TREATING PATIENTS FOR BETTER OUTCOMES IN DEPRESSION

INCORPORATING A PATIENT-CENTERED WELLNESS PROGRAM INTO EVERYDAY PRACTICE

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Despite continuing developments in pharmacotherapy, rates of depression and other mental disorders are increasing the world over.

The World Health Organisation (WHO) estimates that 350 million people of all ages suffer from depression, making it the leading cause of disability worldwide.[1] Suicide, the most severe outcome of a depressive episode, is the second leading cause of death among young adults between the ages of 15 and 29 years and the fifth leading cause of death among 30-49 year olds.[2]

DEPRESSION IS A COMPLEX DISEASE WITH VARIABLE AND DIVERSE PRESENTATIONS. THESE MAY BE SEEMINGLY UNRELATED CONDITIONS, SUCH AS ACCIDENT PRONENESS OR ERECTILE DYSFUNCTION, SUCH THAT THE DEPRESSION ITSELF IS 'MASKED' AND REMAINS UNDIAGNOSED.

Even in those who are diagnosed, treatment is difficult. At least 30% of patients do not respond to pharmacotherapy and more than three quarters are at risk of relapse or chronic symptoms.[3] Furthermore, depression is frequently comorbid, co-occurring with a vast array of pathologies, including anxiety, panic attacks, alcohol and substance abuse, and somatic illnesses such as cancer, diabetes and chronic pain.[4] In recent years, socioeconomic pressures have contributed significantly to increases in the prevalence of depression.

People of all ages are subjected to unrelenting psychosocial stress, which may severely impact on both physical and psychological health.[4,5]

Clearly, pharmacotherapy and the traditional aims of treatment, namely symptom reduction and improved functionality, do not go far enough to effectively manage the causes, symptoms and course of depression. Recently, a third goal of treatment has been described that may improve health, not only in people with depression and other mental health issues, but in society in general. The concept of 'wellness' recognises the need to address the profound detrimental impact of modern lifestyle on physical and mental health, in terms of unhealthy changes and neglect in approaches to nutrition, physical activity, social engagement, thinking and coping skills.

Past president of the American Psychiatric Association, Dilip Jeste, points out that the aim of psychiatric treatment should not only be to reduce symptoms, but rather to help patients 'grow and flourish'.[6] This entails nurturing positive psychological traits, including resilience, optimism, wisdom, self-efficacy (belief in one's own ability to manage and influence one's own life) and social engagement.

These positive traits are tightly linked to human biology and associated with significant positive health outcomes. Indeed, studies have indicated that these attitudes are associated with healthy behaviours, longevity, better functioning and reduced susceptibility to mental and physical disorders, including depression, cancer and cardiometabolic diseases. In depression, resilience in particular is important, being a significant determinant in the ability to manage life stressors and risk of relapse after an initial depressive episode.[7-10]

THE WILD 5 WELLNESS INTERVENTION PROGRAM

The Wellness Interventions for Life's Demands (WILD) 5 program was designed to meet the needs to of a practical and achievable, trackable, accountable, self-directed wellness program for patients with depression.

IT ENCOURAGES AND GUIDES PATIENTS TO DEVELOP AND INCORPORATE FIVE ELEMENTS OF WELLNESS INTO THEIR DAILY ROUTINE, NAMELY PHYSICAL EXERCISE, MINDFULNESS, OPTIMISED SLEEP AND NUTRITION, AND IMPROVEMENT IN SOCIAL CONNECTEDNESS.

These elements were selected because each one of them has been previously demonstrated to improve mental wellness scores with sustainable benefits.[11,12]

WILD 5 is supported by online resources that are available to both the treating clinicians and participating patients.

Patients are introduced to the program during a 30-day induction phase, which is individualised according to their capabilities and modified (e.g. for pain, limitations of movement) if necessary. Thereafter, the behaviours should be continued for life. Program expectations for the initial induction period are listed in Table I. Daily program activities are documented using a Participant Tracking Form.

