NIMH does little to confirm long-term efficacy. In the NIMH-funded study, Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), the effectiveness of SGAs and anticonvulsants were determined among patients diagnosed with bipolar disorder.[64] This hybridized study collected longitudinal data from patients transitioning from naturalistic studies and randomized clinical trials. In one report encompassing data covering 24 months of the STEP-BD study, only 30% of patients experienced no recurrences of symptoms.[65] From 858 patients, some 416 (48.5%) experienced recurrences during 2-years of follow-up, with 298 (34.7%) developing depressive episodes compared to 118 (13.8%) that developed manic, hypomanic, or mixed episodes.[65] In another report on STEP-BD, the recovery rate was rather abysmal and determined to be just under 15%.[66] In another analysis that evaluated bipolar patients during periods of sustained and substantial remission, the degree of functional impairment as determined by the Work and Social Adjustment Scale was deemed to be significant.[67]

Thus, from trials funded by the NIMH, it can be seen that the long-term effectiveness of MPDs is significantly lacking. If we think even more broadly about the implica-

tions of MPD treatment, the work of Whitaker, as reported in a journal publication[48] and a book,[68] reveals even more disturbing long-term trends from MPD treatment. Whitaker reasoned that there has been a significant statistical rise in the percentage of Americans disabled by mental illness since 1955, which coincidentally began with the introduction of Thorazine. Whitaker cites statistics from the U.S. Department of Health and Human Services, which has collected "patient care episodes" (i.e., an estimate of the number of people treated annually for mental illness) over the course of many decades. Whitaker's research focused on the years 1955-2000, and showed a nearly fourfold per-capita increase in patient care episodes (i.e., 1,028 episodes per 100,000 population in 1955 compared to 3,806 per 100,000 population in 2000). He also reviewed data pertaining to the number of mentally ill people who were disabled or required some sort of disability payment (i.e., patients having received a disability payment from the Social Security Disability Insurance or the Supplemental Security Income programmes). His analysis showed that in 1955 3.38 people per 1,000 population were disabled by mental illness, compared to 2003 in which the disability rate had risen to 19.69 people per 1,000 population.

The overarching problem, according to Whitaker, is that this rise in people being treated for mental illness, as well as those disabled by it, have markedly increased primarily as a result of the increased use of MPDs. It is no coincidence that there was a 40-fold increase in the combined sales of antidepressants and antipsychotics during this time period (from an estimated $500 million in 1986 to almost $20 billion in 2004). Additionally, Whitaker noted a substantive increase in roughly 2.4 million Americans designated as disabled from 1987 to 2003 (i.e., a marked acceleration beginning with the introduction of Prozac and other drugs), yielding some 410 people each day in the U.S. being designated as being "disabled" by their mental illness (i.e., requiring some form of social assistance).

These findings are likely not unique to the U.S. since the use of MPDs has prominently increased over the last several decades in many industrialized countries (for examples of increased MPD prescribing trends over a 10- to 12-year period in other countries see data for Ontario, Canada,[69] England,[70] and Australia[71]). Have the rates of mental disability increased in these countries in a manner proportionate to the increased use of MPDs? Given the problems associated with MPD use (as reported here), including the U.S. disability trends highlighted by Whitaker, it is likely that in other industrialized countries the rates of mental disability are rising in a manner proportionate to the increased use of MPDs. In developing countries of the world, policy changes will result in the increased availability of mental health services, including broader access to MPDs.[72,73] I speculate that in the ensuing 10-20 years, data will emerge demonstrating increases in mental disability proportionate to the increased use of MPDs in developing countries as well.

## MPDs Are Associated with Physiological Dependence, Withdrawal Symptoms, and Long-Term Harm

Pharmacological dependence is an expected and biological adaptation of the body becoming habituated to the presence of a psychotropic drug.[74] The mechanisms of withdrawal (i.e., overcoming pharmacological dependence) involve both "pharmacodynamic stress" and psychological reactions.[1] Since psychotropic drugs can induce unpredictable global reactions when used properly,[47,49] there are no reliable ways to predict how patients will overcome pharmacological dependence once their psychotropic drugs are tapered and eventually withdrawn. Every patient's withdrawal process is unique as is their susceptibility to developing withdrawal side effects.[75]

Moncrieff has identified and summarized the data pertaining to several important adverse outcomes caused by MPD withdrawal or reduction, and noted the following possibilities: (1) somatic discontinuation syndromes (also known as withdrawal or rebound reactions); (2) rapid onset psycho-

sis (rebound psychosis, supersensitivity psychosis); and (3) psychological reaction and misattribution.[1] Somatic discontinuation syndromes refer to psychological and behavioural symptoms (e.g., anxiety, restlessness, and insomnia) resulting from withdrawal that might be misinterpreted as early distress signals of relapse. These problems may be associated with MPD withdrawal and patients can experience them to such a heightened degree that coming off their MPDs might be impossible. As such, patients might not be able to overcome their pharmacological dependence and end up taking MPDs for the duration of their lives.

A rapid onset psychosis results shortly after discontinuing antipsychotic (i.e., neuroleptic) medication. This is believed to be an iatrogenic problem since patients without a psychiatric history have also reported this phenomenon. The onset is usually in a few days following discontinuation (e.g., resulting from clozapine due to its short half-life) and results in withdrawal reactions including auditory hallucinations, paranoid delusions, hostility, and sometimes visual hallucinations, grandiosity and elation. With antipsychotic medications having longer half-lives, a withdrawal psychosis might be difficult to identify. Patients are normally managed as though their distress signals indicate a naturally-occurring relapse instead of resulting from MPD withdrawal.

Another major adverse outcome facing patients on MPDs is that withdrawal symptoms might arise due to their psychological concerns or worries about discontinuing or reducing medication dosage. In other words, their expectations of psychiatric illness induce psychiatric illness. Since patients are normally told that they need their medications for life – they often believe this. If patients' doctors and other carers reinforce this notion – patients may become psychologically vulnerable to any decrease or stoppage of MPDs. Their psychological reactions can arise from fear and if so, their ensuing clinical reactions to lowering or stopping their MPDs may be mis-attributed to having relapsed.

Above all, the regular use of MPDs produces a clinical syndrome akin to being addicted to illicit drugs such as cocaine and amphetamines. If we consider addiction to be a "state of being enslaved to a habit or practice or to something psychological or physically habit-forming, as narcotics, to such an extent that its cessation causes severe trauma" (see: http://dictionary.reference.com/browse/addiction), then there are few differences in the addictive process that results from illicit drug use and that which results from MPDs. In both instances, individuals become enslaved to what they are regularly consuming, they experience both physical (i.e., physiological) and psychological dependence, and suffer tremendously when trying to stop. Most authorities on addiction now speak of this as a "brain disorder." If we are honest about what MPDs do to the brain, then understanding the addiction imposed by these drugs as resulting from a medication-induced brain disorder seems to be an appropriate way to understand the significance of the harm they can produce among increasing numbers of patients, especially patients who take MPDs chronically.

Apart from physiological dependence and withdrawal, there are many other ways in which the issue of harm could be further addressed. From the perspective of TI (described previously), it can be inferred that the TIs of MPDs are much lower rather than that of orthomolecules as a result of being more toxic. In other words, the dose of MPD needed to produce a lethal effect would be closer to the dose needed to produce a therapeutic effect. In an experimental study in mice, for example, the TI of diazepam was calculated to be 350 (LD50/ED50 = 49 mg per kg/0.14 mg per kg);[76] compared to the much greater TI of vitamin $B_6$ calculated as 12,791. In this example, and if we compared all the TIs of MPDs and orthomolecules, we would find lower TIs for MPDs indicating a much greater potential for harm.

From a global perspective, prescription drugs result in far more deaths than vitamins, and likely other orthomolecules as well. In a meta-analysis of hospitalized patients, 106,000 patients had fatal adverse drug reactions (ADRs), making medications between

the fourth and sixth leading cause of death in the U.S. in 1994.[77] Another report estimates that deaths due to ADRs from medications to be about 100,000 annually in the U.S.78 If we estimate the annual death rate due to medications in the U.S. from 1983-2011, then 2.8 million deaths can be attributed to medications compared to only 13 from vitamins during the same time period. The deaths attributed to other orthomolecules, such as amino acids, minerals, and essential fatty acids, would also be substantially lower than deaths attributed to medications.