Table I. WILD 5 program expectations

Exercise	Exercise for 30 minutes every day for 30 days, at least moderate intensity. Patient capabilities need to be taken into account. Start with low intensity activity and increase intensity according to developing capability.
Mindfulness	Practice mindfulness at least 8 minutes each day for 30 days.
Sleep	Implement at least 4 of 6 pro-sleep hygiene practices each day for 30 days: • *If you are unable to sleep, get up and go to another room.* • *Do something quiet, calm and relaxing in dim light.* • *Do not fall asleep anywhere other than your bed.* • *Do not watch the clock.* • *Go back to bed when sleepy.* • *Always use the alarm in the morning set for the same time.*
Social connectedness	Text or call family members or friends each day for 30 days.

Protocols for these expectations and a workbook for tracking the activities may be downloaded from www.wild5resources.com (password: wellnessmatters).

It is helpful to remind patients that perfection is not the goal, but that sustained participation to the best of one's ability in all of the five elements is essential if one is to benefit from the program. There is no wear-off effect associated with wellness behaviours, which may be started at any age, and the benefit improves with time and practice. Tracking daily progress motivates patients to adhere to the program, whereas without tracking the drop-out rate is likely to be high.

In a small pilot study, including 36 patients, WILD 5 was shown to significantly improve mental wellness in terms of mood, anxiety, sleep, mindfulness and social connectivity, both in those taking and not taking psychotropic drugs.[11,12]

Patients generally found the program easy to implement into daily life. Compliance with the 30-day program was similar regardless of medication, being highest for social connectedness (28 days) and sleep (25 days), and lowest for mindfulness (18 days).

PARTICIPANTS RANKED EXERCISE, NUTRITION, MINDFULNESS, SLEEP AND SOCIAL CONNECTEDNESS AS MOST TO LEAST HELPFUL, RESPECTIVELY.

Significant improvements were documented in the Patient Health Questionnaire 9 item version (PHQ-9), Generalised Anxiety Disorder 7-item scale (GAD-7), World Health Organisation (Five) Well-Being Index (WHO-5), Mindful Attention Awareness Scale (MAAS) and Pittsburgh Sleep Quality Index (PSQI). The study was positive on all measures and no subjective or objective harm to participants was detected.

WILD 5 IN DIFFICULT TO TREAT POPULATIONS

Positive results using a WILD 5 induction program have also been obtained in two separate populations of patients, one with severe anxiety and one with chronic pain, both of which are frequently difficult to manage.[13]

TO CONTROL FOR THE INFLUENCE OF PERCEIVED SPECIAL CARE, GUIDANCE THROUGH THE PROGRAM WAS CONDUCTED TELEPHONICALLY AND PATIENTS WERE ASKED TO DOWNLOAD A FREE WELLNESS SOFTWARE APPLICATION ON TO THEIR MOBILE DEVICE. A WORKBOOK AND EDUCATIONAL BOOKLETS FOR EACH OF THE FIVE COMPONENTS WAS AVAILABLE TO DOWNLOAD FROM THE WEBSITE.

In patients with severe anxiety (N=50; GAD-7 score ≥10) in addition to depression or bipolar depression, a 30 day induction program was associated with improvements in emotional eating, sleep, depression and anxiety, and markers of wellness, including happiness, optimism, enthusiasm and resilience (Table II).

Table II. Results before and after participation in the WILD 5 30-day program in patients with GAD				
Parameter	**Pre-study score (mean)**	**Post-study score (mean)**	**Percentage change (mean)**	**P value**
Emotional eating (DEBQ)	37.5	33.2	11%	<0.001
Insomnia (PSQI)	12.4	8.5	31%	<0.001
Anxiety (GAD-7)	15.2	8.3	45%	<0.001
Depression (PHQ-9)	15.1	8.4	44%	<0.001
Happiness (NRS)	3.3	4.6	39%	<0.001
Enthusiasm (NRS)	2.5	4.4	76%	<0.001
Optimism (NRS)	3.1	4.6	48%	<0.001
Resilience (NRS)	2.7	4.8	77%	<0.001
DEBQ: Dutch Eating Behaviour Questionnaire; PSQI: Pittsburgh Sleep Quality index; GAD-7: Generalised Anxiety Disorder 7-item scale; PHQ-9: Patient Health Questionnaire 9 item version.				

These latter wellness characteristics were measured using an 11-point numeric rating scale (NRS) from 0 to 10, in which a higher score denotes greater wellbeing. Similar results were obtained in a group of 39 patients with chronic pain, 36 of whom had a comorbid mental disorder.[13] Patients were included if they had experienced pain for at least 4 days per week for 6 months or longer, with or without chronic opioid therapy. After 30 days, there was a 46% improvement in depression score (PHQ-9) and 40% improvement in anxiety score (GAD-7). Total sleep time was increased by 36 minutes. Improvements were also observed in measures of functionality, productivity and performance at work, resilience and optimism (Table III). The mean overall improvement in wellness was 42.8% (standard deviation 22.2%). Individual components of the Brief Pain Inventory (BPI) improved by 21% to 31%, with the exception of pain interference with sleep. Nevertheless, all changes in the BPI were statistically significant. Although WILD 5 should not be seen as a stand-alone management program for chronic pain, this small pilot study suggests that it may be an effective and safe strategy to augment usual treatment.

Table III. Results before and after participation in the WILD 5 30-day program in patients with chronic pain					
Parameter	**Rating Scale**	**Pre-study score (mean)**	**Post-study score (mean)**	**Percentage change (mean)**	**P value**
Depression	PHQ-9	12.1	6.5	46%	<0.0001
Anxiety	GAD-7	9.8	5.8	40%	<0.0001
Wellness	WHO-5	8.3	13.1	57%	<0.0001
Sleep	PSQI	11.5	7.7	33%	<0.0001
Total hours slept	PSQI	6.4	7.0	9%	<0.0001
Mindfulness	MAAS	53.6	64.1	19%	<0.0001
Social connectedness	SCS	28.5	36.8	29%	
Emotional (binge) eating	DEBQ	33.9	29.1	14%	0.003
Disability	SDS	12.2	8.1	33%	<0.0001
Work productivity	EWPS	38.1	28.9	24%	<0.0001
Happiness	NRS (0-10)	3.8	4.9	28%	<0.0001
Mental wellness	NRS (0-10)	3.7	5.4	45%	<0.0001
Optimism	NRS (0-10)	3.4	5.2	52%	<0.0001
Enthusiasm	NRS (0-10)	3.0	4.6	53%	<0.0001
Resilience	NRS (0-10)	3.3	5.3	60%	<0.0001
PHQ-9: Patient Health Questionnaire 9 item version; GAD-7: Generalised Anxiety Disorder 7-item scale; WHO-5: World Health Organisation (Five) Well-Being Index; PSQI: Pittsburgh Sleep Quality index; MAAS: Mindful Attention Awareness Scale; SCS: Social Connectedness Scale; DEBQ: Dutch Eating Behaviour Questionnaire; SDS: Sheehan Disability Scale; EWPS: Endicott Work productivity Scale; NRS (0-10): 11-point numeric rating scale.					

BACKGROUND AND RATIONALE FOR THE INDIVIDUAL COMPONENTS OF WILD 5

1. Exercise

There is a large body of evidence confirming that exercise improves mood and energy levels in patients with depression, which itself is associated with tiredness and fatigue, and reduced motivation and drive. A large Cochrane meta-analysis of 39 studies concluded that exercise improves symptoms of depression, but needs to be continued in the longer term for the benefits to be maintained.[14] Benefits of sustained exercise were greater than control intervention and comparable to those achieved with psychological and antidepressant pharmacological treatments.[14,15]

The mechanisms behind the effects of exercise on mood and wellbeing are multifactorial. Fatigue and impaired executive function, which in turn reduces the motivation to be physically active, in depressed people is linked to disturbed cerebral dopaminergic and noradrenergic transmission.