If we look more specifically at MPD use and death (apart from medication use in general), a more devastating picture emerges about their potential for harm. While numerous studies have shown MPDs to be associated with increased disability (i.e., a reduced healthspan) due to many objectionable side effects (e.g., cardiometabolic risks associated with antidepressant and antipsychotic drugs[79]), the published literature is replete with studies showing significant long-term harm resulting from their use. Only several studies will be cited here to highlight the enormity of this problem. The use of neuroleptics (i.e., both the FGA and SGA) among schizophrenic patients (apart from lifestyle or other factors) when used alone or in combination with other medications is associated with reduced lifespans.[80-83] Benzodiazepine medication is also associated with increased mortality among schizophrenic patients.[84] These results are even more disturbing since it is well-established that schizophrenic patients have a 10-25-year reduction in life expectancy compared to the general population.[85] Drugs used for sleep, i.e., the hypnotics (e.g., zolpidem, temazepam, eszopiclone, zaleplon, other benzodiazepines, barbiturates and sedative antihistamines) have been shown to be associated with increased mortality, even at very low levels of use (<18 pills/year).[86] SSRI medication use among post-menopausal women is associated with increased stroke risk (i.e., hemorrhagic and fatal stroke) and all-cause mortality.[87] Healy and Whitaker in their analysis of SSRI studies found an excess of suicidal acts on active treatments (odds ratio of 2.4) compared to placebo.[88] There are even concerns about SSRI medication and violent crimes. While causality has not been established, we should be very concerned about how MPDs might affect judgment among isolated, vulnerable and highly distressed patients (see: www.ssristories.com/index.php).

Previously, I mentioned that the chronic use of MPDs induce a "brain disorder" in the context of addiction. Breggin has recently highlighted this issue more substantially in his article titled, "Psychiatric drug-induced chronic brain impairment (CBI): implications for long-term treatment with psychiatric medications."[89] Breggin mentions how all MPDs produce effects related to their specific mechanisms of action, but over time these initial specific effects change as the brain and body react to them, eventually causing more extensive changes to take place within the brain and in mental functioning. In proving his hypothesis, Breggin highlights the brain damage induced by long-term antipsychotic treatment. He mentions how these drugs shrink (i.e., atrophy) the brain, inhibit most mitochondrial enzyme systems, chronically block dopamine neurotransmission (resulting in death to the striatal neurons), and cause tardive dyskinesia with "associated impairment of cognitive and affective functioning." These brain changes, however, are not unique to the antipsychotic medications since all classes of MPDs, according to Breggin's research, cause mental dysfunction and atrophy of the brain following long-term exposure.

He asserts that the outcome of being chronically exposed to MPDs (especially, increasing doses over time) results in chronic brain impairment (CBI), which is very similar clinically to the effects arising from a closed-head injury due to trauma. He outlines the 4 major "symptom complexes" associated with CBI that significantly reduce quality of life, which include: (1) cognitive dysfunctions (i.e., short-term memory dysfunction, impaired ability to learn new material, inattention, and concentration problems); (2) apathy or loss of energy and vitality (i.e., indifference, fatigue, loss of creativity, lack of empathy, and

loss of spontaneity); (3) emotional worsening or "affective dysregulation" (i.e., loss of empathy, heightened impatience, irritability, anger, frequent mood changes with depression and anxiety) with a gradual onset such that over time, other people attribute these changes inappropriately to aging, stress, or to the mental illness itself; and (4) anosognosia (i.e., a lack of self-awareness of these symptoms of brain dysfunction).

Even though Breggin does mention several confounding factors that can cause or intensify CBI, his clinical experience has shown that nearly all patients on MPDs for many years develop some symptoms of CBI, with the most noticeable being short-term memory dysfunction and apathy. The apathy, according to Breggin, manifests as "a loss of interest in daily activities, hobbies, creative endeavors, and sometimes family and friends." The only way to recover from CBI is to slowly taper down and eventually stop taking MPDs. Breggin notes that recovery from CBI usually begins at the onset of the withdrawal process, but some patients unfortunately experience withdrawal years after stopping medication. Young children and teenagers can fully recover, even if they had been taking MPDs for years. By comparison, adults might experience persistent CBI problems, typically with memory, attention, and/or concentration, even though their lives will be much more fulfilling after stopping MPDs.

To enable patients to safely withdraw from MPDs, Breggin explains that a "person-centred" approach works best. This therapeutic process allows patients to be in charge of the withdrawal process and only proceed at a pace they are comfortable with. Also, providing psychotherapy during this process, but not insight therapy (e.g., working through childhood trauma), as well as encouraging patients to resume previous pleasurable hobbies (i.e., physical and/or mental activities) that they had neglected due to CBI, can significantly support the process of recovery.