THERE IS A BIDIRECTIONAL RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND MONOAMINE NEUROTRANSMISSION IN THAT EXERCISE MODULATES DOPAMINE AND NORADRENALINE ACTIVITY IN BRAIN REGIONS LINKED TO COGNITIVE AND MOTOR FUNCTION, WHICH IN TURN MAY INCREASE THE ABILITY AND MOTIVATION TO EXERCISE.

It important to note that the individual monoamines do not work in isolation, and dopamine, noradrenaline and serotonin receive reciprocal regulation from each other. This interrelationship is complex. For example, whereas under physiological conditions, serotonin induces dopamine secretion, by selectively increasing serotonin concentrations, selective serotonin re-uptake inhibitors (SSRIs) may worsen deficiencies in dopaminergic activity in areas of the brain associated with movement control and motivation (e.g., prefrontal cortex, striatum and cerebellum) and contribute to fatigue.[16-18]

The synthesis and secretion of serotonin (5-hydroxytriptamine; 5-HT) in the brain and expression of serotonin receptors are also modulated by exercise. These effects depend on the intensity of exercise and vary in different regions of the brain, where 5-HT levels have a significant influence on mood, cognition, fatigue and motor performance.[18]

Changes in tryptophan metabolism during stress and exercise are fundamental to regulation of mood. Tryptophan is an essential amino acid precursor required for the synthesis of proteins, 5-HT and niacin. In peripheral body tissues, including skeletal muscle, liver and white blood cells, the primary pathway by which it is metabolised, accounting for approximately 95% of its metabolism, is the kynurenine pathway.

STRESS HORMONES, SUCH AS CORTISOL, OR INFLAMMATORY MEDIATORS, SUCH AS INTERFERON-γ, INDUCE THE LIVER AND MONOCYTES TO INCREASE EXPRESSION OF ENZYMES THAT DRIVE THIS PATHWAY, RESULTING IN THE FORMATION OF, AND EXCESSIVE INCREASES IN CIRCULATING KYNURENINE. KYNURENINE CROSSES THE BLOOD BRAIN BARRIER, WHEREAFTER IT IS CONVERTED TO A NUMBER OF NEUROACTIVE AND NEUROTOXIC METABOLITES.

In the brain, these metabolites increase inflammation and alter neurotransmission, effects which have been implicated in the pathophysiology of a number of brain disorders, including depression. Animal studies have shown that moderate intensity exercise induces the expression in skeletal muscle of PGC-1αtranscriptional cofactors, and importantly PGC-1α1. In turn, these transcriptional cofactors activate the PGC-1α1-PPARα/β pathway causing increased expression of kynurenine aminotransferases (KATs), which convert kynurenine into kynurenic acid. Because kynurenic acid is incapable of crossing the blood-brain barrier, this additional exercise-associated pathway increases resilience to stress by limiting tahe amount of kynurenine that reaches the brain and thereby reducing the generation of metabolites associated with these pathophysiological states.[19-21]

Importantly, studies have shown that PGC-1α1 expression is reduced in older people and in those with type 2 diabetes. Lower levels of PGC-1α1 may be associated with increased accumulation of kynurenine in the brain, contributing to co-existing depression.[19] By increasing the activity of the PGC-1α1-PPARα/βKAT-kynurenine pathway, exercise may increase resilience to stress and be a helpful adjunct in the management of patients with depression.[20]

STRESS-INDUCED PRO-INFLAMMATORY MEDIATORS MAY ALSO MODULATE DEPRESSION BY A DIRECT EFFECT ON SEROTONIN ITSELF.

Under normal circumstances tryptophan is transported from the periphery across the blood-brain barrier where it is converted to 5-HT in the brain. Increased expression of the kynurenine pathway increases the rate of tryptophan degradation, resulting in a peripheral deficit of the amino acid. This may lead to an insufficient availability of tryptophan to cross into the central nervous system and contribute to a deficiency in 5-HT. Furthermore, in the brain, pro-inflammatory mediators, such as IFN-γ, IFN-α, IL-1β and TNF-α directly upregulate serotonin transporter proteins, leading to increased re-uptake of 5HT, thereby reducing extracellular concentrations of the neurotransmitter.[21]

Neurotoxicity associated with these pathways (and specifically overstimulation of NMDA receptors) may also contribute to neurodegeneration associated with depression and the hippocampal atrophy that has been demonstrated with brain imaging in studies of people with major depression. The associated deficiency in the normal regulatory role of the hippocampus on the activity of the hypothalamic-pituitary-adrenal (HPA) axis may result in HPA axis overactivity, setting up a vicious cycle of stress, chronic inflammation, neurotoxicity and psychopathology.[21] It is interesting that physical exercise has been shown to induce rapid changes in angiogenesis and neuronal cell proliferation in the hippocampus, leading to a significant increase in hippocampal volume within 10 days.[22]

POSITIVE PSYCHOLOGICAL EFFECTS OF EXERCISE ARE WELL DESCRIBED AND CAN ALSO BE DEMONSTRATED OBJECTIVELY BY MEASURING ENDOGENOUS CANNABINOID (CB) OR OPIOID SIGNALLING ACTIVITY.

In animal studies, in comparison to sedentary controls, 8 days of voluntary exercise significantly increased CB1 receptor site binding density. In human athletes, visual analogue scale (VAS) scores taken before and after exercise indicated significant increases in happiness and euphoria after running, which were associated with reductions in opioid receptor availability in prefrontal and limbic/paralimbic brain structures.[23]

Taking both neurophysiological and clinical studies into account, the following is recommended in terms of exercise as part of a management program for patients with depression:

1. Exercise should include both aerobic and resistance training.
2. The optimal number of exercise session per week is no less than 5.
3. Exercise should be of at least moderate intensity.
4. Duration of each individual exercise session may be 20-30 minutes, but it may be acceptable to break this up into several shorter intervals during the day.
5. There appears to be no plateau of the benefits achieved with exercise over time and a daily exercise routine needs to become a life-long practice.
6. Taking into consideration capabilities, available resources and achievable goals, a sustainable exercise plan will need to be individually tailored to each patient.
7. Keeping a diary of mood before and after exercise can help to illustrate the benefit to patients and motivate them to continue.
8. Motivational interviewing is helpful to assist patient in finding solutions to barriers that might prevent them for beginning and sustaining a lifestyle that includes regular exercise.

2. MINDFULNESS

Mindfulness may be defined as "the awareness that emerges through paying attention on purpose, in the present moment, and non-judgmentally, to the unfolding of experience moment by moment." It involves a consciousness of sensations, perceptions, emotions and thoughts and is the attentional state that underlies all forms of meditation.[24,25]

MINDFULNESS-BASED COGNITIVE THERAPY (MBCT) IS BELIEVED TO WORK BY REDUCING COGNITIVE AND EMOTIONAL REACTIVITY TO STRESSFUL EVENTS AND PROMOTING RESILIENCE.

It has been shown to assist in recovery from a variety of painful and psychological conditions, especially depression and anxiety.[25-28] In unstable patients with major depressive disorder who had achieved remission, MBCT was as effective as medication in preventing relapse over a two-year period, reducing the risk of relapse by more than one half in comparison to placebo.[29]

Magnetic resonance imaging studies have demonstrated that regular mindfulness mediation has neuroplastic effects that influence brain structure. In comparison to nonmeditating matched control subjects, meditators had volumetric changes in numerous areas of the brain involved in learning and memory processes, emotion regulation, self-referential processing and perspective, including cortical gray matter, cerebellum, amygdala and hippocampus.[30,31]

The stress response and inflammatory activity is also be affected by mindfulnesss. In comparison to novices, expert yoga practitioners had a markedly attenuated stress response, indicated by lower interleukin-6 (IL6) plasma levels and lower heart rate at baseline and after being exposed to stressful stimuli. Both returned to baseline levels faster in the expert group.

YOGA SESSIONS WERE ASSOCIATED WITH INCREASES IN POSITIVE AFFECT SCORES.