## Conclusion

The scope of harm induced by MPDs is immense. It is conceivable that psychiatrists risk substantial liability if they fail to obtain informed consent, if they do not fully inform their patients of the risks associated with MPD treatment, or if they overstate benefits.[90] Even if there are questions about my interpretation of this data or concerns about my personal biases, we should still be very concerned and re-evaluate the current practice of placing patients on MPDs for long periods. Given the significant increase in the practice of MPD polypharmacy, and fact that most combinations of MPDs are not supported by clinical trials and have unproven efficacy,[91] we need to seriously consider the implications to the healthspan and lifespan of patients when MPD treatment is the only option provided. Orthomolecular psychiatric treatment is a rational and reasonable way to assist patients with mental disorders (**Table 3,** p.29).

Here is a hypothetical example of how a schizophrenic patient's future might be altered from either no treatment, MPD only, or mainly OPT (**Figure 1**, p.29). In all situations this patient's initial psychotic episode occurred around the age of 20. Following that episode, the likely differences in treatment outcomes are substantial, assuming the information contained in this paper is accurate.

When patients are given MPDs as a means to further their stability, the addition of OPT could safely and easily integrate with standard treatment, and allow carefully monitored patients to gradually reduce their medication while remaining mentally stable and physically healthy. We need a mental health system that is life-affirming and not life-impeding. We encourage open-minded and conscientious clinicians to review the extensive literature which documents six decades of research, development, progress and success of orthomolecular medicine. Hopefully this will encourage mental health professionals to recognize and embrace the merits of OPT.

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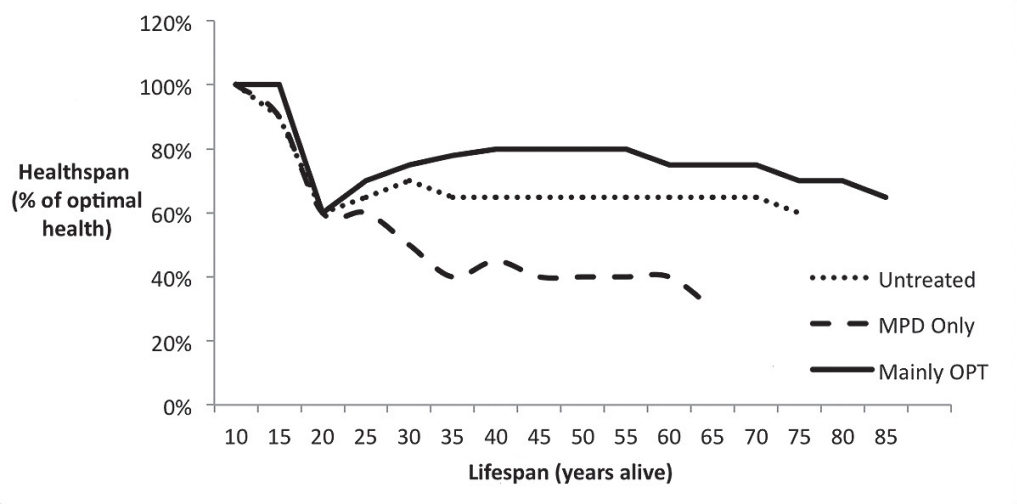
**Table 3.** OPT versus MPDs

| OPT | MPDs |
|---|---|
| Orthomolecules are naturally-occurring in the body and brain. | Xenobiotics are foreign to the body and brain. |
| OPT supports the proper functioning of the brain (and other tissues of the body) without disrupting biochemical and physiological processes resulting in improved or unchanged psychological function. | MPDs artificially alter the functioning of the brain (and other tissues of the body) and produce unpredictable brain-states that might help or harm psychological function. |
| Short-term intervention trials show efficacy. | Short-term intervention trials show efficacy. |
| Quality long-term trials are lacking, but there is a high probability that OPT will sustain both mental and physical health long-term. | Quality long-term trials lack efficacy, even though long-term use is associated with significant morbidity (i.e., decreased healthspan) and increased mortality (i.e., early death). |
| OPT is not associated with physiological dependence, withdrawal symptoms, and long-term harm. | MPDs are associated with physiological dependence, withdrawal symptoms, and long-term harm. |

**Figure 1.** Healthspan and Lifespan of a Hypothetical Schizophrenic Patient.



## Competing Interests

Dr. Prousky is currently a consultant for Pascoe Canada, a company that sells natural health products.

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