These data suggest that regular yoga practice may reduce inflammation below levels predicted by such key risk factors as age, abdominal adiposity, cardiorespiratory fitness, and depressive symptoms.[32]

3. SLEEP

Insomnia is a common problem that is under-recognised and undertreated. In a large telephone survey of more than 10 000 adults in America, Europe and Japan, more than one third reported difficulty falling asleep, maintaining sleep and/or poor quality of sleep that significantly affected quality of life.[33] It is estimated that up to one half of adults suffer from at least subthreshold insomnia problems and up to

one in six has chronic insomnia. More than two thirds of patients consulting their general practitioner complain of insomnia.[34] Parts of the brain that manage memory, concentration, decision-making, emotional regulation and alertness are significantly impaired by insomnia. Obesity, depression, anxiety, drug and alcohol abuse all share a bidirectional relationship with sleep disorders.[35,36] In addition to psychiatric illnesses, many other health problems are associated with insomnia, including cardiovascular disease, gastrointestinal disorders, neurologic diseases and cancer.[34]

Recently, the discovery of the 'glymphatic system' has helped to explain, at least in part, why sleep is so important to health. The glymphatic system is a network of perivascular tunnels formed by astroglial cells in the brain that promotes efficient elimination of soluble proteins, metabolites and potentially neurotoxic waste products, including β-amyloid and tau, from the central nervous system. In addition, it facilitates brain-wide distribution of various compounds including glucose, lipids, amino acids, growth factors and neuromodulators. The glymphatic system functions almost exclusively during sleep and is switched off during wakefulness. Glymphatic dysfunction may provide the link between impaired sleep, disturbed cognition, psychiatric and neurodegenerative diseases.[37,38]

Benzodiazepines and other treatments for insomnia

Use of medication to manage sleep complaints generally tends to compound the problem and should be avoided. Concerns associated with short and long-term benzodiazepine use are listed in Table IV.[39] Depressed patients already taking benzodiazepines should be slowly weaned (over approximately a month) until the medication can be discontinued altogether.

Table IV Concerns associated with short - and long-term use of benzodiazepines

- **Over-sedation**
- **Drug interactions**
- **Cognitive difficulties**
- **Neurodegeneration**
- **Falls and associated trauma**
- **Reduced mobility and driving skills**
- **Poor sleep quality**
- **Depression & emotional blunting**
- **Adverse effects (elderly; pregnancy)**
- **Drug abuse/dependence**
- **Socio-economic costs with long-term use**

Nonpharmacological treatment options to manage insomnia include sleep restriction, cognitive therapy, paradoxical intention and sleep hygiene education. General sleep health recommendations, and those used in WILD 5 are listed in Table V.

Table V Sleep health recommendations

- **The bed is only for sleep & sex.**
- **Avoid daytime napping.**
- **Avoid caffeinated drinks from 14h00.**
- **Electronic devices should be avoided within 90 minutes before bed time.**
- **Enjoy a warm bath or shower before bed**
- **Eliminate ambient light in the bedroom.**
- **If you are unable to sleep, get up & go to another room.**
- **Do something quiet, calm & relaxing in dim light.***
- **Do not fall asleep anywhere other than your bed.***
- **Do not watch the clock.***
- **Go back to bed when sleepy.***
- **Always use the alarm in the morning set for the same time.***
- **Ensure adequate sleep on weekends to compensate for the sleep debt accumulated during the working week.**

* *Patients participating in WILD 5 were asked to observe at least 4 of these 6 recommendations.*

4. SOCIAL CONNECTEDNESS

Although large studies suggest that conversation is one of the activities that people associate with the greatest degree of happiness, technological progress seems to be distancing people from each other and reducing face-to-face interaction.[40] On the other hand, people with depression tend to prefer to isolate themselves from others and do so on purpose.

A wealth of evidence indicates that social isolation and lack of meaningful relationships are risk factors, not only for psychological disorders, but for poor health in general.

Life events involving social rejection are associated with activation of brain areas involved in processing negative affect and distress, and upregulation of the HPA-axis, sympathetic-adrenal-medullary axis and inflammatory response. These neurophysiological events are, in turn, associated with clinical depression.[41] Similarly, social isolation has been linked to increased incidences of psychological stress, depression and coronary artery disease, independent of other cardiovascular risk factors.[42-44]

Community-based studies suggest that positive health benefits of social integration may extend to increased longevity, and lower levels of cancer, fatal cardiovascular events, depression and anxiety; less severe cognitive decline with aging; improved

Social integration helps to promote emotional wellbeing and positive feelings of identity, purpose, self-worth and security independently. In doing so, it induces physiological responses that are beneficial to both mental and overall health. Furthermore, being part of society motivates one to care for oneself. Both quality and quantity of social interactions are important to health. Quality in terms of positivity and happiness of the individuals involved, strength of the bond between individuals, level of conversation and enjoyability of the interaction; and quantity in terms of regularity, where daily contact should be encouraged.

5. NUTRITION

Obesity is a common, multifactorial condition associated with significant health risks, including, among others, cardiovascular disease, type 2 diabetes mellitus, sleep apnoea, other respiratory conditions and cancer.[49] For most people, diet is the primary determinant of whether or not they maintain a healthy body weight as they age.

Obesity also has a significant impact on mental health, and is associated with increased risk of mood and bipolar disorders, generalised anxiety, panic disorder and agoraphobia in both men and women.[50] The relationship between obesity and depression is bidirectional. In comparison to those with normal BMI, obese women were almost 4 times as likely to suffer from depression; whereas depression is significantly associated with reduced physical activity and increased caloric intake.[51] Depression and obesity share common pathophysiologies and both are influenced by gene-environment interactions. Shared neuropeptidergic and neurotransmitter systems include corticotrophin releasing hormone (CRH), neuropeptide Y, serotonin and noradrenaline, insulin-like growth factor-1, and leptin. Both depression and obesity are proinflammatory states. Depression is characterised by overactivation of the HPA axis. Adipose tissue is metabolically active and associated with activation of the immune system and the production of inflammatory cytokines. These cytokines cross the bold-brain barrier and increase the risk of depression through their interaction with virtually every pathophysiologic domain relevant to it, including effects on the serotonergic, dopaminergic, glutaminergic and monoaminergic systems, neuroendocrine function and synaptic plasticity.[52,53]

Modern diets consist of an overabundance of macronutrients, calories, fats, and carbohydrates, but insufficient micronutrients, such as vitamins and minerals. In order to improve mental health and overall wellness, a balanced diet is required that consists of healthy combinations of proteins, healthy fats and carbohydrates, and sufficient intake of micronutrients. However, people with psychiatric symptoms frequently do not consume a balanced, nutrient-rich diet. Deficiency of micronutrients plays a significant causative role in mental illness, exacerbates symptoms and interferes with recovery. In particular, B vitamins (B2, B6, B9 and B12) are required for proper functioning of the methylation cycle, which controls monoamine production (including serotonin, dopamine and noradrenaline), DNA synthesis and maintenance of phospholipids, such as myelin. Fat-soluble vitamins A, D, and E play important roles in genetic transcription, antioxidant recycling and inflammatory regulation in the brain.[54] Deficiencies can therefore directly influence brain function.

*The **MIND** diet*

Both the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets, which emphasise the importance of micronutrient-rich foods, omega-3 fatty acids and fibre-rich foods, and discourage consumption of saturated fats and refined carbohydrates, have been shown to slow cognitive decline or reduce the risk of dementia.[55-58] Moderate adherence to the Mediterranean diet was also associated with reduced risk of depression.[55]

The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet was developed by combining these two diets, with emphasis on antioxidants, omega-3 fatty acids (in particular DHA) and B vitamins - the dietary components linked to neuroprotection and prevention of cognitive decline (Table VI).[59,60] Like the Mediterranean and DASH diets, the MIND diet emphasises natural plant-based foods, but goes further in specifying frequent consumption of berries and green leafy vegetables. Whereas high adherence to the Mediterranean and DASH diets was associated with 54% and 39% reduction in risk of dementia, respectively, even moderate adherence to the MIND diet was associated with reduced risk (35% risk reduction for moderate adherence and 53% risk reduction for high adherence).[60]

Table VI MIND diet

Recommended foods (brain healthy foods)	Unhealthy foods
Green leafy vegetables	Red meats
Other vegetables	Butter and stick margarine
Nuts	Cheese
Berries	Pastries and sweets
Beans	Fried/fast foods
Whole grains	
Fish	
Poultry	
Olive oil	
Wine	

MINDFUL EATING

Mindful eating is a learned mindfulness activity that relates to paying special attention to the experience of eating from moment to moment, nonjudgmentally. It begins with making conscious food choices, being aware of physical vs. psychological hunger and satiety cues, and eating healthily in response to those cues.

During eating, the mindful individual would pay attention to seeing what is on the plate, experiencing the aromas, and being aware of the movements and sensations associated with eating, tasting and swallowing.

Mindfulness shifts attention to the environment to attention to the thoughts, actions and sensations associated with the eating experience, and appreciation of those.[61,62]

Mindful eating has been shown to have numerous benefits, including positive health effects in obese subjects and those with type 2 diabetes. Benefits include healthier food selection, greater cognitive control over eating behaviour, lower calorie intake, reduced binge and emotional eating, weight reduction, reduced fasting glucose and improved overall glycaemic control (HbA1c), and a reduction of depressive symptoms.[62-65]

Wellness behaviour change among subjects participating in WILD 5

Telephonic guidance and provision of detailed written information, combined with online resources and smart phone applications, motivated and empowered patients to positively change their behaviours in each of the five wellness elements. Some of the behaviour changes over one month of study are summarised in Table VII.

Table VII. Positive behaviour change over 30 days in WILD 5 (n=79)

Behaviour	Pre-study score (mean)	Post-study score (mean)	Percentage change (mean)
Exercise			
Days with exercise during 30 day study period		18 (range 3-300)	
Days with exercise per week	2.0	4.3	100% increase
Mean exercise intensity			48% increase
Mean exercise duration			29% increase
Mindfulness			
Number of days with mindfulness practice during 30 day study period		21.4 (range 6-30)	
Number of days with 8 minutes of mindful practice per week	1	5	
Ability to stay in present moment			36% increase
Negative and/or judgemental feelings in response to thoughts (NRS; 0-10)	5.5	3.4	
Sleep			
Total sleep time	6.9	7.3 (additional 24 minutes)	
Quality of sleep (NRS; 0-10)	3.8	5.6	47% improvement
Social connectedness			
Feelings of isolation (NRS; 0-10)	4.5	2.8	37% improvement
How connected do you feel to family and friends in the last 7 days?(NRS; 0-10)	4.7	6.5	38% improvement
How connected do you feel to social life and community in the last 7 days? (NRS; 0-10)	3.4	6.1	79% improvement
Nutrition			
How often have you practiced mindful eating in the last 7 days?	3.2 days	6.1 days	90% increase

NRS; 0-10: 11-point numeric rating scale

CONCLUSIONS

WILD 5 is the first complete wellness program available to clinicians with ready-to-use support materials that can be downloaded free of charge from the internet. Although the WILD 5 pilot study was small and of short duration, the results are extremely encouraging. They suggest that five wellness interventions that are relatively easy for patients to incorporate into their daily routine can significantly improve clinical outcomes in patients with mood disorders and chronic pain. It is important to note that the benefits of WILD 5 are dependent on participation in all five of the wellness components and as an adjunct to usual therapy.

Of course, mindfulness, exercise, sleep, healthy nutrition and socialisation are not new. They are normal life skills. Unfortunately, they are skills that society seems to be losing as it becomes more sedentary, and dependent on technology and the conveniences of modern living.

As such, the WILD 5 program will not only be of benefit to patients. It is a lifestyle of behaviours that would benefit all in the pursuit of living a happy, meaningful, and healthy life. It will help all of us to grow and flourish.

More information about WILD 5 can be obtained from www.wild5resources.com (password: wellnessmatters).

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